Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
November 8, 2017
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – November 8, 2017

DATE: October 25, 2017

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

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

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/2017 Fall Pipeline Update – Appendix B

Action Item – Vote to Prior Authorize Kevzara® (Sarilumab), Siliq™ (Brodalumab), Tremfya™ (Guselkumab), Cyltezo™ (Adalimumab-adbm), and Renflexis™ (Infliximab-abda) – Appendix C

Action Item – Vote to Prior Authorize Blincyto® (Blinatumomab), Besponsa® (Inotuzumab Ozogamicin), Bosulif® (Bosutinib), Gleevec® (Imatinib), Iclusig® (Ponatinib), Kymriah™ (Tisagenlecleucel), Synribo® (Omacetaxine), Sprycel® (Dasatinib), and Tasigna® (Nilotinib) – Appendix D

Action Item – Vote to Prior Authorize Bavencio® (Avelumab) and Update Skin Cancer Medications Prior Authorization Criteria – Appendix E

Action Item – Vote to Prior Authorize Haegarda® [C1 Esterase Inhibitor (Human)] – Appendix F

Action Item – Vote to Prior Authorize Axid® (Nizatidine Capsules and Solution), Tagamet® (Cimetidine Tablets), and Yosprala™ (Aspirin/Omeprazole Delayed-Release Tablets) – Appendix G

Action Item – Vote to Prior Authorize Trulance™ (Plecanatide), Xermelo™ (Telotristat Ethyl), Symproic® (Naldemedine), and Motofen® (Difenoxin/Atropine) – Appendix H

Action Item – Vote to Prior Authorize MiCort™ HC (Hydrocortisone Acetate 2.5% Cream) and Update the Topical Corticosteroids Product Based Prior Authorization Tier Chart and Criteria – Appendix I

Action Item – Vote to Prior Authorize Noctiva™ (Desmopressin Acetate Nasal Spray) – Appendix J

Action Item – Vote to Prior Authorize Sprix® (Ketorolac Tromethamine Nasal Spray) and Cataflam® (Diclofenac Potassium Tablets) – Appendix K

Action Item – Vote to Prior Authorize Promacta® (Eltrombopag) and Update Prior Authorization Criteria for Nplate® (Romiplostim) – Appendix L

Action Item – Vote to Prior Authorize Odactra™ (House Dust Mite Allergen Extract) and Update Allergen Immunotherapy Prior Authorization Criteria – Appendix M

Action Item – Annual Review of Nuedexta® (Dextromethorphan/Quinidine) – Appendix N

Action Item – Annual Review of Orkambi® (Lumacaftor/Ivacaftor) and Kalydeco® (Ivacaftor) – Appendix O

Action Item – Annual Review of Iron Chelating Agents and Vote to Prior Authorize Jadenu® Sprinkle (Deferasirox Oral Granules) – Appendix P

Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Mavyret™ (Glecaprevir/Pibrentasvir) and Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) – Appendix Q

Annual Review of Various Systemic Antibiotic Medications and 30-Day Notice to Prior Authorize Baxdela™ (Delafloxacin Injection and Tablets), Ofloxacin 300mg Tablets, Minolira™ (Minocycline Extended-Release Tablets), Solosec™ (Secnidazole Oral Granules), and Vabomere™ (Meropenem/Vaborbactam Injection) – Appendix R

Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Duzallo® (Lesinurad/Allopurinol) – Appendix S

Annual Review of Pancreatic Enzymes – Appendix T

Industry News and Updates – Appendix U

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – November 8, 2017 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers 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 4, 2017 DUR Minutes – Vote
B. October 4, 2017 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/2017 Fall Pipeline Update – See Appendix B

A. Medication Coverage Activity for October 2017
B. Pharmacy Help Desk Activity for October 2017
C. 2017 Fall Pipeline Update

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

5. Action Item – Vote to Prior Authorize Kevzara® (Sarilumab), Siliq™ (Brodalumab), Tremfya™ (Guselkumab), Cyltezo™ (Adalimumab-adbm), and Renflexis™ (Infliximab-abda) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Blincyto® (Blinatumomab), Besponsa® (Inotuzumab Ozogamicin), Bosulif® (Bosutinib), Gleevec® (Imatinib), Iclusig® (Ponatinib), Kymriah™ (Tisagenlecleucel), Synribo® (Omacetaxine), Sprycel® (Dasatinib), and Tasigna® (Nilotinib) – See Appendix D

A. Introduction
B. Recommendations

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

7. Action Item – Vote to Prior Authorize Bavencio® (Avelumab) and Update Skin Cancer Medications Prior Authorization Criteria – See Appendix E

A. Introduction
B. Recommendations

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

8. Action Item – Vote to Prior Authorize Haegarda® [C1 Esterase Inhibitor (Human)] – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Axid® (Nizatidine Capsules and Solution), Tagamet® (Cimetidine Tablets), and Yosprala™ (Aspirin/Omeprazole Delayed-Release Tablets) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Trulance™ (Plecanatide), Xermelo™ (Telotristat Ethyl), Symproic® (Naldemedine), and Motofen® (Difenoxin/Atropine) – See Appendix H

A. Introduction
B. Cost Comparison: Constipation Medications
C. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize MiCort™ HC (Hydrocortisone Acetate 2.5% Cream) and Update the Topical Corticosteroids Product Based Prior Authorization Tier Chart and Criteria – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

12. Action Item – Vote to Prior Authorize Noctiva™ (Desmopressin Acetate Nasal Spray) – See Appendix J

A. Introduction
B. College of Pharmacy Recommendations

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

13. Action Item – Vote to Prior Authorize Sprix® (Ketorolac Tromethamine Nasal Spray) and Cataflam® (Diclofenac Potassium Tablets) – See Appendix K

A. Introduction
B. College of Pharmacy Recommendations

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

14. Action Item – Vote to Prior Authorize Promacta® (Eltrombopag) and Update Prior Authorization Criteria for Nplate® (Romiplostim) – See Appendix L

A. Introduction
B. College of Pharmacy Recommendations

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

15. Action Item – Vote to Prior Authorize Odactra™ (House Dust Mite Allergen Extract) and Update Allergen Immunotherapy Prior Authorization Criteria – See Appendix M

A. Introduction
B. College of Pharmacy Recommendations

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

16. Action Item – Annual Review of Nuedexta® (Dextromethorphan/Quinidine) – See Appendix N

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Nuedexta® (Dextromethorphan/Quinidine)
D. Prior Authorization of Nuedexta® (Dextromethorphan/Quinidine)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

17. Action Item – Annual Review of Orkambi® (Lumacaftor/Ivacaftor) and Kalydeco® (Ivacaftor) – See Appendix O

A. Current Prior Authorization Criteria

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

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

18. Action Item – Annual Review of Iron Chelating Agents and Vote to Prior Authorize Jadenu® Sprinkle (Deferasirox Oral Granules) – See Appendix P

A. Current Prior Authorization Criteria
B. Utilization of Iron Chelating Agents
C. Prior Authorization of Iron Chelating Agents
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Iron Chelating Agents

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

19. Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Mavyret™ (Glecaprevir/Pibrentasvir) and Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) – See Appendix Q

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Hepatitis C Medications
D. Prior Authorization of Hepatitis C Medications
E. Market News and Updates
F. Regimen Comparison
G. Mavyret™ (Glecaprevir/Pibrentasvir) Product Summary
H. Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Product Summary
I. College of Pharmacy Recommendations
J. Utilization Details of Hepatitis C Medications

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

20. Annual Review of Various Systemic Antibiotic Medications and 30-Day Notice to Prior Authorize Baxdela™ (Delafloxacin Injection and Tablets), Ofloxacin 300mg Tablets, Minolira™ (Minocycline Extended-Release Tablets), Solosec™ (Secnidazole Oral Granules), and Vabomere™ (Meropenem/Vaborbactam Injection) – See Appendix R

A. Current Prior Authorization Criteria
B. Utilization of Various Systemic Antibiotic Medications
C. Prior Authorization of Various Systemic Antibiotic Medications
D. Market News and Updates
E. Baxdela™ (Delafloxacin) Product Summary
F. Minolira™ (Minocycline Extended-Release Tablets) Product Summary
G. Solosec™ (Secnidazole Oral Granules) Product Summary
H. Vabomere™ (Meropenem/Vaborbactam Injection) Product Summary
I. Cost Comparison
J. College of Pharmacy Recommendations
K. Utilization Details of Various Systemic Antibiotic Medications

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

21. Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Duzallo® (Lesinurad/Allopurinol) – See Appendix S

A. Current Prior Authorization Criteria
B. Utilization of Gout Medications
C. Prior Authorization of Gout Medications
D. Market News and Updates
E. Duzallo® (Lesinurad/Allopurinol) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Gout Medications

Non-Presentation; Questions Only:

22. Annual Review of Pancreatic Enzymes – See Appendix T

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

Non-Presentation; Questions Only:

23. Industry News and Updates – See Appendix U

A. Introduction
B. News and Updates

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

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

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

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

A. Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications
B. Phosphate Binding Medications
C. Duchenne Muscular Dystrophy Medications
D. Ocular Allergy Medications
E. Anti-Emetic Medications

**Future business subject to change.*

26. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF OCTOBER 4, 2017

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

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

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

OTHERS PRESENT:		
Kathy Usher, Lexicon	Ani Timourian, Lexicon	Jason Schwier, Amgen
Mai Duong, Novartis	Doug Wood, ViiV Healthcare	Kari Suttee, Novartis
Marc Parker, Sunovion	Matt Forney, Merck	Brandon Ross, Merck
Ron Schnare, Shire	Jim Chapman, AbbVie	Trebla Grant, Kite Pharma
Brian Maves, Pfizer		

PRESENT FOR PUBLIC COMMENT:	
Ani Timourian	Lexicon
Mai Duong	Novartis

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. 15 SPEAKER: MAI DUONG

2B: AGENDA ITEM NO. 16 SPEAKER: ANI TIMOURIAN

ACTION: NONE REQUIRED

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

3A: SEPTEMBER 13, 2017 DUR MINUTES – VOTE

3B: SEPTEMBER 13, 2017 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: VOTE ON 2018 MEETING DATES

4A: MEETINGS ARE HELD THE SECOND WEDNESDAY OF EVERY MONTH AT 4:00 PM

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/MENOPAUSAL HORMONE THERAPY (MHT) FOR VASOMOTOR SYMPTOMS SAFETY MAILING UPDATE

5A: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2017

5B: PHARMACY HELP DESK ACTIVITY FOR SEPTEMBER 2017

5C: MENOPAUSAL HORMONE THERAPY (MHT) FOR VASOMOTOR SYMPTOMS SAFETY MAILING UPDATE

Materials included in agenda packet; presented by Dr. Holderread and Dr. Nichols

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE AFSTYLA® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), SINGLE CHAIN] AND REBINYN® [COAGULATION FACTOR IX (RECOMBINANT), GLYCOPEGYLATED]

6A: INTRODUCTION

6B: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ratterman

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ENDARI™ (L-GLUTAMINE)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
Dr. Garton moved to approve; seconded by Dr. Huddleston
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE NAMENDA XR® (MEMANTINE EXTENDED-RELEASE CAPSULES) AND UPDATE NAMZARIC® (MEMANTINE EXTENDED-RELEASE/DONEPEZIL CAPSULES) CRITERIA
8A: INTRODUCTION
8B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Munoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE ZYPITAMAG™ (PITAVASTATIN MAGNESIUM) AND NIKITA™ (PITAVASTATIN SODIUM)
9A: INTRODUCTION
9B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Dr. Preslar moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE FABRAZYME® (AGALSIDASE BETA)
10A: INTRODUCTION
10B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Munoz moved to approve; seconded by Dr. Huddleston
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE KISQALI® (RIBOCICLIB), KISQALI® FEMARA® CO-PACK (RIBOCICLIB/LETROZOLE), AND NERLYNX™ (NERATINIB)
11A: INTRODUCTION
11B: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders, and Dr. Medina
Dr. Huddleston moved to approve; seconded by Dr. Garton
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 BLINCYTO® (BLINATUMOMAB), BESPONSA® (INOTUZUMAB OZOGAMICIN), BOSULIF® (BOSUTINIB), GLEEVEC® (IMATINIB), ICLUSIG® (PONATINIB), KYMRIAH™ (TISAGENLECLEUCEL), SYNRIBO® (OMACETAXINE), SPRYCEL® (DASATINIB), AND TASIGNA® (NILOTINIB)
12A: INTRODUCTION
12B: UTILIZATION OF ALL/CML MEDICATIONS
12C: MARKET NEWS AND UPDATES
12D: PRODUCT SUMMARIES
12E: RECOMMENDATIONS
12F: UTILIZATION DETAILS OF ALL/CML MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders, and Dr. Medina
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF SKIN CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BAVENCIO® (AVELUMAB)
13A: INTRODUCTION
13B: PREVIOUSLY VOTED PRIOR AUTHORIZATION CRITERIA

13C: UTILIZATION OF SKIN CANCER MEDICATIONS
13D: PRIOR AUTHORIZATION OF SKIN CANCER MEDICATIONS
13E: MARKET NEWS AND UPDATES
13F: BAVENCIO® (AVELUMAB) PRODUCT SUMMARY
13G: RECOMMENDATIONS
13H: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders, and Dr. Medina
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF HEREDITARY ANGIOEDEMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE HAEGARDA® [C1 ESTERASE INHIBITOR (HUMAN)]
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF HEREDITARY ANGIOEDEMA MEDICATIONS
14C: MARKET NEWS AND UPDATES
14D: PRIOR AUTHORIZATION OF HEREDITARY ANGIOEDEMA MEDICATIONS
14E: HAEGARDA® [C1 ESTERASE INHIBITOR (HUMAN)] PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF HEREDITARY ANGIOEDEMA MEDICATIONS
Materials included in agenda packet; presented by Dr. Nichols
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE KEVZARA® (SARILUMAB), SILIQ™ (BRODALUMAB), TREMFYA™ (GUSELKUMAB), CYLTEZO™ (ADALIMUMAB-ADBM), AND RENFLEXIS™ (INFLIXIMAB-ABDA)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS
15C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS
15D: MARKET NEWS AND UPDATES
15E: KEVZARA® (SARILUMAB) PRODUCT SUMMARY
15F: SIILIQ™ (BRODALUMAB) PRODUCT SUMMARY
15G: TREMFYA™ (GUSELKUMAB) PRODUCT SUMMARY
15H: BIOSIMILAR PRODUCT SUMMARIES
15I: GIANT CELL ARTERITIS (GCA) SUMMARY
15J: COLLEGE OF PHARMACY RECOMMENDATIONS
15K: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TRULANCE™ (PLECANATIDE), XERMELO™ (TELOTRISTAT ETHYL), SYMPROIC® (NALDEMEDINE), AND MOTOFEN® (DIFENOXIN/ATROPINE)
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
16C: PRIOR AUTHORIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
16D: MARKET NEWS AND UPDATES
16E: TRULANCE™ (PLECANATIDE) PRODUCT SUMMARY
16F: XERMELO™ (TELOTRISTAT ETHYL) PRODUCT SUMMARY
16G: SYMPROIC® (NALDEMEDINE) PRODUCT SUMMARY
16H: COST COMPARISON: CONSTIPATION MEDICATIONS
16I: COLLEGE OF PHARMACY RECOMMENDATIONS
16J: UTILIZATION DETAILS OF CONSTIPATION AND DIARRHEA MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF THROMBOPOIETIN (TPO) RECEPTOR AGONISTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PROMACTA® (ELTROMBOPAG)**

17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF TPO RECEPTOR AGONISTS
17D: PRIOR AUTHORIZATION OF TPO RECEPTOR AGONISTS
17E: MARKET NEWS AND UPDATES
17F: PROMACTA® (ELTROMBOPAG) PRODUCT SUMMARY
17G: COLLEGE OF PHARMACY RECOMMENDATIONS
17H: UTILIZATION DETAILS OF TPO RECEPTOR AGONISTS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: **ANNUAL REVIEW OF ALLERGEN IMMUNOTHERAPIES AND 30-DAY NOTICE TO PRIOR AUTHORIZE ODACTRA™ (HOUSE DUST MITE ALLERGEN EXTRACT)**

18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF ALLERGEN IMMUNOTHERAPIES
18C: PRIOR AUTHORIZATION OF ALLERGEN IMMUNOTHERAPIES
18D: MARKET NEWS AND UPDATES
18E: ODACTRA™ (HOUSE DUST MITE ALLERGEN EXTRACT) PRODUCT SUMMARY
18F: COLLEGE OF PHARMACY RECOMMENDATIONS
18G: UTILIZATION DETAILS OF ALLERGEN IMMUNOTHERAPIES

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: **ANNUAL REVIEW OF TOPICAL CORTICOSTEROIDS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MICORT™ HC (HYDROCORTISONE ACETATE 2.5% CREAM)**

19A: CURRENT PRIOR AUTHORIZATION CRITERIA
19B: UTILIZATION OF TOPICAL CORTICOSTEROIDS
19C: PRIOR AUTHORIZATION OF TOPICAL CORTICOSTEROIDS
19D: MARKET NEWS AND UPDATES
19E: COLLEGE OF PHARMACY RECOMMENDATIONS
19F: UTILIZATION DETAILS OF TOPICAL CORTICOSTEROIDS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: **ANNUAL REVIEW OF BLADDER CONTROL MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NOCTIVA™ (DESMOPRESSIN ACETATE NASAL SPRAY)**

20A: CURRENT PRIOR AUTHORIZATION CRITERIA
20B: UTILIZATION OF BLADDER CONTROL MEDICATIONS
20C: PRIOR AUTHORIZATION OF BLADDER CONTROL MEDICATIONS
20D: MARKET NEWS AND UPDATES
20E: NOCTURNAL POLYURIA
20F: NOCTIVA™ (DESMOPRESSIN ACETATE NASAL SPRAY) PRODUCT SUMMARY
20G: COLLEGE OF PHARMACY RECOMMENDATIONS
20H: UTILIZATION DETAILS OF BLADDER CONTROL MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler

Dr. Muchmore recommended removing criteria regarding use of concomitant inhaled glucocorticoids.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: **ANNUAL REVIEW OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AND 30-DAY NOTICE TO PRIOR AUTHORIZE SPRIX® (KETOROLAC TROMETHAMINE NASAL SPRAY) AND CATAFLAM® (DICLOFENAC POTASSIUM TABLETS)**

21A: CURRENT PRIOR AUTHORIZATION CRITERIA

21B: UTILIZATION OF NSAIDS
21C: PRIOR AUTHORIZATION OF NSAIDS
21D: MARKET NEWS AND UPDATES
21E: SPRIX® (KETOROLAC TROMETHAMINE NASAL SPRAY) PRODUCT SUMMARY
21F: COST COMPARISON
21G: COLLEGE OF PHARMACY RECOMMENDATIONS
21H: UTILIZATION DETAILS OF NSAIDS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 22: ANNUAL REVIEW OF ANTI-ULCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE YOSPRALA™ (ASPIRIN/OMEPRAZOLE DELAYED-RELEASE TABLETS)
22A: CURRENT PRIOR AUTHORIZATION CRITERIA
22B: UTILIZATION OF ANTI-ULCER MEDICATIONS
22C: PRIOR AUTHORIZATION OF ANTI-ULCER MEDICATIONS
22D: MARKET NEWS AND UPDATES
22E: YOSPRALA™ (ASPIRIN/OMEPRAZOLE DELAYED-RELEASE TABLETS) PRODUCT SUMMARY
22F: COLLEGE OF PHARMACY RECOMMENDATIONS
22G: UTILIZATION DETAILS OF ANTI-ULCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Nichols
ACTION: NONE REQUIRED

AGENDA ITEM NO. 23: INDUSTRY NEWS AND UPDATES
23A: INTRODUCTION
23B: NEWS AND UPDATES
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 24: 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. 25: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
25A: HEPATITIS C MEDICATIONS
25B: OPHTHALMIC ANTI-INFLAMMATORIES
25C: PANCREATIC ENZYMES
25D: CHRONIC IRON OVERLOAD MEDICATIONS
25E: VARIOUS ANTIBIOTICS
25F: CYSTIC FIBROSIS MEDICATIONS
FUTURE BUSINESS SUBJECT TO CHANGE.
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 26: ADJOURNMENT
The meeting was adjourned at 5:38 pm.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: October 5, 2017

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

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

Subject: DUR Board recommendations from meeting of October 4, 2017

Recommendation 1: Vote on 2018 Meeting Dates

MOTION CARRIED by unanimous approval.

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

January 10, 2018
February 14, 2018
March 14, 2018
April 11, 2018
May 9, 2018
June 13, 2018
July 11, 2018
August 8, 2018
September 12, 2018
October 10, 2018
November 14, 2018
December 12, 2018

Recommendation 2: Menopausal Hormone Therapy (MHT) for Vasomotor Symptoms Safety Mailing Update

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] and Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated]

MOTION CARRIED by unanimous approval.

The Oklahoma Health Care Authority recommends the prior authorization of Afstyla® [antihemophilic factor (recombinant), single chain] and Rebinyn® [coagulation factor IX (recombinant), glycoPEGylated] with the following criteria:

Eloctate™, Adynovate®, Afstyla®, Alprolix®, Idelvion®, 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.

Recommendation 4: Vote to Prior Authorize Endari™ (L-Glutamine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Endari™ (L-glutamine) with the following criteria:

Endari™ (L-Glutamine) Approval Criteria:

1. An FDA approved diagnosis of sickle cell disease; and
2. Member must be at least 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 sickle cell disease (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating sickle cell disease); 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 according to package labeling.
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.

Recommendation 5: Vote to Prior Authorize Namenda XR® (Memantine Extended-Release Capsules) and Update Namzaric® (Memantine Extended-Release/Donepezil Capsules) Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Namenda XR® [memantine extended-release (ER) capsules] with the following criteria:

Namenda XR® [Memantine Extended-Release (ER) Capsules] Approval Criteria:

1. An FDA approved diagnosis for the treatment of moderate-to-severe Alzheimer's type dementia; and
2. A patient-specific, clinically significant reason why the member cannot use memantine immediate-release tablets.

Additionally, the College of Pharmacy recommends the following changes noted in red to the Namzaric® (memantine ER/donepezil) prior authorization criteria:

Namzaric® [Memantine Extended-Release (ER)/Donepezil Capsules] Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the separate immediate-release products which do not require prior authorization cannot be used over this combination product; and
2. A quantity limit of 30 capsules per 30 days will apply.

Recommendation 6: Vote to Prior Authorize Zypitamag™ (Pitavastatin Magnesium) and Nikita™ (Pitavastatin Sodium)

MOTION CARRIED by unanimous approval.

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

1. Move rosuvastatin to Tier-1 based on low net cost and add a required trial with rosuvastatin to current Tier-2 criteria, in addition to an atorvastatin trial, based on LDL lowering capability and low net cost.
2. Place Zypitamag™ (pitavastatin magnesium) and Nikita™ (pitavastatin sodium) into the Special Prior Authorization (PA) Tier. Current Special PA criteria will apply.
3. Add criteria for Vascepa® 0.5 gram based on higher net cost compared to Vascepa® 1 gram. Use of Vascepa® 0.5 gram would require a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

The proposed changes can be seen in red in the following criteria and tier chart:

Statin Medications and Ezetimibe Tier-2 Approval Criteria:

1. Member must have ~~a~~ documented trials with atorvastatin and rosuvastatin, consisting of at least eight weeks of continuous therapy each, titrated to a dose of at least 40mg atorvastatin and 20mg rosuvastatin, which did not yield adequate LDL reduction. ~~The minimum starting dose of the Tier-2 medication may only be at the moderate-to-high LDL lowering doses (20mg rosuvastatin or higher)~~; or
2. A documented adverse effect or contraindication to all available lower tiered products; or
3. ~~A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high-risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome, or for pediatric members with homozygous familial hypercholesterolemia (HoFH); or~~

4. Clinical exceptions for ezetimibe include the following:
    a. Documented active liver disease; or
    b. Documented unexplained, persistent elevations of serum transaminases; or
    c. Documented statin-related myopathy.

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

1. 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.

Statin Medications and Ezetimibe*		
Tier-1	**Tier-2**	**Special PA**
atorvastatin (Lipitor®)	ezetimibe (Zetia®)	fluvastatin (Lescol® & Lescol® XL)
lovastatin (Mevacor®)		lovastatin (Altoprev®)
pravastatin (Pravachol®)		pitavastatin **calcium** (Livalo®)
rosuvastatin (Crestor®)		**pitavastatin magnesium (Zypitamag™)**
simvastatin (Zocor®)		**pitavastatin sodium (Nikita™)**
		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.
~~*Crestor® 5mg and Crestor® 10mg require special reason for use.~~

Omega-3 Fatty Acids Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL) and controlled diabetes (fasting glucose <150mg/dL at the time of triglycerides measurement and HgA1c <7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®); and
4. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Recommendation 7: Vote to Prior Authorize Fabrazyme® (Agalsidase Beta)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Fabrazyme® (agalsidase beta) with the following criteria:

Fabrazyme® (Agalsidase Beta) Approval Criteria:

1. An FDA approved diagnosis of Fabry disease. Diagnosis must be confirmed by one of the following:
    a. Genetic testing confirming positive galactosidase alpha (*GLA*) gene mutation; or
    b. Decreased plasma levels of alpha-galactosidase A (less than 5% of normal); and
2. Fabrazyme® (agalsidase beta) will initially be approved for six months. After that time, compliance will be required for continued authorization; 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.

Recommendation 8: Vote to Prior Authorize Kisqali® (Ribociclib), Kisqali® Femara® Co-Pack (Ribociclib/Letrozole), and Nerlynx™ (Neratinib)

MOTION CARRIED by unanimous approval.

The prior authorization of Kisqali® (ribociclib), Kisqali® Femara® Co-Pack (ribociclib/letrozole), and Nerlynx™ (neratinib) with the following criteria:

Kisqali® (Ribociclib) Approval Criteria:

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 (HR)-positive; and
4. Member must be Human Epidermal Receptor Type 2 (HER2)-negative; and
5. Ribociclib must be given in combination with an aromatase inhibitor; and
6. Ribociclib must be used in postmenopausal women only.
7. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ribociclib therapy.

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria:

1. A diagnosis of advanced or metastatic breast cancer, initial therapy; and
2. Member must be Hormone Receptor (HR)-positive; and
3. Member must be Human Epidermal Receptor Type 2 (HER2)-negative; and
4. Ribociclib must be used in postmenopausal women only.
5. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ribociclib/letrozole therapy.

Nerlynx™ (Neratinib) Approval Criteria:

1. For adjuvant treatment in early stage breast cancer; and
2. Member must have Human Epidermal Receptor Type 2 (HER2)-overexpressed breast cancer; and
3. Neratinib must be used to follow adjuvant trastuzumab-based therapy.
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on neratinib therapy.

Recommendation 9: Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications and 30-Day Notice to Prior Authorize Blincyto® (Blinatumomab), Besponsa® (Inotuzumab Ozogamicin), Bosulif® (Bosutinib), Gleevec® (Imatinib), Iclusig® (Ponatinib), Kymriah™ (Tisagenlecleucel), Synribo® (Omacetaxine), Sprycel® (Dasatinib), and Tasigna® (Nilotinib)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Bavencio® (Avelumab)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Hereditary Angioedema Medications and 30-Day Notice to Prior Authorize Haegarda® [C1 Esterase Inhibitor (Human)]

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Kevzara® (Sarilumab), Siliq™ (Brodalumab), Tremfya™ (Guselkumab), Cyltezo™ (Adalimumab-adbm), and Renflexis™ (Infliximab-abda)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Trulance™ (Plecanatide), Xermelo™ (Telotristat Ethyl), Symproic® (Naldemedine), and Motofen® (Difenoxin/Atropine)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Thrombopoietin (TPO) Receptor Agonists and 30-Day Notice to Prior Authorize Promacta® (Eltrombopag)

NO ACTION REQUIRED.

Recommendation 15: Annual Review of Allergen Immunotherapies and 30-Day Notice to Prior Authorize Odactra™ (House Dust Mite Allergen Extract)

NO ACTION REQUIRED.

Recommendation 16: Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize MiCort™ HC (Hydrocortisone Acetate 2.5% Cream)

NO ACTION REQUIRED.

Recommendation 17: Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Noctiva™ (Desmopressin Acetate Nasal Spray)

NO ACTION REQUIRED.

Recommendation 18: Annual Review of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize Sprix® (Ketorolac Tromethamine Nasal Spray) and Cataflam® (Diclofenac Potassium Tablets)

NO ACTION REQUIRED.

Recommendation 19: Annual Review of Anti-Ulcer Medications and 30-Day Notice to Prior Authorize Yosprala™ (Aspirin/Omeprazole Delayed-Release Tablets)

NO ACTION REQUIRED.

Recommendation 20: Industry News and Updates

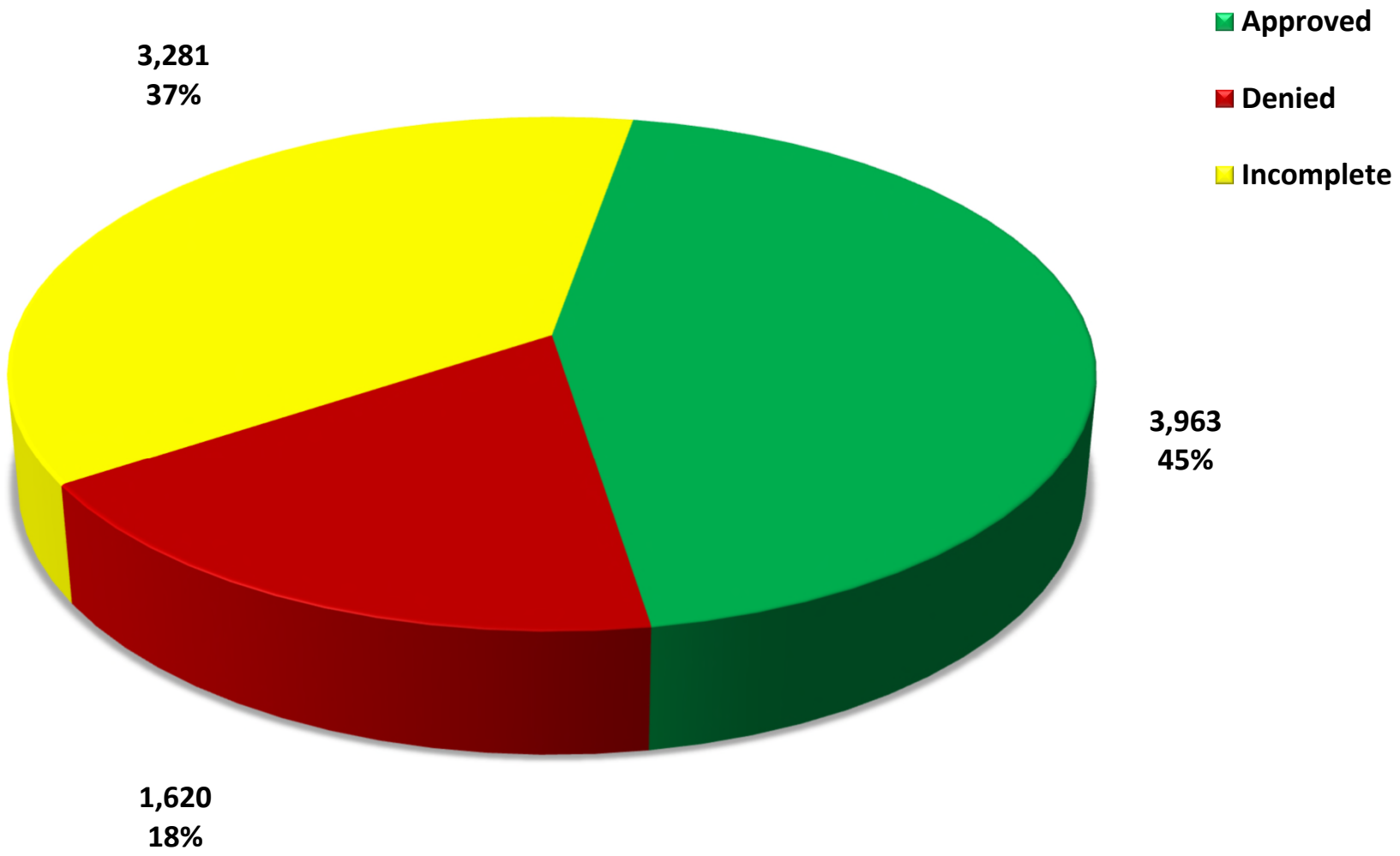
NO ACTION REQUIRED.

Recommendation 21: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

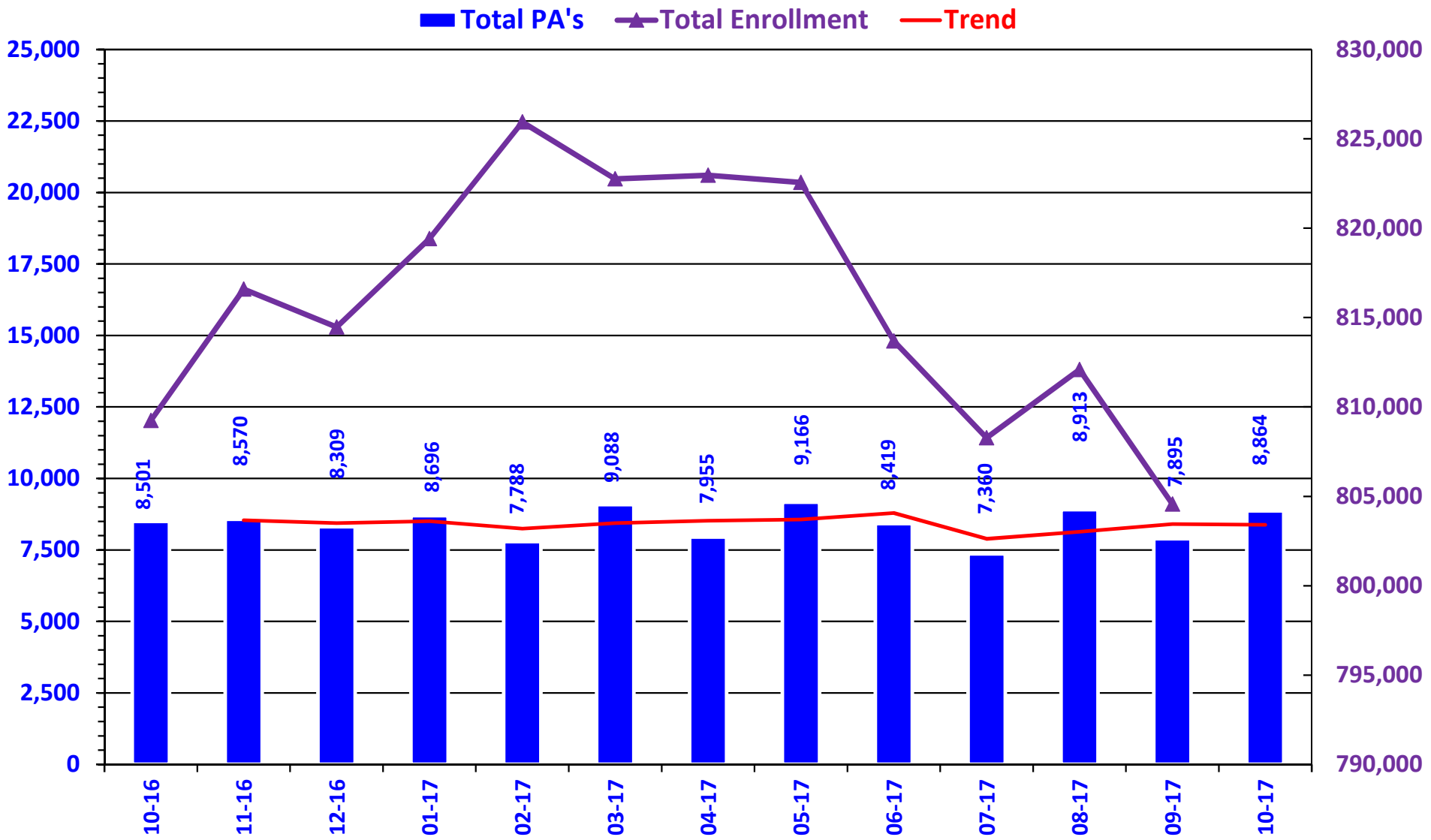
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER 2017



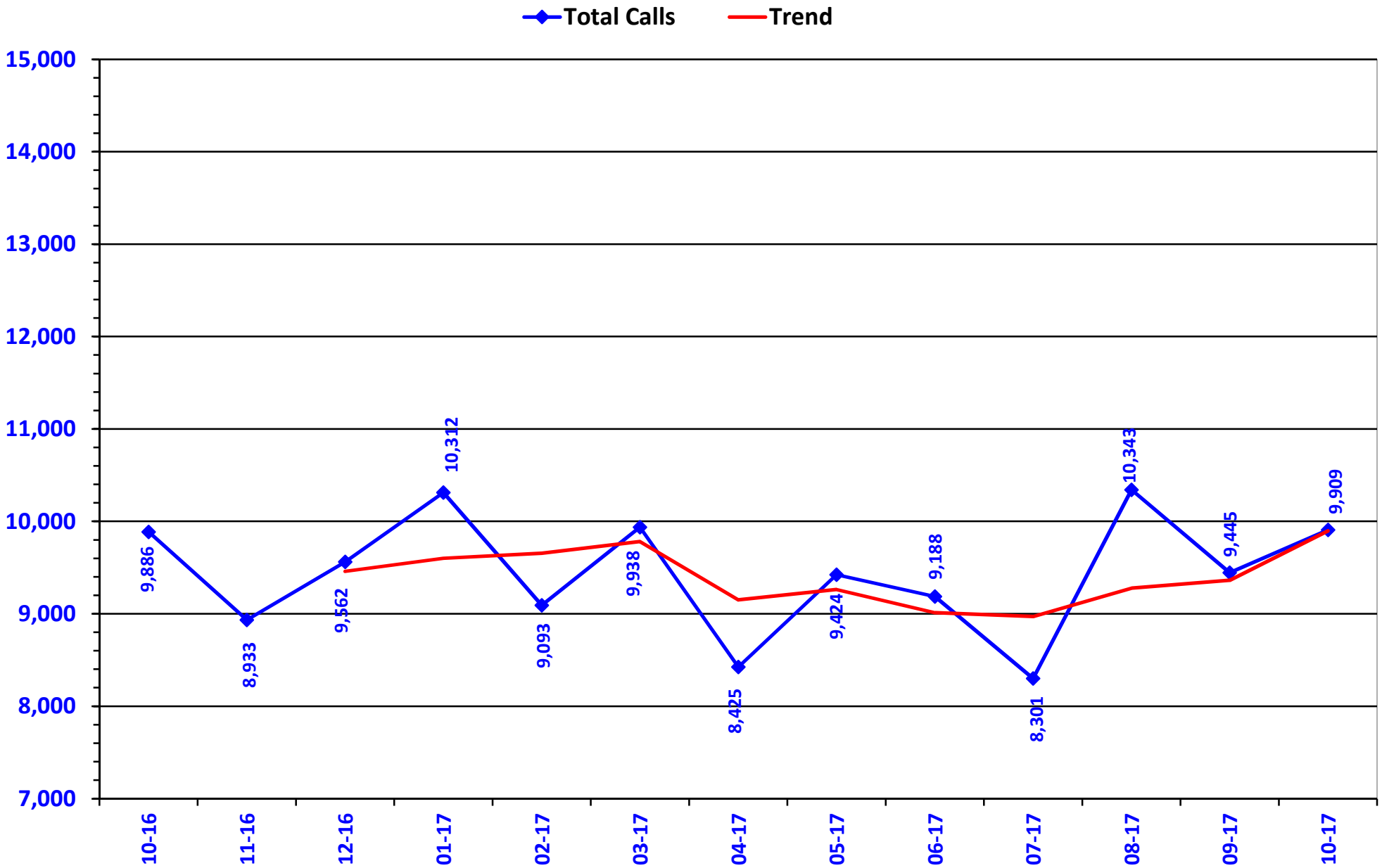
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2016 – NOVEMBER 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
NOVEMBER 2016 – NOVEMBER 2017



Prior Authorization Activity

10/1/2017 Through 10/31/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	135	15	26	94	319
Analgesic - NonNarcotic	22	0	2	20	0
Analgesic - Narcotic	416	219	42	155	165
Angiotensin Receptor Antagonist	16	4	6	6	355
Antiasthma	50	8	13	29	279
Antibiotic	42	18	6	18	263
Anticonvulsant	129	57	12	60	313
Antidepressant	314	129	39	146	333
Antidiabetic	226	86	41	99	347
Antigout	11	2	5	4	354
Antihistamine	110	40	53	17	74
Antimigraine	60	8	20	32	21
Antineoplastic	61	40	3	18	161
Antiparasitic	11	0	3	8	0
Antiulcers	169	40	58	71	152
Anxiolytic	59	34	4	21	308
Atypical Antipsychotics	231	113	32	86	341
Biologics	104	53	16	35	289
Bladder Control	47	9	11	27	357
Blood Thinners	225	156	12	57	331
Botox	38	25	9	4	357
Buprenorphine Medications	316	232	24	60	83
Cardiovascular	95	45	13	37	321
Chronic Obstructive Pulmonary Disease	177	26	41	110	316
Constipation/Diarrhea Medications	153	21	53	79	182
Contraceptive	23	20	0	3	330
Corticosteroid	12	4	2	6	84
Dermatological	199	37	83	79	124
Diabetic Supplies	473	275	11	187	190
Endocrine & Metabolic Drugs	132	72	11	49	148
Erythropoietin Stimulating Agents	11	4	4	3	109
Fibric Acid Derivatives	12	2	5	5	360
Fibromyalgia	219	30	110	79	304
Fish Oils	10	1	2	7	115
Gastrointestinal Agents	125	21	33	71	128
Genitourinary Agents	11	4	4	3	25
Glaucoma	11	3	3	5	96
Growth Hormones	127	96	7	24	135
Hepatitis C	242	164	34	44	8
HFA Rescue Inhalers	47	14	10	23	325
Insomnia	32	8	8	16	116
Insulin	87	31	11	45	324
Miscellaneous Antibiotics	18	3	5	10	9
Multiple Sclerosis	68	38	11	19	150
Muscle Relaxant	51	7	22	22	35
Nasal Allergy	71	6	22	43	140
Neurological Agents	72	33	19	20	330
NSAIDs	166	14	54	98	204
Ocular Allergy	39	7	12	20	116
Ophthalmic	15	0	6	9	0

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	22	6	8	8	354
Other*	273	41	72	160	222
Otic Antibiotic	17	6	2	9	11
Respiratory Agents	16	10	1	5	200
Statins	22	5	11	6	357
Stimulant	850	376	117	357	343
Synagis	387	101	154	132	149
Testosterone	46	13	13	20	356
Topical Antifungal	43	4	13	26	8
Topical Corticosteroids	134	3	55	76	288
Vitamin	71	14	40	17	270
Pharmacotherapy	44	41	0	3	228
Emergency PAs	0	0	0	0	
Total	**7,415**	**2,894**	**1,519**	**3,002**	
Overrides					
Brand	33	20	5	8	320
Compound	39	32	1	6	140
Cumulative Early Refill	4	3	1	0	180
Diabetic Supplies	1	1	0	0	4
Dosage Change	349	327	1	21	12
High Dose	3	1	1	1	91
Ingredient Duplication	32	24	0	8	12
Lost/Broken Rx	101	95	0	6	14
NDC vs Age	264	172	27	65	241
Nursing Home Issue	39	38	0	1	11
Opioid Quantity	28	21	4	3	163
Other*	31	26	0	5	52
Quantity vs. Days Supply	533	327	61	145	243
STBS/STBSM	25	11	4	10	43
Stolen	10	10	0	0	14
Temporary Unlock	1	1	0	0	27
Third Brand Request	28	17	2	9	16
Overrides Total	**1,449**	**1,069**	**101**	**279**	
Total Regular PAs + Overrides	**8,864**	**3,963**	**1,620**	**3,281**	

Denial Reasons	
Unable to verify required trials.	2,564
Does not meet established criteria.	1,654
Lack required information to process request.	683
Other PA Activity	
Duplicate Requests	643
Letters	11,245
No Process	7
Changes to existing PAs	629
Helpdesk Initiated Prior Authorizations	670
PAs Missing Information	82

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

2017 Fall Pipeline Update

Oklahoma Health Care Authority
November 2017

Introduction

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.

Benralizumab[1,2,3,4,5]

Anticipated Indication(s): An interleukin-5 (IL-5) receptor antagonist for the treatment of severe, uncontrolled asthma.

Clinical Trials: Benralizumab was evaluated in six multicenter, randomized, double-blind, parallel-group, placebo-controlled trials including a total of 3,068 patients with severe uncontrolled asthma with an eosinophilic phenotype. The results of these Phase 3 trials included reductions in annual rate of asthma exacerbations of 51% to 70% and a 93% reduction in exacerbations requiring emergency room visits or hospitalizations compared to placebo. Additionally, benralizumab use was associated with a significant reduction in oral corticosteroid (OCS) required dose; 52% of benralizumab-treated patients discontinued OCS therapy completely per trial protocol compared to 19% of patients receiving placebo.

Place in Therapy: Currently there are three monoclonal antibodies on the market indicated for treatment of severe, uncontrolled asthma: Nucala® (mepolizumab) and Cinqair® (reslizumab) which target IL-5 cytokine, and Xolair® (omalizumab), which targets immunoglobulin E (IgE). Unlike mepolizumab or reslizumab, dosed every 4 weeks, or omalizumab, dosed every 2 to 4 weeks, benralizumab has been studied with dosing every 8 weeks.

Projected FDA Decision: 12/2017

SoonerCare Impact: During state fiscal year 2017, a total of 33 members had paid medical or pharmacy claims for omalizumab, accounting for $569,415.68 in drug spending and an average cost per claim of $3,558.85. There were no paid claims for mepolizumab or reslizumab during state fiscal year 2017.

Semaglutide [1,2,6,7,8,9]

Anticipated Indication(s): A once-weekly, glucagon-like peptide 1 (GLP-1) analogue for the treatment of type 2 diabetes mellitus (T2DM).

Clinical Trials: Semaglutide was evaluated in seven multicenter, randomized, double-blind, placebo-controlled trials and a cardiovascular (CV) outcomes trial involving more than 8,000 adults with T2DM. The results of these trials showed a clinically meaningful reduction in HbA_{1c} and reduction in body weight versus comparator treatments, including Januvia® (sitagliptin), Lantus® (insulin glargine), Bydureon® [exenatide extended-release (ER)], and Trulicity® (dulaglutide). In the CV outcomes trial, which included 3,297 adult patients with T2DM at high CV risk, semaglutide significantly reduced the risk of the primary composite endpoint of time to first occurrence of either CV death, non-fatal myocardial infarction, or non-fatal stroke by 26% versus placebo when added to the standard of care; however, there was no improvement in CV death or overall mortality.

Place in Therapy: There are currently six GLP-1 analogue products on the market, three of which are dosed once-weekly. Novo Nordisk's other GLP-1 analogue, Victoza® (liraglutide), which is dosed once daily, is the only GLP-1 analogue that has an additional indication of reduction of major adverse CV events (MACE) in adults with T2DM and established CV disease. Even though a CV outcomes trial was included in its Phase 3 trials, it is not known at this time if semaglutide will also apply for the additional MACE prophylaxis indication.

Projected FDA Decision: 12/05/2017

SoonerCare Impact: During state fiscal year 2017, a total of 832 members utilized GLP-1 analogue medications, accounting for $2,607,879.94 in drug spending and an average cost per claim of $655.41.

Rhopressa™ (Netarsudil Ophthalmic Solution) [2,10,11,12]

Anticipated Indication(s): A first-in-class, once-daily ophthalmic solution for lowering intraocular pressure (IOP) in patients with glaucoma. Netarsudil reduces IOP by inhibiting both Rho kinase (ROCK) and norepinephrine transporter (NET).

Clinical Trials: Netarsudil was evaluated in four Phase 3 efficacy and safety trials, which demonstrated non-inferiority of once-daily netarsudil to twice-daily timolol. In the final Phase 3 trial, ROCKET 4, which included 708 patients, netarsudil once-daily achieved its primary and secondary efficacy endpoints demonstrating non-inferiority compared to timolol twice-daily for patients with baseline IOP from >20mmHg to <25mmHg. It also demonstrated a consistent level of IOP lowering across all baseline IOPs throughout the 90-day efficacy period. The safety analysis of netarsudil showed the most common adverse event was hyperemia, which was reported in approximately 40% of patients, 85% of which was scored as mild.

Place in Therapy: There are currently five different classes of ophthalmic drops on the market for decreasing IOP in patients with glaucoma. In pre-clinical trials, netarsudil had shown it may

have disease-modifying properties, including an anti-fibrotic effect on trabecular meshwork cells and potential to increase perfusion of the trabecular meshwork.

Projected FDA Decision: 02/28/2018

SoonerCare Impact: During state fiscal year 2017, a total of 1,287 members utilized glaucoma medications, accounting for $549,769.68 in drug spending and an average cost per claim of $90.41.

Tezacaftor/Ivacaftor [2,13,14]

Anticipated Indication(s): Treatment of cystic fibrosis (CF) in patients age 12 years and older who have two copies of the *F508del* mutation or one copy of *F508del* and one residual function mutation.

Clinical Trials: Tezacaftor/ivacaftor was evaluated in two global, randomized, double-blind, placebo-controlled Phase 3 trials. The EVOLVE study evaluated the efficacy and safety of tezacaftor/ivacaftor in approximately 500 patients with CF age 12 years and older who have two copies of the *F508del* mutation over 24 weeks. The study met its primary endpoint with the mean absolute improvement in percent predicted forced expiratory volume in one second ($ppFEV_1$) of 4 percentage points from baseline compared to placebo ($p<0.0001$). The EXPAND study evaluated the efficacy and safety of tezacaftor/ivacaftor as well as ivacaftor monotherapy in patients with CF age 12 years and older who have one mutation that results in residual CF transmembrane conductance regulator (CFTR) function and one copy of the *F508del* mutation. The study met its primary endpoints of mean absolute improvement of $ppFEV_1$ with an improvement of 6.8 percentage points from baseline for those treated with tezacaftor/ivacaftor compared to placebo ($p<0.0001$) and a 4.7 percentage point improvement compared to placebo for those receiving ivacaftor monotherapy ($p<0.0001$), which indicated a significant improvement in $ppFEV_1$ with tezacaftor/ivacaftor compared to ivacaftor alone.

Place in Therapy: Tezacaftor/ivacaftor has the same mechanism of action as Orkambi® (lumacaftor/ivacaftor), Vertex's other oral combination therapy for CF. However, Orkambi® is only indicated in patients that are homozygous for the *F508del* mutation in the CFTR gene. Tezacaftor/ivacaftor is being developed for CF patients that may only have one *F508del* mutation and one residual function mutation. In North America, Europe, and Australia, there are more than 22,000 people age 12 years and older who have two copies of the *F508del* mutation, and there are more than 1,500 people age 12 years and older who have at least one residual function mutation that is responsive to tezacaftor/ivacaftor.

Projected FDA Decision: 02/28/2018

SoonerCare Impact: During state fiscal year 2017, a total of 58 members utilized oral CF medications, accounting for $7,983,972.96 in drug spending. Orkambi® (lumacaftor/ivacaftor) 200mg-125mg accounted for $4,248,080.31 of the total spending for CF medications and had an average cost per claim of $20,522.13.

Aimovig™ (Erenumab)[2,15,16,17,18,19,20]

Anticipated Indication(s): A calcitonin gene-related peptide (CGRP) receptor antagonist for migraine prevention.

Clinical Trials: Erenumab was evaluated in two randomized, double-blind, placebo-controlled Phase 3 trials. The ARISE trial included 577 patients that experienced an average of 4 to 14 migraine days each month, with an average of 8 migraine days per month at baseline. Patients were randomized to receive either placebo or erenumab 70mg subcutaneously (SC) once monthly for three months. The results of the ARISE trial showed those receiving erenumab experienced a statistically significant 2.9-day reduction from baseline in monthly migraine days compared to a 1.8-day reduction in the placebo arm. The second Phase 3 trial, the STRIVE study, included 955 patients that were experiencing an average of 8.3 migraine days per month, who were randomized to receive either placebo or one of two erenumab doses (70mg or 140mg) SC once monthly for six months. Results of the STRIVE study showed patients in the erenumab 70mg and 140mg treatment arms experienced statistically significant reductions of 3.2 and 3.7 days from baseline in monthly migraine days, respectively, compared to a 1.8-day reduction seen in the placebo arm.

Place in Therapy: Erenumab is the first biologic product specifically for migraine prevention. Approximately 39 million adults and children in the United States suffer from migraines, ranking as the sixth most disabling illness in the world. Current standard of therapy for migraine prophylaxis includes various oral medications including but not limited to antiepileptic medications (e.g., divalproex sodium, topiramate), antidepressants (e.g., amitriptyline, venlafaxine), and beta-blocker medications (e.g., metoprolol, propranolol) in addition to triptan medications (e.g., sumatriptan) for acute symptom relief. Botox® (onabotulinumtoxinA) therapy is also recommended for chronic migraine prophylaxis.

Projected FDA Decision: 05/17/2018

SoonerCare Impact: During state fiscal year 2017, a total of 5,281 members utilized triptan medications, accounting for $263,993.38 in drug spending with an average cost per claim of $22.95. During state fiscal year 2016, a total of 167 members utilized Botox®, accounting for $422,393.20 in drug spending with an average cost per claim of $1,431.84. The utilization of Botox® accounted for all covered indications and was not limited to use for chronic migraine prophylaxis.

Pipeline Table[1,2]

Medication Name*	Manufacturer	Therapeutic Use	Route of Administration	Approval Status	Anticipated FDA Response
eptacog beta	Revo Biologics	hemophilia A or B	IV	Filed BLA	11/2017
Auryxia® (ferric citrate)	Keryx Biopharmaceuticals	IDA in non-dialysis CKD	Oral	Filed sNDA	11/08/2017
letermovir	Merck	cytomegalovirus	Oral	Filed NDA	11/08/2017
Cinvanti™ (aprepitant)	Heron Therapeutics	CINV	IV	Filed NDA	11/10/2017
beta-glucuronidase	Ultragenyx	Sly syndrome	IV	Filed BLA	11/16/2017

Medication Name*	Manufacturer	Therapeutic Use	Route of Administration	Approval Status	Anticipated FDA Response
Briviact® (brivaracetam)	UCB	partial-onset seizures (monotherapy)	Oral	Filed sNDA	11/17/2017
exenatide SC pump (ITCA 650)	Intarcia	T2DM	SC	Filed NDA	11/27/2017
buprenorphine depot	Indivior	opioid use disorder	SC	Filed NDA	11/30/2017
ertugliflozin ertugliflozin/metformin ertugliflozin/sitagliptin	Merck/Pfizer	T2DM	Oral	Filed NDA	12/2017
Xeljanz®/Xeljanz® XR (tofacitinib citrate)	Pfizer	psoriatic arthritis	Oral	Filed sNDA	12/2017
benralizumab	AstraZeneca	asthma (severe eosinophilic)	SC	Filed BLA	12/2017
Abilify® (aripiprazole sensor tablet)	Otsuka/Proteus	bipolar I (acute); schizophrenia; MDD	Oral	Filed NDA	12/2017
Ryplazim™ (plasminogen)	Prometic Life Sciences	plasminogen deficiency	IV	Filed BLA	12/2017
Vesicare® (solifenacin)	Astellas	neurogenic detrusor overactivity in pediatrics	Oral	Filed sNDA	12/2017
Sensipar® (cinacalcet)	Amgen	pediatric HPT	Oral	Filed sNDA	12/2017
Corlanor® (ivabradine)	Amgen	CHF/cardiomyo-pathies (pediatric)	Oral	Filed sNDA	12/2017
rizatriptan	Redhill	migraines	Oral	Filed NDA	12/2017
Vimpat® (lacosamide)	UCB	partial onset seizures (4yrs+)	Oral, IV	Filed sNDA	12/2017
Makena® (hydroxyprogesterone caproate auto injector)	AMAG	preterm labor	SC	Filed sNDA	12/2017
Repatha® (evolocumab)	Amgen	MACE prevention	SC	Filed sBLA	12/02/2017
semaglutide	Novo Nordisk	T2DM	SC	Filed NDA	12/05/2017
Zelboraf® (vemurafenib)	Genentech	ECD with BRAF V600 mutation	Oral	Filed sNDA	12/07/2017
A-101	Aclaris	seborrheic dermatitis	Topical	Filed NDA	12/14/2017
SUN-101/eFlow® (glycopyrrolate)	Sunovion	COPD	Inhalation	Filed NDA	12/15/2017
sirolimus	Santen	uveitis	Intraocular	Filed NDA	12/22/2017
Jatenzo™ (testosterone undecanoate)	Clarus	hypogonadism	Oral	Filed NDA	12/26/2017
Macrilen™ (macimorelin)	Aeterna Zentaris	evaluation of GHD in adults	Oral	Filed NDA	12/30/2017
ibalizumab	Theratechnologies/ Genentech	HIV-1 (multi-drug resistant)	IV	Filed BLA	01/03/2018
Sinuva™ (mometasone furoate)	Intersect ENT	recurrent ethmoid sinus obstruction	Implant	Filed NDA	01/07/2018

Medication Name*	Manufacturer	Therapeutic Use	Route of Administration	Approval Status	Anticipated FDA Response
Luxturna™ (voretigene neparvovec)	Spark Therapeutics	inherited retinal disease	Ophthalmic	Filed BLA	01/12/2018
Trulance® (plecanatide)	Synergy	IBS-C	Oral	Filed sNDA	01/24/2018
Linhaliq™ (ciprofloxacin)	Aradigm	NCFBE in patients with chronic lung infections with *Pseudomonas aeruginosa*	Inhalation	Filed NDA	01/26/2018
Auvi-Q® (epinephrine)	Kaleo	anaphylaxis (infants/small children)	IM, SC	Filed sNDA	01/26/2018
dolutegravir/rilpivirine	Janssen/ViiV	HIV-1 (maintenance)	Oral	Filed NDA	02/01/2018
AndexXa® (andexanet alfa)	Portola	Factor Xa anticoagulant antidote	IV	Filed BLA	02/02/2018
Tlando™ (testosterone undecanoate)	Lipocine	hypogonadism	Oral	Filed NDA	02/08/2018
emicizumab	Roche	hemophilia A	Oral	Filed NDA	02/23/2018
Rhopressa™ (netarsudil)	Aerie	glaucoma	Ophthalmic	Filed NDA	02/28/2018
tezacaftor/ivacaftor	Vertex	≥12yrs old with CF who have 2 copies of *F508del* mutation or 1 *F508del* mutation and 1 residual function mutation	Oral	Filed NDA	02/28/2018
bictegravir, emtricitabine, and tenofovir alafenamide	Gilead	HIV	Oral	Filed NDA	02/28/2018
ZTlido™ (lidocaine patch)	Scilex	post-herpetic neuralgia	Topical	Filed NDA	02/28/2018
Xeljanz®/Xeljanz XR® (tofacitinib citrate)	Pfizer	UC	Oral	Filed sNDA	03/2018
tildrakizumab	Sun	plaque psoriasis	SC	Filed BLA	03/2018
Plenvu® (PEG)	Salix/Valeant	colonoscopy prep	Oral	Filed NDA	03/2018
Esmya® (ulipristal acetate)	Allergan	uterine fibroids	Oral	Filed NDA	03/2018
Latuda® (lurasidone)	Sunovion	bipolar depression monotherapy (10-17yrs)	Oral	Filed sNDA	03/2018
Hizentra® (immune globulin)	CSL Behring	CIDP	SC	Filed sBLA	03/2018
Otiprio® (ciprofloxacin otic)	Otonomy	acute otitis externa	Intratympanic	Filed sNDA	03/02/2018
Akynzeo® (netupitant/ palonosetron)	Helsinn	CINV	IV	Filed sNDA	04/2018
Taltz® (ixekizumab)	Lilly	psoriatic arthritis	SC	Filed sBLA	04/13/2018

Medication Name*	Manufacturer	Therapeutic Use	Route of Administration	Approval Status	Anticipated FDA Response
Tavalisse™ (fostamatinib)	Rigel	ITP	Oral	Filed NDA	04/17/2018
burosumab	Ultragenyx	X-linked hypophosphatemia	SC	Filed BLA	04/17/2018
Nucala® (mepolizumab)	BMS/GSK	EGPA	SC	Filed sBLA	04/28/2018
mirabegron/solifenacin	Astellas	OAB	Oral	Filed sNDA	04/30/2018
Aimovig™ (erenumab)	Amgen	migraines	SC	Filed BLA	05/17/2018
Arnuity® Ellipta® (fluticasone furoate)	GSK	asthma (age 5-11yrs)	Inhalation	Filed sNDA	05/24/2018
Cimzia® (certolizumab pegol)	UCB/Dermira	plaque psoriasis	SC	Filed sBLA	05/25/2018
KIT-302 (amlodipine/celecoxib)	Kitov	HTN, OA	Oral	Filed NDA	05/31/2018
Xeglyze™ (abametapir)	Hatchtech	lice	Topical	Filed NDA	Unknown
Trevyent® (treprostinil)	Cardiome Pharma	PAH	IV	Filed NDA	Unknown
Scenesse® (afamelanotide)	Clinuvel	erythropoietic protoporphyria	SC implant	Filed NDA	Unknown
Vyndaqel® (tafamidis meglumine)	Pfizer	transthyretin familial amyloid polyneuropathy; transthyretin cardiomyopathy	Oral	Filed NDA	Unknown
FK506 (tacrolimus)	Astellas	prevention of organ rejection	Oral	Filed NDA	Unknown
Travivo™ (gepirone ER)	GSK	MDD	Oral	Filed NDA	Unknown

NDA = New Drug Application; BLA = Biologic License Application; sBLA = supplemental Biologic License Application; sNDA = supplemental New Drug Application; IV = intravenous; IM = intramuscular; SC = subcutaneous; ER = extended-release; IDA = iron deficiency anemia; CKD = chronic kidney disease; CINV = chemotherapy-induced nausea and vomiting; T2DM = type 2 diabetes mellitus; MDD = major depressive disorder; HPT = hyperparathyroidism; CHF = chronic heart failure; yrs = years; MACE = major adverse cardiovascular event; ECD = Erdheim-Chester disease; COPD = chronic obstructive pulmonary disease; GHD = growth hormone deficiency; HIV = human immunodeficiency virus; IBS-C = irritable bowel syndrome with constipation; NCFBE = non-cystic fibrosis bronchiectasis; CF = cystic fibrosis; UC = ulcerative colitis; PEG = polyethylene glycol; CIDP = chronic inflammatory demyelinating polyneuropathy; ITP = idiopathic thrombocytopenic purpura; EGPA = eosinophilic granulomatosis with polyangiitis; OAB = overactive bladder; HTN = hypertension; OA = osteoarthritis; PAH = pulmonary arterial hypertension; *Biosimilars and oncology medications excluded from table. Medications known to have received a Complete Response Letter from the FDA that have not resubmitted were excluded.

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Appendix C

Vote to Prior Authorize Kevzara® (Sarilumab), Siliq™ (Brodalumab), Tremfya™ (Guselkumab), Cyltezo™ (Adalimumab-adbm), and Renflexis™ (Infliximab-abda)

Oklahoma Health Care Authority
November 2017

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16]

- **Kevzara® (sarilumab)** is an interleukin (IL)-6 receptor antagonist indicated for the treatment of adult patients with moderate-to-severe, active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease modifying anti-rheumatic drugs (DMARDs). Kevzara® is supplied as 150mg/1.14mL or 200mg/1.14mL single-dose, pre-filled syringes, and the recommended dose of sarilumab is 200mg via subcutaneous (SC) injection once every two weeks. Sarilumab has a boxed warning for risk of serious infections. The wholesale acquisition cost (WAC) for six months of sarilumab therapy is $18,000.00.
- **Siliq™ (brodalumab)** is a human interleukin-17 receptor A (IL-17RA) antagonist indicated for the treatment of moderate-to-severe plaque psoriasis (PsO) in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies. Siliq™ is supplied as 210mg/1.5mL single-dose, pre-filled syringes, and the recommended dose of brodalumab is 210mg via SC injection at weeks 0, 1, and 2 followed by 210mg once every two weeks. If an adequate response has not been achieved after 12 to 16 weeks of treatment with brodalumab, consideration should be given to discontinuing therapy. Continued treatment beyond 16 weeks in patients who have not achieved an adequate response is not likely to result in greater success. Brodalumab has a boxed warning for risk of suicidal ideation and behavior and is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Siliq™ REMS Program. Brodalumab is contraindicated in patients with Crohn's disease (CD) as it may cause worsening of disease. The WAC for six months of brodalumab therapy is $21,000.06.
- **Tremfya™ (guselkumab)** is an IL-23 blocker indicated for the treatment of adult patients with moderate-to-severe PsO who are candidates for systemic therapy or phototherapy. Tremfya™ is supplied as 100mg/mL single-dose, pre-filled syringes, and the recommended dose of guselkumab is 100mg via SC injection at weeks 0, 4, and every 8 weeks thereafter. The WAC for six months of guselkumab therapy is $29,052.00.
- **Cyltezo™ (adalimumab-adbm)**, a biosimilar to Humira® (adalimumab), is a tumor necrosis factor (TNF) blocker indicated for RA, juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), adult CD, ulcerative colitis (UC), and PsO; Cyltezo™ is indicated for all Humira® indications except ages 2 to 4 years in JIA, pediatric CD, hidradenitis suppurativa (HS), and uveitis (UV). Cyltezo™ is supplied as 40mg/0.8mL single-use, pre-filled syringes intended for SC use. The recommended dosing varies by disease state; maintenance dosing ranges from 40mg every other week to 40mg every week. Cost information for Cyltezo™ is not yet available.

- **Renflexis™ (infliximab-abda)**, a biosimilar to Remicade® (infliximab), is a TNF blocker indicated for CD, pediatric CD, UC, RA in combination with methotrexate, AS, PsA, and PsO. Renflexis™ is indicated for all Remicade® indications except pediatric UC. Renflexis™ is supplied as a 100mg/10mL vial intended for intravenous (IV) administration, and the recommended dosing varies by disease state; maintenance dosing ranges from 3mg/kg to 10mg/kg every 4 to 8 weeks. The WAC for six months of infliximab-abda therapy in a 70kg patient receiving 5mg/kg every 8 weeks is $9,040.68.
- In May 2017, the U.S. Food and Drug Administration (FDA) approved SC **Actemra® (tocilizumab)** for the treatment of adults with **giant cell arteritis (GCA)**, also known as temporal arteritis, a chronic, systemic, inflammatory vasculitis of medium and large vessels, particularly the superficial temporal arteries. Common symptoms of GCA include headache, visual disturbances, jaw claudication, neck pain, scalp tenderness, fever, fatigue, and weight-loss. The laboratory hallmarks of GCA are an elevation in erythrocyte sedimentation rate (ESR) >30mm/hr and C-reactive protein (CRP) ≥1mg/dL. Temporal artery biopsy remains the gold standard for GCA diagnosis. GCA typically progressively improves with corticosteroid treatment, and treatment often results in complete resolution.
- Astellas Pharma U.S. Incorporated voluntarily discontinued **Amevive® (alefacept)**. The decision to discontinue alefacept was based on business reasons and not due to safety or efficacy concerns.
- In August 2017, the FDA approved IV **Actemra® (tocilizumab)** for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in patients 2 years of age and older. CRS, which is caused by an overactive immune response, has been identified as a potentially severe and life-threatening side effect of CAR T cell therapy for certain cancers.

Recommendations

The College of Pharmacy recommends the addition of Kevzara® (sarilumab), Siliq™ (brodalumab), Tremfya™ (guselkumab), Cyltezo™ (adalimumab-adbm), and Renflexis™ (infliximab-abda) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply.

- If the net cost of Cyltezo™ (adalimumab-adbm) and Renflexis™ (infliximab-abda) is determined to be greater than the net cost of the reference product formulations of Cyltezo™ and Renflexis™, authorization would also require a patient-specific, clinically significant reason why the member could not use the reference product formulations of Cyltezo™ and Renflexis™.
- The following criteria will also apply for authorization of Siliq™ (brodalumab):
    - Initial authorizations of Siliq™ (brodalumab) will be for the duration of 12 weeks at which time the prescriber must verify the member is responding to treatment. If an adequate response has not been achieved after 12 to 16 weeks of treatment with brodalumab, consideration should be given to discontinuing therapy.
    - Members must also be enrolled in the Siliq™ REMS Program for approval.
    - Members with a concomitant diagnosis of Crohn's disease will not be approved.

Additionally, the College of Pharmacy recommends the following criteria for Actemra® (tocilizumab) for a diagnosis of giant cell arteritis:

Actemra® (Tocilizumab) Approval Criteria [Giant Cell Arteritis (GCA) Diagnosis]:

1. An FDA approved diagnosis of GCA; and
2. Member must be 50 years of age or older; and
3. A history of erythrocyte sedimentation rate (ESR) of ≥30mm/hr or a history of C-reactive protein (CRP) ≥1mg/dL; and
4. Member should have a trial of glucocorticoids for a minimum of four weeks or a reason why this is not appropriate; and
5. Actemra® will be taken in combination with tapering course of a glucocorticoid upon initiation; and
6. Member must have baseline liver enzymes, absolute neutrophil count (ANC), lipid panel, and platelet count and verification that they are acceptable to prescriber; and
7. Member must not have severe hepatic impairment; and
8. Actemra® should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
9. Approval quantity will be based on Actemra® prescribing information and FDA approved dosing regimen.

Lastly, the College of Pharmacy recommends the following criteria for Actemra® (tocilizumab) for a diagnosis of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS):

Actemra® (Tocilizumab) Approval Criteria [Chimeric Antigen Receptor (CAR) T Cell-Induced Cytokine Release Syndrome (CRS) Diagnosis]:

1. An FDA approved diagnosis of CAR T cell-induced 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.

Humira® (Adalimumab) Approval Criteria [Hidradenitis Suppurativa Diagnosis]:

1. A diagnosis of moderate-to-severe hidradenitis suppurativa (HS); and

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

Humira® (Adalimumab) Approval Criteria [Noninfectious Intermediate and Posterior Uveitis or Panuveitis Diagnosis]:

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

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

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

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

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

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

*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.

DMARDs = Disease modifying anti-rheumatic drugs, NSAIDs = Nonsteroidal anti-inflammatory drugs

±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.

€Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) or noninfectious intermediate and posterior uveitis or panuveitis.

+May be rebated to Tier-2 status only.

¥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).

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

πUnique criteria applies for a diagnosis of giant cell arteritis (GCA) or chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS).

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Appendix D

Vote to Prior Authorize Blincyto® (Blinatumomab), Besponsa® (Inotuzumab Ozogamicin), Bosulif® (Bosutinib), Gleevec® (Imatinib), Iclusig® (Ponatinib), Kymriah™ (Tisagenlecleucel), Synribo® (Omacetaxine), Sprycel® (Dasatinib), and Tasigna® (Nilotinib)

Oklahoma Health Care Authority
November 2017

Introduction[1,2,3,4,5,6,7,8,9,10]

Blincyto® (Blinatumomab):

- **Therapeutic Class:** Anti-CD19/CD3 monoclonal antibody (bispecific T-cell engager, BiTE®)
- **Indication(s):** Treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)
- **How Supplied:** 35mcg vials for intravenous (IV) solution
- **Dose:** Weight and cycle dependent; ranges from 5mcg/m^2/day to 15mcg/m^2/day in patients weighing <45kg and 9mcg daily to 28mcg daily in patients weighting ≥45kg
- **Cost:** $4,319.43 per 35mcg vial

Besponsa® (Inotuzumab Ozogamicin):

- **Therapeutic Class:** Anti-CD22 monoclonal antibody
- **Indication(s):** Treatment of relapsed or refractory B-cell precursor ALL in adults
- **How Supplied:** 0.9mg vial for IV solution
- **Dose:** Weight and cycle dependent; ranges from 0.5mg/m^2 to 0.8mg/m^2 on days 1, 8, and 15 of a 21 to 28-day treatment cycle
- **Cost:** $18,700 per 0.9mg vial

Bosulif® (Bosutinib):

- **Therapeutic Class:** BCR-ABL Tyrosine Kinase Inhibitor (TKI)
- **Indication(s):** Chronic, accelerated, or blast phase chronic myeloid leukemia (CML)
- **How Supplied:** 100mg and 500mg oral tablets
- **Dose:** 500mg once daily, may increase to 600mg daily
- **Cost:** $13,539 for a 1-month supply of 500mg tablets

Gleevec® (Imatinib):

- **Therapeutic Class:** BCR-ABL TKI
- **Indication(s):**
  - Philadelphia positive (Ph+) ALL (pediatric and adult)
  - Aggressive, systemic mastocytosis
  - Chronic, accelerated, or blast phase CML
  - Dermatofibrosarcoma protuberans

- Gastrointestinal (GI) stromal tumors
- Hypereosinophilic syndrome and/or chronic eosinophilic leukemia
- Myelodysplastic/myeloproliferative diseases

- **How Supplied:** 100mg and 400mg oral tablets
- **Dose:** 400mg daily; may be increased to 800mg daily
- **Cost:** $10,122.30 for a 1-month supply of 400mg tablets

Iclusig® (Ponatinib):

- **Therapeutic Class:** BCR-ABL TKI
- **Indication(s):**
  - Ph+ ALL in patients for whom no other TKI therapy is indicated
  - Chronic phase, accelerated phase, or blast phase CML for which no other TKI therapy is indicated
  - T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL
- **How Supplied:** 15mg and 45mg oral tablets
- **Dose:** 45mg once daily
- **Cost:** $16,560.90 for a 1-month supply of 45mg tablets

Kymriah™ (Tisagenlecleucel):

- **Therapeutic Class:** CD19-directed genetically modified autologous T cell immunotherapy
- **Indication(s):** Patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse
- **How Supplied:** Patient-specific infusion bag
- **Dose:** Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells and body weight
- **Cost:** $475,000 per one-time treatment

Synribo® (Omacetaxine):

- **Therapeutic Class:** Cephalotaxine, protein synthesis inhibitor
- **Indication(s):** Chronic or accelerated phase CML
- **How Supplied:** 3.5mg vial for subcutaneous (SC) solution
- **Dose:** 1.25mg/m^2 twice daily for 7 to 14 consecutive days of a 28-day treatment cycle
- **Cost:** $957.00 per 3.5mg vial

Sprycel® (Dasatinib):

- **Therapeutic Class:** BCR-ABL TKI
- **Indication(s):**
  - Ph+ ALL
  - Chronic, accelerated, or blast phase CML
- **How Supplied:** 20mg, 50mg, 70mg, 80mg, 100mg, and 140mg oral tablets
- **Dose:** 100mg to 140mg daily
- **Cost:** $11,616.00 for a 1-month supply of 100mg tablets

Tasigna® (Nilotinib):

- **Therapeutic Class:** BCR-ABL TKI
- **Indication(s):** Chronic or accelerated phase CML
- **How Supplied:** 150mg and 200mg oral tablets
- **Dose:** 300mg to 400mg twice daily
- **Cost:** $12,415.20 for a 1-month supply of 150mg tablets

Recommendations

Blincyto® (Blinatumomab) Approval Criteria:

1. Blincyto® should be used as a single-agent only; and
2. For **one** of the following diseases:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) acute lymphoblastic leukemia (ALL); or
    b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL after failure of two Tyrosine Kinase Inhibitors (TKIs); or
    c. Ph- ALL as consolidation in adult/young adolescent or patients younger than 65 years without substantial comorbidity with persistent or late clearance minimal residual disease positive (MRD+) following a complete response to induction.

Besponsa® (Inotuzumab Ozogamicin) Approval Criteria:

1. Besponsa® must be used as a single-agent only; and
2. Member must have **one** of the following:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) acute lymphoblastic leukemia (ALL); or
    b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL who are intolerant/refractory to two or more Tyrosine Kinase Inhibitors (TKIs).

Bosulif® (Bosutinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Bosulif® may be authorized for relapsed/refractory ALL either as:
    a. Single-agent; or
    b. In combination with an induction regimen not previously given; and
2. Bosulif® must be only used in patients with E255K/V, F317L/VI/C, F359V/C/I, T315A, or Y253H mutations.

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

1. Patients with chronic, accelerated, or blast phase CML 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.

Gleevec® (Imatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Gleevec® may be approved for **one** of the following indications:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or
    c. In relapsed/refractory ALL and as a single-agent or in combination with multi-agent chemotherapy.

Gleevec® (Imatinib) Approval Criteria [Bone Cancer – Chordoma Diagnosis]:

1. Single-agent therapy or in combination with cisplatin or sirolimus for the treatment of recurrent disease.

Gleevec® (Imatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have **one** of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Gleevec® (Imatinib) Approval Criteria [Melanoma Diagnosis]:

1. Member must meet **all** of the following criteria:
    a. Gleevec® must be used as a single-agent; and
    b. Second-line or subsequent therapy for disease progression or after maximum clinical benefit from BRAF targeted therapy; and
    c. Metastatic or unresectable tumors; and
    d. Activating mutations of C-KIT; and
    e. Member must have an ECOG performance status of 0 to 2.

Gleevec® (Imatinib) Approval Criteria [Myelodysplastic Syndrome (MDS) Diagnosis]:

1. Chronic myelomonocytic leukemia (CMML) for 5q31-33 translocations and/or PDGFRβ gene rearrangements.

Gleevec® (Imatinib) Approval Criteria [Non-Melanoma Skin Cancers – Dermatofibrosarcoma Protuberans (DFSP) Diagnosis]:

1. Tumors with t(17;22) translocation; and
2. Member must have **one** of the following:
    a. Adjuvant therapy for positive surgical margins following excision; or
    b. Recurrent disease if disease is unresectable or if additional resection would lead to unacceptable functional or cosmetic outcomes; or
    c. For metastatic disease.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Desmoid Tumors (Aggressive Fibromatosis) Diagnosis]:

1. Primary, recurrent, or progressive disease with **one** of the following:

a. Initial treatment for resectable disease; or
b. Adjuvant treatment for gross residual disease; or
c. Initial treatment for unresectable disease or for disease for which surgery would be unacceptably morbid.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Primary/preoperative treatment for patients with documented GIST with **one** of the following:
   a. Resectable with risk of significant morbidity; or
   b. Unresectable; or
   c. Recurrent; or
   d. Metastatic; or
2. Postoperative treatment with **one** of the following:
   a. Complete resection of primary GIST; or
   b. Persistent gross residual disease; or
3. Continued treatment for **one** of the following:
   a. Limited progression; or
   b. Generalized progression.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor Diagnosis]:

1. Gleevec® must be used as a single-agent only.

Iclusig® (Ponatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have **one** of the following:
   a. Induction/consolidation with HyperCVAD; or
   b. Maintenance therapy in combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
   c. Maintenance therapy post-hematopoietic stem cell transplant; or
   d. Relapsed/refractory disease either as a single-agent, in combination with chemotherapy not previously given, or in patients with T315I mutations.

Iclusig® (Ponatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have **one** of the following:
   a. In patients with a T315I mutation; or
   b. Intolerant or resistant to all other Tyrosine Kinase Inhibitors (TKIs); or
   c. Post-hematopoietic stem cell transplantation in patients with prior accelerated or blast phase prior to transplant or who have relapsed.

Kymriah™ (Tisagenlecleucel) Approval Criteria:

1. **All** of the following must be met for approval:
   a. B-Cell precursor acute lymphoblastic leukemia (ALL); and
   b. Member must be 25 years of age or younger; and

c. Refractory or in second or later relapse:
    i. Philadelphia chromosome negative (Ph-) ALL: must be refractory or with ≥2 relapses; or
    ii. Philadelphia chromosome positive (Ph+) ALL: must have failed ≥2 Tyrosine Kinase Inhibitors (TKIs); and
d. Therapies to consider prior to tisagenlecleucel if appropriate: clinical trial, multi-agent chemotherapy with or without hematopoietic cell transplantation (HCT), blinatumomab (category 1 recommendation), and inotuzumab (category 1 recommendation).

2. Healthcare facilities must be on the certified list to administer CAR T cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

Synribo® (Omacetaxine) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Synribo® must be used as a single-agent only; and
2. Member must have **one** of the following:
    a. Primary treatment of advanced phase CML with disease progression to accelerated phase; or
    b. Post-hematopoietic stem cell transplant in patients who have relapsed; or
    c. Patients with T315I mutation; or
    d. Patients who are intolerant or resistant to two or more Tyrosine Kinase Inhibitors (TKIs).

Sprycel® (Dasatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have **one** of the following:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or
    c. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

Sprycel® (Dasatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have **one** of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Sprycel® (Dasatinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Member must have **all** of the following:
    a. Progressive disease and failed imatinib, sunitinib, or regorafenib; and
    b. PDGFRA D842V mutation.

Tasigna® (Nilotinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have **one** of the following:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or
    c. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

Tasigna® (Nilotinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have **one** of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Tasigna® (Nilotinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Member must have progressive disease and failed imatinib, sunitinib, or regorafenib.

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Appendix E

Vote to Prior Authorize Bavencio® (Avelumab) and Update Skin Cancer Medications Prior Authorization Criteria

Oklahoma Health Care Authority
November 2017

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15]

- **Opdivo® (nivolumab)** received the following updates and indication(s) from the U.S. Food and Drug Administration (FDA) during fiscal year 2017:
    - Modified dosage regimen approved for renal cell carcinoma, metastatic melanoma, and non-small cell lung cancer (NSCLC); single-dose regimen of nivolumab (3mg/kg intravenously [IV] every two weeks) replaced with new regimen of 240mg IV every two weeks.
    - Approved for treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after a platinum-based therapy.
    - Approved for treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy.
    - Approved for treatment of patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
    - Approved for treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.
- **Keytruda® (pembrolizumab)** received the following updates and indication(s) from the FDA during fiscal year 2017:
    - Approved for metastatic NSCLC in patients whose tumors express programmed death-ligand 1 (PD-L1) (tumor proportion score ≥50%); also expanded the indication in second-line treatment of lung cancer to include all patients with PD-L1-expressing NSCLC.
    - Approved for treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or those who have relapsed after three or more prior lines of therapy.
    - Approved for locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy.
    - Approved for treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

- Approved for use in combination with pemetrexed and carboplatin (pem/carbo) for the first-line treatment of metastatic nonsquamous NSCLC, irrespective of PD-L1 expression.
- Approved for treatment of adult and pediatric patients with unresectable or metastatic solid tumors that have biomarker MSI-H or dMMR. This indication covers patients with solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options and patients with colorectal cancer that has progressed following treatment with certain chemotherapy drugs (i.e., fluoropyrimidine, oxaliplatin, and irinotecan).
- Approved for patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1], with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.

- **Bavencio® (avelumab)**, a PD-L1 blocking antibody, was approved for adults and pediatric patients 12 years of age and older with metastatic Merkel Cell Carcinoma (MCC), and in patients with locally advanced or metastatic urothelial carcinoma. Bavencio® is supplied as a 200mg/10mL single-dose vial intended to be administered as 10mg/kg via IV infusion over 60 minutes every 2 weeks. The wholesale acquisition cost (WAC) of avelumab is $150.40 per mL or $1,504.00 per 10mL vial.

Recommendations

- 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 Bavencio® (avelumab) with the following criteria listed in red:

Bavencio® (Avelumab) Approval Criteria [Merkel Cell Carcinoma (MCC) Diagnosis]:

1. A diagnosis of metastatic MCC; and
2. Member must be 12 years of age or older.

Bavencio® (Avelumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Disease has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

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

1. A diagnosis of metastatic NSCLC; and
2. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for PD-L1 expression as follows:
    a. Single-agent, first-line: ≥50%; or

b. First-line in combination with carboplatin and pemetrexed: no expression required; or
c. Single-agent, second-line: ≥1%; and

4. Member meets **one** of the following:
   a. Previously untreated metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
   b. New diagnosis as first-line therapy (patient has not received chemotherapy to treat disease) if:
      i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; and
      ii. Member has an ECOG performance status of 0 to 1; or
   c. Single-agent for disease progression on or after platinum-containing chemotherapy (e.g., cisplatin or carboplatin):
      i. Patients with EGFR-mutation-positive disease should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
         1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*
      ii. Patients with ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
         1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*
      iii. Member has an ECOG performance status of 0 to 2.

Keytruda® (Pembrolizumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. Locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy; or
2. Within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; or
3. Frontline pembrolizumab for patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.
   a. Cisplatin ineligibility is defined as:
      i. Baseline creatinine clearance of <60mL/min, or an ECOG performance status of 2, or Class III heart failure, or grade 2 or greater peripheral neuropathy, or grade 2 or greater hearing loss.

Keytruda® (Pembrolizumab) Approval Criteria [Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumor (Tissue/Site-Agnostic) or Metastatic Colorectal Cancer Diagnosis]:

1. MSI-H or dMMR solid tumors that have progressed following prior treatment with no satisfactory alternative treatment options; or

2. MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Keytruda® (Pembrolizumab) Approval Criteria [Gastric or Gastroesophageal Junction Tumor Diagnosis]:

1. Recurrent, locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. Tumors must express PD-L1; and
3. Disease progression on or after two or more prior systemic therapies (including fluoropyrimidine- and platinum-containing chemotherapy, and if appropriate, HER2/neu-targeted therapy).

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

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

Opdivo® (Nivolumab) Approval Criteria [Urothelial Bladder Cancer Diagnosis]:

1. A diagnosis of metastatic or unresectable locally advanced cancer; and
2. Used as second-line or greater therapy; and
3. Patient has failed a platinum containing regimen; and
4. Member has an ECOG performance status of 0 to 1.

Opdivo® (Nivolumab) Approval Criteria [Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer Diagnosis]:

1. Diagnosis of MSI-H or dMMR metastatic colorectal cancer; and
2. Progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Opdivo® (Nivolumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Relapsed or progressive disease; and
2. Member must have been previously treated with sorafenib.

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

1. A diagnosis of relapsed or surgically unresectable stage IV disease; and
~~2. Tumor histology: predominantly clear cell; and~~
3. Failed prior therapy with one of the following medications:
    a. Sunitinib; or
    b. Sorafenib; or
    c. Pazopanib; or
    d. Axitinib; and
4. Nivolumab must be used as a single-agent; and
5. Member has an ECOG performance status of 0 to 2; and

6. The patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
7. Dose as follows:
    a. Single-agent: 240mg every two weeks.

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[1] U.S. Food and Drug Administration (FDA). FDA approves first treatment for rare form of skin cancer. Available online at: https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm548278.htm. Issued 03/23/2017. Last accessed 10/23/2017.

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[6] U.S. Food and Drug Administration (FDA). Pembrolizumab (KEYTRUDA) for classical Hodgkin lymphoma. Available online at: https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm546893.htm. Issued 03/14/2017. Last accessed 10/23/2017.

[7] Merck. FDA Approves Merck's KEYTRUDA® (pembrolizumab) for Certain Patients with Locally Advanced or Metastatic Urothelial Carcinoma, a Type of Bladder Cancer. *Business Wire*. Available online at: http://investors.merck.com/news/press-release-details/2017/FDA-Approves-Mercks-KEYTRUDA-pembrolizumab-for-Certain-Patients-with-Locally-Advanced-or-Metastatic-Urothelial-Carcinoma-a-Type-of-Bladder-Cancer/default.aspx. Issued 05/18/2017. Last accessed 10/23/2017.

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Appendix F

Vote to Prior Authorize Haegarda® [C1 Esterase Inhibitor (Human)]

Oklahoma Health Care Authority
November 2017

Introduction[1]

Indication(s): Haegarda® is a plasma-derived concentrate of C1 esterase inhibitor (human) (C1-INH) indicated for routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescent and adult patients.

Dosing:

- Haegarda® is supplied as a kit with a white lyophilized powder in single-use vials containing 2,000 or 3,000 International Units (IU) of C1-INH with sterile water for injection and one Mix2Vial® filter transfer set.
  - Haegarda® should be reconstituted with sterile water for injection prior to administration. Once reconstituted, Haegarda® should be administered within 8 hours.
- The recommended dose is 60 IU per kg body weight by subcutaneous (SC) injection twice weekly (every 3 or 4 days).

Cost Comparison:

Medication	Cost Per Vial	Cost for 28 Days of Therapy*
Haegarda® [C1 esterase inhibitor (human)]	**$1,880.00 – $2,820.00**	**$37,600.00◊**
Cinryze® [C1 esterase inhibitor (human)]	$2,758.79	$44,140.64

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.
*28 days of therapy based on recommended dosing.
◊Weight-based dosing based on 70kg patient

Recommendations

The College of Pharmacy recommends the prior authorization of Haegarda® [C1 esterase inhibitor (human)] similar to the other prior authorized hereditary angioedema (HAE) prophylaxis medications with the following criteria:

Cinryze® (C1 Esterase Inhibitor) and Haegarda® (C1 Esterase Inhibitor) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. History of at least one or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or three or more emergency medical treatments per year; and
4. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and

5. Member meets the following:
    a. Documented intolerance, insufficient response, or contraindication to attenuated androgens (e.g., danazol, stanozolol, oxandrolone, methyltestosterone); and
    b. Documented intolerance, insufficient response, or contraindication to antifibrinolytic agents (e.g., ε – aminocaproic acid, tranexamic acid); or
    c. Recent hospitalization for severe episode of angioedema; and
6. Cinryze® Dosing:
    a. The recommended dose of Cinryze® is 1,000 units IV every 3 to 4 days, approximately two times per week, to be infused at a rate of 1mL/min; and
    b. Initial doses should be administered in an outpatient setting by a healthcare provider. Patients can be taught by their healthcare provider to self-administer Cinryze® intravenously; and
    c. A quantity limit of 8,000 units per month will apply (i.e., two treatments per week or eight treatments per month); or
7. Haegarda® Dosing:
    a. 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
    b. A quantity limit of two treatments per week or eight treatments per month will apply.

[1] Haegarda® Prescribing Information. CSL Behring. Available online at: http://labeling.cslbehring.com/PI/US/HAEGARDA/EN/HAEGARDA-Prescribing-Information.pdf. Last revised 06/2017. Last accessed 10/09/2017.

Appendix G

Vote to Prior Authorize Axid® (Nizatidine Capsules and Solution), Tagamet® (Cimetidine Tablets), and Yosprala™ (Aspirin/Omeprazole Delayed-Release Tablets)

Oklahoma Health Care Authority
November 2017

Introduction[1]

Yosprala™ (aspirin/omeprazole delayed-release tablets) is a combination of aspirin and omeprazole, which is indicated for patients who require aspirin for secondary prevention of cardiovascular and cerebrovascular events and who are at risk of developing aspirin-associated gastric ulcers.

Cost Comparison:

Medication	Cost Per Unit	Cost for 30 Days of Therapy*
Yosprala™ (aspirin/omeprazole delayed-release tablets)	**$5.00**	**$150.00**
aspirin 81mg enteric-coated tablets◊	$0.05	$1.50
omeprazole 40mg capsules	$0.09	$2.70

*30 days of therapy based on usual dose of medication.
◊Cost based on Walgreens generic 120-count bottle from walgreens.com, last checked 10/09/2017.
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.

Recommendations

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

1. Place Yosprala™ (aspirin/omeprazole delayed-release tablets) into the Special Prior Authorization (PA) Tier of the Anti-Ulcer PBPA category. The following criteria will apply:
    a. A patient-specific, clinically significant reason why the separate products (aspirin and omeprazole) cannot be used in place of this combination product.
2. Place nizatidine solution (Axid®) into the Special PA Tier of the Anti-Ulcer PBPA category based on net cost. The following criteria will apply:
    a. A previous trial of ranitidine syrup or a patient-specific, clinically significant reason why ranitidine syrup is not appropriate for the member.
3. Place cimetidine tablets (Tagamet®) and nizatidine capsules (Axid®) into the Special PA Tier of the Anti-Ulcer PBPA category based on net costs. The following criteria will apply:
    a. A previous trial of ranitidine and famotidine or a patient-specific, clinically significant reason why ranitidine and famotidine are not appropriate for the member.

4. Move esomeprazole (Nexium® packets) and pantoprazole (Protonix® I.V.) to Tier-2 based on net costs. Current Tier-2 criteria and special formulation criteria will apply.
5. For famotidine suspension (Pepcid®), add a previous trial of ranitidine syrup or a patient-specific, clinically significant reason why ranitidine syrup is not appropriate for the member.

The proposed changes can be seen in red in the following criteria and tier chart:

Tagamet® (Cimetidine Tablets) Approval Criteria:

1. A previous 14-day trial of ranitidine and famotidine or a patient-specific, clinically significant reason why ranitidine and famotidine are not appropriate for the member.

Pepcid® (Famotidine Suspension) Approval Criteria:

1. A previous 14-day trial of ranitidine syrup or a patient-specific, clinically significant reason why ranitidine syrup is not appropriate for the member; and
2. Famotidine suspension (Pepcid®) will have an age restriction of 6 years of age and younger. Members older than 6 years of age will require a reason why the member needs the liquid formulation and cannot use the oral tablet formulation.

Axid® (Nizatidine Capsules) Approval Criteria:

1. A previous 14-day trial of ranitidine and famotidine or a patient-specific, clinically significant reason why ranitidine and famotidine are not appropriate for the member.

Axid® (Nizatidine Solution) Approval Criteria:

1. A previous 14-day trial of ranitidine syrup or a patient-specific, clinically significant reason why ranitidine syrup is not appropriate for the member; and
2. Nizatidine solution (Axid®) will have an age restriction of 6 years of age and younger. Members older than 6 years of age will require a reason why the member needs the liquid formulation and cannot use the oral capsule formulation.

Yosprala™ (Aspirin/Omeprazole Delayed-Release Tablets) Approval Criteria:

1. A patient-specific, clinically significant why the separate products (aspirin and omeprazole) cannot be used in place of this combination product.

Anti-Ulcer Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
omeprazole (Prilosec® caps)	dexlansoprazole (Dexilant® caps)	esomeprazole (Nexium® caps, ~~**packets**~~, I.V.)	**aspirin/omeprazole DR tabs (Yosprala™)**
pantoprazole (Protonix® tabs)	**esomeprazole (Nexium® packets)**	esomeprazole strontium caps	**cimetidine tabs (Tagamet®)**
	lansoprazole (Prevacid® caps, ODT)	dexlansoprazole (Dexilant® SoluTab)	famotidine (Pepcid® susp)
	pantoprazole (Protonix® I.V.)	omeprazole (Prilosec® susp, powder)	**nizatidine caps & sol (Axid®)**
	rabeprazole sodium (Aciphex® tabs)	pantoprazole (Protonix® susp, ~~**I.V.**~~)	omeprazole/sodium bicarbonate (Zegerid®)
		rabeprazole sodium (Aciphex® Sprinkles)	ranitidine (caps, ~~**Zantac® Effervescent Tabs**~~)
			sucralfate susp UD cups

ODT = orally disintegrating tablets; caps = capsules; tabs = tablets; I.V. = intravenous; susp = suspension; sol = solution; DR = delayed-release; UD = unit dose

*Special formulations including ODTs, granules, suspension, sprinkle capsules, and solution for I.V. require special reason for use.

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

[1] Yosprala Prescribing Information. Aralez Pharmaceuticals US, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/205103s000lbl.pdf. Last revised 09/2016. Last accessed 10/09/2017.

Appendix H

Vote to Prior Authorize Trulance™ (Plecanatide), Xermelo™ (Telotristat Ethyl), Symproic® (Naldemedine), and Motofen® (Difenoxin/Atropine)

Oklahoma Health Care Authority
November 2017

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18]

- **Trulance™ (plecanatide)** was approved by the U.S. Food and Drug Administration (FDA) in January 2017 for the treatment of chronic idiopathic constipation (CIC) in adult patients. Plecanatide, taken orally once daily, functions as a guanylate cyclase-C agonist and works locally in the upper gastrointestinal (GI) tract to stimulate secretion of intestinal fluid and support regular bowel function. Plecanatide has a boxed warning for the risk of serious dehydration in pediatric patients. The safety and effectiveness of plecanatide in patients younger than 18 years of age have not been established, and plecanatide is contraindicated in patients younger than 6 years of age. Plecanatide is also contraindicated in patients with known or suspected mechanical GI obstruction. The national average drug acquisition cost (NADAC) of Trulance™ is $11.26 per tablet, resulting in a monthly cost of $337.80.
- **Xermelo™ (telotristat ethyl)** was FDA approved in February 2017 as an orphan drug for use in combination with somatostatin analog (SSA) therapy [e.g., Somatuline® (lanreotide), Sandostatin® (octreotide)] for the treatment of adults with carcinoid syndrome diarrhea that SSA therapy alone has inadequately controlled. Telotristat ethyl, in a regimen with SSA therapy, is approved in tablet form to be taken orally three times daily with food. A carcinoid tumor is a specific type of neuroendocrine tumor (NET) and most often develops in the GI tract or lungs. When carcinoid tumors become large or spread to other parts of the body, they can release extra serotonin into the body, which can cause carcinoid syndrome. Telotristat ethyl targets the overproduction of serotonin by NETs and reduces the frequency of carcinoid syndrome diarrhea. The wholesale acquisition cost (WAC) of Xermelo™ is $61.48 per tablet, resulting in a monthly cost of $5,533.20.
- **Symproic® (naldemedine)** was FDA approved in March 2017 as a once-daily, oral, peripherally-acting mu-opioid receptor antagonist (PAMORA) for the treatment of opioid-induced constipation (OIC) in adult patients with chronic, non-cancer pain. In August 2017, the FDA approved a supplemental New Drug Application (sNDA) for Symproic® to provide clarification of the OIC indication, specifically stating that it is indicated for the treatment of OIC in adult patients 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.* Naldemedine is contraindicated in patients with known or suspected GI obstruction and patients at risk of recurrent obstruction, due to the potential for GI perforation, and is also

contraindicated in patients with a history of hypersensitivity reaction to naldemedine. The WAC of Symproic® is $10.47 per tablet, resulting in a monthly cost of $314.10.

- An sNDA for **Motofen® (difenoxin 1mg/atropine 0.025mg oral tablets)** was FDA approved in March 2017 to transfer the ownership to Sebela Pharmaceuticals, and it is anticipated to be available on the market soon. First FDA approved in 1978, Motofen® is an antiperistaltic anti-diarrheal medication indicated as adjunctive therapy in the management of acute nonspecific diarrhea and acute exacerbations of chronic functional diarrhea. Motofen® is contraindicated in patients with diarrhea associated with organisms that penetrate the intestinal mucosa (e.g., toxigenic *Escherichia coli*, *Salmonella* species, *Shigella*) and pseudomembranous colitis associated with broad spectrum antibiotics. The recommended dosing for patients age 12 years and older is an initial dose of two tablets orally, followed by one tablet orally after each loose stool or every 3 to 4 hours as needed, with a maximum of eight tablets per 24 hours. If clinical improvement is not observed in 48 hours, continued administration of this type of medication is not recommended. For acute diarrhea and acute exacerbations of functional diarrhea, treatment beyond 48 hours is usually not necessary. The safety and effectiveness of Motofen® in children younger than 12 years of age have not been established, and Motofen® is contraindicated in children younger than 2 years of age. The current WAC of Motofen® is $6.88 per tablet, resulting in a cost of $55.04 per day at maximum dosing (eight tablets/day). The NADAC of diphenoxylate/atropine (generic Lomotil®) is $0.42 per tablet, resulting in a cost of $3.36 per day at maximum dosing (eight tablets/day). Lomotil® is indicated in children ages 2 years and older and is also available generically as an oral solution ($8.80 per day at maximum dosing).
- The FDA issued a Drug Safety Communication in July 2016 to update the warnings for oral and injectable fluoroquinolone antibiotics due to disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system that can occur together in the same patient. The FDA determined that fluoroquinolones should be reserved for use in patients who have no other treatment options for acute bacterial sinusitis (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTI) because the risk of these serious side effects generally outweighs the benefits in these patients. The current approval criteria for **Xifaxan® (rifaximin) 200mg** for the diagnosis of traveler's diarrhea requires a reason why the member cannot use a fluoroquinolone antibiotic, which is recommended in The American Academy of Family Physicians treatment guidelines as the antibiotic of choice for traveler's diarrhea in most parts of the world because of their efficacy against most enteropathogens. Rifaximin is FDA approved for the treatment of traveler's diarrhea due to noninvasive strains of *Escherichia coli (E. coli)* and is recommended as an option in places where noninvasive *E. coli* is the predominant pathogen (e.g., Mexico). Treatment guidelines for traveler's diarrhea have not been updated since the FDA updated the warnings for fluoroquinolones.
- The FDA issued a Drug Safety Communication in March 2017 to warn about an increased risk of serious pancreatitis with **Viberzi® (eluxadoline)** in patients without a gallbladder. An FDA review found that these patients have an increased risk of developing serious pancreatitis that could result in hospitalization or death, and the FDA concluded that

healthcare professionals should not prescribe eluxadoline to patients who do not have a gallbladder and should consider alternative treatment options in these patients. Eluxadoline is indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D), and the package labeling for eluxadoline has been updated to include patients without a gallbladder as a contraindication.

Cost Comparison: Constipation Medications

Medication	Recommended Dose	Cost/Month*
Chronic Idiopathic Constipation (CIC) Indication		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$336.60
Linzess® (linaclotide) 145mcg cap	72mcg or 145mcg PO QDay	$340.20
Trulance™ (plecanatide) 3mg tab	3mg PO QDay	$337.80
Irritable Bowel Syndrome with Constipation (IBS-C) Indication		
Amitiza® (lubiprostone) 8mcg cap	8mcg PO BID	$336.60
Linzess® (linaclotide) 290mcg cap	290mcg PO QDay	$339.60
Opioid-Induced Constipation (OIC) Indication⁺		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$336.60
Movantik® (naloxegol) 25mg tab	12.5mg or 25mg PO QDay	$301.20
Relistor® (methylnaltrexone) 150mg tab	450mg PO QDay	$1,431.00
Relistor® (methylnaltrexone) 12mg/0.6mL inj¥	12mg subQ QDay	$2,876.76α
Symproic® (naldemedine) 0.2mg tab	0.2mg PO QDay	$314.10

cap = capsule, tab = tablet, inj = injection, PO = by mouth, BID = twice daily, QDay = once daily, subQ = subcutaneous
*Costs are based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC is unavailable and do not reflect rebated prices or net costs.
⁺Medications included in the table are indicated for the treatment of OIC in adult patients 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.
¥Relistor® injection is also indicated for the treatment of OIC in patients with severe terminal disease who are receiving only palliative care, with recommended dosing of weight-based every other day subcutaneous injections as needed.
αCost/month for Relistor® injection is based on once daily use of 12mg/0.6mL syringes.

Recommendations

The College of Pharmacy recommends the prior authorization of Trulance™ (plecanatide), Xermelo™ (telotristat ethyl), Symproic® (naldemedine), and Motofen® (difenoxin/atropine) with the following criteria:

Trulance™ (Plecanatide) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) 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 the prescriber documents the member is responding well to treatment.
6. A quantity limit of 30 tablets for a 30-day supply will apply.

Xermelo™ (Telotristat Ethyl) Approval Criteria:

1. An FDA approved diagnosis of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy; and
2. Member must be 18 years of age or older; and
3. Member must have been taking a stable dose of SSA therapy for the last three months and be inadequately controlled (four or more bowel movements per day); and
4. Prescriber must verify member will continue taking SSA therapy in combination with Xermelo™; 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 90 tablets for a 30-day supply will apply.

Criteria number six for Symproic® was removed (see below in red) due to cost information recently becoming available; the cost of Symproic® is comparable to Amitiza® and Movantik®.

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 the 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 the prescriber documents the 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.

Motofen® (Difenoxin/Atropine) Approval Criteria:

1. An FDA approved diagnosis of acute nonspecific diarrhea or acute exacerbations of chronic functional diarrhea; and
2. Member must not be 2 years of age or younger; and
3. Member must not have diarrhea associated with organisms that penetrate the intestinal mucosa (e.g., toxigenic *Escherichia coli, Salmonella species, Shigella*) or pseudomembranous colitis associated with broad spectrum antibiotics; and
4. A patient-specific, clinically significant reason why the member cannot use Lomotil® (diphenoxylate/atropine) and loperamide must be provided; and
5. A quantity limit of 16 tablets per 2 days will apply.

Additionally, the College of Pharmacy recommends updating the current approval criteria for Xifaxan® (rifaximin) 200mg to remove from the approval criteria the required reason why the member cannot use a fluoroquinolone antibiotic, which addresses the FDA Drug Safety Communication that updated the warnings for fluoroquinolone antibiotics. The College of Pharmacy also recommends updating the current approval criteria for Viberzi® (eluxadoline) to exclude members with any contraindications to taking Viberzi®, which addresses the recent FDA Drug Safety Communication regarding use of Viberzi® in patients without a gallbladder. The proposed changes can be seen in red in the following criteria:

Xifaxan® (Rifaximin) 200mg Approval Criteria:

1. An FDA approved diagnosis of traveler's diarrhea (TD); and
2. Member must be 12 years of age or older; and
3. TD must be due to noninvasive strains of *Escherichia coli*; and
4. ~~A patient-specific, clinically significant reason why the member cannot use a fluoroquinolone antibiotic (e.g., ciprofloxacin, levofloxacin) must be provided.~~
5. A quantity limit of 9 tablets for a 3-day supply will apply.

Viberzi® (Eluxadoline) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
2. Member must be 18 years of age or older; and
3. Member must not have any of the contraindications for use of Viberzi® (e.g., removed gallbladder; biliary duct obstruction or sphincter of Oddi disease or dysfunction; alcoholism, alcohol abuse, or alcohol addiction; history of pancreatitis or structural diseases of the pancreas; severe hepatic impairment; history of chronic or severe constipation; mechanical gastrointestinal obstruction); and
4. Documentation of trials of two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10 to 14 consecutive days at the recommended dosing). Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure.

5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents the member is responding well to treatment.
6. A quantity limit of 60 tablets for a 30-day supply will apply.

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Appendix I

Vote to Prior Authorize MiCort™ HC (Hydrocortisone Acetate 2.5% Cream) and Update Topical Corticosteroids Product Based Prior Authorization Tier Chart and Criteria

Oklahoma Health Care Authority
November 2017

Introduction[1]

MiCort™ HC (hydrocortisone acetate 2.5% cream) was approved by the U.S. Food and Drug Administration (FDA) as an Abbreviated New Drug Application (ANDA) in February 2001; however, the market start date for MiCort™ HC was September of 2016. MiCort™ HC is a topical corticosteroid indicated for the relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. It is available as a topical external 2.5% w/w cream and should be applied to the affected area as a thin film two to four times daily depending on the severity of the condition. The wholesale acquisition cost (WAC) for MiCort™ HC is $7.42 per gram or $210.73 per 28.4 gram tube with applicator. In comparison, Proctosol-HC® (hydrocortisone 2.5% cream) has a national average drug acquisition cost (NADAC) of $1.40 per gram or $39.69 for a 28.35 gram tube with applicator and is currently available without prior authorization.

Recommendations

The College of Pharmacy recommends the prior authorization of MiCort™ HC (hydrocortisone acetate 2.5% cream) with the criteria noted in red:

MiCort™ HC (Hydrocortisone Acetate 2.5% Cream) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Proctosol-HC® (hydrocortisone 2.5% cream).

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

Topical Corticosteroid PBPA Tier Chart and Criteria Recommendations:

1. The creation of a third Tier to account for very high net cost products.
2. Move Aclovate® (alclometasone dipropionate cream and ointment) from Tier-1 to Tier-2 under Low Potency of the Topical Corticosteroid PBPA Tier Chart based on cost.
3. Move Derma-Smoothe® and Derma-Smoothe FS® (fluocinolone acetonide 0.01% oil) from Tier-2 to Tier-3 under Low Potency of the Topical Corticosteroid PBPA Tier Chart based on cost.
4. Move Desonate® (desonide 0.05% gel) and Capex® (fluocinolone acetonide 0.01% shampoo) from Tier-2 to Tier-1 under Low Potency of the Topical Corticosteroid PBPA Tier Chart based on cost.

5. Move Sernivo™ (betamethasone dipropionate 0.05% spray) spray and Westcort® (hydrocortisone valerate 0.2% cream and ointment) from Tier-2 to Tier-3 under Medium/High to Medium Potency of the Topical Corticosteroid PBPA Tier Chart based on cost.
6. Move Temovate® (clobetasol propionate 0.05% cream and solution) from Tier-2 to Tier-1 under the Ultra-high to High Potency of the Topical Corticosteroid PBPA Tier Chart based on cost.
7. Move Clobex® (clobetasol propionate 0.05% shampoo and spray), Olux-E® and Olux® (clobetasol propionate 0.05% foam), Temovate® (clobetasol propionate 0.05% ointment), and Topicort® (desoximetasone 0.25% cream, ointment, and spray) from Tier-2 to Tier-3 under the Ultra-high to High Potency of the Topical Corticosteroid PBPA Tier Chart based on 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, the member must also provide a patient-specific, clinically significant reason for requesting a Tier-2 in the same potency instead of trying a higher potency; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (foams, shampoos, sprays, kits, etc.); 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, the member must also provide a patient-specific, clinically significant reason for requesting a Tier-3 in the same potency instead of trying a higher potency; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-3 (foams, shampoos, sprays, kits, etc.); 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 (**Diprolene AF®**)	**C**	amcinonide	**C,O,L**	**clobetasol propionate 0.05% (Clobex®)**	**Sh,Spr**
augmented betamethasone dipropionate (**Diprolene®**)	**G**	augmented betamethasone dipropionate (**Diprolene®**)	**O,L**	**clobetasol propionate 0.05% (Olux®, Olux-E®)**	**F**
betamethasone dipropionate (**Diprosone®**)	**O**	betamethasone dipropionate (**Diprosone®**)	**C**	**clobetasol propionate 0.05% (Temovate®)**	**O**
clobetasol propionate 0.05% (Temovate®)	**C,So**	clobetasol propionate 0.05% (**Clobex®**)	**L**	**desoximetasone 0.25% (Topicort®)**	**C,O,Spr**
fluocinonide 0.05%	**C,O,So**	clobetasol propionate 0.05% (**Temovate®**)	**G**		
halobetasol propionate (**Ultravate®**)	**C**	desoximetasone 0.05% (**Topicort®**)	**G**		
		diflorasone diacetate 0.05% (**Apexicon®**)	**C**		
		diflorasone diacetate 0.05% (**Apexicon E®**)	**C,O**		
		fluocinonide 0.05%	**G**		
		fluocinonide 0.1% (**Vanos®**)	**C**		
		flurandrenolide tape (**Cordran®**)	**Tape**		
		halcinonide (**Halog®**)	**C,O**		
		halobetasol propionate 0.05% (**Ultravate®**)	**L,O**		
		halobetasol propionate/lactic acid (**Ultravate X®**)	**C**		
Medium/High to Medium Potency					
betamethasone dipropionate	**L**	betamethasone dipropionate/calcipotriene (**Taclonex®**)	**O,Sus, Spr**	**betamethasone dipropionate 0.05% (Sernivo™)**	**Spr**
betamethasone valerate 0.1% (**Beta-Val®**)	**C,O,L**	betamethasone valerate 0.12% (**Luxiq®**)	**F**	**hydrocortisone valerate 0.2% (Westcort®)**	**C,O**
fluticasone propionate (**Cutivate®**)	**C,O**	calcipotriene/betamethasone dipropionate (**Enstilar®**)	**F**		
mometasone furoate (**Elocon®**)	**C,L**	desoximetasone 0.05% (**Topicort LP®**)	**C,O**		
triamcinolone acetonide	**C,O,L**	fluocinolone acetonide 0.025% (**Synalar®**)	**C,O**		
		fluocinonide emollient (**Lidex E®**)	**C**		
		flurandrenolide 0.05%	**C,L,O**		
		fluticasone propionate (**Cutivate®**)	**L**		
		hydrocortisone butyrate 0.1%	**C,O,So**		
		hydrocortisone probutate (**Pandel®**)	**C**		

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
		mometasone furoate 0.1%	**O**		
		prednicarbate (**Dermatop®**)	**O,C**		
		triamcinolone acetonide (**Kenalog®**)	**Spr**		
Low Potency					
desonide 0.05% (Desonate®)	**G**	**alclometasone dipropionate (Aclovate®)**	**C,O**	**fluocinolone acetonide 0.01% (Derma-Smoothe®; Derma-Smoothe FS®)**	**Oil**
fluocinolone acetonide 0.01% (Capex®)*	**Sh**	clocortolone pivalate (**Cloderm®**)	**C**		
fluocinolone acetonide 0.01% (**Synalar®**)	**C**	desonide 0.05% (**Verdeso®**)	**F**		
hydrocortisone acetate 2.5%	**C,O,L**	desonide emollient	**C,O**		
hydrocortisone/urea (**U-Cort®**)	**C**	fluocinolone acetonide 0.01% (**Synalar®**)	**So**		
		hydrocortisone 2.5% (**Texacort®**)	**So**		
		hydrocortisone/pramoxine (**Pramosone®**)	**C,L**		

C = Cream; O = Ointment; L = Lotion; G = Gel; Sh = Shampoo; So = Solution; Spr = Spray; Sus = Suspension; F = Foam
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Capex® (fluocinolone acetonide 0.1% shampoo) is not a required trial for non-scalp conditions.

[1] MiCort™ HC Prescribing Information. Sebela Pharmaceuticals Inc. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3c634bbe-cf9b-0db5-e054-00144ff8d46c. Last revised 09/2016. Last accessed 10/11/2017.

Appendix J

Vote to Prior Authorize Noctiva™ (Desmopressin Acetate Nasal Spray)

Oklahoma Health Care Authority
November 2017

Introduction[1,2]

Noctiva™ (desmopressin acetate nasal spray) is a vasopressin analog indicated for the treatment of nocturnal polyuria in adults who awaken at least two times per night to void. It was not studied in patients younger than 50 years of age. Nocturnal polyuria is an overproduction of urine at night, with a normal 24-hour urine output. Noctiva™ acts as a selective agonist at V2 receptors on renal cells in the collecting ducts. This increases water re-absorption in the kidneys and reduces urine production. Noctiva™ is a preservative-free nasal spray delivering 0.83mcg or 1.66mcg of desmopressin acetate in each spray. It is supplied in a 3.5mL amber glass bottle containing 30 doses. For patients younger than 65 years of age who are not at increased risk for hyponatremia, the recommended dose is one spray of 1.66mcg in either nostril nightly approximately 30 minutes before going to bed. For patients 65 years of age and older or younger patients at risk for hyponatremia, the recommended starting dose is one spray of 0.83mcg nightly in either nostril, which can be increased to one spray of 1.66mcg after at least seven days, if needed, provided the serum sodium has remained normal. Noctiva™ can cause hyponatremia that, if severe, can be life-threatening. As such, within seven days and approximately one month after initiating, resuming, or increasing the dose of Noctiva™, serum sodium concentrations should be checked. It is contraindicated in patients with an estimated glomerular filtration rate (eGFR) below 50mL/min/1.73m^2 and in concomitant use with loop diuretics, inhaled or systemic glucocorticoids, and other medications via the nasal route.

Cost Comparison:

Medication	Cost Per Unit	Cost Per 30 days
Noctiva™ (desmopressin acetate nasal spray)	**Unknown**	**Unknown**
desmopressin 0.1mg tablet	$0.78	$23.40*

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per 30 days based on off-label dosing for nocturia of 100mcg at bedtime.

Recommendations

The College of Pharmacy recommends placement of Noctiva™ (desmopressin acetate) into the Special Prior Authorization (PA) Tier of the Bladder Control Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Noctiva™ (Desmopressin Acetate) 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; ~~or~~
    ~~c. Inhaled or systemic glucocorticoids;~~ and
9. The prescriber must confirm the member does not have renal impairment with estimated glomerular filtration rate (eGFR) below 50mL/min/1.73m^2; and
10. Initial approvals will be for the duration of 3 months, and 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.

Bladder Control Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
fesoterodine (Toviaz®)	tolterodine (Detrol®)	darifenacin (Enablex®)	**desmopressin acetate nasal spray (Noctiva™)[+]**
oxybutynin (Ditropan®)	trospium (Sanctura®)	mirabegron (Myrbetriq®)	oxybutynin patch (Oxytrol®)[+]
oxybutynin ER (Ditropan XL®)		oxybutynin gel (Gelnique®)	
		solifenacin (VESIcare®)	
		tolterodine ER (Detrol LA®)	
		trospium ER (Sanctura XR®)	

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended release
[+]Unique criteria specific to Oxytrol® (oxybutynin patch) and Noctiva™ (desmopressin acetate nasal spray) applies.

[1] Noctiva™ Prescribing Information. Serenity Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/201656lbl.pdf. Last revised 03/2017. Last accessed 10/03/2017.
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Appendix K

Vote to Prior Authorize Sprix® (Ketorolac Tromethamine Nasal Spray) and Cataflam® (Diclofenac Potassium Tablets)

Oklahoma Health Care Authority
November 2017

Introduction[1,2]

Sprix® (ketorolac tromethamine nasal spray) is a nonsteroidal anti-inflammatory drug (NSAID) indicated for use in adults for the short-term (not to exceed 5 days and not to be used with other forms of ketorolac or other NSAIDs) management of moderate-to-moderately severe pain that requires analgesia at the opioid level. It is supplied in single-day, preservative-free spray bottles containing eight sprays per bottle. Each spray delivers 15.75mg of ketorolac tromethamine. The recommended dose for adults younger than 65 years of age is 31.5mg (one 15.75mg spray in each nostril) every 6 to 8 hours with a maximum daily dose of 126mg (eight sprays). The recommended dose for adults 65 years of age and older, renally impaired patients, and adult patients weighing less than 50kg is 15.75mg (one 15.75mg spray in only one nostril) every 6 to 8 hours with a maximum daily dose of 63mg (four sprays).

Cost Comparison:

Medication	Cost Per Unit	Cost Per 5 Days
Sprix® (ketorolac tromethamine 15.75mg nasal spray)*	**$295.85**	**$1,479.25**
ketorolac injection 30mg/1mL	$3.48	$69.60
ketorolac 10mg tablet	$0.98	$19.60

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Unit = bottle, tablet, or vial
*Sprix® is dispensed exclusively through Cardinal Health Specialty Pharmacy.

Diclofenac potassium 50mg (Cataflam®) has a national average drug acquisition cost (NADAC) of $0.48 per tablet resulting in a 30-day supply costing $43.20. As shown in the following Tier-1 products table, the cost of a similar product, diclofenac sodium 75mg, is $0.14 per tablet with a 30-day supply costing $8.40.

Tier-1 Products:

Medication	Cost Per Tablet	Cost for 30 Days of Therapy*
diclofenac potassium 50mg tablet	**$0.48**	**$43.20**
diclofenac sodium 75mg tablet	$0.14	$8.40
meloxicam 15mg tablet	$0.02	$0.60

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost for 30 days of therapy based on recommended dosing for osteoarthritis.

Fenoprofen 600mg (Nalfon®) and meclofenamate 100mg (Meclomen®) also demonstrate substantial cost differences between similar medications as noted in the following Tier-2 products table. The NADAC for fenoprofen 600mg tablets is $312.00 for a 30-day supply, while

the wholesale acquisition cost (WAC) for meclofenamate 100mg capsules is $742.80 for a 30-day supply. This compares to etodolac 300mg capsules with a NADAC of $94.50 for a 30-day supply.

Tier-2 Products:

Medication	Cost Per Unit	Cost for 30 Days of Therapy*
fenoprofen 600mg tablet	**$2.60**	**$312.00**
meclofenamate 100mg capsule	**$6.19**	**$742.80**
etodolac 300mg capsule	$1.05	$94.50
naproxen sodium 550mg tablet	$1.17	$70.20

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 = tablet or capsule
*Cost for 30 days of therapy based on recommended dosing for osteoarthritis.

Celecoxib 400mg (Celebrex®) is one of several strengths of celecoxib available for patients requiring treatment with an NSAID; however, the cost of celecoxib 400mg is significantly greater. Also, celecoxib 400mg is the only strength indicated for Familial Adenomatous Polyposis (FAP). The NADAC of celecoxib 400mg is $1.82 per capsule. This results in a 30-day supply costing $54.60. As shown in the following table, the cost of the other available strengths of celecoxib, at an equivalent dose, is significantly less.

Medication	Cost Per Capsule	Cost for 30 Days of Therapy*
celecoxib 400mg capsule	**$1.82**	**$54.60**
celecoxib 200mg capsule	$0.42	$25.20
celecoxib 100mg capsule	$0.38	$45.60

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*30 days of therapy based on 400mg/day of celecoxib.

Recommendations

The College of Pharmacy recommends the following:

1. The placement of Cataflam® (diclofenac potassium tablets) into Tier-2 of the NSAID Product Based Prior Authorization (PBPA) category based on national average drug acquisition cost (NADAC).
2. The placement of Sprix® (ketorolac tromethamine nasal spray), Nalfon® (fenoprofen), Meclomen® (meclofenamate), and Celebrex® (celecoxib) 400mg capsules into the Special Prior Authorization (PA) Tier of the NSAID PBPA category based on wholesale acquisition cost (WAC) and NADAC. Current Special PA Tier criteria will apply. Additionally, for Celebrex® (celecoxib) 400mg capsules the following criteria will apply:
    a. **Celebrex® (Celecoxib 400mg Capsules) Approval Criteria:**
        i. A diagnosis of Familial Adenomatous Polyposis (FAP); and
        ii. A patient-specific, clinically significant reason why the member cannot use two celecoxib 200mg capsules to achieve a 400mg dose.
3. Move Celebrex® (celecoxib) 50mg, 100mg, and 200mg capsules from Tier-2 to Tier-1 based on NADAC.

NSAIDs Tier-2 Approval Criteria:

1. Previous use of at least two Tier-1 NSAID products (from different product lines) plus a proton pump inhibitor (PPI) within the last 120 days.

NSAIDs Special Prior Authorization (PA) Approval Criteria:

1. A unique indication for which a Tier-1 or Tier-2 product is not appropriate; or
2. Previous use of at least two Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically-significant reason why a special formulation is needed over a Tier-1 product.
4. Additionally, use of Tivorbex® (indomethacin) will require a patient-specific, clinically significant reason why the member cannot use all other available generic indomethacin products.
5. Additionally, use of Celebrex® (celecoxib) 400mg capsules will require a diagnosis of Familial Adenomatous Polyposis (FAP) and a patient-specific, clinically significant reason why the member cannot use two celecoxib 200mg capsules to achieve a 400mg dose.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	**Tier-2**	**Special PA**
celecoxib (Celebrex®) 50mg, 100mg, & 200mg caps	**diclofenac potassium (Cataflam®)**	**celecoxib (Celebrex®) 400mg caps**
diclofenac ER (Voltaren® XR)	diclofenac sodium/ misoprostol (Arthrotec®)	diclofenac (Zorvolex®)
diclofenac sodium (Voltaren®) 50mg & 75mg tabs	diclofenac sodium (Voltaren®) 25mg tabs	diclofenac epolamine (Flector® patch)
etodolac (Lodine®) 400mg & 500mg tabs	etodolac (Lodine®) 200mg & 300mg caps	diclofenac potassium (Cambia®) powder pack
flurbiprofen (Ansaid®)	etodolac ER (Lodine® XL)	diclofenac potassium (Zipsor®) caps
ibuprofen (Motrin®)	naproxen sodium (Anaprox®) 275mg & 550mg tabs	diclofenac sodium (Dyloject™)
ketoprofen (Orudis®)	oxaprozin (Daypro®)	diclofenac sodium (Pennsaid®) topical drops
meloxicam (Mobic®)	piroxicam (Feldene®)	diclofenac sodium (Voltaren® Gel
nabumetone (Relafen®)	tolmetin (Tolectin®)	**fenoprofen (Nalfon®)**
naproxen (Naprosyn®)		ibuprofen/famotidine (Duexis®)
naproxen EC (Naprosyn®)		Indomethacin (Indocin®) susp & ER caps
sulindac (Clinoril®)		indomethacin (Tivorbex®)
		ketoprofen ER (Oruvail®)
		ketorolac tromethamine (Sprix®) nasal spray
		meclofenamate (Meclomen®)
		mefenamic acid (Ponstel®)
		meloxicam (Vivlodex®) caps
		naproxen sodium ER (Naprelan®)
		naproxen/esomeprazole (Vimovo®)

ER = extended-release, EC = enteric coated, caps = capsules, tabs = tablets, susp = suspension
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

[1] National Institute of Health. Sprix® (ketorolac tromethamine spray, metered). *U.S. National Library of Medicine: DailyMed*. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=97005a1c-167e-4676-bae7-e49b38c36f9e. Last revised 07/08/2016. Last accessed 10/03/2017.

[2] Celebrex® Prescribing Information. Pfizer. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/020998s017lbl.pdf. Last revised 02/2005. Last accessed 10/23/2017.

Appendix L

Vote to Prior Authorize Promacta® (Eltrombopag) and Update Prior Authorization Criteria for Nplate® (Romiplostim)

Oklahoma Health Care Authority
November 2017

Introduction[1,2]

Promacta® (eltrombopag) is a thrombopoietin receptor agonist indicated for the treatment of:

- Thrombocytopenia in adult and pediatric patients 1 year of age and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Eltrombopag should only be used in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
- Thrombocytopenia in patients with chronic hepatitis C (CHC) to allow initiation and maintenance of interferon (IFN)-based therapy. Eltrombopag should only be used in patients with CHC whose degree of thrombocytopenia prevents the initiation of IFN-based therapy or limits the ability to maintain IFN-based therapy.
- Patients with severe aplastic anemia (SAA) who have had an insufficient response to immunosuppressive therapy.
- Limitations of Use:
    - Eltrombopag is not indicated for the treatment of patients with myelodysplastic syndrome (MDS).
    - The safety and efficacy of eltrombopag have not been established in combination with direct-acting antiviral (DAA) agents used without IFN for treatment of CHC infection.
- Boxed Warning: Eltrombopag has a boxed warning for the risk for hepatic decompensation in patients with CHC and risk of hepatotoxicity.
- In October 2017, the *Warnings and Precautions* section of the Promacta® label was updated to include the increased risk of death and progression of MDS to acute myeloid leukemia (AML). The *Indications and Usage* section was also updated with a new limitation of use to state that Promacta® is not indicated for the treatment of patients with MDS. A randomized, double-blind, placebo-controlled, multicenter trial in patients with International Prognostic Scoring System intermediate-1, intermediate-2, or high risk MDS with thrombocytopenia receiving azacitidine in combination with either eltrombopag or placebo was terminated due to lack of efficacy and safety reasons, including progression to AML.

Recommendations

The College of Pharmacy recommends the prior authorization of Promacta® (eltrombopag) with the following criteria:

Promacta® (Eltrombopag) Approval Criteria:

1. An FDA approved indication of chronic immune (idiopathic) thrombocytopenia (ITP); and
    a. Previous insufficient response to at least one of the following:
        i. Corticosteroids; or
        ii. Immunoglobulins; or
        iii. Splenectomy; and
    b. Degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
    c. Must be prescribed by, or in consultation with, a hematologist or oncologist; or
2. An FDA approved indication of thrombocytopenia in patients with chronic hepatitis C (CHC) to allow initiation and maintenance of interferon (IFN)-based therapy; and
    a. Promacta® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
    b. Patient must be prescribed IFN for treatment of CHC infection; or
3. An FDA approved indication of severe aplastic anemia (SAA); and
    a. Previous insufficient response or documented contraindication or intolerance to immunosuppressive therapy; and
    b. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
4. For the diagnoses of chronic ITP and CHC associated thrombocytopenia, initial approvals will be for the duration of 1 month. For the diagnosis of SAA, initial approvals will be for the duration of 4 months. Subsequent approvals may be authorized if the prescriber documents the member is responding well to therapy and the following criteria is met, based upon member's diagnoses:
    a. For All Diagnoses:
        i. Must not have excessive platelet count responses. Promacta® should be discontinued if platelets exceed 400 x 10^9/L after two weeks of therapy at the lowest dose; and
        ii. Prescriber documents liver function tests are being monitored and levels are acceptable to the prescriber.
    b. Chronic ITP:
        i. Documentation that platelet count has increased to a level sufficient to avoid clinically important bleeding or that a dose increase is planned, if not already on maximum dose. Promacta® should be discontinued if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after four weeks of therapy at the maximum daily dose of 75mg.
    c. CHC-Associated Thrombocytopenia:
        i. Documentation that member continues to be on antiviral therapy. Promacta® should be discontinued when antiviral therapy is discontinued.
    d. SAA:
        i. Documentation that member has had a hematologic response (e.g., increase in platelet count, increase in hemoglobin, increase in absolute neutrophil

count, reduction in frequency of platelet or red blood cell transfusions). Promacta® should be discontinued if no hematologic response has occurred after 16 weeks of therapy.

Additionally, the College of Pharmacy recommends to update the Nplate® (romiplostim) prior authorization criteria with the following changes noted in red:

Nplate® (Romiplostim) Approval Criteria:

1. An FDA approved indication of chronic immune (idiopathic) thrombocytopenia purpura (ITP); and
2. Previous insufficient response with at least ~~two~~ one of the following treatments:
   a. Corticosteroids; or
   b. Immunoglobulins; or
   c. Splenectomy; and
3. ~~Recent platelet count of < 50 x 10^9/L; and~~
4. Degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
5. Nplate® (romiplostim) is not being used in an attempt to normalize platelet counts; and
6. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
7. Initial dosing of 1mcg/kg once weekly as a subcutaneous injection with recent patient weight in kilograms provided; and
8. Continuation criteria:
   a. Weekly CBCs with platelet count and peripheral blood smears until stable platelet count (≥50 x 10^9/L for at least four weeks without dose adjustment) has been achieved, then obtain monthly thereafter; and
   b. Dosing adjustments:
      i. Platelets <50 x 10^9/L, increase dose by 1mcg/kg; or
      ii. Platelets >200 x 10^9/L for two consecutive weeks, reduce dose by 1mcg/kg; or
      iii. Platelets >400 x 10^9/L, do not dose. Continue to assess platelet count weekly. When platelets <200 x 10^9/L, resume at a dose reduced by 1mcg/kg; and
9. Discontinuation criteria:
   a. Platelet count does not increase to a level sufficient to avoid clinically important bleeding after four weeks of therapy at the maximum weekly dose of 10mcg/kg; and
10. Approval period will be for four weeks initially, and then quarterly.

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[1] Promacta® Prescribing Information. Novartis Pharmaceuticals Corporation. Available online at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/promacta.pdf. Last revised 10/2017. Last accessed 10/11/2017.

[2] Promacta® (eltrombopag) – New Warning. OptumRx. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-safety/drugsafety_promacta_2017-1006.pdf. Issued 10/2017. Last accessed 10/23/2017.

Appendix M

Vote to Prior Authorize Odactra™ (House Dust Mite Allergen Extract) and Update Allergen Immunotherapy Prior Authorization Criteria

Oklahoma Health Care Authority
November 2017

Introduction[1,2]

Odactra™ (house dust mite allergen extract) was approved by the U.S. Food and Drug Administration (FDA) in March of 2017 for the treatment of house dust mite (HDM)-induced nasal inflammation (allergic rhinitis), with or without eye inflammation (conjunctivitis), in adults 18 to 65 years of age. This is the first approval of an allergen extract to be administered sublingually for this indication. Odactra™ exposes patients to HDM allergens, training the immune system to reduce the severity and frequency of eye and nasal allergy symptoms. It is recommended for patients to dissolve one tablet under the tongue daily and the tablets are taken year round. The safety and efficacy of Odactra™ was evaluated in studies conducted in the United States, Canada, and Europe involving approximately 2,500 subjects. During treatment, participants in the Odactra™ treatment group reported a 16 to 18 percent reduction in symptoms and the need for additional medications compared to the placebo group. Information regarding the cost of Odactra™ is currently unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Odactra™ (house dust mite allergen extract) with the following criteria:

Odactra™ (House Dust Mite Allergen Extract) Approval Criteria:

1. Member must be 18 to 65 years of age; and
2. Member must have a positive skin test (labs required) to licensed house dust mite allergen extracts or *in vitro* testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each; and
    b. **Montelukast:** One 14-day trial in combination with an antihistamine; and
    c. **Intranasal corticosteroids:** Trials of two different products for 21 days each; and
6. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and

7. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as “allergy shots”; and
8. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
9. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist; and
10. A quantity limit of one tablet daily will apply; and
11. Initial approvals will be for the duration of six months of therapy, at which time the prescriber must verify the patient is responding well to Odactra™ therapy. Additionally, compliance will be evaluated for continued approval.

The College of Pharmacy also recommends updating the existing prior authorization criteria for Grastek® (Timothy grass pollen allergen extract), Ragwitek® (short ragweed pollen allergen extract), and Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue grass mixed pollens allergen extract) to include an upper limit age restriction of 65 years of age, as shown in red, based on FDA approved indication(s):

Grastek® (Timothy Grass Pollen Allergen Extract) Approval Criteria:

1. Member must be 5 to 65 years of age; and
2. Member must have a positive skin test (labs required) or *in vitro* testing for pollen specific IgE antibodies for Timothy grass or cross-reactive grass pollen (cool season grasses); and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Intranasal corticosteroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of the grass pollen season (November 15th) and continue throughout the season; and
7. The first dose must be given in the physician’s office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as “allergy shots”; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and

12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Ragwitek® (Short Ragweed Pollen Allergen Extract) Approval Criteria:

1. Member must be 18 to 65 years of age; and
2. Member must have a positive skin test (labs required) or *in vitro* testing for pollen specific IgE antibodies to short ragweed pollen; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis symptoms; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Intranasal corticosteroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of ragweed pollen season (May 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) Approval Criteria:

1. Member must be 10 to 65 years of age; and
2. Member must have a positive skin test (labs required) or *in vitro* testing for pollen specific IgE antibodies to one of the five grass pollens contained in Oralair®; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and

   b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
   c. **Intranasal corticosteroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 16 weeks prior to the start of the grass pollen season (October 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 16 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

[1] U.S. Food and Drug Administration (FDA). FDA News Release: FDA Approved Odactra for House Dust Mite Allergies. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm544330.htm. Issued 03/01/2017. Last accessed 10/11/2017.

[2] Odactra™ Prescribing Information. Merck & Co., Inc. Available online at: https://www.fda.gov/downloads/biologicsbloodvaccines/allergenics/ucm544382.pdf. Last revised 03/2017. Last accessed 10/11/2017.

Appendix N

Fiscal Year 2017 Annual Review of Nuedexta® (Dextromethorphan/Quinidine)

Oklahoma Health Care Authority
November 2017

Introduction[1,2,3,4]

PseudoBulbar Affect (PBA) is a condition that causes sudden outbursts of uncontrollable crying and/or laughing that is exaggerated or not connected to the patient's emotional state. PBA typically occurs in patients with neurological conditions or injuries, such as stroke, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), traumatic brain injury (TBI), Alzheimer's disease, and Parkinson's disease. The goal of treatment for PBA is to reduce the severity and frequency of emotional outbursts. Treatment options include antidepressants, such as selective serotonin reuptake inhibitors and tricyclic antidepressants, and Nuedexta® (dextromethorphan/ quinidine).

Nuedexta® was approved by the U.S. Food and Drug Administration (FDA) in 2010 and is the only FDA approved treatment for PBA. The efficacy of Nuedexta® was evaluated in a 12-week, randomized, double-blind, placebo controlled trial of 326 patients with MS or ALS with clinically significant PBA, as determined by a score of at least 13 in the Center for Neurologic Study-Lability Scale (CNS-LS), a 7-item self-assessment of PBA frequency and severity. At 12 weeks, patients on Nuedexta® experienced a PBA episode reduction of -3.9 from a 6.8 baseline versus a -3.0 reduction from a 4.5 baseline for placebo ($p=0.005$ vs placebo). In an open-label study, Nuedexta® was studied in patients with dementia, stroke, or TBI and a clinical diagnosis of PBA. The primary endpoint was change from baseline to day 90 in CNS-LS score. CNS-LS score in all cohorts combined was 20.5 at baseline to 12.8 at day 90 ($p<0.001$ vs baseline). The CNS-LS reductions were similar across all three disease cohorts (dementia, stroke, and TBI) at day 90. The recommended starting dose of Nuedexta® is one capsule daily by mouth for the initial seven days of therapy. On the eighth day of therapy and thereafter, the recommended dose is two capsules per day, given as one capsule every 12 hours. The need for continued treatment should be reassessed periodically, as spontaneous improvement of PBA occurs in some patients. The National Average Drug Acquisition Cost (NADAC) of Nuedexta® is $12.09 per capsule, resulting in a monthly cost for maintenance dosing of $725.40.

Current Prior Authorization Criteria

Nuedexta® (Dextromethorphan/Quinidine) Approval Criteria:

1. An FDA approved diagnosis of Pseudobulbar Affect (PBA); and
2. Member must be 18 years of age or older; and
3. A quantity limit of 60 capsules per 30 days will apply.
4. Approvals will be for the duration of one year.

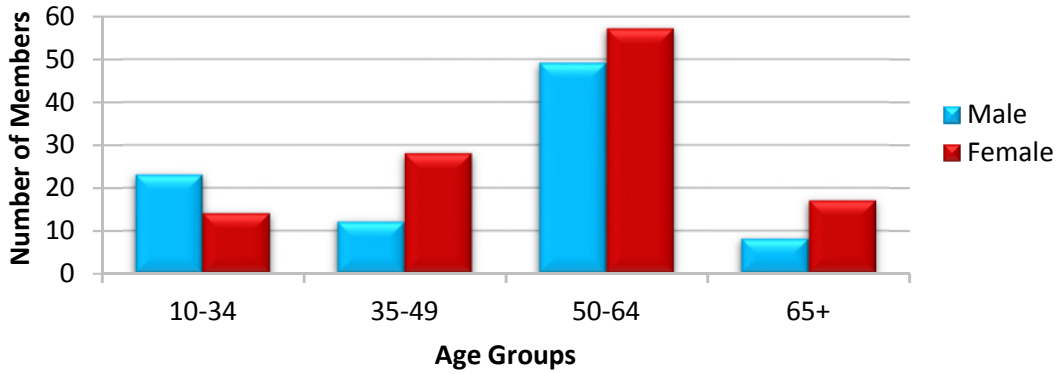
Utilization of Nuedexta® (Dextromethorphan/Quinidine): Fiscal Year 2017

Comparison of Fiscal Years

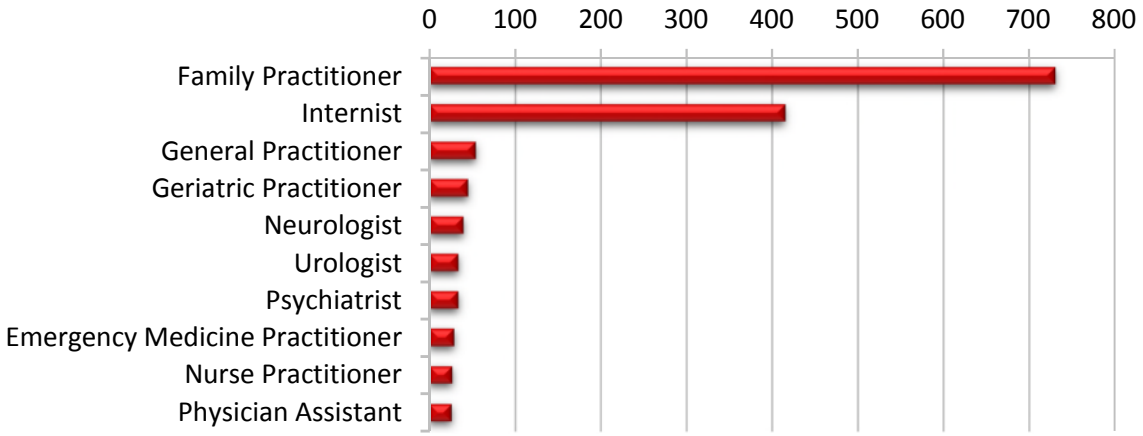
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	124	955	$548,729.36	$574.59	$23.45	45,657	23,403
2017	208	1,447	$918,193.89	$634.55	$23.85	75,252	38,498
% Change	**67.70%**	**51.50%**	**67.30%**	**10.40%**	**1.70%**	**64.80%**	**64.50%**
Change	**84**	**492**	**$369,464.53**	**$59.96**	**$0.40**	**29,595**	**15,095**

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

Demographics of Members Utilizing Nuedexta® (Dextromethorphan/Quinidine)



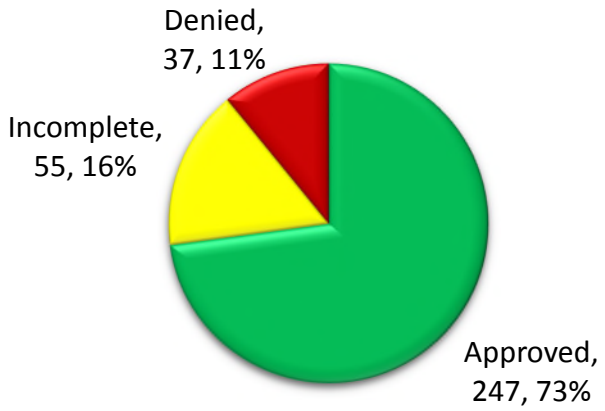
Top Prescriber Specialties of Nuedexta® (Dextromethorphan/Quinidine) by Number of Claims



Prior Authorization of Nuedexta® (Dextromethorphan/Quinidine)

There were 339 prior authorization requests submitted for Nuedexta® during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



Market News and Updates[5,6,7,8,9]

Anticipated Patent Expiration:

- Nuedexta® (dextromethorphan/quinidine): August 2026

Pipeline:

- **AVP-786:** In June 2017, Avanir Pharmaceuticals, the manufacturer of Nuedexta®, announced enrollment had begun in a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of AVP-786 for the treatment of neurobehavioral disinhibition, including aggression, agitation, and irritability in patients with TBI. Avanir is also studying AVP-786 for residual schizophrenia and agitation associated with Alzheimer's disease. AVP-786 is a novel, next-generation investigational product consisting of deudextromethorphan and an ultra-low dose of quinidine. Incorporation of deuterium into dextromethorphan reduces first-pass liver metabolism and therefore requires an ultra-low dose of quinidine in the AVP-786 formulation. A lower dose may result in a reduced potential for drug interactions and cardiac effects.

Other News:

- **May 2017:** A television advertisement regarding PBA has raised questions about the role of direct-to-consumer advertising in promoting the use of medicines for uncommon conditions beyond the narrow population of patients who benefit most from them. The ad did not specifically mention any drug by name, but was sponsored by the manufacturer of Nuedexta®, Avanir. According to EvaluatePharma, which tracks pharmaceutical pricing and markets, sales of Nuedexta® rose from $37 million in 2012 to $218 million in 2016. Dr. Adriane Fugh-Berman, a doctor who teaches at Georgetown University Medical Center and has investigated pharmaceutical marketing practices, states that she "suspects this disease is being redefined to include overly emotional people", through advertising. The United States is one of two countries that allows advertising of prescription drugs. The pharmaceutical company states that efforts are "focused on raising awareness about PBA to help people better understand the symptoms of a condition that is often overlooked, misunderstood, and misdiagnosed." After the ad ran, a survey found that awareness of PBA among primary care doctors

rose to 72 percent, up from about one-third in pre-marketing surveys. Additionally, awareness rose to 52 percent among patients. In 2017, the drug maker unveiled a new advertising campaign that specifically calls on viewers to "ask about Nuedexta®." Dr. Laura Boylan, a neurologist and adjunct professor at New York University School of Medicine who treats patients with psychiatric concerns related to neurological diseases, acknowledges that PBA may be under-recognized by the medical profession. However, she still worries about overprescribing of Nuedexta®.

- **October 2017:** A CNN investigation has found that the maker of Nuedexta® is aggressively targeting frail and elderly nursing home residents for whom the drug may be unnecessary or even unsafe. According to the investigation, the medication's financial success is being driven by a sales force focused on expanding the use of the medication among elderly patients suffering from Alzheimer's disease and dementia and by high-volume prescribing and advocacy efforts by doctors receiving payments from the company. More than half of all Nuedexta® pills have gone to long-term care facilities since 2012. According to data obtained from QuintilesIMS, which tracks pharmaceutical sales, the number of pills rose to roughly 14 million in 2016, a jump of nearly 400% in four years. Nuedexta® is being prescribed more frequently in nursing homes despite the medication having limited data in the elderly. One study conducted in patients with Alzheimer's disease had 194 subjects and found that those on Nuedexta® experienced falls at more than twice the rate of those on placebo. Furthermore, a company website states that PBA can afflict up to approximately 40% of patients with dementia, a figure based on an Avanir-funded survey; however, this number was repeatedly disputed by medical experts interviewed by CNN. Geriatric physicians, dementia researchers, and other medical experts told CNN that PBA is extremely rare in dementia patients and several stated that it affects 5% or less of patients. Additionally, state regulators have found doctors inappropriately diagnosing nursing home residents with PBA to justify using Nuedexta® to treat patients with confusion, agitation, and unruly behavior. The CNN analysis also found that nearly half of the Nuedexta® claims filed with Medicare in 2015 came from doctors who received money or other benefits from the drug company. During the FDA approval process, two key doctors on the committee raised concerns about the use of Nuedexta® in patients with Alzheimer's disease to treat PBA. Both doctors recommended that Nuedexta® only be approved for PBA in patients with MS or ALS. They said that evidence that it would be effective in other diseases was "weak", that not enough was known about the safety of the medication in the elderly, and that it was unclear that PBA even existed in Alzheimer's patients. However, despite these concerns, the FDA approved Nuedexta® for treating PBA in patients who have neurological conditions such as dementia.

Recommendations

The College of Pharmacy recommends updating the Nuedexta® (dextromethorphan/quinidine) prior authorization criteria with the following changes noted in red:

Nuedexta® (Dextromethorphan/Quinidine) Approval Criteria:

1. An FDA approved diagnosis of Pseudobulbar Affect (PBA) secondary to a neurological condition; and
2. Documentation of the secondary neurological condition must be submitted; and
3. Member must be 18 years of age or older; and
4. Nuedexta® must be prescribed by, or in consultation with, a neurologist or psychiatrist (or be an advanced care practitioner with a supervising physician who is a neurologist or psychiatrist); and
5. Member must not have a contraindication to therapy [e.g., concomitant use with quinidine, quinine, or mefloquine; history of quinidine, quinine, or mefloquine-induced thrombocytopenia, hepatitis, or other hypersensitivity reactions; known hypersensitivity to dextromethorphan; use with a monoamine oxidase inhibitor (MAOI) or within 14 days of stopping an MAOI; prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, or heart failure; complete atrioventricular (AV) block without implanted pacemaker, or at high risk of complete AV block; currently taking other drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine or pimozide)]; and
6. Prescriber must document baseline number of PBA laughing or crying episodes per day; and
7. A quantity limit of 60 capsules per 30 days will apply; and
8. Initial approvals will be for the duration of ~~one year~~ 12 weeks. Reauthorizations may be granted if the prescriber documents the member is responding well to treatment as indicated by a reduction in the number of PBA episodes of laughing or crying per day compared to baseline.

[1] Avanir Pharmaceuticals. PseudoBulbar Affect. Available online at: https://www.pbainfo.org/. Last accessed 10/17/2017.
[2] Cruz MP. Nuedexta for the Treatment of Pseudobulbar Affect: A Condition of Involuntary Crying or Laughing. *Pharmacy and Therapeutics* 2013; 38(6):325-328.
[3] Avanir Pharmaceuticals. Nuedexta Effective for Pseudobulbar Affect (PBA) in Patients with Alzheimer's Disease and other Dementias, Stroke, and Traumatic Brain Injury. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/nuedexta-effective-for-pseudobulbar-affect-pba-in-patients-with-alzheimers-disease-and-other-dementias-stroke-and-traumatic-brain-injury-300281888.html. Issued 06/08/2016. Last accessed 10/18/2017.
[4] Nuedexta Prescribing Information. Avanir Pharmaceuticals. Available online at: https://www.nuedextahcp.com/sites/default/files/content/Prescribing_Information.pdf. Last revised 01/2015. Last accessed 10/17/2017.
[5] 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 08/2017. Last accessed 10/14/2017.
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[9] Ellis B, Hicken M. The Little Red Pill Being Pushed on the Elderly. *CNN*. Available online at: http://www.cnn.com/2017/10/12/health/nuedexta-nursing-homes-invs/. Issued 10/12/2017. Last accessed 10/17/2017.

Appendix O

Fiscal Year 2017 Annual Review of Orkambi® (Lumacaftor/Ivacaftor) and Kalydeco® (Ivacaftor)

Oklahoma Health Care Authority
November 2017

Current Prior Authorization Criteria

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the *F508del* mutation in the CFTR gene detected by genetic testing; and
2. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the CFTR gene; and
3. Orkambi® will not be approved for patients with CF other than those homozygous for the *F508del* mutation; and
4. Member must be 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_1, will be required for continued approval.

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis with a *G551D, G1244E, G1349D, G178R, G551S, R117H, S1251N, S1255P, S549N,* or *S549R* mutation in the CFTR gene detected by genetic testing; and
2. Member must be 2 years of age or older; and
3. A quantity limit of two tablets per day or 56 tablets per 28 days will apply.
4. Initial approval will be for the duration of six months, after which time, compliance and information regarding efficacy, such as improvement in FEV_1, will be required for continued approval.

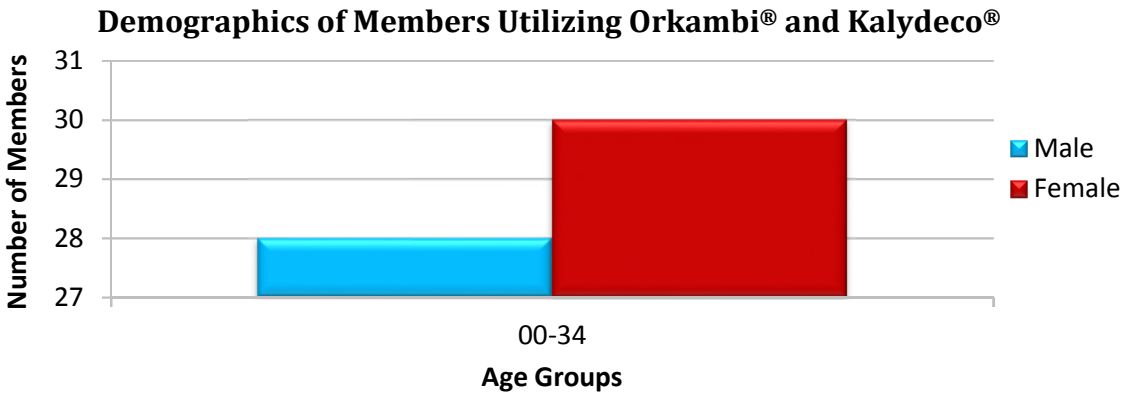
Utilization of Orkambi® and Kalydeco®: Fiscal Year 2017[1]

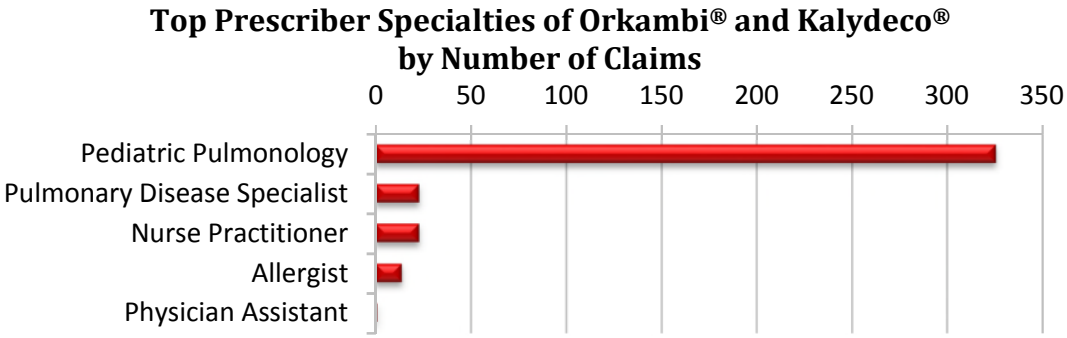
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	33	197	$4,274,100.28	$21,695.94	$774.01	18,200	5,522
2017	58	387	$7,983,972.96	$20,630.42	$735.85	39,816	10,850
% Change	**75.80%**	**96.40%**	**86.80%**	**-4.90%**	**-4.90%**	**118.80%**	**96.50%**
Change	**25**	**190**	**$3,709,872.68**	**-$1,065.52**	**-$38.16**	**21,616**	**5,328**

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

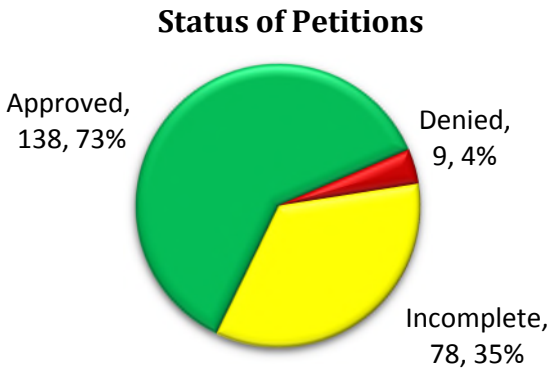
- In May 2017, the United States Food and Drug Administration (FDA) expanded the approved use of Kalydeco® (ivacaftor) in treating cystic fibrosis from treating 10 mutations to treating 33 mutations.





Prior Authorization of Orkambi® and Kalydeco®

There were 225 prior authorization requests submitted for Orkambi® and Kalydeco® during fiscal year 2017. The following chart shows the status of the submitted petitions during fiscal year 2017.



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

Anticipated Patent Expiration(s):

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

New FDA Approval(s):

- **May 2017:** The FDA expanded the approved use of Kalydeco® (ivacaftor) in treating CF from treating 10 mutations to treating 33 mutations. The agency based its decision in part on results of laboratory testing in conjunction with evidence from earlier human clinical trials due to the small patient populations of many rare CF mutations making clinical studies unfeasible. The approved mutations include the following: *G551D, G1244E, G1349D, G178R, G551S, R117H, S549N, S549R, S1251N, S1255P, A455E, A1067T, D110E, D110H, D579G, D1152H, D1270N, E56K, E193K, F1052V, F1074L, G1069R, K1060T, L206W, P67L, R74W, R117C, R347H, R352Q, R1070Q, R1070W, S945L*, and *S977F*.
- **July 2017:** The FDA approved Kalydeco® (ivacaftor) for the treatment of patients with CF 2 years of age and older who have 1 of 5 residual function mutations that result in a splicing defect in the CF transmembrane conductance regulator (CFTR) gene. The approval was based on the Phase 3 EXPAND study in the following mutations: *2789+5G—>A, 3272-26A—>G, 3849+10kbC—>T, 711+3A—>G*, and *E831X*.

News:

- **July 2017:** Vertex Pharmaceuticals raised the price of its best-selling CF medication, Orkambi®, by 5% in a move to boost revenues for the company.

Pipeline:

- **March 2017:** PTC Therapeutics announced ataluren has failed to significantly improve respiratory function in nonsense mutation cystic fibrosis (nmCF) according to the results of a Phase 3 trial. The company plans to abandon its effort to continue developing ataluren as a cystic fibrosis (CF) treatment. However, ataluren will continue to be marketed in Europe under the brand name Translarna™ for nonsense mutation Duchenne muscular dystrophy.

- **July 2017:** Vertex Pharmaceuticals is testing multiple triple combination regimens to find the best cocktail for the majority of patients with CF. Vertex Pharmaceuticals announced positive results from the initial studies including two Phase 2 clinical trials and one Phase 1 study evaluating tezacaftor and ivacaftor with three different experimental drugs. In the two Phase 2 studies, one experimental drug known as VX-152 showed a 9.7 percentage point average improvement in forced expiratory volume (FEV_1), on top of the two drug combination. Another experimental drug, VX-440, showed a 12 percentage point average improvement. A third drug, VX-659, in a Phase 1 study, improved FEV_1 by an average 9.6 percentage points. Vertex also said the regimens were generally well-tolerated across all three studies.
- **August 2017:** Vertex Pharmaceuticals announced the FDA and the European Medicines Agency (EMA) accepted for priority review applications of a combination product of Kalydeco® (ivacaftor) and tezacaftor as treatment for a subset of CF patients. The applications were based on positive results from previous Phase 3 clinical trials, the EVOLVE and the EXPAND studies, that showed that combining tezacaftor with ivacaftor significantly improved lung function in CF patients carrying either one or two copies of the *F508del* mutation in the CFTR gene. The FDA has set an action date of February 28, 2018.

Recommendations

The College of Pharmacy recommends updating the Kalydeco® (ivacaftor) approval criteria to reflect the new FDA approved indications:

Kalydeco® (Ivacaftor) Approval Criteria:

1. 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
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 six months, after which time compliance and information regarding efficacy, such as improvement in FEV_1, will be required for continued approval.

Utilization Details of Orkambi® and Kalydeco®: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
IVACAFTOR PRODUCTS						
KALYDECO TAB 150MG	63	8	$1,403,634.25	$793.01	$22,279.91	17.58%
SUBTOTAL	**63**	**8**	**$1,403,634.25**	**$793.01**	**$22,279.91**	**17.58%**
LUMACAFTOR/IVACAFTOR PRODUCTS						
ORKAMBI TAB 200-125	207	29	$4,248,080.31	$732.93	$20,522.13	53.21%
ORKAMBI TAB 100-125	117	21	$2,332,258.40	$710.19	$19,933.83	29.21%
SUBTOTAL	**324**	**50**	**$6,580,338.71**	**$724.71**	**$20,309.69**	**82.42%**
TOTAL	**387**	**58***	**$7,983,972.96**	**$735.85**	**$20,630.42**	**100%**

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

[1] U.S. Food and Drug Administration (FDA). FDA expands approved use of Kalydeco to treat additional mutations of cystic fibrosis. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm559212.htm. Issued 05/2017. Last accessed 09/28/2017.
[2] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 08/2017. Last accessed 09/27/2017.
[3] Vertex Pharmaceuticals, Inc. FDA Approves Kayldeco® (ivacaftor) for More Than 600 People Ages 2 and Older with Cystic Fibrosis Who Have Certain Residual Function Mutations. *Business Wire*. Available online at: http://www.businesswire.com/news/home/20170801005866/en/FDA-Approves-KALYDECO%C2%AE-ivacaftor-600-People-Ages. Issued 08/01/2017. Last accessed 10/24/2017.
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[6] Fernandes J. Ataluren Fails to Pass Muster as Treatment for Severe Form of Cystic Fibrosis. *Cystic Fibrosis News Today*. Available online at: https://cysticfibrosisnewstoday.com/2017/03/06/ataluren-fizzles-in-clinical-trial-against-severe-form-of-cystic-fibrosis/. Issued 03/2017. Last accessed 09/27/2017.
[7] Inacio P. FDA, EMA Accept Tezacaftor-Kalydeco Combo for Priority Review. *Cystic Fibrosis News Today*. Available online at: https://cysticfibrosisnewstoday.com/2017/08/25/cf-subset-therapy-candidate-tezacaftor-kalydeco-combo-accepted-for-review-by-fda-and-ema-vertex-announces/. Issued 08/2017. Last accessed 09/27/2017.
[8] Tirrell M. Vertex Pharma's three-drug combinations improve breathing in some cystic fibrosis patients. *CNBC*. Available online at: https://www.cnbc.com/2017/07/18/vertex-pharmas-3-drug-combo-aids-breathing-in-cystic-fibrosis-patients.html. Issued 07/2017. Last accessed 09/28/2017.

Appendix P

Fiscal Year 2017 Annual Review of Iron Chelating Agents and Vote to Prior Authorize Jadenu® Sprinkle (Deferasirox Oral Granules)

Oklahoma Health Care Authority
November 2017

Current Prior Authorization Criteria

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

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

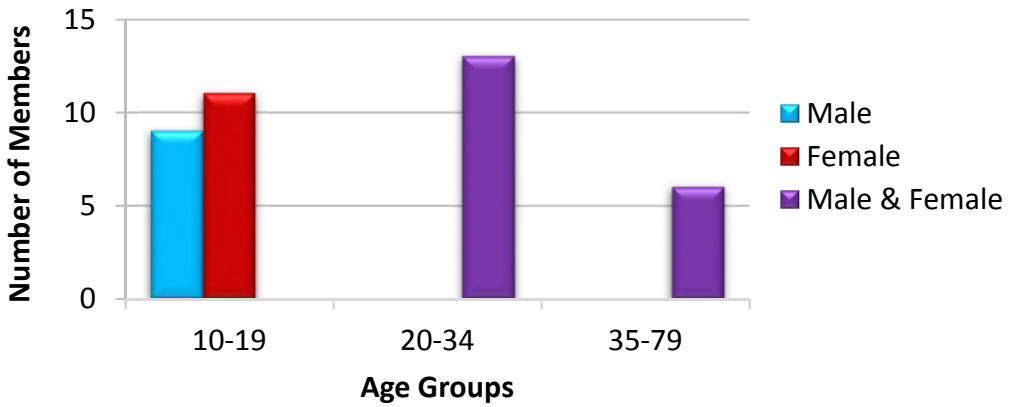
Utilization of Iron Chelating Agents: Fiscal Year 2017

Comparison of Fiscal Years

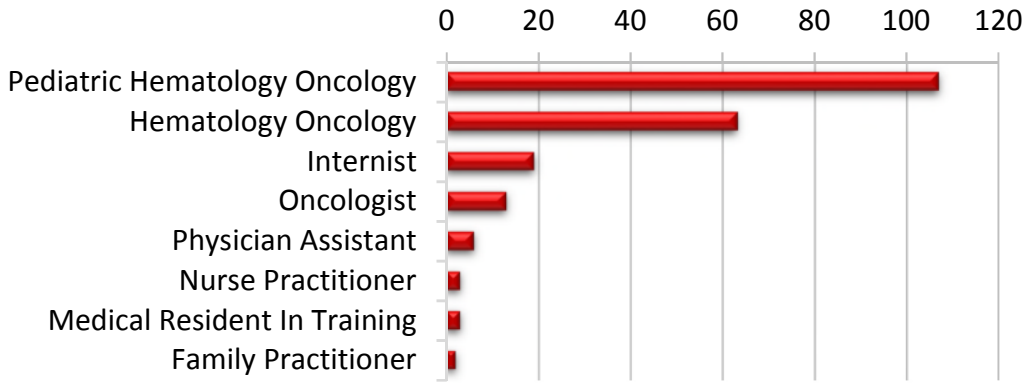
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	48	249	$1,914,074.72	$7,687.05	$255.72	19,861	7,485
2017	39	216	$1,771,728.92	$8,202.45	$269.59	16,617	6,572
% Change	**-18.80%**	**-13.30%**	**-7.40%**	**6.70%**	**5.40%**	**-16.30%**	**-12.20%**
Change	**-9**	**-33**	**-$142,345.80**	**$515.40**	**$13.87**	**-3,244**	**-913**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Please note, the current prior authorization criteria for Jadenu® and Ferriprox® went into effect 02/20/2017 (during fiscal year 2017).

Demographics of Members Utilizing Iron Chelating Agents



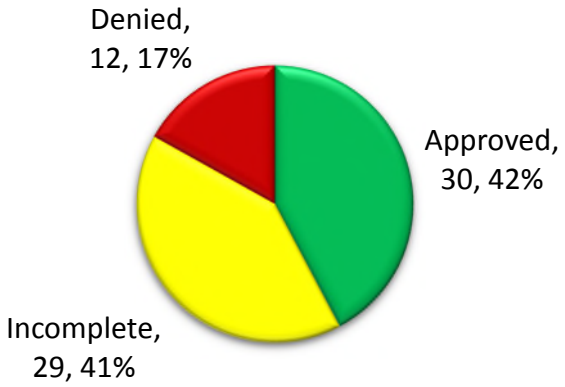
Top Prescriber Specialties of Iron Chelating Agents by Number of Claims



Prior Authorization of Iron Chelating Agents

There were 71 prior authorization requests submitted for iron chelating agents during fiscal year 2017. The current prior authorization criteria for Jadenu® and Ferriprox® went into effect 02/20/2017 (during fiscal year 2017). The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

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

New FDA Approval(s):

- **May 2017:** The U.S. Food and Drug Administration (FDA) approved Jadenu® Sprinkle (deferasirox oral granules) for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older and for

the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes. Jadenu® Sprinkle is available in single-dose sachets containing granules equivalent to 90mg, 180mg, or 360mg deferasirox. Jadenu® oral tablets were first FDA approved in 2015 for the same indications and are available in the same strengths (90mg, 180mg, and 360mg). Currently, there are no clinical data in patients with Jadenu® tablets and Jadenu® Sprinkle granules, and FDA approval was based on clinical trials conducted with Exjade® (deferasirox tablets for oral suspension), as they contain the same active ingredient. Jadenu® tablets may be crushed and mixed with soft foods immediately prior to use for patients who have difficulty swallowing whole tablets. Deferasirox is dosed orally once daily, with recommended dosing based on diagnosis and on body weight (ranges from 7mg/kg/day to 28mg/kg/day). The wholesale acquisition cost (WAC) of Jadenu® Sprinkle granules is currently the same as Jadenu® tablets, and is as follows: $35.58 per 90mg tablet or granule sachet, $71.15 per 180mg tablet or granule sachet, and $142.31 per 360mg tablet or granule sachet.

Recommendations

The College of Pharmacy recommends the prior authorization of Jadenu® Sprinkle (deferasirox oral granules) with the following criteria:

Jadenu® (Deferasirox), Jadenu® Sprinkle (Deferasirox), and Ferriprox® (Deferiprone) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason other than convenience why the member cannot use Exjade® (deferasirox) must be provided; and
3. For Jadenu® Sprinkle (deferasirox oral granules), an age restriction of six years and younger will apply. Members older than six years of age will require a patient-specific, clinically significant reason why Jadenu® oral tablets cannot be used even when the tablets are crushed; 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.

Utilization Details of Iron Chelating Agents: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
DEFERASIROX PRODUCTS						
JADENU TAB 360MG	150	30	$1,277,179.77	5	$8,514.53	72.09%
EXJADE TAB 500MG	22	5	$232,478.01	4.4	$10,567.18	13.12%
JADENU TAB 180MG	22	9	$94,743.46	2.44	$4,306.52	5.35%
JADENU TAB 90MG	9	4	$21,649.16	2.25	$2,405.46	1.22%
EXJADE TAB 250MG	2	2	$16,495.87	1	$8,247.94	0.93%
SUBTOTAL	**205**	**39***	**$1,642,546.27**	**5.86**	**$8,012.42**	**92.71%**
DEFERIPRONE PRODUCTS						
FERRIPROX TAB 500MG	11	1	$129,182.65	11	$11,743.88	7.29%
SUBTOTAL	**11**	**1***	**$129,182.65**	**11**	**$11,743.88**	**7.29%**
TOTAL	**216**	**39***	**$1,771,728.92**	**5.54**	**$8,202.45**	**100%**

*Total number of unduplicated members. Costs do not reflect rebated prices or net costs. Please note, the current prior authorization criteria for Jadenu® and Ferriprox® went into effect 02/20/2017 (during fiscal year 2017).

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 08/2017. Last accessed 10/09/2017.

[2] Hee Han D. New Formulation of Jadenu® Approved. *MPR*. Available online at: http://www.empr.com/news/jadenu-sprinkle-deferasirox-granules-chronic-iron-overload/article/663449/. Issued 05/22/2017. Last accessed 10/13/2017.

[3] Jadenu® (Deferasirox) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/jadenu-1/. Last revised 05/18/2017. Last accessed 10/13/2017.

[4] Jadenu® (Deferasirox) Prescribing Information. Novartis Pharmaceuticals Corporation. Available online at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/jadenu.pdf. Last revised 05/2017. Last accessed 10/13/2017.

Appendix Q

Fiscal Year 2017 Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Mavyret™ (Glecaprevir/Pibrentasvir) and Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir)

Oklahoma Health Care Authority
November 2017

Introduction

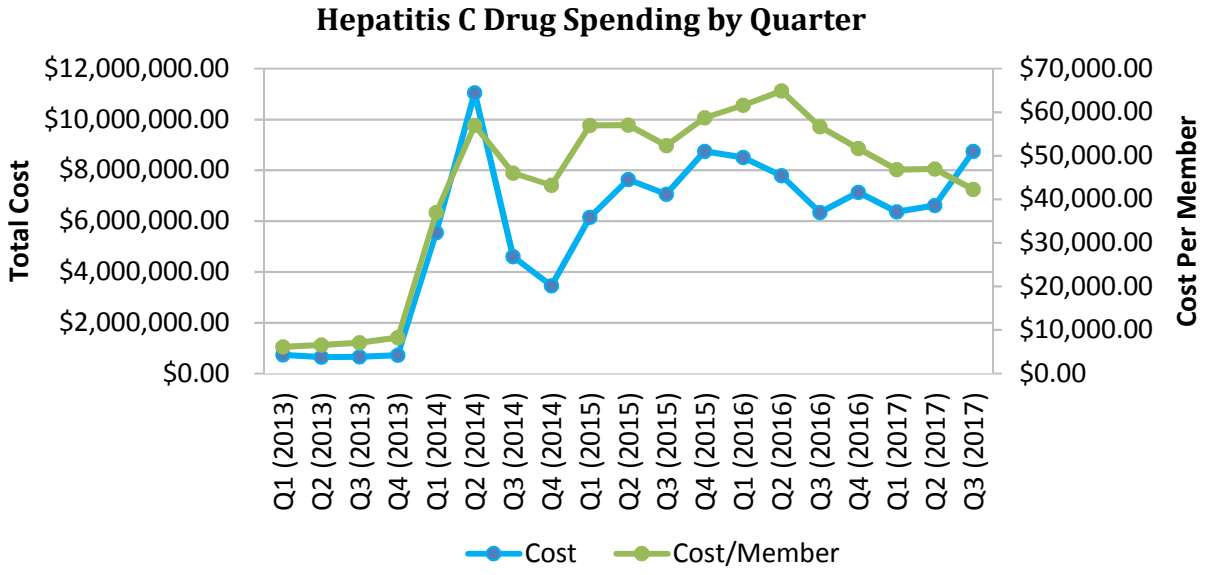
Sovaldi® (sofosbuvir) and Olysio® (simeprevir), both approved by the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2013, were previously restricted under Oklahoma law, preventing prior authorization management by the Oklahoma Health Care Authority. The state law was changed in May of 2014 allowing for prior authorization implementation of the hepatitis C 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, and Epclusa® (sofosbuvir/velpatasvir) and Viekira XR™ [dasabuvir/ombitasvir/ paritaprevir/ritonavir extended-release (ER)] were reviewed in December 2016.

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. The state fiscal year runs from July 1st to June 30th, and therefore data reflecting the lowering of the fibrosis score to F1 is not reflected in the state fiscal year 2017 data.

	Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015	Fiscal Year 2016	Fiscal Year 2017
Total HCV Drug Spending	$2,990,929.48	$17,993,807.47	$21,863,385.60	$32,105,818.63	$26,475,372.50

Costs do not reflect rebated prices or net costs.
State fiscal year = 07/01 to 06/30
Fibrosis score lowered to F1 07/01/17 and not reflected in state fiscal year 2017 data.



Current Prior Authorization Criteria

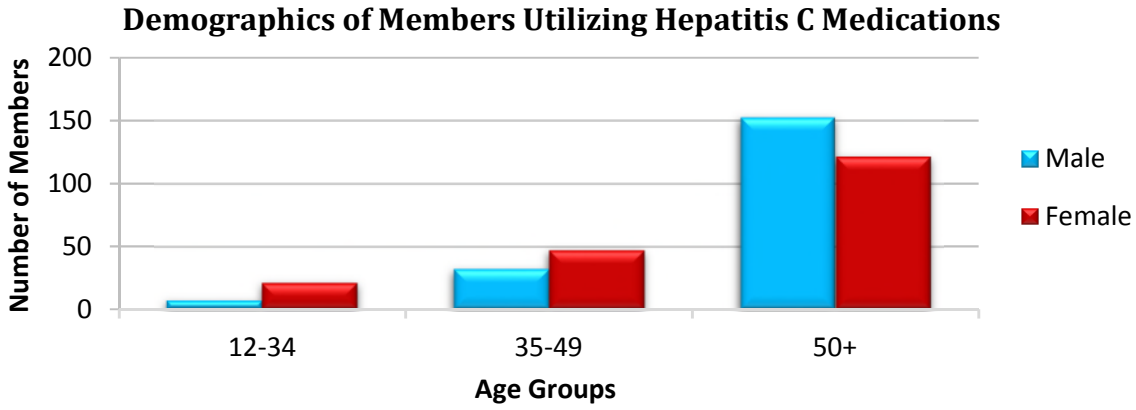
Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir ER), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), Zepatier™ (elbasvir/grazoprevir), Epclusa® (sofosbuvir/velpatasvir), Mavyret™ (glecaprevir/pibrentasvir), and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) are the preferred DAAs for the treatment of chronic HCV genotype 1. Use of an alternative regimen including Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) 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. Detailed prior authorization criteria can be found at the end of this report in the recommendations section.

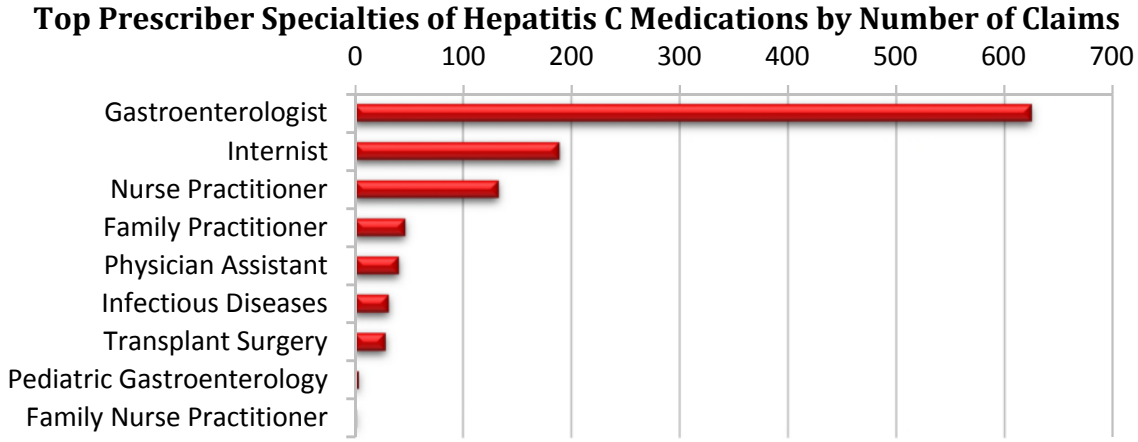
Utilization of Hepatitis C Medications: Fiscal Year 2017

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	371	1,355	$32,105,818.63	$23,694.33	$847.57	75,856	37,880
2017	380	1,103	$26,475,372.50	$24,003.06	$856.75	50,134	30,902
% Change	**2.40%**	**-18.60%**	**-17.50%**	**1.30%**	**1.10%**	**-33.90%**	**-18.40%**
Change	**9**	**-252**	**-$5,630,446.13**	**$308.73**	**$9.18**	**-25,722**	**-6,978**

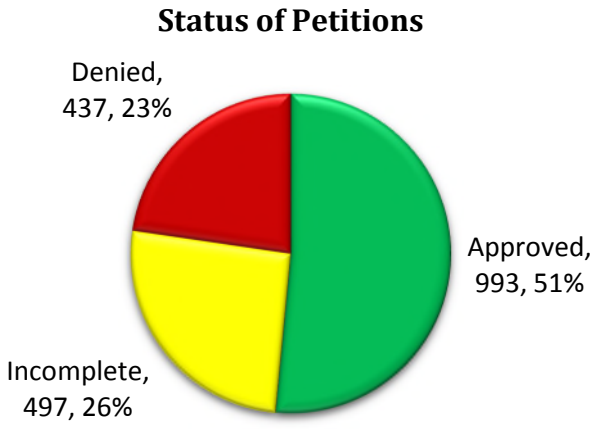
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Hepatitis C Medications

There were 1,927 prior authorization requests submitted for 621 unique members for hepatitis C medications during fiscal year 2017. 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 2017.



Hepatitis C Summary Statistics for Treated Members*

Parameter	Details
Number of Unduplicated Treated Members*	1,221 Unduplicated Members
Genotype	**Genotype 1:** 68.2% **Genotype 2:** 16.2% **Genotype 3:** 14.3% **Genotype 4:** 0.6% **Multiple Genotypes:** 0.6%
Fibrosis Score	**Average:** 2.88 **F1:** 8.1% **F2:** 32.3% **F3:** 20.0% **F4:** 38.5% **Decompensated:** 0.2% **Other:** 1.0%
Pre-Treatment Viral Load (HCV RNA)	**Average:** 4,102,405 IU/mL
Prior Treatment Experience	**Treatment-Experienced Members:** 13.9% **Treatment-Naïve Members:** 86.1%
Treatment Length	**Average:** 12.05 weeks **8 weeks:** 24.2% **12 weeks:** 66.2% **16 weeks:** 1.6% **24 weeks:** 8.0%
Compliance¥	**Before PA:** 18.8% of members noncompliant **After PA:** 2.2% of members noncompliant
SVR Cure Rate/Cost Per Cure	93.2% Cure Rate+ Based on cure rate and drug spending during allotted time frame (01/01/2014-03/31/2017), the estimated cost per cure in the SoonerCare population is $99,024.86-$200,459.62. Range due to partial SVR response rate.

*Table includes data collected from 07/01/2014 to 09/30/2017; total number of unduplicated members treated includes data from 01/01/2014 to 09/30/2017 (treated members are those with at least one paid claim).

HCV RNA = Hepatitis C Virus Ribonucleic Acid; PA = Prior Authorization; SVR = Sustained Virologic Response at least 12 weeks after therapy completion

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

+SVR Cure rate includes data from members who started therapy from 12/01/2013-03/31/2017. The cure rate is based only on members for whom SoonerCare was able to obtain SVR responses (SVR response rate: 52.8%).

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

Anticipated Patent Expiration(s):

- Olysio® (simeprevir): September 2029
- Sovaldi® (sofosbuvir): December 2030
- Zepatier™ (elbasvir/grazoprevir): May 2031
- Daklinza™ (daclatasvir): June 2031
- Technivie™ (ombitasvir/paritaprevir/ritonavir): April 2032
- Harvoni® (ledipasvir/sofosbuvir): September 2032
- Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir): October 2033

- Epclusa® (sofosbuvir/velpatasvir): January 2034
- Vosevi® (sofosbuvir/velpatasvir/voxilaprevir): July 2034
- Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir ER): January 2035

New FDA Approval(s):

- **July 2017:** The FDA approved Vosevi® (sofosbuvir/velpatasvir/voxilaprevir), an oral combination of an HCV nucleotide analog NS5B polymerase inhibitor, an HCV NS5A inhibitor, and an HCV NS3/4A protease inhibitor, for the treatment of all six major genotypes of chronic hepatitis C (CHC) in patients without cirrhosis or with mild cirrhosis. Sofosbuvir/velpatasvir/voxilaprevir is the first treatment approved for patients who have been previously treated with sofosbuvir or NS5A inhibitors.
- **August 2017:** The FDA approved Mavyret™ (glecaprevir/pibrentasvir), an oral combination of an HCV NS3/4A protease inhibitor and an HCV NS5A inhibitor, to treat adults with chronic HCV genotypes 1 to 6 without cirrhosis or with mild cirrhosis, including patients with moderate-to-severe kidney disease and those who are on dialysis. Glecaprevir/pibrentasvir is also approved for adult patients with HCV genotype 1 infection who have been previously treated with a regimen either containing an NS5A inhibitor or an NS3/4A protease inhibitor but not both. Glecaprevir/pibrentasvir is the first eight-week regimen approved for all 6 major genotypes in treatment-naïve, noncirrhotic patients.

New Indication(s):

- **April 2017:** The FDA approved a supplemental New Drug Application (sNDA) for Sovaldi® (sofosbuvir) and Harvoni® (ledipasvir/sofosbuvir) to treat HCV in pediatric patients 12 to 17 years of age. Both sofosbuvir and ledipasvir/sofosbuvir were previously approved only in adults, and are the first DAA agents approved for children and adolescents with HCV.
- **August 2017:** Gilead Sciences Inc. announced the FDA approval of updated labeling for Epclusa® (sofosbuvir/velpatasvir) to include use in patients co-infected with HCV and human immunodeficiency virus (HIV).

Regimen Comparison[6,7,8,9,10,11]

The following table shows the current American Association for the Study of Liver Disease (AASLD)/Infectious Diseases Society of America (IDSA) guidance recommended regimens of DAA medications for the treatment of chronic HCV infection in treatment-naïve patients with or without compensated cirrhosis. The table is not all-inclusive and excludes regimens considered "alternative" in the guidelines as opposed to "recommended"; regimens are ordered as they are recommended in the guidelines. 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. Sustained virologic response (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	$53,276.16	92%-100%[+]
		GLEC/PIB 8 wks	$26,399.52	99% (1a & 1b)[Ω]
		LED/SOF 8 or 12 wks	$60,739.84-$91,109.76	93% or 96%
		VEL/SOF 12 wks	$72,910.32	98%[¥]
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$53,276.16	92%-100%[+]
		GLEC/PIB 12 wks	$39,599.28	99% (1a & 1b)[Ω]
		LED/SOF 12 wks	$91,109.76	94% (1a & 1b)
		VEL/SOF 12 wks	$72,910.32	98%[¥]
Genotype 1b	Treatment-naïve, Non-cirrhotic	**EBR/GZR** 12 wks	$53,276.16	98%
		GLEC/PIB 8 wks	$26,399.52	99% (1a & 1b)[Ω]
		LED/SOF 8 or 12 wks	$60,739.84-$91,109.76	98%
		VEL/SOF 12 wks	$72,910.32	99%[¥]
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$53,276.16	98%
		GLEC/PIB 12 wks	$39,599.28	99% (1a & 1b)[Ω]
		LED/SOF 12 wks	$91,109.76	94% (1a & 1b)
		VEL/SOF 12 wks	$72,910.32	98%[¥]
Genotype 2	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$26,399.52	98%[Ω]
		VEL/SOF 12 wks	$72,910.32	99%-100%[¥]
	Treatment-naïve, Cirrhotic	**VEL/SOF** 12 wks	$72,910.32	99%-100%[¥]
		GLEC/PIB 12 wks	$39,599.28	100%[Ω]
Genotype 3	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$26,399.52	94.9%
		VEL/SOF 12 wks	$72,910.32	98%
	Treatment-naïve, Cirrhotic	**GLEC/PIB** 12 wks	$39,599.28	98%
		VEL/SOF 12 wks	$72,910.32	93%
Genotype 4	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$26,399.52	93%[Ω]
		VEL/SOF 12 wks	$72,910.32	100%[¥]
		EBR/GZR 12 wks	$53,276.16	97%
		LED/SOF 12 wks	$91,109.76	93%
	Treatment-naïve, Cirrhotic	**GLEC/PIB** 12 wks	$39,599.28	100%[Ω]
		VEL/SOF 12 wks	$72,910.32	100%[¥]
		EBR/GZR 12 wks	$53,276.16	97%
		LED/SOF 12 wks	$91,109.76	93%
Genotype 5 or 6	Treatment-naïve, Cirrhotic & Non	**GLEC/PIB** 8 wks (non) 12 wks (cirrhotic)	$26,399.52-$39,599.28	GT5: 100%, GT6: 100%[Ω] GT5: 100%, GT6: 100%[Ω]
		VEL/SOF 12 wks	$72,910.32	GT5: 97%, GT6: 100%
		LED/SOF 12 wks	$91,109.76	GT5: 93%, GT6: 96%

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

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

[Ω]May include some treatment-experienced patients.

[¥]Percentage includes cirrhotic & non-cirrhotic patients.

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.

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

Mavyret™ (Glecaprevir/Pibrentasvir) Product Summary[7]

Indication(s): Mavyret™ [glecaprevir (GLEC)/pibrentasvir (PIB)] is a fixed-dose combination of GLEC, an HCV NS3/4A protease inhibitor, and PIB, an HCV NS5A inhibitor, and is indicated for the treatment of patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). GLEC/PIB is also indicated for the treatment of adult patients with HCV genotype 1 infection, who have been previously treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.

Dosing:

- Mavyret™ is supplied as oral tablets containing 100mg GLEC and 40mg PIB to be dispensed in a carton for a total of 28 days or 56 days of therapy.
- The recommended dosing is three tablets (total daily dose: GLEC 300mg and PIB 120mg) taken orally once daily with food.
- The length of therapy of GLEC/PIB is dependent upon patient cirrhosis status, prior treatment experience, and viral genotype. Recommended regimen durations can be seen in the following table:

Genotype	Prior Treatment Experience	No Cirrhosis	Compensated Cirrhosis
1, 2, 3, 4, 5, or 6	Treatment Naïve	8 weeks	12 weeks
1	NS5A w/o NS3/4A PI	16 weeks	16 weeks
1	NS3/4A PI w/o NS5A	12 weeks	12 weeks
1, 2, 4, 5, or 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks

w/o = without; PI = protease inhibitor; PRS = pegylated interferon, ribavirin, and/or sofsobuvir
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
Examples of NS3/4A PIs include: boceprevir, glecaprevir, grazoprevir, paritaprevir, simeprevir, telaprevir, voxilaprevir

- GLEC/PIB is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated in severe hepatic impairment (Child-Pugh C).

Boxed Warning: Risk of hepatitis B virus (HBV) reactivation in patients coinfected with HCV and HBV
All patients should be tested for evidence of current or prior HBV infection before initiating treatment with GLEC/PIB. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV DAAs and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. HCV/HBV coinfected patients should be monitored for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up.

Contraindication(s):

- GLEC/PIB is contraindicated in patients with severe hepatic impairment (Child-Pugh C).
- GLEC/PIB is contraindicated with atazanavir or rifampin.

Warnings and Precaution(s):

- Risk of Reduced Therapeutic Effect: Carbamazepine, efavirenz, and St. John's wort may significantly decrease plasma concentrations of GLEC and PIB, leading to reduced therapeutic effect. The use of these agents with GLEC/PIB is not recommended.

Use in Specific Populations:

- Pregnancy: No adequate human data are available to establish whether or not GLEC/PIB poses a risk to pregnancy outcomes. In animal reproduction studies, no adverse developmental effects were observed when the components of GLEC/PIB were administered separately during organogenesis at exposures up to 53 times (rats; GLEC) or 51 and 1.5 times (mice and rabbits, respectively; PIB) the human exposures at the recommended dose of GLEC/PIB.
- Lactation: It is not known whether the components of GLEC/PIB are excreted in human breast milk, affect human milk production, or have effects on the breastfed infant.
- Pediatric Use: The safety and effectiveness of GLEC/PIB in children younger than 18 years of age have not been established.
- Geriatric Use: In clinical trials of GLEC/PIB, 328 subjects were age 65 years and older (14% of the total number of subjects in the Phase 2 and 3 clinical trials) and 47 subjects were age 75 years and older (2%). No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger subjects.
- Renal Impairment: No dosage adjustment of GLEC/PIB is required in patients with mild, moderate, or severe renal impairment, including those on dialysis.
- Hepatic Impairment: No dosage adjustment of GLEC/PIB is required in patients with mild hepatic impairment (Child-Pugh A). GLEC/PIB is not recommended in patients with moderate hepatic impairment (Child-Pugh B). GLEC/PIB is contraindicated in patients with severe hepatic impairment (Child-Pugh C).

Drug Interactions:

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comments**
Antiarrhythmics digoxin	↑ digoxin	Digoxin concentration monitoring is recommended; dose of digoxin may need to be ↓
Anticoagulants dabigatran	↑ dabigatran	May require dabigatran dose modifications
Anticonvulsants carbamazepine	↓ GLEC ↓ PIB	Coadministration not recommended
Antimycobacterials rifampin	↓ GLEC ↓PIB	Coadministration is contraindicated
Ethinyl Estradiol-Containing Products combined oral contraceptives	Not applicable	Coadministration may increase risk of ALT elevations and is not recommended
Herbal Products St. John's wort	↓ GLEC ↓ PIB	Coadministration not recommended

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comments**
HIV-Antiviral Agents atazanavir, darunavir, lopinavir, ritonavir, efavirenz	↑ GLEC and PIB w/ atazanavir, darunavir, lopinavir, & ritonavir ↓ GLEC and PIB w/ efavirenz	Atazanavir coadministration is contraindicated due to ↑ ALT elevations Coadministration w/ darunavir, lopinavir, ritonavir, or efavirenz is not recommended
HMG-CoA Reductase Inhibitors atorvastatin, lovastatin, simvastatin, pravastatin, rosuvastatin, fluvastatin, pitavastatin	↑ atorvastatin, lovastatin, simvastatin, pravastatin, rosuvastatin, fluvastatin, & pitavastatin	Coadministration w/ atorvastatin, lovastatin, & simvastatin is not recommended due to risk of myopathy Dose of pravastatin should be ↓ by 50% if coadministered Rosuvastatin dose should not exceed 10mg per day Lowest approved dose should be used of fluvastatin or pitavastatin
Immunosuppressants cyclosporine	↑ GLEC ↑ PIB	Coadministration not recommended in patients requiring >100mg cyclosporine per day

Table modified from: Mavyret™ Product Information. AbbVie Inc.
Consult the prescribing information for a detailed list of clinically significant drug interactions.
GLEC = glecaprevir; PIB = pibrentasvir; ↑ = increased; ↓ = decreased; HIV = human immunodeficiency virus; w/ = with; ALT = alanine transaminase; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A

Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Product Summary[11]

Indication(s): Vosevi™ (sofosbuvir [SOF]/velpatasvir [VEL]/voxilaprevir [VOX]) is a fixed-dose combination of SOF, an HCV nucleotide analog NS5B polymerase inhibitor, VEL, an HCV NS5A inhibitor, and VOX, an HCV NS3/4A protease inhibitor indicated for the treatment of adult patients with chronic HCV infection with or without compensated cirrhosis who have:

- Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor; or
- Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing SOF without an NS5A inhibitor
    - Additional benefit of SOF/VEL/VOX over SOF/VEL was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with SOF without an NS5A inhibitor

Dosing:

- Vosevi® is available as a fixed-dose oral tablet containing 400mg of SOF, 100mg of VEL, and 100mg of VOX. It is dispensed in a bottle for a total of 28 days of therapy.
- The recommended dosage of SOF/VEL/VOX is one tablet by mouth once daily with food. The recommended treatment regimens and duration can be found in the following table:

Genotype	Prior Treatment Experience	Treatment Regimen and Duration
1, 2, 3, 4, 5, or 6	NS5A inhibitor	**SOF/VEL/VOX** for 12 weeks
1a or 3	SOF w/o NS5A inhibitor	**SOF/VEL/VOX** for 12 weeks

w/o = without; SOF = sofosbuvir; VEL = velpatasvir; VOX = voxilaprevir
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir

- No dosage recommendation for SOF/VEL/VOX can be given for patients with severe renal impairment [estimated Glomerular Filtration Rate (eGFR) less than 30 mL/min/1.73m^2] or with end-stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the SOF metabolite.
- SOF/VEL/VOX is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to higher exposures of VOX in these patients.

Boxed Warning: Risk of hepatitis B virus (HBV) reactivation in patients coinfected with HCV and HBV
All patients should be tested for evidence of current or prior HBV infection before initiating treatment with SOF/VEL/VOX. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV DAAs and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. HCV/HBV coinfected patients should be monitored for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up.

Contraindication(s):
- SOF/VEL/VOX is contraindicated with rifampin.

Warnings and Precautions:
- Serious Symptomatic Bradycardia When SOF Is Coadministered with Amiodarone and Another HCV DAA: Postmarketing cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is coadministered with a SOF containing regimen. Bradycardia has generally occurred within hours to days, but cases have been observed up to two weeks after initiating HCV treatment. Bradycardia generally resolved after discontinuation of HCV treatment. Coadministration of amiodarone with SOF/VEL/VOX is not recommended.
- Risk of Reduced Therapeutic Effect Due to Concomitant Use of SOF/VEL/VOX with Inducers of P-glycoprotein (P-gp) and/or Moderate-to-Potent Inducers of Cytochrome (CYP) P450: Drugs that are inducers of P-gp and/or moderate-to-potent inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., rifampin, St. John's wort, carbamazepine) may significantly decrease plasma concentrations of SOF, VEL, and/or VOX, leading to potentially reduced therapeutic effect of SOF/VEL/VOX. The use of these agents with SOF/VEL/VOX is not recommended.

Use in Special Populations:
- Pregnancy: No adequate human data are available to establish whether or not SOF/VEL/VOX poses a risk to pregnancy outcomes. In animal reproduction studies, no evidence of adverse developmental outcomes was observed with SOF/VEL/VOX at exposures greater than those in humans.
- Nursing Mothers: It is not known whether SOF/VEL/VOX and its metabolites are present in human breast milk, affect human milk production, or have effects on the breastfed infant. The predominant circulating metabolite of SOF (GS-331007) and VEL were detected in the milk of lactating rats without effect on nursing pups.

- Pediatric Use: The safety and effectiveness of SOF/VEL/VOX in pediatric patients have not been established.
- Geriatric Use: Clinical trials of SOF/VEL/VOX included 74 subjects aged 65 years and older (17% of total number of subjects in the POLARIS-1 and POLARIS-4 Phase 3 clinical trials). No overall differences in safety or effectiveness have been observed between geriatric subjects and younger subjects.
- Renal Impairment: No dosage adjustment of SOF/VEL/VOX is required for patients with mild or moderate renal impairment. The safety and efficacy of SOF/VEL/VOX have not been established in patients with severe renal impairment (eGFR <30mL/min/1.73 m^2) or ESRD requiring hemodialysis.
- Hepatic Impairment: No dosage adjustment of SOF/VEL/VOX is required for patients with mild hepatic impairment (Child-Pugh A). SOF/VEL/VOX is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to higher exposures of VOX (up to 6-fold).

Drug Interactions:

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comment**
Acid Reducing Agents antacids, H_2-receptor antagonists, PPIs	↓ VEL	Drugs that increase gastric pH are expected to ↓ concentration of VEL Antacids should be separated by 4 hours H_2-receptor antagonists may be administered simultaneously w/ or staggered at a dose that does not exceed equivalent to famotidine 40mg twice daily Omeprazole 20mg can be coadministered; use w/ other PPIs has not been studied
Antiarrhythmics digoxin, amiodarone	↑ digoxin Effect on amiodarone, SOF, VEL, & VOX unknown	Digoxin concentration monitoring is recommended Coadministration with amiodarone is not recommended
Anticoagulants dabigatran	↑dabigatran	Monitoring of dabigatran is recommended
Anticonvulsants carbamazepine, phenytoin, phenobarbital, oxcarbazepine	↓ SOF ↓ VEL ↓ VOX	Coadministration is not recommended
Antimycobacterials rifampin, rifabutin, rifapentine	↓SOF, VEL, & VOX w/ multiple doses of rifampin ↓SOF, VEL, and ↑ VOX w/ a single dose of rifampin ↓ SOF, VEL, & VOX w/ rifabutin & rifapentine	Coadministration w/ rifampin is contraindicated Coadministration w/ rifabutin & rifapentine is not recommended

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comment**
HIV-Antiviral Agents atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, tenofovir DF	↑VOX w/ atazanavir & lopinavir ↓ SOF & VEL w/ tipranavir/ritonavir ↓ VEL & VOX w/efavirenz ↑ tenofovir DF	Coadministration with atazanavir, lopinavir, tipranavir/ritonavir, or efavirenz is not recommended Monitoring for tenofovir-associated adverse reactions is recommended
Herbal Supplements St. John's wort	↓ SOF ↓ VEL ↓ VOX	Coadministration is not recommended
HMG-CoA Reductase Inhibitors pravastatin, rosuvastatin, pitavastatin, atorvastatin, fluvastatin, lovastatin, simvastatin	↑ pravastatin, rosuvastatin, pitavastatin, atorvastatin, fluvastatin, lovastatin, & simvastatin	Dose of pravastatin should be not exceed 40mg per day if coadministered Coadministration of rosuvastatin or pitavastatin is not recommended due to risk of myopathy Lowest approved dose should be used of atorvastatin, fluvastatin, lovastatin, & simvastatin
Immunosuppressants cyclosporine	↑ VOX	Coadministration is not recommended

Table modified from: Vosevi™ Product Information. Gilead Sciences Inc.
Consult the prescribing information for a detailed list of clinically significant drug interactions.
SOF = sofosbuvir; VEL = velpatasvir; VOX = voxilaprevir; H_2 = histamine-2; PPI = proton pump inhibitor; ↑ = increased; ↓ = decreased; w/ = with; HIV = human immunodeficiency virus; DF = disproxil fumarate; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A

Recommendations

The College of Pharmacy recommends the following:

1. The prior authorization of Mavyret™ (glecaprevir/pibrentasvir) and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) with criteria similar to the other prior authorized hepatitis C medications.
2. Adding the following criteria regarding short life expectancy in accordance with the hepatitis C treatment guidelines: 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.

The following table highlights the preferred regimens for each genotype in treatment-naïve members (listed in alphabetical order). Additional regimens for treatment-experienced members are covered, just not included in the following table. Additional regimens other than those listed may be considered based on patient-specific clinical situations. Preferred regimens are based on treatment guidelines and supplemental rebate participation and are subject to change if the manufacturer chooses not to participate in supplemental rebates.

Genotype	Patient Factors	Preferred Regimen(s)
Genotype 1		
1	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 8 or 12 weeks Mavyret™ for 8 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 12 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Harvoni® for 12 weeks (with RBV if decompensated) Mavyret™ for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 24 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
Genotype 2		
2	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Mavyret™ for 12 weeks Sovaldi® + RBV for 12 weeks
Genotype 3		
3	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa® or Mavyret™)
3	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Mavyret™ for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa® or Mavyret™)
Genotype 4		
4	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Mavyret™ for 8 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks

Genotype	Patient Factors	Preferred Regimen(s)
4	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Harvoni® for 12 weeks (with RBV if decompensated) Mavyret™ for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
Genotype 5 or 6		
5 or 6	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks Harvoni® for 12 weeks (with RBV if decompensated)
5 or 6	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Mavyret™ for 12 weeks Harvoni® for 12 weeks (with RBV if decompensated)

If not specified, regimen applies to all genotypic subtypes.
RBV = ribavirin; PEG IFN = peginterferon alfa; RAV= resistance-associated polymorphisms
Preferred regimens based on clinical efficacy data, guideline recommendations, supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir ER), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), 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 Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) 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. Detailed criteria for medications with no changes to the coverage criteria are not included in the criteria on the following pages. The criteria for each medication may include FDA approved regimens or AASLD guideline recommended regimens that are not included in the SoonerCare preferred regimens table. Preferred regimens for each genotype can be found in the preferred regimens table. Additional regimens other than those listed in the preferred regimens table may be considered based on patient-specific clinical situations.

Mavyret™ (Glecaprevir/Pibrentasvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype 1, genotype 2, genotype 3, genotype 4, genotype 5, or genotype 6; and
3. Member must have a METAVIR fibrosis score of F1 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and
4. Mavyret™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and

5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on the prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on cirrhosis status, viral genotype, and treatment history will apply (new regimens will apply as approved by the FDA):

Genotype	Prior Treatment Experience	No Cirrhosis	Compensated Cirrhosis
1, 2, 3, 4, 5, or 6	Treatment Naïve	8 weeks	12 weeks
1	NS5A w/o NS3/4A PI	16 weeks	16 weeks
1	NS3/4A PI w/o NS5A	12 weeks	12 weeks
1, 2, 4, 5, or 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks

w/o = without; PI = protease inhibitor; PRS = pegylated interferon, ribavirin, and/or sofsobuvir
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
Examples of NS3/4A PIs include: boceprevir, glecaprevir, grazoprevir, paritaprevir, simeprevir, telaprevir, voxilaprevir

8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Prescriber must agree to counsel members on the potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
14. 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
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy; and
16. Member must not be taking the following medications: carbamazepine, rifampin, ethinyl estradiol-containing medications, St. John's wort, atazanavir, darunavir, lopinavir, ritonavir, efavirenz, atorvastatin, lovastatin, simvastatin, rosuvastatin doses greater than 10mg per day, cyclosporine doses greater than 100mg per day; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and

18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Approval of the 8-week carton (in place of the 4-week carton) requires a patient-specific, clinically significant reason why the member requires the 8-week carton in place of the 4-week carton; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
21. Approvals for treatment regimen initiation for 12 weeks or 16 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype 1, genotype 2, genotype 3, genotype 4, genotype 5, or genotype 6; and
3. Member must have a METAVIR fibrosis score of F1 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and
4. Vosevi® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on the prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on treatment history will apply:
    a. **Adult patients without cirrhosis or with compensated cirrhosis (Child-Pugh A):**
        i. **Genotype 1, 2, 3, 4, 5, or 6 patients who were previously treated with an HCV regimen containing an NS5A inhibitor** (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir): Vosevi® for 12 weeks; or
        ii. **Genotype 1a or 3 patients who were previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor:** Vosevi® for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and

11. Prescriber must agree to counsel members on the potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
14. 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
15. Member must not have severe renal impairment [estimated Glomerular Filtration Rate (eGFR) <30mL/min/1.73m^2)]; and
16. 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
17. Member must not be taking the following medications: H_2-receptor antagonists at doses greater than 40mg famotidine twice daily equivalent, omeprazole doses greater than 20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses greater than 40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and
18. If member is using antacids they must agree to separate antacid and Vosevi® administration by four hours; and
19. 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
20. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
21. 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
22. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Utilization Details of Hepatitis C Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	% COST	COST/ CLAIM
SOFOSBUVIR/LEDIPASVIR PRODUCTS						
HARVONI TAB 90-400MG	482	214	$15,291,534.37	2.25	57.76%	$31,725.18
SUBTOTAL	**482**	**214**	**$15,291,534.37**	**2.25**	**57.76%**	**$31,725.18**
SOFOSBUVIR/VELPATASVIR PRODUCTS						
EPCLUSA TAB 400-100MG	293	107	$7,384,922.39	2.74	27.89%	$25,204.51
SUBTOTAL	**293**	**107**	**$7,384,922.39**	**2.74**	**27.89%**	**$25,204.51**
ELBASVIR/GRAZOPREVIR PRODUCTS						
ZEPATIER TAB 50-100MG	88	33	$1,563,736.47	2.67	5.91%	$17,769.73
SUBTOTAL	**88**	**33**	**$1,563,736.47**	**2.67**	**5.91%**	**$17,769.73**
SOFOSBUVIR PRODUCTS						
SOVALDI TAB 400MG	56	25	$1,645,327.71	2.24	6.21%	$29,380.85
SUBTOTAL	**56**	**25**	**$1,645,327.71**	**2.24**	**6.21%**	**$29,380.85**
DACLATASVIR PRODUCTS						
DAKLINZA TAB 60MG	22	8	$487,896.96	2.75	1.84%	$22,177.13
SUBTOTAL	**22**	**8**	**$487,896.96**	**2.75**	**1.84%**	**$22,177.13**
OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR PRODUCTS						
VIEKIRA PAK TAB	2	1	$56,602.30	2	0.21%	$28,301.15
VIEKIRA XR TAB	1	1	$27,783.55	1	0.10%	$27,783.55
SUBTOTAL	**3**	**2**	**$84,385.85**	**1.5**	**0.31%**	**$28,128.62**
RIBAVIRIN PRODUCTS						
RIBAVIRIN TAB 200MG	107	44	$10,766.74	2.43	0.04%	$100.62
RIBASPHERE TAB 200MG	33	14	$4,006.68	2.36	0.02%	$121.41
RIBAVIRIN CAP 200MG	15	9	$2,285.45	1.67	0.01%	$152.36
MODERIBA TAB 200MG	4	2	$509.88	2	0.00%	$127.47
SUBTOTAL	**159**	**66**	**$17,568.75**	**2.41**	**0.07%**	**$110.50**
TOTAL	**1,103**	**380***	**$26,475,372.50**	**2.9**	**100%**	**$24,003.06**

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

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Appendix R

Fiscal Year 2017 Annual Review of Various Systemic Antibiotic Medications and 30-Day Notice to Prior Authorize Baxdela™ (Delafloxacin Injection and Tablets), Ofloxacin 300mg Tablets, Minolira™ (Minocycline Extended-Release Tablets), Solosec™ (Secnidazole Oral Granules), and Vabomere™ (Meropenem/ Vaborbactam Injection)

Oklahoma Health Care Authority
November 2017

Current Prior Authorization Criteria

Oral Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the immediate-release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.
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 ER 775mg tablets (Moxatag®)
    - Cephalexin 500mg tablets
    - Cephalexin 750mg capsules
    - Ciprofloxacin 100mg tablets
    - Ciprofloxacin 500mg and 1,000mg ER tablets
    - Doxycycline hyclate 75mg capsules (Acticlate®)
    - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
    - Doxycycline monohydrate 75mg and 150mg capsules and tablets
    - Doxycycline monohydrate DR 40mg capsules (Oracea®)
    - Minocycline ER tablets (Solodyn®)
    - Minocycline immediate-release tablets
    - Tetracycline 250mg and 500mg capsules

Avycaz® (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infections (cUTI), including pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Avycaz® must be used in combination with metronidazole; and

4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/ tazobactam), a carbapenam (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Dalvance® (Dalbavancin) Approval Criteria:

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

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.

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

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

Orbactiv® (Oritavancin) Approval Criteria:

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

Sivextro® (Tedizolid Tablets) Approval Criteria:

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

Suprax® (Cefixime), Cedax® (Ceftibuten), and Spectracef® (Cefditoren) 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 medication(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 carbapenam (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Utilization of Various Systemic Antibiotic Medications: Fiscal Year 2017

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

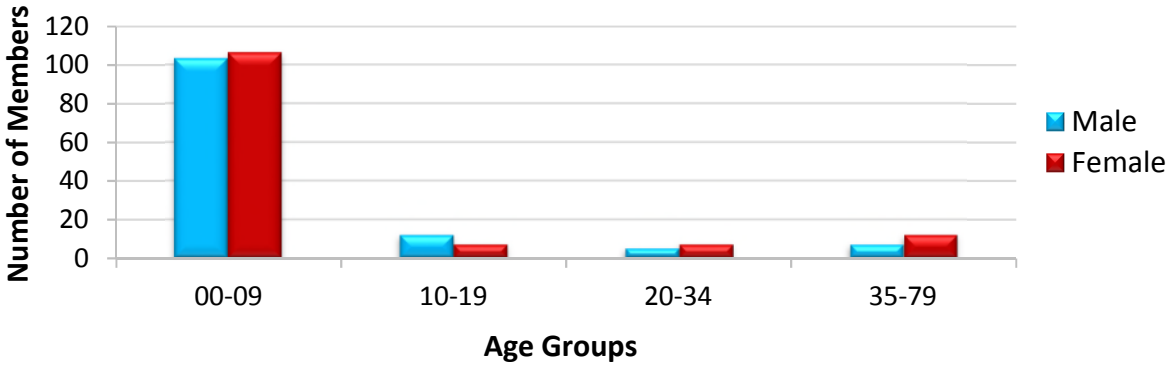
Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	641	813	$162,205.31	$199.51	$15.05	71,629	10,781
2017	259	367	$111,910.18	$304.93	$23.72	36,391	4,718
% Change	**-59.60%**	**-54.90%**	**-31.00%**	**52.80%**	**57.60%**	**-49.20%**	**-56.20%**
Change	**-382**	**-446**	**-$50,295.13**	**$105.42**	**$8.67**	**-35,238**	**-6,063**

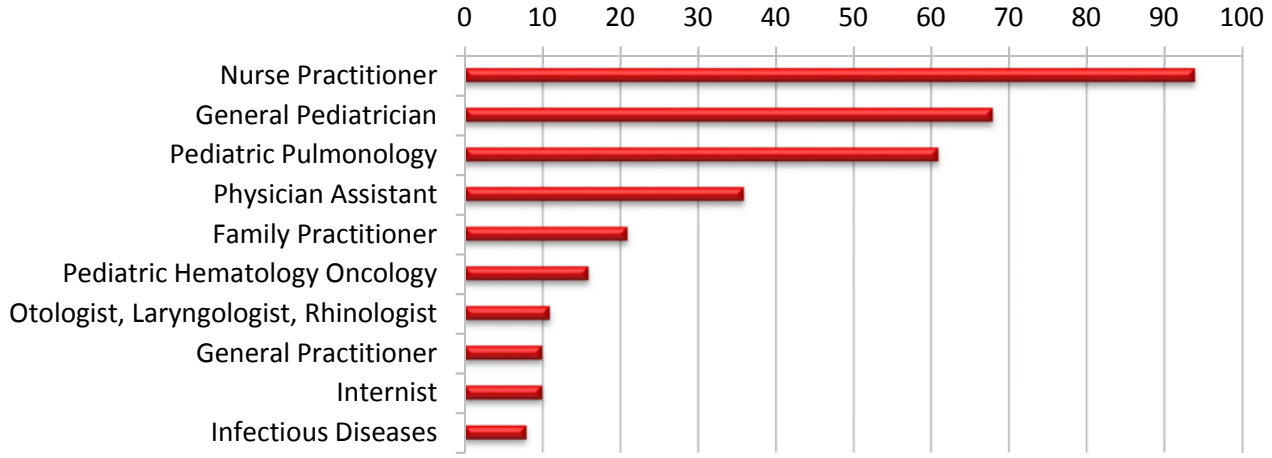
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- There were no medical claims for the various systemic antibiotic medications during fiscal year 2017.

Demographics of Members Utilizing Various Systemic Antibiotic Medications



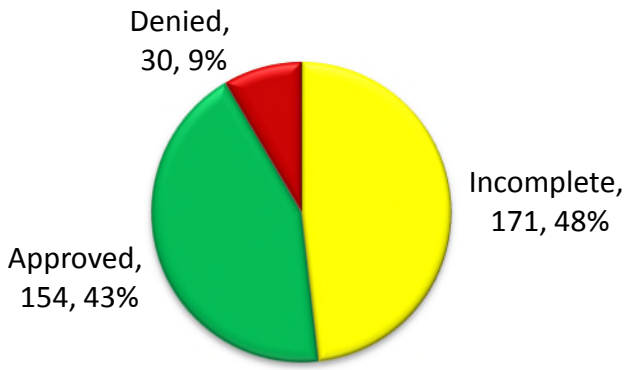
Top Prescriber Specialties of Various Systemic Antibiotic Medications by Number of Claims



Prior Authorization of Various Systemic Antibiotic Medications

There were 355 prior authorization requests submitted for various systemic antibiotic medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34]

Anticipated Patent Expiration(s):

- Augmentin XR® [amoxicillin/clavulanate potassium extended-release (ER)]: April 2020
- Dalvance® (dalbavancin): November 2023
- Solodyn® (minocycline ER): March 2027
- Moxatag® (amoxicillin ER): May 2027
- Dificid® (fidaxomicin): July 2027
- Doryx® [doxycycline hyclate delayed-release (DR) tablet]: February 2028
- Suprax® (cefixime oral 500mg/5mL suspension): December 2028
- Baxdela™ (delafloxacin): December 2029
- Orbactiv® (oritavancin): April 2030

- Sivextro® (tedizolid): December 2030
- Vabomere® (meropenem/vaborbactam): August 2031
- Avycaz® (ceftazidime/avibactam): June 2032
- Zerbaxa® (ceftolozane/tazobactam): March 2034

New FDA Approval(s):

- **May 2016:** The U.S. Food and Drug Administration (FDA) approved a supplemental New Drug Application (sNDA) for Teflaro® (ceftaroline fosamil) granting new indications for pediatric patients 2 months of age to younger than 18 years of age with acute bacterial skin and skin structure infection (ABSSSI), including infections caused by methicillin-resistant *Staphylococcus (S.) aureus* (MRSA), and community-acquired bacterial pneumonia (CABP) caused by *Streptococcus pneumoniae* and other designated susceptible bacteria.
- **March 2017:** The FDA approved an expanded indication for Cubicin® and Cubicin® RF (daptomycin injection) for complicated skin and skin structure infections (cSSSI) in pediatric patients 1 to 17 years of age caused by susceptible isolates of the following Gram-positive bacteria: *S. aureus* (including methicillin-resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae* subsp. *equisimilis*, and *Enterococcus faecalis* (vancomycin-susceptible isolates only). Daptomycin was previously only approved in adult patients with cSSSI.
- **May 2017:** Minolira™ (minocycline ER tablets) was approved by the FDA for the treatment of inflammatory lesions of non-nodular moderate-to-severe acne vulgaris in patients 12 years of age and older.
- **June 2017:** Baxdela™ (delafloxacin) was approved by the FDA for the treatment of adults with ABSSSI caused by designated susceptible bacteria.
- **June 2017:** Clindamycin ready-to-use injection was approved by the FDA for the treatment of a variety of bacterial infections caused by susceptible anaerobic bacteria and strains of streptococci, pneumococci, and staphylococci in three commonly prescribed formulations (300mg/50mL, 600mg/50mL, and 900mg/50mL). This is the first premixed clindamycin formulation.
- **August 2017:** Vabomere™ (meropenem/vaborbactam injection) was approved by the FDA for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by designated bacteria in adults.
- **September 2017:** The FDA approved an expanded indication for Cubicin® and Cubicin® RF (daptomycin injection) for *S. aureus* bloodstream infections (bacteremia) in pediatric patients 1 to 17 years of age. Daptomycin was previously only approved in adult patients with bacteremia.
- **September 2017:** Solosec™ (secnidazole oral granules) was approved by the FDA for treatment of bacterial vaginosis in adult women.

News:

- **April 2016:** The FDA announced Spectracef® (cefditoren) has been discontinued from marketing and that the product was not discontinued or withdrawn for safety or efficacy reasons.

- **October 2016:** A quality improvement report from the Veterans Affairs Western New York Healthcare System in Buffalo, NY reported that patients with an elevated body mass index (BMI) and/or a diagnosis of heart failure (HF) have an increased likelihood of treatment failure for skin and soft tissue infections (SSTI). The report retrospectively reviewed the charts of 293 outpatients who received a coded diagnosis of cellulitis or abscess by a primary care provider or emergency department physician and were treated with an oral antibiotic between January 1, 2006 and July 1, 2015. At baseline, 67% of the patients were overweight/obese (BMI 25-40kg/m^2), 16% had extreme obesity (BMI >40kg/m^2), and 17% were normal weight (<25kg/m^2). Of the total cohort, 69 patients were deemed to be treatment failures. Of the subgroup of patients that failed oral antibiotics, mean BMI was elevated at 34.2kg/m^2 (p=0.01), 47.8% had diabetes (p=0.03), and 15.9% had heart failure (p=0.05). There was no statistically significant differences in antibiotic regimens or treatment duration in the patients that failed compared to those who did not fail. An elevated BMI raised the chances of failure by 1.05 (1.01-1.1; p<0.009) for every 1kg/m^2 unit increment and a diagnosis of heart failure raised the chances of failure by 2.56 (1.1-5.8; p<0.03). If a patient had a BMI of 40kg/m^2 and heart failure, the risk of antibiotic failure was 49.7%; this increased to 70.9% for a BMI of 60kg/m^2. In contrast, those with a BMI of 40kg/m^2 or 60kg/m^2 without heart failure had antibiotic failure rates of 28.7% and 48.7%, respectively.
- **November 2016:** The American Academy of Pediatrics (AAP) released updated guidelines for use of systemic and topical fluoroquinolone (FQ) antibiotics in pediatric patients. The guideline outlined the updated information concerning safety and efficacy and currently FDA-approved indications for FQs in children. Concerns for safety have limited FQ use in children; however, they remain a drug of choice for specific indications and should not be used if an alternative agent is available.
- **May 2017:** The FDA updated a previous warning for oral and injectable FQ antibiotics due to disabling side effects. The revision indicates as part of an ongoing review, patient cases identified previously by the FDA and from published studies currently do not support reports that these medications may result in detachment of the retina in the eyes, or bulges or tears in the aorta blood vessel (i.e., aortic aneurysm and aortic dissection).
- **June 2017:** A recent study showed *S. aureus* infections among U.S. hospital patients have been less resistant to key antibiotics. The study tested antibiotic resistance in 19,036 *S. aureus* samples from 42 medical centers between 2009 and 2015. The results found that the rates of resistance to oxacillin fell from 47.2% in 2009 to 43.6% in 2015 and 42.2% in 2016. *S. aureus* resistance to other antibiotics, such as levofloxacin, clindamycin, and erythromycin, also decreased and resistances to ceftaroline, trimethoprim-sulfamethoxazole, and tetracycline remained stable. The study also showed that *S. aureus* resistance to daptomycin, linezolid, vancomycin, and tigecycline stayed extremely rare with no sign of increasing.
- **June 2017:** The World Health Organization (WHO) released its updated Essential Medicines List, which included a revision of the antibiotics section. In an effort to ensure that antibiotics are available when needed and that the right antibiotics are prescribed for the right infections, antibiotics were grouped into three categories

(ACCESS, WATCH, and RESERVE) with recommendations on when each category should be used. The new categories only apply to antibiotics used to treat 21 of the most common general infections, and if shown to be useful, it could be broadened in future versions.

- **July 2017:** GlaxoSmithKline announced that they will be discontinuing Ceftin® (cefuroxime axetil) oral suspension. The product was not discontinued or withdrawn for safety or efficacy reasons. Ceftin® (cefuroxime axetil) will continue to be available in 250mg and 500mg tablet formulation.
- **September 2017:** A nested case-control study using data from a national health insurance claims database between 1998 and 2011 showed FQ use is associated with a non-negligible increased risk of gastrointestinal (GI) perforation. The study compared a cohort of 17,510 patients diagnosed with GI perforation to a matched group of controls. The results showed that current use of a FQ was associated with the greatest increase in risk of GI perforations after disease risk score adjustment (RR 1.90; 95% CI 1.62-2.22) and the risk of GI perforation was attenuated for past and any prior year use (RR 1.33; 95% CI 1.20-1.47 and RR 1.46; 95% CI 1.34-1.59, respectively).
- **October 2017:** A study published in *JAMA Pediatrics* concluded co-administration of intravenous (IV) vancomycin and piperacillin/tazobactam is associated with increased risk of acute kidney injury (AKI) in hospitalized children. The retrospective cohort study included data from 1,915 children hospitalized for three or more days and who received IV vancomycin plus one other antipseudomonal β-lactam combination therapy. The study found that 8.2% of patients had antibiotic-associated AKI, including 11.7% who received IV vancomycin plus piperacillin/tazobactam combination therapy.

Pipeline Update(s):

- **Amphora®:** Amphora® (L-lactic acid/citric acid/potassium bitartrate vaginal gel) is a novel, non-hormonal, surfactant-free drug, currently in Phase 3 trials for contraception and treating sexually transmitted infections (STI). The FDA has given Amphora® Qualified Infectious Disease Product (QIDP) status for the prevention of urogenital gonorrhea infection in women and for the reduction of recurrent episodes of bacterial vaginosis.
- **ASN100:** ASN100 is currently in Phase 2 development for prevention of hospital-acquired *S. aureus* pneumonia in mechanically-ventilated patients who are heavily-colonized with *S. aureus* in their respiratory tracts. ASN100 is a combination of two monoclonal antibodies, ASN-1 and ASN-2, which together neutralize six clinically important *S. aureus* cytotoxins, including those that inflict damage to lung epithelial cells that inhibit an effective immune response. Results of the Phase 2 efficacy and safety study are anticipated in the second half of 2018.
- **Cadazolid:** Cadazolid is a novel quinoxolidinone antibiotic in development for the treatment of *Clostridium (C.) difficile*-associated diarrhea. Cadazolid is a strong inhibitor of *C. difficile* protein synthesis, leading to suppression of toxin production and spore formation. In August 2017, the FDA granted cadazolid Orphan Drug Designation for treatment of *C. difficile* infection in pediatric patients.
- **Cefiderocol:** Cefiderocol is a novel siderophore cephalosporin currently in Phase 3 trials for the treatment of cUTI and for treatment of patients with carbapenem-resistant

pathogens at various sites. Cefiderocol has a novel mechanism of action, which allows it to more efficiently penetrate the outer cell membrane of gram-negative pathogens by binding to ferric iron and is actively transported into bacterial cells via the bacterial iron transporters, which function to incorporate this essential nutrient for bacteria. Shionogi anticipates submission of a New Drug Application (NDA) to the FDA in 2017.

- **Eravacycline:** Eravacycline is a novel tetracycline antibiotic currently in Phase 3 trials for the treatment of complicated intra-abdominal infections (cIAI) and cUTI. The FDA has granted eravacycline Fast Track Designation and QIDP status. Tetraphase anticipates submission of an NDA to the FDA in the first quarter of 2018.
- **Iclaprim:** Iclaprim is a novel antibiotic in development for treatment of ABSSSI. Iclaprim has received Orphan Drug Designation from the FDA for the treatment of *S. aureus* lung infections in patients with cystic fibrosis. Motif Bio plans to submit an NDA for iclaprim during the first quarter of 2018.
- **Lefamulin:** Lefamulin is a novel pleuromutilin antibiotic in development for treatment of CABP. In September 2017, Nabriva Therapeutics announced a global, Phase 3 trial evaluating the safety and efficacy of IV to oral lefamulin in patients with CABP met its primary endpoint of non-inferiority compared to moxifloxacin with or without adjunctive linezolid for early clinical response.
- **Omadacycline:** Omadacycline is an antibiotic in a new class of compounds, aminomethylcyclines, which are related to the tetracycline class, currently in Phase 3 trials. Omadacycline has broad spectrum activity for gram-positive, gram-negative, aerobes, anaerobes, and atypical bacteria, including MRSA, penicillin-resistant and multi-drug resistant *Streptococcus pneumoniae* (PRSP and MDRSP), vancomycin-resistant *Enterococcus* species (VRE), and extended spectrum β-lactamase producing *enterobacteriaceae* (ESBL). Paratek anticipates submission of an NDA to the FDA as early as the first quarter of 2018.
- **Plazomicin:** Plazomicin is a novel aminoglycoside currently in Phase 3 clinical trials for indications including serious bacterial infections due to multi-drug resistant *Enterobacteriaceae*, including carbapenem-resistant *Enterobacteriaceae* (CRE). Achaogen, the developers of plazomicin, plan to submit an NDA in the second half of 2017.
- **Sarecycline:** Sarecycline is a once-daily, oral, narrow spectrum, tetracycline-derived antibiotic with anti-inflammatory properties for the potential treatment of moderate-to-severe acne. Allergan anticipates submission of an NDA by the end of 2017.
- **Solithera™ (Solithromycin):** In December 2016, the FDA issued a complete response letter (CRL) for oral and IV Solithera™ (solithromycin) to treat CABP in adults.
- **SYN-004 (Ribaxamase):** Ribaxamase, currently in Phase 2 trials, is a first-in-class oral enzyme designed to degrade certain IV beta-lactam antibiotics within the GI tract and maintain the natural balance of the gut microbiome for the prevention of *C. difficile* infection (CDI), pathogenic overgrowth, and the emergence of antimicrobial resistance (AMR).
- **Taksta™ (Fusidic Acid):** Fusidic acid is a novel, orally active antibiotic against gram-positive bacteria, including all *S. aureus* strains such as HA-MRSA, CA-MRSA, and linezolid-resistant strains, by inhibiting protein synthesis by blocking aminoacyl-tRNA

transfer to protein in susceptible bacteria. Fusidic acid is currently in Phase 2 trials for treatment of ABSSSI and for patients with prosthetic joint infections.

- **WCK 5222 (Cefepime/Zidebactam):** WCK 5222 is a combination of a novel drug, zidebactam, and cefepime. Zidebactam is an antibiotic with a novel β-lactam enhancer mechanism that facilitates overcoming of multiple resistance mechanisms in gram-negative superbugs, including the most dreaded mechanism called New Delhi metallo β-lactamase (NDM) which renders the last line of antibiotics (carbapenems) ineffective. WCK 5222 is also active against the recently reported colistin-resistant strains of gram-negative pathogens. This drug meets the urgent threat of CRE and serious threats like multidrug-resistant *Acinetobacter*, ESBLs, drug-resistant *Salmonella typhi,* and multidrug-resistant *Pseudomonas aeruginosa*. The FDA has agreed to an abridged Phase 3 trial based on evaluation of its preclinical and clinical data from Phase 1 studies. The FDA has granted WCK 5222 Fast Track Designation and QIDP status. Wockhardt expects global launch of WCK 5222 during the year 2020 to 2021.
- **Zolyd™ (Fosfomycin Injection):** Fosfomycin injection is currently being studied as a first-line treatment for cUTI suspected to be caused by multidrug-resistant pathogens. Fosfomycin injection is an epoxide antibiotic with a broad spectrum of bactericidal gram-negative and gram-positive activity. Zavante expects to file an NDA with the FDA in early 2018.

Baxdela™ (Delafloxacin) Product Summary[35]

Indication(s): Baxdela™ (delafloxacin) is indicated for the treatment of ABSSSI caused by designated susceptible bacteria.

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

Microbiology: Delafloxacin has been shown to be active against the following bacteria:

- Gram-Positive Bacteria: *S. aureus* (including methicillin-resistant and -sensitive strains), *S. haemolyticus, S. lugdunensis, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus* Group, and *Enterococcus faecalis*
- Gram-Negative Bacteria: *Escherichia (E.) coli, Klebsiella pneumoniae, Enterobacter cloacae,* and *Pseudomonas aeruginosa*

Dosing:

- Delafloxacin is available as a 300mg sterile, lyophilized powder for reconstitution in single-dose vials and as 450mg tablets.
- Recommended dosing:
    - 300mg IV every 12 hours over 60 minutes for 5 to 14 days; or
    - 300mg IV every 12 hours over 60 minutes, then 450mg via oral tablet every 12 hours for a total duration of 5 to 14 days; or
    - 450mg tablet orally every 12 hours for a total duration of 5 to 14 days

- Delafloxacin dosage should be adjusted in patients with severe renal impairment, and serum creatinine levels and estimated glomerular filtration rate (eGFR) should be closely monitored.
    - eGFR 30-89mL/min/1.73m^2: No dosage adjustment
    - eGFR 15-29mL/min/1.73m^2:
        - Tablets: no dosage adjustment
        - IV: 200mg IV over 60 minutes every 12 hours; or 200mg IV over 60 minutes every 12 hours, then 450mg via oral tablet every 12 hours
    - eGFR <15mL/min/1.73m^2 (including patients on hemodialysis): Not recommended
- Delafloxacin should be administered at least 2 hours before or 6 hours after antacids containing magnesium or aluminum, sucralfate, medications with metal cations (i.e., iron or multivitamins containing zinc or iron), or didanosine buffered tablets for oral suspension or powder for oral solution.

Boxed Warning: Serious Adverse Reactions Including Tendinitis, Tendon Rupture, Peripheral Neuropathy, Central Nervous System (CNS) Effects, and Exacerbation of Myasthenia Gravis

- FQs have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including tendinitis, tendon rupture, peripheral neuropathy, and CNS effects. If a patient experiences any of these adverse effects, delafloxacin should be discontinued immediately and patients should avoid the use of FQs, including delafloxacin. FQs may exacerbate muscle weakness in patients with myasthenia gravis and should be avoided in patients with a known history of myasthenia gravis.

Mechanism of Action: FQs exhibit a concentration-dependent bactericidal activity against gram-positive and gram-negative bacteria in vitro. The antibacterial activity of delafloxacin is due to the inhibition of both bacterial topoisomerase IV and DNA gyrase (topoisomerase II) enzymes, which are required for bacterial DNA replication, transcription, repair, and recombination.

Contraindication(s): Patients with known hypersensitivity to delafloxacin or any of the FQ class of antibacterial drugs

Warnings and Precautions:

- Tendinitis and Tendon Rupture: FQs have been associated with an increased risk of tendinitis and tendon rupture in all ages. Tendinitis can occur within hours or days of starting a FQ, or as long as several months after completion of FQ therapy.
- Peripheral Neuropathy: FQs have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesia, hypoesthesias, dysesthesias, and weakness have been reported in patients receiving FQs, including delafloxacin. Symptoms may occur soon after initiation and may be irreversible in some patients.

- CNS Effects: FQs have been associated with increased risk of CNS reactions, including convulsions, increased intracranial pressure, and toxic psychosis. FQs, including delafloxacin, may also cause CNS reactions of nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression, and suicidal thoughts or acts.
- Exacerbation of Myasthenia Gravis: FQs have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis.
- Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity reactions, some following the first dose, have been reported in patients receiving FQs.
- *C. difficile*-Associated Diarrhea: *C. difficile*-associated diarrhea (CDAD) has been reported in users of nearly all systemic antibacterial drugs, including delafloxacin, with severity ranging from mild diarrhea to fatal colitis.
- Development of Drug-Resistant Bacteria: Prescribing delafloxacin in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions: The most common adverse reactions experienced with delafloxacin (incidence ≥2%) include nausea, diarrhea, headache, transaminase elevations, and vomiting.

Use in Specific Populations:

- Pregnancy: The limited available data with delafloxacin use in pregnant women are insufficient to inform a drug-associated risk of major birth defects and miscarriages. When delafloxacin was administered orally to rats during the period of organogenesis, no malformations or fetal death were observed at up to 7 times the estimated clinical exposure. When rats were dosed intravenously in late pregnancy and through lactation, there were no adverse effects on offspring at exposures approximating the clinical IV exposure.
- Lactation: There are no data available on the presence of delafloxacin in human milk, on the breast-fed infant, or the effects on milk production. Delafloxacin is excreted in the breast milk of rats.
- Pediatric Use: The safety and effectiveness in pediatrics patients has not been established. Use in patients younger than 18 years of age is not recommended.
- Geriatric Use: Geriatric patients are at increased risk for developing severe tendon rupture when being treated with FQ. Caution should be used when prescribing delafloxacin to elderly patients, especially those on corticosteroids.
- Hepatic Impairment: No dosage adjustment is necessary for delafloxacin in patients with hepatic impairment.
- Renal Impairment: The dosage of delafloxacin should be adjusted in patients with severe renal impairment and serum creatinine levels and eGFR should be closely monitored.

Efficacy: A total of 1,510 adults with ABSSSI were randomized in two multicenter, multinational, double-blind, double-dummy, non-inferiority trials. Trial 1 compared delafloxacin 300mg via IV infusion every 12 hours to comparator. Trial 2 compared delafloxacin 300mg via IV infusion every 12 hours for six doses then made a mandatory switch to oral delafloxacin 450mg tablets to comparator. In both studies, the comparator was the combination of IV vancomycin

15mg/kg actual body weight and aztreonam. Aztreonam therapy was discontinued if no gram-negative pathogens were identified in the baseline cultures. The table below summarizes the clinical response from both Phase 3 trials.

Table 1. Clinical Response[¥] at 48-72 Hours in the ITT Population

	Baxdela™ (300mg IV) (Responders/total n) (%)	Vancomycin 15mg/kg + Aztreonam (Responders/total n) (%)	Treatment Difference (2-sided 95% CI)
Trial 1	259/331 (78.2%)	266/329 (80.9%)	-2.6% (-8.8%, 3.6%)
	Baxdela™ (300mg IV + 450mg oral) (Responders/total n) (%)	**Vancomycin 15mg/kg + Aztreonam (Responders/total n) (%)**	**Treatment Difference (2-sided 95% CI)**
Trial 2	354/423 (83.7%)	344/427 (80.6%)	3.1% (-2.0%, 8.3%)

ITT = intent to treat (includes all randomized patients); IV = intravenous; CI = confidence interval

[¥]Objective clinical response was defined as a 20% or greater decrease in lesion size as determined by digital planimetry of the leading edge of erythema at 48 to 72 hours after initiation of treatment without any reasons for failure (less than 20% reduction in lesion size, administration of rescue antibacterial therapy, use of another antibacterial or surgical procedure to treat for lack of efficacy, or death). Missing patients were treated as failures.

Cost Comparison:

Product	Cost Per Unit	Cost for 14 Days of Treatment
Baxdela™ (delafloxacin injection)	**$132.50**	**$3,710.00**
Baxdela™ (delafloxacin tablets)	**$67.50**	**$1,890.00**
Baxdela™ (delafloxacin injection and tablets)[#]	**See above**	**$2,280.00**
vancomycin injection[§]	$5.51	$154.28
linezolid 600mg injection	$41.74	$1,168.72
doxycycline 100mg tablets	$0.55	$15.40
trimethoprim/sulfamethoxazole 800/160mg tablets	$0.14	$3.92

[#]Dosing recommendations include IV to oral formulation regimen. The cost of a 14-day course of treatment using 3 days of IV then switching to the oral for the remaining 11 days is shown in the table.

[§]Dosing based on dose of 2 grams every 12 hours.

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.

Minolira™ (Minocycline Extended-Release Tablets) Product Summary[36]

Indication(s): Minolira™ (minocycline ER tablets) is a tetracycline-class drug indicated to treat only inflammatory lesions of non-nodular moderate-to-severe acne vulgaris in patients 12 years of age and older.

Dosing:

- Minolira™ is available as 105mg and 135mg functionally scored, ER oral tablets. Minolira™ should not be chewed or crushed.
- Minolira™ should be dosed approximately 1g/kg once daily, with or without food, for 12 weeks. Dosing recommendations based on patient weight are outlined in the following table.

Patient's Weight (kg)	Daily Dose (mg)	Recommended Tablet Strength and Size to Administer	Actual Dose (mg/kg)
45-59	52.5	Half of the 105mg tablet	1.16-0.88
60-89	67.5	Half of the 135mg tablet	1.13-0.75
90-125	105	One 105mg tablet	1.17-0.84
126-136	135	One 135mg tablet	10.7-0.99

- Patients with renal impairment should have the total dosage decreased by either reducing the recommended individual doses and/or extending the time intervals between doses.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost for 30 Days[+]
Minolira™ (minocycline ER tablet)	**Unknown**	**Unknown**
minocycline capsules	$0.22 – $0.48	$13.20 – $28.80

[+]30-day supply based on recommended dosing regimen.
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.

Solosec™ (Secnidazole Oral Granules) Product Summary[37]

Indication(s): Solosec™ (secnidazole) is a nitroimidazole antimicrobial indicated for the treatment of bacterial vaginosis in adult women.

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

Microbiology: Culture and sensitivity testing of bacteria are not routinely performed to establish the diagnosis of bacterial vaginosis. The following *in vitro* data are available, but their clinical significance is unknown:

- *Bacteroides* species
- *Gardnerella vaginalis*
- *Prevotella* species
- *Mobiluncus* species
- *Megasphaera*-like type I/II

Dosing:

- Secnidazole is available in a unit-of-use child resistant foil packet containing 2 grams of oral granules.
- The recommended dosage of secnidazole is 2 grams (1 packet) once daily, as a single-dose, without regard to timing of meals.
    - The entire contents of 1 packet should be sprinkled onto applesauce, yogurt, or pudding and should be consumed within 30 minutes, without chewing or crunching the granules.
    - Secnidazole is not intended to be dissolved in any liquid.

Mechanism of Action: Secnidazole is a nitroimidazole antibiotic, which exhibits its antimicrobial activity by entering the bacterial cell as an inactive prodrug where the nitro group is reduced by

bacterial enzymes to radical anions. It is believed that these radical anions interfere with bacterial DNA synthesis of susceptible isolates.

Contraindication(s): Secnidazole is contraindicated in patients who have shown hypersensitivity to secnidazole, other ingredients of the formulation, or other nitroimidazole derivatives.

Warnings and Precautions:

- Vulvo-Vaginal Candidiasis: In controlled clinical trials of non-pregnant women with bacterial vaginosis, vulvo-vaginal candidiasis developed in 19/197 (9.6%) of subjects who received secnidazole 2 grams and 4/136 (2.9%) of subjects who received placebo. Symptomatic vulvo-vaginal candidiasis may require treatment with an antifungal agent.
- Potential Risk of Carcinogenicity: Carcinogenicity has been seen in mice and rats treated chronically with nitroimidazole derivatives, which are structurally related to secnidazole. It is unclear if the positive tumor findings in lifetime rodent studies of those nitroimidazoles indicate a risk to potential patients taking a single dose of secnidazole to treat bacterial vaginosis. Chronic use of secnidazole should be avoided.
- Drug Resistance: Secnidazole should not be prescribed in the absence of proven or strongly suspected bacterial infection or for a prophylactic indication as it is unlikely to provide a benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions: The most common adverse reactions observed in clinical trials, with an incidence of 2% or greater, were vulvo-vaginal candidiasis, headache, nausea, dysgeusia, vomiting, diarrhea, abdominal pain, and vulvo-vaginal pruritus.

Use in Specific Populations:

- Pregnancy: There is insufficient human data to establish whether there is a drug-associated risk of major birth defects or miscarriages with secnidazole in pregnant women.
- Lactation: There is no information on the presence of secnidazole in human milk, the effects on the breast-fed child, or the effects on milk production. Other nitroimidazole derivatives are present in human milk. Due to the potential for serious adverse reactions, including tumorigenicity, patients that are breastfeeding should be advised breastfeeding is not recommended during treatment with secnidazole and for 96 hours (based on half-life) after administration of secnidazole.
- Pediatric Use: The safety and effectiveness of secnidazole in pediatric patients younger than 18 years of age have not been established.
- Geriatric Use: Clinical studies with secnidazole did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently than younger subjects.

Efficacy: Two randomized, placebo-controlled Phase 3 trials, with similar design, were conducted to evaluate the efficacy of secnidazole 2 grams for the treatment of bacterial vaginosis. Trial 1 enrolled 144 non-pregnant female patients 19 to 54 years of age and Trial 2 enrolled 189 non-pregnant female patients 18 to 54 years of age, with 54% of subjects in both trials being African American. Efficacy was assessed by clinical outcome evaluated 21 to 30

days following a single-dose of secnidazole. A clinical responder was defined as "normal" vaginal discharge, negative "whiff" test, and clue cells less than 20%. Additional endpoints included Nugent score cure (Nugent score of 0 to 3) and therapeutic outcome. A therapeutic responder was defined as a clinical responder with a Nugent score cure. The results of both trials can be seen in the table below.

Table 1. Efficacy of Secnidazole for Treatment of Bacterial Vaginosis in MITT at 21-30 Days

	Trial 1		Trial 2	
	Secnidazole (N=62); n (%)	**Placebo (N=62); n (%)**	**Secnidazole (N=107); n (%)**	**Placebo (N=57); n (%)**
Clinical Responder^	42 (67.7%)	11 (17.7%)	57 (53.3%)	11 (19.3%)
Nugent Score Cure#	25 (40.3%)	4 (6.5%)	47 (43.9%)	3 (5.3%)
Therapeutic Responder	25 (40.3%)	4 (6.5%)	37 (34.6%)	2 (3.5%)

All outcomes were statistically significant ($p<0.001$).
N = number of patients in treatment group; MITT = modified intent-to-treat population, defined as all patients randomized who had a baseline Nugent score of 4 or greater and were negative for other sexually transmitted infections at baseline.
^Patients missing one or more of the clinical assessments were considered as non-responders/not cured.
#Patients with missing Nugent scores were considered Nugent score failures.

Cost Comparison:

Product	Cost Per Unit	Cost per Treatment
Solosec™ (secnidazole 2 gram oral granules)	**Unknown**	**Unknown**
metronidazole 500mg tablets	$0.30	$4.20
tinidazole 500mg tablets	$3.35	$26.80

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.

Vabomere™ (Meropenem/Vaborbactam Injection) Product Summary[38]

Indication(s): Vabomere™ (meropenem/vaborbactam) is indicated for the treatment of patients 18 years of age and older with cUTI including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae* species complex.

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

Microbiology: Meropenem/vaborbactam has been shown to be active against the following bacteria:

- Gram-Negative Bacteria: *Enterbacter cloacae* species complex, *Escherichia coli*, and *Klebsiella pneumoniae*

Dosing:

- Vabomere™ is available in a 2 gram (meropenem 1 gram/vaborbactam 1 gram) vial for reconstitution.

- The recommended dosage of meropenem/vaborbactam is 4 grams (meropenem 2 grams/vaborbactam 2 grams) via IV every 8 hours, infused over 3 hours, for up to 14 days.
- The dosage of meropenem/vaborbactam should be adjusted in patients with renal impairment and serum creatinine levels and eGFR should be closely monitored daily and the dosage be adjusted accordingly. All doses should be administered via IV over 3 hours.
    - eGFR 30-49mL/min/1.73m^2: No dosage adjustment
    - eGFR 15-29mL/min/1.73m^2: Meropenem/vaborbactam 2 grams IV every 12 hours
    - eGFR <15mL/min/1.73m^2: Meropenem/vaborbactam 1 gram IV every 12 hours
    - For patients on hemodialysis, meropenem/vaborbactam should be administered after a hemodialysis session.

Mechanism of Action: Vabomere™ is a combination of meropenem and vaborbactam. Meropenem is a carbapenem antibiotic that exhibits bactericidal action by inhibiting cell wall synthesis. Vaborbactam is a non-suicidal beta-lactamase inhibitor that protects meropenem from degradation by certain serine beta-lactamases such as *Klebsiella pneumoniae* carbapenemase (KPC). Vaborbactam does not have any antibacterial activity.

Contraindication(s): Meropenem/vaborbactam is contraindicated in patients with known hypersensitivity to any components of Vabomere™, to other drugs in the same class, or those that have demonstrated anaphylactic reactions to beta-lactam antibacterial drugs.

Warnings and Precautions:
- Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity reactions and serious skin reactions have been reported in patients receiving therapy with beta-lactam antibacterial drugs or patients with a history of penicillin hypersensitivity.
- Seizure Potential: Seizure and other adverse CNS experiences have been reported during treatment with meropenem. These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions, history of seizures), bacterial meningitis, and/or compromised renal function.
- Risk of Breakthrough Seizures Due to Drug Interaction with Valproic Acid: Concomitant use of meropenem/vaborbactam and valproic acid or divalproex sodium is generally not recommended. Case reports have shown that co-administration of carbapenems to patients receiving valproic acid or divalproex sodium results in a reduction in valproic acid concentrations that may drop below a therapeutic range, increasing the risk of breakthrough seizures. Increasing the dose of valproic acid or divalproex sodium may not be sufficient to overcome this reaction.
- CDAD: CDAD has been reported in users of nearly all systemic antibacterial drugs, including meropenem/vaborbactam, with severity ranging from mild diarrhea to fatal colitis.
- Thrombocytopenia: In patients with renal impairment, thrombocytopenia has been observed in patients treated with meropenem, but no clinical bleeding has been reported.

- Potential for Neuromotor Impairment: Patients receiving meropenem/vaborbactam in the outpatient setting should be counseled on potential adverse reactions such as seizures, delirium, headaches, and/or paresthesia that could interfere with mental alertness and/or cause motor impairment.
- Development of Drug-Resistant Bacteria: Prescribing meropenem/vaborbactam in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions: The most frequently reported adverse reactions (3% or greater) in patients receiving meropenem/vaborbactam were headache, phlebitis/infusion site reaction, and diarrhea.

Use in Specific Populations:

- Pregnancy: There is insufficient human data to establish whether there is a drug-associated risk of major birth defects or miscarriages with Vabomere™, meropenem, or vaborbactam in pregnant women.
- Lactation: Meropenem has been reported to be excreted in human milk. It is unknown whether vaborbactam is excreted in human milk. No information is available on the effects of meropenem and vaborbactam on the breast-fed child or on milk production.
- Pediatric Use: The safety and effectiveness of meropenem/vaborbactam in pediatric patients (younger than age 18 years of age) have not been established.
- Geriatric Use: No overall differences in safety or effectiveness were observed between geriatric patients (age 65 years and older) and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.
- Renal Impairment: Dosage adjustments for meropenem/vaborbactam are recommended in patients with renal impairment (eGFR <50mL/min/1.73m^2). For patients with changing renal function, serum creatinine and eGFR should be monitored at least daily and dose should be adjusted accordingly.

Efficacy: A total of 545 adults with cUTI, including pyelonephritis, were randomized into a double-blind, double-dummy, multi-center trial comparing meropenem/vaborbactam 4 grams (meropenem 2 grams and vaborbactam 2 grams) to piperacillin/tazobactam (piperacillin 4 grams/tazobactam 0.5 grams) IV every 8 hours. Switching to an oral antibacterial drug, such as levofloxacin, was allowed after a minimum of 15 doses of IV therapy. The microbiologically modified intent to treat population (m-MITT) included all randomized patients who received any study drug and had at least one baseline uropathogen. Clinical and microbiological response at the end of IV treatment (EOIVT) required both a clinical outcome of cure or improvement and a microbiologic outcome of eradication (all baseline uropathogens at >10^5 CFU/mL reduced to <10^4 CFU/mL). Clinical and microbiological response was also assessed at the Test of Cure (TOC) visit (approximately 7 days after completion of treatment) in the m-MITT population and required both a clinical outcome of cure and a microbiological outcome of eradication. Mean duration of IV treatment in both treatment groups was 8 days and mean total treatment duration (IV and oral) was 10 days. Approximately 10% of patients in each

treatment group in the m-MITT population had a levofloxacin-resistant pathogen at baseline and received levofloxacin as the oral switch therapy. This protocol violation may have impacted the assessment of the outcomes at the TOC visit, however, these patients were not excluded from the analysis. The table below summarizes the trial results.

Table 1. Clinical Microbiological Response Rates (m-MITT Population)

	Vabomere™ n/N (%)	Piperacillin/Tazobactam n/N (%)	Difference (95% CI)
Clinical cure/improvement AND microbiological eradication at the EOIVT visit^	183/186 (98.4%)	165/175 (94.3%)	4.1% (0.3%, 8.8%)
Clinical cure/improvement AND microbiological eradication at the TOC visit$^{\Delta}$	124/162 (76.5%)	112/153 (73.2%)	3.3% (-6.2%, 13.0%)

CI = confidence interval; EOIVT = end of intravenous treatment; TOC = test of cure; N = microbiologically modified intent to treat population

^EOIVT visit includes patients with organisms resistant to piperacillin/tazobactam at baseline.

$^{\Delta}$TOC visit excludes patients with organisms resistant to piperacillin/tazobactam at baseline.

Cost Comparison:

Product	Cost Per Unit	Cost per 10-Day Course of Therapy^{+}
Vabomere™ (meropenem/vaborbactam)	**$165.00**	**$13,860.00**
piperacillin/tazobactam (Zosyn®)	$9.45	$378.00

$^{+}$Vabomere™ may be dosed for up to 14 days, pricing listed based on 10-day course.

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

Cost Comparison

There are several cost effective generic options available for SoonerCare members who require antibiotic therapy. As shown in the following tables, several generic medications cost significantly more than similar medications. In the following cephalexin products table, the state maximum allowable cost (SMAC) of cephalexin 250mg tablet at $1.13 per tablet, resulting in a 7-day course of therapy costing $31.64. The cost of a similar product, cephalexin 250mg capsules, has a national average drug acquisition cost (NADAC) of $0.08 per capsule resulting in a 7-day course of therapy costing $2.24. The fluoroquinolone products table shows additional substantial cost differences between similar medications. The wholesale acquisition cost (WAC) of ofloxacin 300mg tablets is $172.20 for a 7-day course of therapy. The NADAC of levofloxacin 500mg tablets and ciprofloxacin 500mg tablets are $1.33 and $2.10 for a 7-day course of therapy, respectively.

Cephalexin Products:

Product	Cost Per Unit	Cost per 7-Day Course of Therapy[+]
cephalexin 250mg tablet	**$1.13**	**$31.64**
cephalexin 500mg tablet	$2.29	$32.06
cephalexin 250mg capsule	$0.08	$2.24
cephalexin 500mg capsule	$0.09	$1.26

[+]Based on recommended dosing regimen per package insert, duration of therapy can vary based on indication.
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.

Fluoroquinolone Products:

Product	Cost Per Unit	Cost per 7-Day Course of Therapy[+]
ofloxacin 300mg tablet	**$12.30**	**$172.20**
ofloxacin 400mg tablet	$14.91	$208.74
moxifloxacin 400mg tablet	$5.14	$35.98
levofloxacin 500mg tablet	$0.19	$1.33
ciprofloxacin 500mg tablet	$0.15	$2.10

[+]Based on recommended dosing regimen per package insert, duration of therapy can vary based on indication.
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Baxdela™ (delafloxacin injection and tablets), Solosec™ (secnidazole oral granules), and Vabomere™ (meropenem/vaborbactam injection) with the following criteria:

Baxdela™ (Delafloxacin Injection and Tablets) 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.
    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.

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.

Vabomere™ (Meropenem/Vaborbactam Injection) 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.

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

1. Add cephalexin 250mg tablets to the Antibiotic Special Formulation category based on net cost. Current special formulation criteria will apply.
2. Add Minolira™ (minocycline hydrochloride ER tablets) to the Antibiotic Special Formulation category. Current special formulation criteria will apply.
3. Add oflaxacin 300mg tablets with criteria similar to ofloxacin 400mg tablets and moxifloxacin prior authorization criteria based on net cost. Current criteria will apply.
4. Add Sivextro® (tedizolid) vial formulation with criteria similar to Sivextro® tablet formulation based on net cost. Current criteria will apply.

The proposed changes can be seen in red in the following criteria:

Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the immediate-release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.
2. The following oral antibiotic currently require prior authorization and the special formulation approval criteria will apply:
    - Amoxicillin/clavulanate potassium extended-release (ER) tablets (Augmentin XR®)
    - Amoxicillin ER 775mg tablets (Moxatag®)
    - Cephalexin **250mg and** 500mg tablets
    - Cephalexin 750mg capsules
    - Ciprofloxacin 100mg tablets
    - Ciprofloxacin 500mg and 1,000mg ER tablets
    - Doxycycline hyclate 75mg capsules (Acticlate®)
    - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
    - Doxycycline monohydrate 75mg and 150mg capsules and tablets
    - Doxycycline monohydrate DR 40mg capsules (Oracea®)
    - **Minocycline ER tablets (Minolira™)**
    - Minocycline ER tablets (Solodyn®)
    - Minocycline immediate-release tablets
    - Tetracycline 250mg and 500mg capsules

Ofloxacin 300mg and 400mg Tablets and Moxifloxacin 400mg Tablets Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, and/or other cost effective therapeutic equivalent medication(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 medication(s).
3. A quantity limit of six tablets **or vials** per six days will apply.

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

1. 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 medication(s).

Utilization Details of Various Systemic Antibiotic Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ CLIENT	COST/ CLAIM
CEFIXIME PRODUCTS					
CEFIXIME SUS 200/5ML	24	18	$8,488.39	1.33	$353.68
CEFIXIME SUS 100/5ML	21	15	$5,265.90	1.4	$250.76
SUPRAX CAP 400MG	5	5	$778.35	1	$155.67
SUPRAX CHW 200MG	3	3	$1,184.32	1	$394.77
SUPRAX CHW 100MG	2	2	$509.33	1	$254.67
SUBTOTAL	**55**	**41**	**$16,226.29**	**1.34**	**$295.02**
CEFTOLOZANE/TAZOBACTAM PRODUCTS					
ZERBAXA INJ 1.5GM	10	1	$31,540.65	10	$3,154.07
SUBTOTAL	**10**	**1**	**$31,540.65**	**10**	**$3,154.07**
CIPROFLOXACIN PRODUCTS					
CIPRO (5%) SUS 250MG/5mL	97	82	$14,588.49	1.18	$150.40
CIPRO (10%) SUS 500MG/5mL	72	60	$11,633.40	1.2	$161.58
CIPROFLOXACN SUS 250MG/5mL	7	7	$1,055.50	1	$150.79
SUBTOTAL	**176**	**141**	**$27,277.39**	**1.25**	**$154.99**
DOXYCYCLINE PRODUCTS					
DOXYCYCL HYC TAB 200MG DR	3	1	$3,157.86	3	$1,052.62
SUBTOTAL	**3**	**1**	**$3,157.86**	**3**	**$1,052.62**
LEVOFLOXACIN PRODUCTS					
LEVOFLOXACIN SOL 25MG/ML	80	59	$9,221.34	1.36	$115.27
SUBTOTAL	**80**	**59**	**$9,221.34**	**1.36**	**$115.27**
MINOCYCLINE PRODUCTS					
SOLODYN TAB 65MG	11	1	$12,033.86	11	$1,093.99
SUBTOTAL	**11**	**1**	**$12,033.86**	**11**	**$1,093.99**
MOXIFLOXACIN PRODUCTS					
MOXIFLOXACIN TAB 400MG	6	4	$937.59	1.5	$156.27
SUBTOTAL	**6**	**4**	**$937.59**	**1.5**	**$156.27**
ORITAVANCIN PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ CLIENT	COST/ CLAIM
ORBACTIV SOL 400MG	1	1	$3,070.16	1	$3,010.16
SUBTOTAL	**1**	**1**	**$3,070.16**	**1**	**$3,010.16**
TETRACYCLINE PRODUCTS					
TETRACYCLINE CAP 250MG	13	7	$3,721.83	1.86	$286.29
TETRACYCLINE CAP 500MG	12	12	$4,723.21	1	$393.60
SUBTOTAL	**25**	**19**	**$8,445.04**	**1.32**	**$337.80**
TOTAL	**367**	**259***	**$111,910.18**	**1.42**	**$304.93**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Please note the utilization data only includes antibiotics that currently require prior authorization; antibiotics available without prior authorization are not included in the data.

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Appendix S

Fiscal Year 2017 Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Duzallo® (Lesinurad/ Allopurinol)

Oklahoma Health Care Authority
November 2017

Current Prior Authorization Criteria

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

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

Uloric® (Febuxostat) Approval Criteria:

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels greater than 6.0mg/dL; and
2. A patient-specific, clinically significant reason why allopurinol would not be a viable option for the member.
3. A quantity limit of 30 tablets per 30 days will apply.

Zurampic® (Lesinurad) Approval Criteria:

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

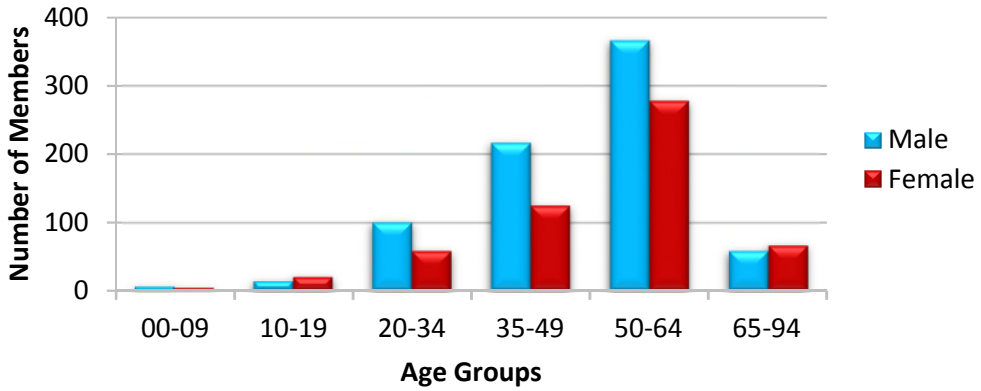
Utilization of Gout Medications: Fiscal Year 2017

Comparison of Fiscal Years

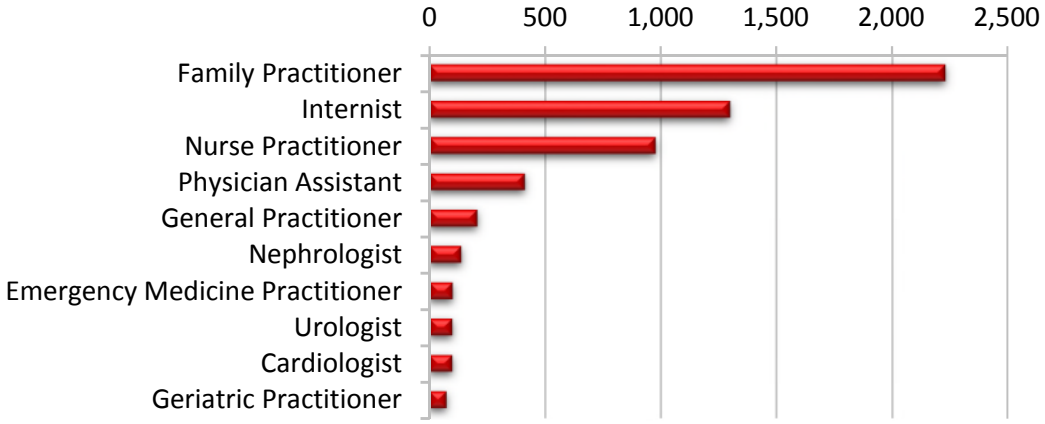
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	1,332	5,930	$173,962.79	$29.34	$0.79	307,982	220,018
2017	1,309	5,943	$169,459.42	$28.51	$0.76	299,847	221,892
% Change	**-1.70%**	**0.20%**	**-2.60%**	**-2.80%**	**-3.80%**	**-2.60%**	**0.90%**
Change	**-23**	**13**	**-$4,503.37**	**-$0.83**	**-$0.03**	**-8,135**	**1,874**

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

Demographics of Members Utilizing Gout Medications

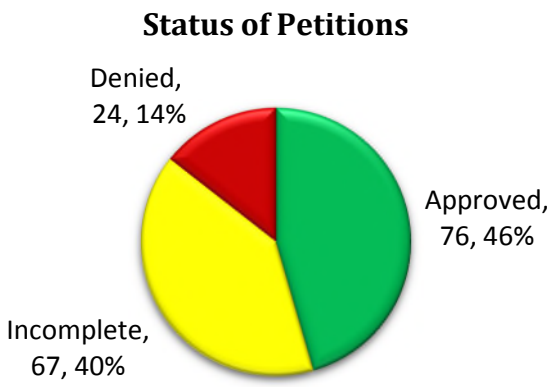


Top Prescriber Specialties of Gout Medications by Number of Claims



Prior Authorization of Gout Medications

There were 167 prior authorization requests submitted for gout medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.



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

Anticipated Patent Expiration(s):

- Colcrys® (colchicine tablets): February 2029
- Uloric® (febuxostat): September 2031
- Zurampic® (lesinurad): February 2032
- Mitigare® (colchicine capsules): August 2033

Both Colcrys® and Mitigare® have unexpired patents, but unconventional actions led to generic product availability. In 2009, the U.S. Food and Drug Administration (FDA) approved the first branded version of colchicine, Colcrys® (colchicine 0.6mg tablets). All other formulations, which had not gone through FDA's review process, were removed from the market at that time under the FDA's regulatory authorities. In September 2014, another branded formulation, Mitigare® (colchicine) 0.6mg capsules, was approved by the FDA. Soon after, in January 2015, West-Ward Pharmaceuticals Corp. launched the authorized generic, colchicine 0.6mg capsules. Prasco Laboratories and Takeda Pharmaceuticals U.S.A., Inc. followed suit in January 2015 by entering into a distribution and supply agreement for the rights to distribute colchicine tablets, the authorized generic of Colcrys® (colchicine 0.6mg tablets).

New FDA Approval(s):

- Duzallo® (lesinurad/allopurinol): August 2017

News:

- **January 2017:** The American College of Physicians (ACP) published clinical practice guidelines on the management of acute and recurrent gout in the *Annals of Internal Medicine*. The following recommendations were provided:
    - Recommendation 1: Clinicians should choose corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine to treat patients with acute gout. (Grade: strong recommendation, high-quality evidence)
    - Recommendation 2: Clinicians should use low-dose colchicine when using colchicine to treat acute gout. (Grade: strong recommendation, moderate-quality evidence)

- Recommendation 3: Initiating long-term urate-lowering therapy (ULT) in most patients after a first gout attack or in patients with infrequent attacks is not recommended. (Grade: strong recommendation, moderate-quality evidence)
- Recommendation 4: Clinicians should discuss benefits, harms, costs, and individual preferences with patients before initiating ULT, including concomitant prophylaxis, in patients with recurrent gout attacks. (Grade: strong recommendation, moderate-quality evidence)

- **April 2017:** An article published in the *ACP Internist* pointed out that the ACP guideline differs from the American College of Rheumatology (ACR) 2012 guidelines, and the European League Against Rheumatism (EULAR) 2016 guidelines on several management strategies of gout. The ACP, ACR, and EULAR are in agreement that a patient with only one attack and normal kidney function need not begin ULT. Both ACR and EULAR recommend that ULT can, however, be considered from the first presentation of the disease. Additionally, the ACR and EULAR guidelines strongly recommend that a patient's uric acid level be monitored and that ULT should aim to lower that level to the target range (<6mg/dL for maintenance or <5mg/dL for faster dissolution of crystals for patients with severe gout). The ACP guideline noted that while a treat-to-target strategy "has logical appeal and is supported by observational evidence," the strategy has not been experimentally tested. The ACR and EULAR guidelines recommend talking to patients about their diet and the need to avoid or limit certain foods and beverages; however, the ACP guideline indicates there is insufficient evidence for gout-specific dietary advice or therapies to improve symptomatic outcomes.

Duzallo® (Lesinurad/Allopurinol) Product Summary[7,8]

Indication(s): Duzallo® (lesinurad/allopurinol) is a combination of lesinurad, a URAT1 inhibitor, and allopurinol, a xanthine oxidase inhibitor, indicated for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of allopurinol alone. It lowers sUA levels by increasing excretion and inhibiting production of uric acid.

- Limitation of Use: Not recommended for the treatment of asymptomatic hyperuricemia.

Boxed Warning: Risk of Acute Renal Failure
- Acute renal failure has occurred with lesinurad, one of the components of Duzallo®.

Dosing:
- Duzallo® is supplied as film-coated tablets containing 200mg of lesinurad and 200mg of allopurinol or 200mg of lesinurad and 300mg of allopurinol.
- It is to be taken once daily by mouth with food and water. Patients should stay well hydrated (2L of liquid per day).
- The recommended dose is one 200mg lesinurad/300mg allopurinol tablet per day [or one 200mg lesinurad/200mg allopurinol tablet per day for patients with a creatinine clearance (CrCl) 45mL/min to less than 60mL/min].

- Lesinurad/allopurinol is not recommended for patients taking daily doses of allopurinol less than 300mg (or less than 200mg in patients with CrCl less than 60mL/min).
- One tablet of lesinurad/allopurinol should be used in place of an equivalent portion of the total daily allopurinol dose. The total daily dose of allopurinol should be maintained at the time of initiating treatment.
- One tablet contains the maximum daily lesinurad dose (200mg). Patients should not take more than one tablet of lesinurad/allopurinol per day.

Contraindication(s):

- Severe renal impairment (CrCl less than 30mL/min), end-stage renal disease (ESRD), kidney transplant recipients, or patients on dialysis
- Tumor lysis syndrome or Lesch-Nyhan syndrome
- Known hypersensitivity to allopurinol, including previous occurrence of skin rash

Warnings and Precautions:

- Renal Events: Adverse reactions related to renal function, including acute renal failure, can occur after initiating lesinurad/allopurinol. Treatment with lesinurad 200mg in combination with allopurinol was associated with an increased incidence of serum creatinine elevations, most of which were reversible. Treatment should be interrupted if serum creatinine is elevated to greater than two times the value when lesinurad treatment was initiated. Treatment should not be initiated in patients with a CrCl less than 45mL/min. Renal function should be evaluated prior to initiation of lesinurad/ allopurinol and periodically thereafter.
- Cardiovascular (CV) Events: In clinical trials with lesinurad and allopurinol, major adverse CV events (CV deaths, nonfatal myocardial infarctions, and non-fatal strokes) were observed. A causal relationship has not been established.

Adverse Reactions: The most common adverse reactions reported by at least 2% of patients on lesinurad in combination with allopurinol and at least 1% greater than that observed in patients on placebo with allopurinol include: headache, influenza, and gastroesophageal reflux.

Use in Specific Populations:

- Pregnancy: There are no available human data on use of lesinurad/allopurinol or lesinurad alone in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Limited data on allopurinol use in pregnant women do not demonstrate an increase in frequency of adverse development outcomes.
- Lactation: There is no information regarding the presence of lesinurad/allopurinol or lesinurad alone in human milk, the effects on the breastfed infant, or the effects on milk production. Lesinurad was present in the milk of rats. There was no report of effects of allopurinol on the breastfed infant or on milk production.
- Pediatric Use: The safety and effectiveness of lesinurad/allopurinol in pediatric patients has not been established.
- Geriatric Use: No dose adjustment is necessary in elderly patients; however, greater sensitivity of some older individuals cannot be ruled out.

- Renal Impairment: The efficacy and safety of lesinurad in combination with allopurinol were evaluated in studies that included gout patients with mild and moderate renal impairment. There were no clear differences in safety and effectiveness of lesinurad in combination with allopurinol in patients with mild renal impairment compared to patients with normal renal function. The efficacy and safety of lesinurad/allopurinol have not been evaluated in gout patients with severe renal impairment (CrCl less than 30mL/min), with ESRD, or receiving dialysis. Lesinurad/allopurinol is not expected to be effective in these patient populations.
- Hepatic Impairment: No dose adjustment is necessary in patients with mild or moderate hepatic impairment (Child-Pugh classes A and B). Neither lesinurad/allopurinol nor its individual components have been studied in patients with severe hepatic impairment; therefore, it is not recommended in these patients.
- Secondary Hyperuricemia: No studies with lesinurad/allopurinol have been conducted in patients with secondary hyperuricemia. It is contraindicated for use in tumor lysis syndrome or Lesch-Nyhan syndrome, where the rate of uric acid formation is greatly increased.

Efficacy: Bioequivalence of Duzallo® to co-administered lesinurad and allopurinol was demonstrated, and efficacy of the combination of allopurinol and lesinurad was demonstrated in two Phase 3 studies. Both studies were 12-month multicenter, randomized, double-blind, placebo-controlled clinical studies in adult patients with hyperuricemia and gout. Study 1 and Study 2 enrolled patients with gout who were on a stable dose of allopurinol of at least 300mg (or 200mg for moderate renal impairment), had a sUA less than 6.5mg/dL, and reported at least two gout flares in the prior 12 months. The primary study endpoint was the proportion of patients reaching target sUA. Patients were randomized 1:1:1 to receive lesinurad 200mg, lesinurad 400mg, or placebo once daily; all were to continue on their stable allopurinol dose. The primary endpoint was met in both studies. When added to allopurinol, lesinurad 200mg and 400mg resulted in statistically significant increases in the proportion of patients who achieved the target goal of sUA less than 6mg/dL by month 6 compared with allopurinol alone. At each time-point during the 12-month treatment period, the mean percent decrease and absolute change from baseline sUA was greater on lesinurad 200mg plus allopurinol compared with allopurinol alone ($p<0.0001$). In Study 1 and Study 2, the rates of gout flare requiring treatment from the end of month 6 to the end of month 12 were not statistically different between lesinurad 200mg in combination with allopurinol compared with allopurinol alone.

Cost Comparison:

Medication	Cost Per Tablet	Cost Per 30 Days
Duzallo® (lesinurad/allopurinol) 200mg/200mg tablet	**$12.37**	**$371.10**
Duzallo® (lesinurad/allopurinol) 200mg/300mg tablet	**$12.37**	**$371.10**
Zurampic® (lesinurad) 200mg tablet	$12.37	$371.10
allopurinol 100mg tablet	$0.13	$17.10*
allopurinol 300mg tablet	$0.21	$6.30*

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

*Cost for 30 days of allopurinol based on equivalent maximum dosing of Duzallo® (allopurinol 300mg/day).

Recommendations

The College of Pharmacy recommends the prior authorization of Duzallo® (lesinurad/ allopurinol) with criteria similar to Zurampic® (lesinurad):

Duzallo® (Lesinurad/Allopurinol) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved indication for the treatment of symptomatic hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of allopurinol alone; and
3. Failure of allopurinol or febuxostat alone defined by serum urate levels greater than 6.0mg/dL; and
4. Prior to starting treatment with Duzallo®, member must be on at least 300mg of allopurinol daily, unless creatinine clearance (CrCl) is less than 60mL/min then 200mg daily is required. Duzallo® 200mg/200mg will only be approved for members with a CrCl less than 60mL/min; and
5. Prescriber must verify that member has a CrCl greater than 45mL/min prior to initiating treatment. For continued approval, prescriber must verify CrCl is greater than 45mL/min and serum creatinine is not greater than two times baseline when Duzallo® was initiated; and
6. Prescriber must document member has no contraindications for use of Duzallo® including any of the following**:** Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl less than 30mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis.
7. A quantity limit of one tablet daily will apply.

Utilization Details of Gout Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ALLOPURINOL PRODUCTS					
ALLOPURINOL TAB 300MG	2,948	618	$50,721.12	$0.43	$17.21
ALLOPURINOL TAB 100MG	2,160	585	$24,767.04	$0.28	$11.47
SUBTOTAL	**5,108**	**1,203**	**$75,488.16**	**$0.36**	**$14.78**
COLCHICINE PRODUCTS					
COLCHICINE TAB 0.6MG	428	156	$23,623.64	$7.58	$55.20
PROBEN/COLCH TAB 500-0.5MG	89	28	$3,506.77	$1.13	$39.40
COLCRYS TAB 0.6MG	55	31	$2,880.43	$11.16	$52.37
COLCHICINE CAP 0.6MG	39	21	$2,030.84	$8.68	$52.07
SUBTOTAL	**611**	**236**	**$32,041.68**	**$4.78**	**$52.44**
FEBUXOSTAT PRODUCTS					
ULORIC TAB 40MG	151	26	$40,253.45	$9.31	$266.58
ULORIC TAB 80MG	73	12	$21,676.13	$9.90	$296.93
SUBTOTAL	**224**	**38**	**$61,929.58**	**$9.50**	**$276.47**
TOTAL	**5,943**	**1,309***	**$169,459.42**	**$0.76**	**$28.51**

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

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[2] Mitigare®. Physicians: Colchicine History. West-Ward Pharmaceuticals. Available online at: https://www.mitigare.com/physicians/colchicine-history/. Last revised 10/22/2015. Last accessed 10/23/2017.

[3] Takeda Pharmaceutical Company Limited. Prasco and Takeda Enter into Agreement to Market Authorized Generic of Colcrys® (colchicine, USP) in the United States. Available online at: https://www.takeda.com/newsroom/newsreleases/2015/prasco-and-takeda-enter-into-agreement-to-market--authorized-generic-of-colcrys-colchicine-usp-in-the-united-states/. Issued 01/13/2015. Last accessed 10/23/2017.

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[6] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Annals of the Rheumatic Diseases* 2017; 76:29-42.

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[8] Ardea Biosciences. Lesinurad in Combination With a Xanthine Oxidase Inhibitor for Treatment of Hyperuricemia Associated With Gout. Available online at: https://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/arthritisadvisorycommittee/ucm467951.pdf. Issued 10/26/2015. Last accessed 10/09/2017.

Appendix T

Fiscal Year 2017 Annual Review of Pancreatic Enzymes

Oklahoma Health Care Authority
November 2017

Current Prior Authorization Criteria

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

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

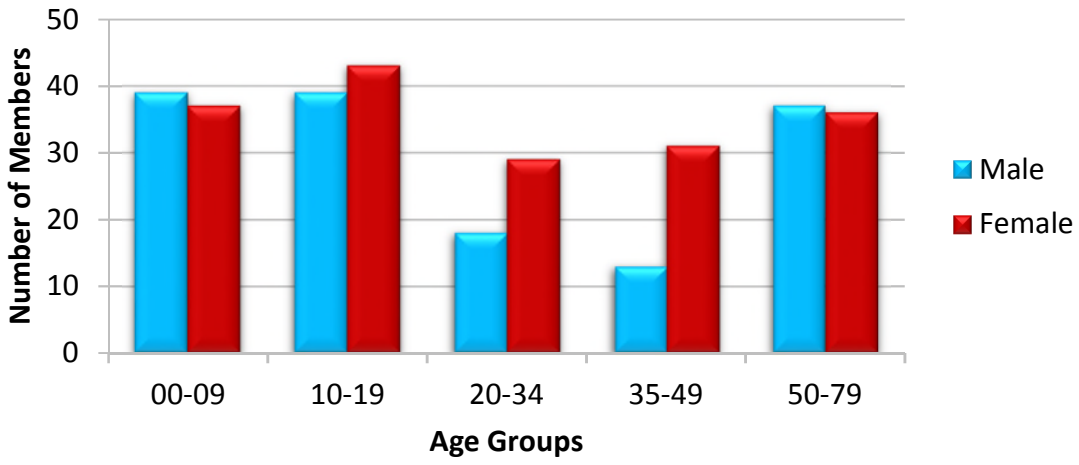
Utilization of Pancreatic Enzymes: Fiscal Year 2017

Comparison of Fiscal Years

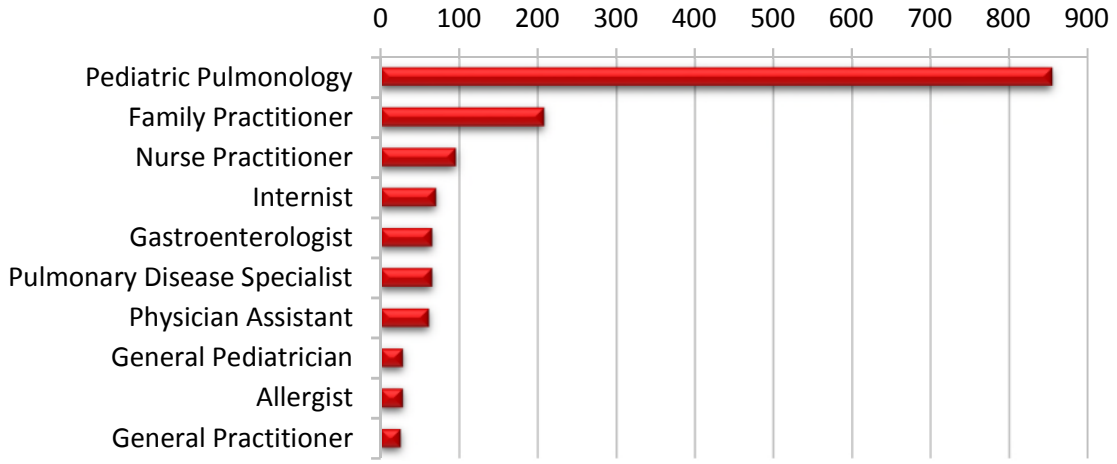
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	333	1,636	$2,133,366.46	$1,304.01	$45.72	513,283	46,665
2017	322	1,614	$2,469,781.19	$1,530.22	$52.93	546,541	46,659
% Change	**-3.30%**	**-1.30%**	**15.80%**	**17.30%**	**15.80%**	**6.50%**	**0.00%**
Change	**-11**	**-22**	**$336,414.73**	**$226.21**	**$7.21**	**33,258**	**-6**

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

Demographics of Members Utilizing Pancreatic Enzymes



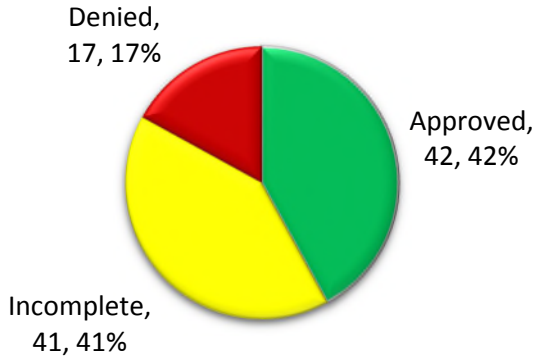
Top Prescriber Specialties of Pancreatic Enzymes by Number of Claims



Prior Authorization of Pancreatic Enzymes

There were 100 prior authorization requests submitted for pancreatic enzymes during fiscal year 2017. The prior authorization for pancreatic enzymes was implemented on March 27, 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Zenpep®: February 2028
- Creon®: February 2030

New FDA Approval(s):

- **July 2017:** The U.S. Food and Drug Administration (FDA) approved Pertzye® 24,000 USP lipase unit capsules. Pertzye® was previously available as delayed-release capsules in the following strengths: 4,000 USP units of lipase; 8,000 USP units of lipase; and 16,000 USP units of lipase. The new dosing strength allows for the use of fewer capsules to reach the needed weight-based dose when compared to the other capsule sizes.

Pipeline:

- **July 2017:** Anthera Pharmaceuticals announced that the RESULT Phase 3 clinical study of Sollpura® (liprotamase), a novel, non-porcine pancreatic enzyme replacement therapy (PERT), for exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF) had been approved by the Cystic Fibrosis Foundation Therapeutics Development Network Protocol Review Committee. Topline data are expected at the end of 2017 or in early 2018. The Phase 3 study is designed to evaluate the non-inferiority of liprotamase at individualized doses compared to approved, porcine-derived, enteric-coated PERT when administered to patients with EPI due to CF. The study will enroll approximately 150 patients who are well-controlled on stable porcine PERT at screening. Being that liprotamase is non-porcine, it mitigates the porcine-associated risks such as supply limitations and the potential for contamination with pig-associated viral or other infectious agents. Additionally, given its stability in the absence of enteric coating, a soluble, drinkable formulation of liprotamase is in development.

Recommendations

The College of Pharmacy does not recommend any changes to the pancreatic enzyme replacement therapy prior authorization criteria at this time.

Utilization Details of Pancreatic Enzymes: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CREON®						
CREON CAP 24000 UNIT	324	75	$617,918.45	$64.66	$1,907.16	25.02%
CREON CAP 12000 UNIT	235	63	$201,123.68	$29.81	$855.85	8.14%
CREON CAP 36000 UNIT	198	50	$444,200.66	$75.74	$2,243.44	17.99%
CREON CAP 6000 UNIT	90	29	$33,026.57	$13.65	$366.96	1.34%
CREON CAP 3000 UNIT	27	9	$6,208.53	$8.48	$229.95	0.25%
SUBTOTAL	**874**	**226**	**$1,302,477.89**	**$51.44**	**$1,490.25**	**52.74%**
ZENPEP®						
ZENPEP CAP 25000 UNIT	94	22	$259,636.83	$95.45	$2,762.09	10.51%
ZENPEP CAP 20000 UNIT	91	24	$161,416.71	$59.78	$1,773.81	6.54%
ZENPEP CAP 15000 UNIT	85	20	$99,678.89	$39.98	$1,172.69	4.04%
ZENPEP CAP 10000 UNIT	59	13	$41,955.16	$25.18	$711.10	1.70%
ZENPEP CAP 5000 UNIT	59	15	$14,684.53	$8.93	$248.89	0.59%
ZENPEP CAP 40000 UNIT	32	13	$114,945.36	$122.28	$3,592.04	4.65%
ZENPEP CAP 3000 UNIT	1	1	$439.16	$17.57	$439.16	0.02%
PANCRELIPASE CAP 5000 UNIT	1	1	$72.01	$3.13	$72.01	0.00%
SUBTOTAL	**422**	**109**	**$692,828.65**	**$56.73**	**$1,641.77**	**28.05%**
PERTZYE®						
PERTZYE CAP 16000 UNIT	195	35	$392,300.06	$68.79	$2,011.80	15.88%
PERTZYE CAP 8000 UNIT	66	16	$47,823.65	$24.90	$724.60	1.94%
SUBTOTAL	**261**	**51**	**$440,123.71**	**$57.73**	**$1,686.30**	**17.82%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
PANCREAZE®						
PANCREAZE CAP 4200 UNIT	25	3	$2,484.61	$4.48	$99.38	0.10%
PANCREAZE CAP 10500 UNIT	8	3	$2,457.08	$10.24	$307.14	0.10%
PANCREAZE CAP 21000 UNIT	7	4	$13,527.06	$67.98	$1,932.44	0.55%
PANCREAZE CAP 16800 UNIT	5	2	$1,915.22	$12.77	$383.04	0.08%
SUBTOTAL	**45**	**12**	**$20,383.97**	**$17.82**	**$452.98**	**0.83%**
VIOKACE®						
VIOKACE TAB 10440 UNIT	8	1	$8,809.61	$36.71	$1,101.20	0.36%
VIOKACE TAB 20880 UNIT	4	1	$5,157.36	$42.98	$1,289.34	0.21%
SUBTOTAL	**12**	**2**	**$13,966.97**	**$38.80**	**$1,163.91**	**0.57%**
TOTAL	**1,614**	**322***	**$2,469,781.19**	**$52.93**	**$1,530.22**	**100%**

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

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 08/2017. Last accessed 09/20/2017.

[2] Chiesi USA, Inc. Digestive Care, Inc. Announces FDA Approval of a 24,000 USP Lipase Units Capsules of Pertzye (pancrelipase) Delayed Release Capsules to Treat Exocrine Pancreatic Insufficiency (EPI) Due to Cystic Fibrosis and Other Conditions. *Market Wired*. Available online at: http://www.marketwired.com/press-release/digestive-care-inc-announces-fda-approval-24000-usp-lipase-units-capsule-pertzyer-pancrelipase-2226235.htm. Issued 07/14/2017. Last accessed 10/10/2017.

[3] Pertzye® Prescribing Information. Digestive Care, Inc. Available online at: https://resources.chiesiusa.com/Pertzye/PERTZYE_PI.pdf. Last revised 07/2017. Last accessed 10/10/2017.

[4] Anthera Pharmaceuticals, Inc. Anthera Pharmaceuticals Announces RESULT Phase 3 Clinical Study of Sollpura will be included in the Cystic Fibrosis Foundation Therapeutics Development Network. *GlobeNewswire*. Available online at: https://globenewswire.com/news-release/2017/07/10/1042001/0/en/Anthera-Pharmaceuticals-Announces-RESULT-Phase-3-Clinical-Study-of-Sollpura-will-be-included-in-the-Cystic-Fibrosis-Foundation-Therapeutics-Development-Network.html. Issued 07/10/2017. Last accessed 09/20/2017.

Appendix U

Industry News and Updates

Oklahoma Health Care Authority
November 2017

Introduction

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

News and Updates[1,2,3]

News:

- **Seamless Trial:** A recent report by the AARP Public Policy Institute looked at longitudinal trends in drug pricing, focusing on changes in the cost of specialty medications between 2006 and 2015. The institute looked at the 101 most commonly used specialty medications and tracked the percentage by which prices increased over the course of nine years. The largest annual increase in the period of 2006 to 2015 was in 2015 and the increase was 9.6%. The report noted that the average 2015 cost for a single specialty medication used on a chronic basis was $52,486, which is slightly less than the median United States household income of $55,775. The U.S. Food and Drug Administration (FDA) is also concerned with the trends reported in the AARP's report. At the Regulatory Affairs Professionals Society's 2017 Regulatory Conference, the FDA commissioner, Dr. Scott Gottlieb, said that drug development is getting costlier and taking longer. One of the issues that Dr. Gottlieb identified was the frontloading of development costs in the early stages, with late-stage development inflation rising slower than early stages. He stated that as a result, fewer new ideas get advanced and drugs that do succeed are priced to reflect the high cost of development. He stated that the agency is focused on efforts to modernize how it collects clinical information, and he discussed the growth of trial designs that avoid the three-stage design for other ways of testing a drug's efficacy by using a combined-phase, or "seamless" trial. Seamless trials use a long, continuous trial to reduce costs, save time, and minimize the number of patients necessary. Dr. Gottlieb noted the usefulness for seamless trials among candidates for cancer therapy.
- **Return on Investment:** A study published in the *Journal of the American Medical Association Internal Medicine* evaluated the research and development (R&D) costs of certain drugs in comparison to their ultimate revenue. According to the study, when it comes to drug pricing, the exorbitant R&D costs are almost immaterial. To figure out what it costs to bring a new drug to market, a team led by Sham Mailankody identified pharmaceutical companies that had only one drug on the market. They then determined when the company first started working on that molecule and added up the company's R&D costs for each year from that point until FDA approval. The R&D costs also include the costs for other drugs that the company was working on that never made it to the market. An example of one of the drugs analyzed was eculizumab, developed by Alexion

Pharmaceuticals. The company started working on the drug in January of 2002 and it was FDA approved in March of 2007. The total R&D costs over that time was $817 million. Since eculizumab was FDA approved, it has brought in $13 billion or a 15-fold return on investment. The drug costs more than $400,000 per year per patient. The sales in the first quarter of 2017 exceeded the total R&D costs for the drug. One caveat is that eculizumab is difficult to manufacture, therefore this is not pure profit following R&D. A spokesperson for Alexion stated that R&D costs really do not capture all the expenses in bringing a drug to market. He also pointed out that "revenues today enable us to find answers tomorrow for some of the most complicated genetic and medical challenges in other rare and ultra-rare diseases that others deem impossible."

- **Abbreviated New Drug Application (ANDA):** The FDA approved 763 generic drug applications in fiscal year 2017, a 17 percent increase from the previous year. According to the Office of Generic Drugs, 70 ANDAs were approved in September 2017.

[1] Salazar D. AARP Highlights Rising Specialty Prices as FDA Looks to Tackle Development Costs, Speed. *Drug Store News*. Available online at: http://www.drugstorenews.com/article/aarp-highlights-rising-specialty-prices-fda-looks-tackle-development-costs-speed?tp=i-H55-Q5U-4UI-6XmxX-1v-6lz-1c-181s-6XmbT-1bNYW8&utm_campaign=Daily&utm_source=Experian&utm_medium=email&cid=17283&mid=96711043. Issued 09/14/2017. Last accessed 09/15/2017.

[2] Wilson FP. What Does ROI Say About Drug Pricing. *MedPage Today®*. Available online at: https://www.medpagetoday.com/PublicHealthPolicy/HealthPolicy/67819. Issued 09/11/2017. Last accessed 09/15/2017.

[3] Fiscal 2017 Ends With Record High in ANDA Approvals. *FDANews*. Available online at: http://www.fdanews.com/articles/183881-fiscal-2017-ends-with-record-high-in-anda-approvals?utm_campaign=Drug%20Daily%20Bulletin&utm_source=hs_email&utm_medium=email&utm_content=57176991&_hsenc=p2ANqtz-8-c6YBURYA9UaeOga9USwOIwxaJ7YmP9bx0OXkg07PWR0llDgBHRMc4_lg8OR2vKT4IHaEiAnFJ3tca6sVILlQIYW1-VB92AZ311pRw419u-HihoM&_hsmi=57176991. Issued 10/10/2017. Last accessed 10/10/2017.

Appendix V

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

FDA NEWS RELEASE

For Immediate Release: September 28th, 2017
FDA approves new treatment for certain advanced or metastatic breast cancers

The U.S. Food and Drug Administration (FDA) approved Verzenio (abemaciclib) to treat adult patients who have hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer that has progressed after taking therapy that alters a patient's hormones (endocrine therapy). Verzenio is approved to be given in combination with an endocrine therapy, called fulvestrant, after the cancer had grown on endocrine therapy. It is also approved to be given on its own, if patients were previously treated with endocrine therapy and chemotherapy after the cancer had metastasized.
Verzenio works by blocking certain molecules (known as cyclin-dependent kinases 4 and 6), involved in promoting the growth of cancer cells. There are two other drugs in this class that are approved for certain patients with breast cancer, palbociclib, approved in February 2015, and ribociclib, approved in March 2017.
Breast cancer is the most common form of cancer in the United States. The National Cancer Institute at the National Institutes of Health estimates approximately 252,710 women will be diagnosed with breast cancer this year, and 40,610 will die of the disease. Approximately 72 percent of patients with breast cancer have tumors that are HR-positive and HER2-negative.
The safety and efficacy of Verzenio in combination with fulvestrant were studied in a randomized trial of 669 patients with HR-positive, HER2-negative breast cancer that had progressed after treatment with endocrine therapy and who had not received chemotherapy once the cancer had metastasized. The study measured the length of time tumors did not grow after treatment (progression-free survival). The median progression-free survival for patients taking Verzenio with fulvestrant was 16.4 months compared to 9.3 months for patients taking placebo with fulvestrant.
The safety and efficacy of Verzenio as a stand-alone treatment were studied in a single-arm trial of 132 patients with HR-positive, HER2-negative breast cancer that had progressed after treatment with endocrine therapy and chemotherapy after the cancer metastasized. The study measured the percent of patients whose tumors completely or partially shrank after treatment (objective response rate). In the study, 19.7 percent of patients taking Verzenio experienced complete or partial shrinkage of their tumors for a median 8.6 months.
Common side effects of Verzenio include diarrhea, neutropenia and leukopenia, nausea, abdominal pain, infections, fatigue, anemia, decreased appetite, vomiting, and headache.
Serious side effects of Verzenio include diarrhea, neutropenia, elevated liver blood tests, and deep venous thrombosis/pulmonary embolism. Women who are pregnant should not take Verzenio because it may cause harm to a developing fetus.
The FDA granted this application Priority Review and Breakthrough Therapy designations.
The FDA granted the approval of Verzenio to Eli Lilly and Company.

Safety Announcements

FDA Drug Safety Communication: A case of hemorrhagic occlusive retinal vasculitis (HORV) following intraocular injections of a compounded triamcinolone, moxifloxacin, and vancomycin formulation (TMV)

[10/03/2017] Introduction
Hemorrhagic occlusive retinal vasculitis (HORV) is a rare, potentially blinding postoperative complication that has been observed in dozens of patients who have received intraocular injections of vancomycin formulations toward the end of otherwise uncomplicated cataract surgeries. The following is a report on a case of HORV following injections of a compounded triamcinolone, moxifloxacin, and vancomycin formulation (TMV).
Adverse Event
FDA received an adverse event report on August 14, 2017, from a physician concerning a patient who was diagnosed postoperatively with bilateral HORV after being administered injections of a compounded TMV

formulation in each eye at the conclusion of cataract surgery procedures that were done two weeks apart. The TMV formulation was compounded by Imprimis Pharmaceuticals, Inc., located in Ledgewood, New Jersey.

Vancomycin-Associated HORV

Many ophthalmologists use intraocular vancomycin during cataract surgery with the intent of preventing postoperative endophthalmitis. The FDA is unaware of any adequately controlled studies demonstrating the safety and efficacy of intraocular vancomycin in preventing endophthalmitis. There is no FDA-approved vancomycin formulation for intraocular injection. The formulation is usually prepared at the surgical site or obtained in advance of surgery from a compounding pharmacy.

The use of intraocular vancomycin has recently been associated with the newly described condition HORV. Characteristics of HORV include a delayed onset (up to three weeks) of sudden painless decreased vision, intraocular inflammation, intraretinal hemorrhage, retinal vasculitis, vascular occlusion, and retinal ischemia. If vancomycin is administered to both eyes, legal blindness is a likely consequence of HORV.

No cases of HORV were reported in a retrospective analysis of medical records of 922 patients (1,541 eyes) who underwent cataract surgeries with intravitreal injections of compounded TMV formulations from November 2013 to December 2015. However, this chart review of non-controlled data is limited in its ability to identify rare events and may not necessarily be generalizable to a larger population who may undergo cataract surgery. The adverse event being reported here serves as a reminder that intraocular administration of vancomycin, including when the vancomycin is one of multiple active ingredients in a compounded drug, can result in HORV.

HORV Warning on FDA-Approved Vancomycin Injection, USP

FDA approved on September 28, 2017, a supplemental New Drug Application (sNDA) that adds a subsection about HORV to the WARNINGS section in the labeling of Vancomycin Injection, USP. The warning states: Hemorrhagic occlusive retinal vasculitis, including permanent loss of vision, occurred in patients receiving intracameral or intravitreal administration of vancomycin during or after cataract surgery. The safety and efficacy of vancomycin administered by the intracameral or the intravitreal route have not been established by adequate and well-controlled trials. Vancomycin is not indicated for prophylaxis of endophthalmitis.

FDA Recommendation

The prophylactic use of intraocular vancomycin, alone or in a compounded drug combining multiple active ingredients, during cataract surgery is generally not recommended because of the risk of HORV.

Current Drug Shortages Index (as of October 31st, 2017):

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

Amino Acids	***Currently in Shortage***
Aminocaproic Acid Injection, USP	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended Release Tablets	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***

Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Folic Acid Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Hydromorphone Hydrochloride (Dilaudid) Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nitrous Oxide, Gas	***Currently in Shortage***
Pantoprazole (Protonix) Powder for Injection	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine (Transderm Scop) Transdermal System Patch	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tolmetin Sodium Tablets, USP	***Currently in Shortage***