OKLAHOMA
Health Care Authority

Drug Utilization Review Board

OHCA Webinar
Wednesday,
May 12, 2021
4:00pm

Please register for the webinar at:
https://zoom.us/webinar/register/WN_RctXaWJVRsClG2uvcRqTyQ
After registering, you will receive a confirmation email
containing information about joining the webinar.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Michyla Adams, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – May 12, 2021

DATE: April 28, 2021

NOTE: In response to COVID-19, the May 2021 DUR Board meeting will be held via OHCA webinar at 4:00pm. Please register for the meeting using the following website address: https://zoom.us/webinar/register/WN_RctXaWJVRsClG2uvcRqTyQ After registering, you will receive a confirmation email containing information about joining the webinar.

Enclosed are the following items related to the May 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/Prenatal Vitamin Utilization Update – Appendix B

Action Item – Vote to Prior Authorize Lyumjev™ (Insulin Lispro-aabc) – Appendix C

Action Item – Vote to Prior Authorize Amondys 45™ (Casimersen), Viltepso® (Viltolarsen), and Vyondys 53™ (Golodirsen) – Appendix D

Action Item – Vote to Prior Authorize Verquvo™ (Vericiguat) – Appendix E

Action Item – Vote to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel) – Appendix F

Action Item – Vote to Prior Authorize Cosela™ (Trilaciclib), Gavreto™ (Pralsetinib), Retevmo® (Selpercatinib), Tabrecta™ (Capmatinib), Tepmetko® (Tepotinib), and Zepzelca™ (Lurbinectedin) – Appendix G

Annual Review of Balversa® (Erdafitinib) and 30-Day Notice to Prior Authorize Cabometyx® (Cabozantinib), Fotivda® (Tivozanib), Jelmyto® (Mitomycin), and Padcev® (Enfortumab Vedotin-ejfv) – Appendix H

Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Gemtesa® (Vibegron) – Appendix I

Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Zilxi® (Minocycline 1.5% Topical Foam) – Appendix J

Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Fetroja® (Cefiderocol) and Kimyrsa™ (Oritavancin) – Appendix K

Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Kynmobi™ (Apomorphine) and Ongentys® (Opicapone) – Appendix L

Annual Review of Alzheimer's Disease Medications – Appendix M

Annual Review of Allergen Immunotherapies – Appendix N

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – May 12, 2021 @ 4:00pm

Oklahoma Health Care Authority (OHCA) Webinar
Please register for the meeting at:
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AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Wilcox

DUR Board Members:	**Telephone Conference Participants**
Dr. Stephen Anderson –	participating via Zoom teleconference
Dr. Jennifer de los Angeles –	participating via Zoom teleconference
Ms. Jennifer Boyett –	participating via Zoom teleconference
Dr. Markita Broyles –	participating via Zoom teleconference
Dr. Theresa Garton –	participating via Zoom teleconference
Dr. Megan Hanner –	participating via Zoom teleconference
Dr. Lynn Mitchell –	participating via Zoom teleconference
Dr. John Muchmore –	participating via Zoom teleconference
Dr. Lee Muñoz –	participating via Zoom teleconference
Dr. James Osborne –	participating via Zoom teleconference

Public Access to Meeting via Zoom:

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Dial: +1-602-753-0140 or +1-669-219-2599
Webinar ID: 936 4044 2965
Passcode: 52923318

Public Comment for Meeting:

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing by visiting www.okhca.org/DUR and completing the Speaker Registration Form. Completed Speaker Registration forms should be submitted to *DURPublicComment@okhca.org*. Forms must be received after the DUR Board agenda has been posted and no later than 24 hours before the meeting.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. April 14, 2021 DUR Minutes – Vote
B. April 14, 2021 DUR Recommendation Memorandum
C. Correspondence

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

4. Update on Medication Coverage Authorization Unit/Prenatal Vitamin Utilization Update – See Appendix B

A. Pharmacy Helpdesk Activity for April 2021
B. Medication Coverage Activity for April 2021
C. Prenatal Vitamin Utilization Update

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

5. Action Item – Vote to Prior Authorize Lyumjev™ (Insulin Lispro-aabc) – See Appendix C

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. News
C. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Amondys 45™ (Casimersen), Viltepso® (Viltolarsen), and Vyondys 53™ (Golodirsen) – See Appendix D

A. Introduction
B. Cost Comparison: Duchenne Muscular Dystrophy (DMD) Exon-Skipping Therapies
C. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Verquvo™ (Vericiguat) – See Appendix E

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel) – See Appendix F

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. Breyanzi® (Lisocabtagene Maraleucel) Product Summary
C. Cost Comparison: Chimeric Antigen Receptor (CAR) T-Cell Therapies for Lymphoma
D. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Cosela™ (Trilaciclib), Gavreto™ (Pralsetinib), Retevmo® (Selpercatinib), Tabrecta™ (Capmatinib), Tepmetko® (Tepotinib), and Zepzelca™ (Lurbinectedin) – See Appendix G

A. New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
B. College of Pharmacy Recommendations

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

10. Annual Review of Balversa® (Erdafitinib) and 30-Day Notice to Prior Authorize Cabometyx® (Cabozantinib), Fotivda® (Tivozanib), Jelmyto® (Mitomycin), and Padcev® (Enfortumab Vedotin-ejfv) – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Balversa® (Erdafitinib)
D. Prior Authorization of Balversa® (Erdafitinib)

E. Market News and Updates
F. Product Summaries
G. College of Pharmacy Recommendations

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

11. Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Gemtesa® (Vibegron) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Bladder Control Medications
C. Prior Authorization of Bladder Control Medications
D. Market News and Updates
E. Gemtesa® (Vibegron) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Bladder Control Medications

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

12. Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Zilxi® (Minocycline 1.5% Topical Foam) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Topical Acne and Rosacea Products
C. Prior Authorization of Topical Acne and Rosacea Products
D. Market News and Updates
E. Zilxi® (Minocycline 1.5% Topical Foam) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Topical Acne and Rosacea Products

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

13. Annual Review of Various Systemic Antibiotics and 30-Day to PA Fetroja® (Cefiderocol) and Kimyrsa™ (Oritavancin) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Various Systemic Antibiotics
C. Prior Authorization of Various Systemic Antibiotics
D. Market News and Updates
E. Fetroja® (Cefiderocol) Product Summary
F. Kimyrsa™ (Oritavancin) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Various Systemic Antibiotics

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

14. Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Kynmobi™ (Apomorphine) and Ongentys® (Opicapone) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of PD Medications
C. Prior Authorization of PD Medications
D. Market News and Updates
E. Kynmobi™ (Apomorphine) Product Summary
F. Ongentys® (Opicapone) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of PD Medications

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

15. Annual Review of Alzheimer's Disease Medications – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Alzheimer's Disease Medications

C. Prior Authorization of Alzheimer's Disease Medications
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Alzheimer's Disease Medications

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

16. Annual Review of Allergen Immunotherapies – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Allergen Immunotherapies
C. Prior Authorization of Allergen Immunotherapies
D. Market News and Updates
E. College of Pharmacy Recommendations

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

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

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

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

A. Annual Review of the SoonerCare Pharmacy Benefit
B. Attention-Deficit/Hyperactivity Disorder (ADHD) and Narcolepsy Medications
C. Atypical Antipsychotic Medications
D. Ophthalmic Anti-Inflammatories
E. Various Special Formulations

**Future product and class reviews subject to change*.

19. Adjournment

NOTE: An analysis of the atypical [Aged, Blind, and Disabled (ABD)] patient subgroup of the Oklahoma Medicaid population has been performed pertaining to all recommendations included in this DUR Board meeting packet to ensure fair and knowledgeable deliberation of the potential impact of the recommendations on this patient population.

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING APRIL 14, 2021

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.	x	
Jennifer de los Angeles, Pharm.D., BCOP	x	
Jennifer Boyett, MHS; PA-C	x	
Markita Broyles, D.Ph.; MBA	x	
Theresa Garton, M.D.	x	
Megan A. Hanner, D.O.	x	
Lynn Mitchell, M.D.; Vice Chairwoman	x	
John Muchmore, M.D.; Ph.D.; Chairman	x	
Lee Muñoz, D.Ph.	x	
James Osborne, Pharm.D.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; DUR Manager	x	
Rebekah Bargewell; Administrative Assistant		x
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Andrew Craig; Database Analyst	x	
Lisa Daniel, Pharm.D.; Pharmacy Resident	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Mark Fuelling; Client Support Analyst		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Katrina Harris, Pharm.D.; Clinical Pharmacist		x
Robert Klatt, Pharm.D.; Clinical Pharmacist	x	
Amy Miller; Operations Coordinator		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Karen O'Neill, Pharm.D.; Clinical Pharmacist		x
Wynn Phung, Pharm.D.; Clinical Pharmacist		x
Leslie Robinson, D.Ph.; Pharmacy PA Coordinator		x
Vickie Sams, CPhT.; Quality/Training Coordinator	x	
Grant H. Skrepnek, Ph.D.; Associate Professor		x
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Devin Wilcox, D.Ph.; Pharmacy Director	x	
Justin Wilson, Pharm.D.; Clinical Pharmacist	x	
PA Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		x
Emily Borders, Pharm.D., BCOP	x	
Sarah Schmidt, Pharm.D., BCPS, BCOP		x
Graduate Students: Matthew Dickson, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): Alicia O'Halloran	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		x
Ellen Buettner, Chief of Staff		x
Kevin Corbett, C.P.A.; Chief Executive Officer		x
Terry Cothran, D.Ph.; Pharmacy Director	x	
Susan Eads, J.D.; Director of Litigation	x	
Michael Herndon, D.O.; Chief Medical Officer		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Paula Root, M.D.; Senior Medical Director	x	
Michelle Tahah, Pharm.D.; Clinical Pharmacist	x	

OTHERS PRESENT:	
Frank Alvarado, Johnson & Johnson	Brent Parker, Merck
Robert Greely, Biogen	Tara McKinley, Otsuka
Leo Pratt, NS Pharma	Porscha Showers, Gilead
Shellie Keast, Mercer	John Omick, Global Blood Therapeutics
Melanie Curlett, Takeda	Audrey Rattan, Alkermes
Matthew Wright, Artia Solutions	Roger Grotzinger, Bristol Myers Squibb
Brian Maves, Pfizer	Brandon Ross, Merck
Mark Kaiser, Otuska	David Prather, Novo Nordisk
Dave Miley, Teva	Kathrin Kucharski, Sarepta
David Poskey, UCB	Nima Nabavi, Amgen
Andrew Delgado, Bristol Myers Squibb	Jean Ritter, Zealand Pharmaceuticals
Burl Beasley, OMES	John Ford, NS Pharma
Marc Parker, Sunovion	Jennifer Shumsky, Little Hercules Foundation
Dana Pipkin, Sarepta	Lindsey Walter, Novartis
Bob Atkins, Biogen	

PRESENT FOR PUBLIC COMMENT:	
Andrew Delgado	Bristol Myers Squibb
Kathrin Kucharski	Sarepta
Leo Pratt	NS Pharma

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA ITEM NO. 11 ANDREW DELGADO
2B: AGENDA ITEM NO. 16 KATHRIN KUCHARSKI
2C: AGENDA ITEM NO. 16 LEO PRATT
ACTION: NONE REQUIRED

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

3A: MARCH 10, 2021 DUR MINUTES – VOTE
3B: MARCH 10, 2021 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore
Dr. Garton moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/SOONERPSYCH PROGRAM UPDATE**

4A: PHARMACY HELPDESK ACTIVITY FOR MARCH 2021
4B: MEDICATION COVERAGE ACTIVITY FOR MARCH 2021
4C: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Nawaz, Dr. Ha

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE BAFIERTAM™ (MONOMETHYL FUMARATE), KESIMPTA® (OFATUMUMAB), AND ZEPOSIA® (OZANIMOD)**

5A: NEW U.S FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Anderson moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE SEVENFACT® [COAGULATION FACTOR VIIA (RECOMBINANT)-JNCW]**

6A: INTRODUCTION
6B: OKLAHOMA HEALTH CARE AUTHORITY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ratterman
Dr. Anderson moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE SOGROYA® (SOMAPACITAN-BECO)**

7A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Wilson
Dr. Garton moved to approve; seconded by Dr. Hanner

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE NYVEPRIA™ (PEGFILGRASTIM-APGF)**

8A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
8B: NYVEPRIA™ (PEGFILGRASTIM-APGF) PRODUCT SUMMARY
8C: COST COMPARISON: PEGFILGRASTIM PRODUCTS
8D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE BARHEMSYS® (AMISULPRIDE)**

9A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
9B: BARHEMSYS® (AMISULPRIDE) PRODUCT SUMMARY
9C: COST COMPARISON: ANTI-EMETICS FOR POSTOPERATIVE NAUSEA AND VOMITING (PONV)
9D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ha
Dr. Anderson moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE ORLADEYO™ (BEROTRALSTAT)

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Broyles moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE BREYANZI® (LISOCABTAGENE MARALEUCEL), MONJUVI® (TAFASITAMAB-CXIX), ROMIDEPSIN 27.5MG/5.5ML VIAL, TECARTUS™ (BREXUCABTAGENE AUTOLEUCEL), AND UKONIQ™ (UMBRALISIB)

11A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND INDICATION(S)

11B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders
Following public comment by the manufacturer of Breyanzi®, Dr. Borders recommended to table the vote to prior authorize Breyanzi® until the next DUR Board meeting in May to allow additional time to review the data presented by the manufacturer
Dr. Broyles moved to approve all recommendations except for Breyanzi® which will be tabled until the May DUR Board meeting; seconded by Dr. Anderson

ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF ANTIHYPERTENSIVE MEDICATIONS

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF ANTIHYPERTENSIVE MEDICATIONS

12C: PRIOR AUTHORIZATION OF ANTIHYPERTENSIVE MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: COLLEGE OF PHARMACY RECOMMENDATIONS

12F: UTILIZATION DETAILS OF ANTIHYPERTENSIVE MEDICATIONS

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF LUNG CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE COSELA™ (TRILACICLIB), GAVRETO™ (PRALSETINIB), RETEVMO® (SELPERCATINIB), TABRECTA™ (CAPMATINIB), TEPMETKO® (TEPOTINIB) AND ZEPZELCA™ (LURBINECTEDIN)

13A: INTRODUCTION

13B: CURRENT PRIOR AUTHORIZATION CRITERIA

13C: UTILIZATION OF LUNG CANCER MEDICATIONS

13D: MARKET NEWS AND UPDATES

13E: PRODUCT SUMMARIES

13F: COLLEGE OF PHARMACY RECOMMENDATIONS

13G: UTILIZATION DETAILS OF LUNG CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Borders
Dr. Broyles moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 14: **ANNUAL REVIEW OF AYVAKIT™ (AVAPRITINIB), BYNFEZIA PEN™ (OCTREOTIDE), AND TAZVERIK® (TAZEMETOSTAT)**

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF AYVAKIT™ (AVAPRITINIB), BYNFEZIA PEN™ (OCTREOTIDE), AND TAZVERIK® (TAZEMETOSTAT)
14C: PRIOR AUTHORIZATION OF AYVAKIT™ (AVAPRITINIB), BYNFEZIA PEN™ (OCTREOTIDE), AND TAZVERIK® (TAZEMETOSTAT)
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **ANNUAL REVIEW OF ANTI-DIABETIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE LYUMJEV™ (INSULIN LISPRO-AABC)**

15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF ANTI-DIABETIC MEDICATIONS
15C: PRIOR AUTHORIZATION OF ANTI-DIABETIC MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: LYUMJEV™ (INSULIN LISPRO-AABC) PRODUCT SUMMARY
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF NON-INSULIN ANTI-DIABETIC MEDICATIONS
15H: UTILIZATION DETAILS OF INSULIN MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **ANNUAL REVIEW OF MUSCULAR DYSTROPHY MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AMONDYS 45™ (CASIMERSEN), VILTEPSO® (VILTOLARSEN), AND VYONDYS 53™ (GOLODIRSEN)**

16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF MUSCULAR DYSTROPHY MEDICATIONS
16C: PRIOR AUTHORIZATION OF MUSCULAR DYSTROPHY MEDICATIONS
16D: MARKET NEWS AND UPDATES
16E: PRODUCT SUMMARIES
16F: COST COMPARISON: DUCHENNE MUSCULAR DYSTROPHY (DMD) EXON-SKIPPING THERAPIES
16G: COLLEGE OF PHARMACY RECOMMENDATIONS
16H: UTILIZATION DETAILS OF MUSCULAR DYSTROPHY MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF HEART FAILURE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VERQUVO™ (VERICIGUAT)**

17A: CURRENT PRIOR AUTHORIZATION CRITERIA
17B: UTILIZATION OF HEART FAILURE MEDICATIONS
17C: PRIOR AUTHORIZATION OF HEART FAILURE MEDICATIONS
17D: MARKET NEWS AND UPDATES
17E: VERQUVO™ (VERICIGUAT) PRODUCT SUMMARY
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF HEART FAILURE MEDICATIONS

Materials included in agenda packet; presented by Dr. Wilson

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Ha

ACTION: NONE REQUIRED

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

19A: ANNUAL REVIEW OF THE PHARMACY BENEFIT
19B: ALZHEIMER'S DISEASE MEDICATIONS
19C: BLADDER CONTROL MEDICATIONS
19D: VARIOUS SYSTEMIC ANTIBIOTICS

**Future business subject to change.*

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: **ADJOURNMENT**

The meeting was adjourned at 5:37pm.

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

Memorandum

Date: April 16, 2021

To: Terry Cothran, D.Ph.
Pharmacy Director
Oklahoma Health Care Authority

From: Michyla Adams, Pharm.D.
Drug Utilization Review (DUR) Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting on April 14, 2021

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Bafiertam™ (Monomethyl Fumarate), Kesimpta® (Ofatumumab), and Zeposia® (Ozanimod)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Bafiertam™ (monomethyl fumarate), Kesimpta® (ofatumumab), and Zeposia® (ozanimod) with the following criteria:

Bafiertam™ (Monomethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no serious active infection(s); and
4. Complete blood counts (CBC), including lymphocyte count, and verification that levels are acceptable to the prescriber; and

5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Intolerable adverse effects associated with a trial of Tecfidera® (dimethyl fumarate) and Vumerity® (diroximel fumarate) that are not expected to occur with Bafiertam™ or a patient-specific, clinically significant reason why trials of Tecfidera® and Vumerity® are not appropriate for the member must be provided; and
7. Verification that CBC, including lymphocyte count, levels are acceptable to the prescriber in addition to compliance will be required for continued approval every 6 months; and
8. A quantity limit of 120 capsules per 30 days will apply.

Kesimpta® (Ofatumumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Member must have had at least 1 relapse in the previous 12 months; and
3. The prescriber must verify hepatitis B virus (HBV) screening is performed before the first dose of Kesimpta® and the member does not have an active HBV infection; and
4. Prescriber must agree to monitor quantitative serum immunoglobulin level before, during, and after discontinuation of treatment with Kesimpta® until B-cell repletion; and
5. Prescriber must verify the member has no active infection(s); and
6. Prescriber must verify the first injection of Kesimpta® will be administered by a health care professional prepared to manage injection-related adverse reactions; and
7. Kesimpta® must be shipped via cold chain supply and the member or member's caregiver must be trained on the proper storage and subcutaneous (sub-Q) administration of Kesimpta®; and
8. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of treatment with Kesimpta®; and
9. Female members of reproductive potential must use an effective method of contraception during treatment and for 6 months after discontinuing Kesimpta®; and
10. A quantity limit of 1 syringe or prefilled Sensoready® Pen per month will apply. Initial dosing titration will be approved for a quantity limit override upon meeting Kesimpta® approval criteria; and
11. Compliance will be checked for continued approval every 6 months.

Zeposia® (Ozanimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Member must not have any contraindications for use of Zeposia® including:

    a. Experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or NYHA Class III/IV HF in the last 6 months; or
    b. Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless member has a functioning pacemaker; or
    c. Severe untreated sleep apnea; or
    d. Concurrent use of monoamine oxidase inhibitors (MAOIs); and
3. Member must not have received prior treatment with alemtuzumab; and
4. Member must not be concurrently using strong CYP2C8 inhibitors/inducers or breast cancer resistance protein (BCRP) inhibitors; and
5. Verification from the prescriber that member has no active infection(s); and
6. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
7. Prescriber must conduct an electrocardiogram (ECG) to determine whether preexisting conduction abnormalities are present before initiating Zeposia®; and
8. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
9. Ophthalmic evaluation and verification that member will be monitored for changes in vision throughout therapy; and
10. Verification from the prescriber that the member has been assessed for medications and conditions that cause reduction in heart rate or AV conduction delays and that the member will be followed with appropriate monitoring per package labeling; and
11. Verification from the prescriber that the member has been assessed for previous confirmed history of chickenpox or vaccination against varicella. Members without a history of chickenpox or varicella vaccination should receive a full course of the varicella vaccine prior to commencing treatment with Zeposia®; and
12. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
13. Female members of reproductive potential must be willing to use effective contraception during treatment with Zeposia® and for at least 3 months after discontinuing treatment; and
14. Member must have had an inadequate response to Gilenya® (fingolimod) or a patient-specific, clinically significant reason why fingolimod is not appropriate for the member must be provided; and
15. Compliance will be checked for continued approval every 6 months; and
16. A quantity limit of 30 capsules per 30 days will apply.

Recommendation 3: Vote to Prior Authorize Sevenfact® [Coagulation Factor VIIa (Recombinant)-jncw]

MOTION CARRIED by unanimous approval.

The Oklahoma Health Care Authority recommends the prior authorization of Sevenfact® [coagulation factor VIIa (recombinant)-jncw] with the following criteria:

Sevenfact® [Coagulation Factor VIIa (Recombinant)-jncw] Approval Criteria:

1. An FDA approved diagnosis; and
2. Sevenfact® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

Recommendation 4: Vote to Prior Authorize Sogroya® (Somapacitan-beco)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Sogroya® (somapacitan-beco) into Tier-2 of the growth hormone products Product Based Prior Authorization (PBPA) category with the following criteria:

Sogroya® (Somapacitan-beco) Approval Criteria:

1. Member must have a confirmed diagnosis of adult growth hormone deficiency (GHD) confirmed by 1 of the following:
   a. Insulin tolerance test (ITT) or glucagon test with a peak growth hormone (GH) response <3ng/mL; or
   b. ≥3 pituitary hormone deficiencies and insulin like growth factor-1 (IGF-1) standard deviation score (SDS) <-2.0; and
2. Member must be 18 years of age or older; and
3. Sogroya® must be prescribed by an endocrinologist; and
4. Member's baseline IGF-1 level and SDS must be provided; and
5. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use all Tier-1 product(s) must be provided; and
6. Prescriber must verify the member does not have active malignancy or active proliferative or severe non-proliferative diabetic retinopathy; and
7. Prescriber must verify the member has been counseled on proper administration and storage of Sogroya®; and
8. Approval quantity will be based on the FDA approved dosing in accordance with the Sogroya® *Prescribing Information*; and
9. Initial approvals will be for the duration of 6 months. For additional approval consideration, compliance will be evaluated and the prescriber must verify the member is responding well to treatment as

demonstrated by a reduction in truncal fat percentage or normalization of IGF-1 level (IGF-1 SDS of -0.5 to 1.75); and

10. A maximum approved dose of 8mg per week will apply.

Growth Hormone Products	
Tier-1*	**Tier-2**
Genotropin® (Pfizer) - Cartridge, MiniQuick	**Humatrope®** (Eli Lilly) - Vials, Cartridge Kits
	Norditropin® (NovoNordisk) - FlexPro® Pens
	Nutropin® and Nutropin AQ® (Genentech) - Vials, Pen Cartridge, NuSpin®
	Omnitrope® (Sandoz) - Vials, Cartridge
	Saizen® (EMD Serono) - Vials, click.easy®
	†Serostim® (EMD Serono) - Vials
	†Sogroya® (somapacitan-beco) (NovoNordisk) - Pens
	Zomacton® and Zoma-Jet® (Ferring) - Vials, Injection Device
	†Zorbtive® (EMD Serono) - Vials

*Supplementally rebated product(s); 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).
†Additional approval criteria applies.
All products, other than Sogroya®, contain the identical 191 amino acid sequence found in pituitary-derived human growth hormone (hGH). For Sogroya®, 1 amino acid has been substituted and linked to an albumin-binding side chain.

Recommendation 5: Vote to Prior Authorize Nyvepria™ (Pegfilgrastim-apgf)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Nyvepria™ (pegfilgrastim-apgf), removing the prior authorization for Ziextenzo® (pegfilgrastim-bmez) based on net costs, and updating the current pegfilgrastim approval criteria with the following changes shown in red:

Fulphila® (Pegfilgrastim-jmdb), Nyvepria™ (Pegfilgrastim-apgf), and Udenyca® (Pegfilgrastim-cbqv)~~, Ziextenzo® (Pegfilgrastim-bmez)~~ Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Granix® (tbo-filgrastim), Neulasta® (pegfilgrastim), Neupogen® (filgrastim), Zarxio® (filgrastim-sndz), or Ziextenzo® (pegfilgrastim-bmez) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Additionally, the College of Pharmacy recommends removing the prior authorization for Granix® (tbo-filgrastim) and Zarxio® (filgrastim-sndz) based on net costs and updating the current filgrastim approval criteria with the following changes shown in red:

~~**Granix® (Tbo-filgrastim),**~~ **Nivestym® (Filgrastim-aafi)**~~**, and Zarxio® (Filgrastim-sndz)**~~ **Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Granix® (tbo-filgrastim), Neupogen® (filgrastim), or Zarxio® (filgrastim-sndz) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Recommendation 6: Vote to Prior Authorize Barhemsys® (Amisulpride)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Barhemsys® (amisulpride) with the following criteria:

Barhemsys® (Amisulpride) Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an anti-emetic of a different class; or
   b. Treatment of PONV in members who have received anti-emetic prophylaxis with an agent of a different class or who have not received prophylaxis; and
2. Member must be 18 years of age or older; and
3. Member must not have received a preoperative dopamine-2 (D_2) antagonist (e.g., metoclopramide); and
4. A patient-specific, clinically significant reason why the member cannot use other cost-effective therapeutic alternatives for the prevention or treatment of PONV (e.g. ondansetron, dexamethasone) must be provided.

Recommendation 7: Vote to Prior Authorize Orladeyo™ (Berotralstat)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Orladeyo™ (berotralstat) and recommends updating the Cinryze® (C1 esterase inhibitor), Haegarda® (C1 esterase inhibitor), and Takhzyro® (lanadelumab-flyo) approval

criteria to be consistent with the current treatment guidelines with the following criteria (changes and additions noted in red):

Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), Orladeyo™ (Berotralstat), and Takhzyro® (Lanadelumab-flyo) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
4. ~~History of at least 1 or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or 3 or more emergency medical treatments per year; or~~ Based on HAE attack frequency, attack severity, comorbid conditions, and member's access to emergent treatment, the prescriber has determined long-term prophylaxis is appropriate for the member; or
5. Approval consideration will be given if the member has a recent hospitalization for a severe episode of angioedema; and
6. Authorization of Cinryze® or Haegarda® will also require a patient-specific, clinically significant reason why the member cannot use Orladeyo™; and
7. Authorization of Takhzyro® (lanadelumab-flyo) will also require a patient-specific, clinically significant reason why the member cannot use Cinryze®, Haegarda®, or Orladeyo™; and
8. Cinryze® Dosing:
    a. The recommended dose of Cinryze® is 1,000 units intravenously (IV) every 3 to 4 days, approximately 2 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 health care provider; members can be taught by their health care provider to self-administer Cinryze® IV; and
    c. A quantity limit of 8,000 units per month will apply (i.e., 2 treatments per week or 8 treatments per 28 days); or
9. Haegarda® Dosing:
    a. The recommended dose of Haegarda® is 60 IU/kg subcutaneously (sub-Q) twice weekly; and
    b. 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
    c. A quantity limit of 2 treatments per week or 8 treatments per 28 days will apply; or
10. Orladeyo™ Dosing:
    a. The recommended dose of Orladeyo™ is 150mg by mouth once daily; and
    b. A quantity limit of 28 capsules per 28 days will apply; or

11. Takhzyro® Dosing:
    a. The recommended dose of Takhzyro® is 300mg sub-Q every 2 weeks (dosing every 4 weeks may be considered in some members); and
    b. Prescriber must verify member or caregiver has been trained by a health care professional on proper storage and sub-Q administration of Takhzyro®; and
    c. A quantity limit of (2) 300mg/2mL vials per 28 days will apply.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Berinert® (C1 esterase inhibitor), Firazyr® (icatibant), Kalbitor® (ecallantide), and Ruconest® (C1 esterase inhibitor) based on net costs with the following criteria (changes noted in red):

Berinert® (C1 Esterase Inhibitor), Firazyr® (Icatibant), Kalbitor® (Ecallantide), and Ruconest® (C1 Esterase Inhibitor) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for the *treatment* of acute attacks of HAE; and
3. For authorization consideration of Firazyr® (icatibant) or Kalbitor® (ecallantide), a patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor) ~~and Firazyr® (icatibant)~~ must be provided; or
4. For authorization consideration of Ruconest® (C1 esterase inhibitor), a patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor), Firazyr® (icatibant), or Kalbitor® (ecallantide) must be provided.

Recommendation 8: Vote to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel), Monjuvi® (Tafasitamab-cxix), Romidepsin 27.5mg/5.5mL Vial, Tecartus™ (Brexucabtagene Autoleucel), and Ukoniq™ (Umbralisib)

MOTION TABLED on the following recommendations for Breyanzi® (lisocabtagene maraleucel); the vote to prior authorize Breyanzi® (lisocabtagene maraleucel) will be a May action item.

The College of Pharmacy recommends the prior authorization of Breyanzi® with the following criteria, including an update based on net cost in comparison to other available chimeric antigen receptor (CAR) T-cell therapies indicated for large B-cell lymphoma (items shown in red are changes from what was included in the March 2021 DUR Board packet):

Breyanzi® (Lisocabtagene Maraleucel) Approval Criteria [Lymphoma Diagnosis]:

1. Diagnosis of large B-cell lymphoma; and
2. Relapsed or refractory disease; and
3. Member must have received at least 2 lines of systemic therapy; and

4. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategy (REMS) requirements; and
5. A patient-specific, clinically significant reason why Yescarta® (axicabtagene) or Kymriah® (tisagenlecleucel) is not appropriate for the member must be provided.

MOTION CARRIED by unanimous approval on all of the following recommendations for Monjuvi® (tafasitamab-cxix), Tecartus™ (brexucabtagene autoleucel), Ukoniq™ (umbralisib), romidepsin 27.5mg/5.5mL vial, Opdivo® (nivolumab), Tazverik® (tazemetostat), Xalkori® (crizotinib), and Yescarta® (axicabtagene ciloleucel).

The College of Pharmacy also recommends the prior authorization of Monjuvi® (tafasitamab-cxix), Tecartus™ (brexucabtagene autoleucel), and Ukoniq™ (umbralisib) with the following criteria (shown in red):

Monjuvi® (Tafasitamab-cxix) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. Diagnosis of DLBCL in adults; and
2. Relapsed or refractory disease; and
3. Used in combination with lenalidomide.

Tecartus™ (Brexucabtagene Autoleucel) Approval Criteria [Lymphoma Diagnosis]:

1. Diagnosis of mantle cell lymphoma; and
2. Relapsed or refractory disease; and
3. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategy (REMS) requirements.

Ukoniq™ (Umbralisib) Approval Criteria [Marginal Zone Lymphoma (MZL) Diagnosis]:

1. Diagnosis of MZL; and
2. Relapsed or refractory disease; and
3. Member must have received at least 1 prior anti-CD20-based regimen.

Ukoniq™ (Umbralisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Diagnosis of FL; and
2. Relapsed or refractory disease; and
3. Member must have received at least 3 prior lines of systemic therapy.

Additionally, the College of Pharmacy recommends the prior authorization of romidepsin 27.5mg/5.5mL vial with the same criteria as the Istodax® (romidepsin) approval criteria (changes noted in red):

Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Finally, the College of Pharmacy recommends updating the Opdivo® (nivolumab), Tazverik® (tazemetostat), Xalkori® (crizotinib), and Yescarta® (axicabtagene ciloleucel) approval criteria based on recent FDA approvals (changes and new criteria noted in red; only criteria with updates are listed):

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

1. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
2. Used in 1 of the following settings:
    a. For nivolumab monotherapy:
        i. Diagnosis of relapsed or surgically unresectable stage IV disease; and
        ii. Failed prior therapy with 1 of the following medications:
            1. Sunitinib; or
            2. Sorafenib; or
            3. Pazopanib; or
            4. Axitinib; or
    b. For nivolumab use in combination with ipilimumab:

i. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; or

c. For nivolumab use in combination with cabozantinib:

i. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with advanced RCC; and

3. Dose as follows:
   a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
   b. In combination with ipilimumab: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks thereafter.

Tazverik® (Tazemetostat) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Treatment of adult members with relapsed/refractory disease; and
2. *EZH2* mutation detected; and
3. Member must have received 2 lines of therapy or as subsequent therapy with no satisfactory alternative treatment options.

Xalkori® (Crizotinib) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL) Diagnosis]:

1. Members 1 to 21 years of age:
   a. Diagnosis of systemic ALCL that is anaplastic lymphoma kinase (ALK)-positive; and
   b. Relapsed or refractory disease; or
2. Members older than 21 years of age:
   a. Diagnosis of systemic ALCL that is ALK-positive; and
   b. Second-line or initial palliative intent therapy and subsequent therapy.

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

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

Recommendation 9: Annual Review of Antihypertensive Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends moving all strengths of candesartan tablets except the 32mg from Tier-2 to Tier-1 of the Antihypertensive Medications PBPA category based on net costs (changes shown in red):

Angiotensin Receptor Blockers (ARBs) and ARB Combination Products		
Tier-1	**Tier-2**	**Special PA**
candesartan (Atacand®)*	candesartan **32mg** (Atacand®)	azilsartan (Edarbi®)
irbesartan (Avapro®)	olmesartan/amlodipine/HCTZ (Tribenzor®)	azilsartan/chlorthalidone (Edarbyclor®)
irbesartan/HCTZ (Avalide®)	telmisartan/HCTZ (Micardis® HCT)	candesartan/HCTZ (Atacand® HCT)
losartan (Cozaar®)		eprosartan (Teveten®)
losartan/HCTZ (Hyzaar®)		eprosartan/HCTZ (Teveten® HCT)
olmesartan (Benicar®)		telmisartan/amlodipine (Twynsta®)
olmesartan/amlodipine (Azor®)		
olmesartan/HCTZ (Benicar HCT®)		
telmisartan (Micardis®)		
valsartan (Diovan®)		
valsartan/amlodipine (Exforge®)		
valsartan/amlodipine/HCTZ (Exforge® HCT)		
valsartan/HCTZ (Diovan HCT®)		

***All strengths other than 32mg.**
HCTZ = hydrochlorothiazide

Recommendation 10: Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Cosela™ (Trilaciclib), Gavreto™ (Pralsetinib), Retevmo® (Selpercatinib), Tabrecta™ (Capmatinib), Tepmetko® (Tepotinib), and Zepzelca™ (Lurbinectedin)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik® (Tazemetostat)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Anti-Diabetic Medications and 30-Day Notice to Prior Authorize Lyumjev™ (Insulin Lispro-aabc)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Muscular Dystrophy Medications and 30-Day Notice to Prior Authorize Amondys 45™ (Casimersen), Viltepso® (Viltolarsen), and Vyondys 53™ (Golodirsen)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Heart Failure (HF) Medications and 30-Day Notice to Prior Authorize Verquvo™ (Vericiguat)

NO ACTION REQUIRED.

Recommendation 15: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 16: Future Business

NO ACTION REQUIRED.

Parent Project Muscular Dystrophy
JOIN THE FIGHT. END DUCHENNE.

April 12, 2021

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

To Whom It May Concern,

On behalf of Parent Project Muscular Dystrophy (PPMD) and Americans who live with the devastating diagnosis of Duchenne muscular dystrophy, we are writing today to urge you to support coverage for access to FDA approved therapies aimed at treating Duchenne muscular dystrophy, including EXONDYS 51, VYONDYS 53, VILTEPSO, and AMONDYS 53. **PPMD believes therapies for Duchenne should never be restricted for access based on age, function, or stage of disease.** Strict requirements for prior authorization and reauthorization should not limit access for patients in dire need of these therapies. In a slow, progressive, debilitating disease like Duchenne, every day marks another day of muscle cell death, patients should be able to try these medications without delay and be monitored over time to determine if their progression of disease has been slowed, the sole purpose of these FDA approved therapies. PPMD believes that patients should be afforded the right to start treatment if issued a prescription in consultation with their Duchenne medical provider.

Parent Project Muscular Dystrophy (PPMD) is the nation's leading patient advocacy organization dedicated to ending Duchenne. As you may know, Duchenne muscular dystrophy is a universally fatal, genetic disorder that affects approximately 1 in 5,000 live male births. People with Duchenne face a relentless deterioration of muscle strength leading to loss of mobility followed by severe cardiac and respiratory compromise in early adulthood. There is no escape.

Notwithstanding rising investments in research and development following the 1986 discovery of the Duchenne gene and the protein it specifies, there had been no FDA approved therapy to treat the underlying cause of Duchenne prior to September 2016 when the FDA approved market authorization for EXONDYS 51[1]. Following that, the Duchenne community enthusiastically celebrated FDA approvals of Emflaza[2] (February 9, 2017), VYONDYS 53[3] (December 12, 2019) and more recently VILTEPSO[4] (August 2020) and AMONDYS 45[20](February 2020). The fact that all dystrophin restoration therapies were advanced under the agency's accelerated approval pathway is a clear indication of the **high unmet medical need** in Duchenne.

The FDA package label inserts for EXONDYS 51[5], VYONDYS 53[6], VILTEPSO[7], and AMONDYS 45[20] provided no restriction on administrating this therapy based on age or disease progression. We strongly recommend coverage for EXONDYS 51, VYONDYS 53, VILTEPSO, or AMONDYS 45 for all patients who have a confirmed genetic mutation amenable to therapy and have been issued a prescription by a treating physician. This would be in agreement with the Medicaid Drug Rebate Program Notice - For State Technical Contacts (Release No. 185) which states "as with any other drug, if the drug is labeled by a manufacturer that has signed a Medicaid National Drug Rebate Agreement, and the drug meets the definition of covered outpatient drug, then the drug is covered by the Medicaid Drug Rebate Program (MDRP) and is to be covered by state Medicaid programs" [8].

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Parent Project Muscular Dystrophy JOIN THE FIGHT. END DUCHENNE.

PPMD supports all therapy development in an independent and objective manner as our mission dictates. Our work has included an emphasis in recent years on patient-focused drug development strategies as the Duchenne therapy pipeline has become more robust. One of our efforts included a rigorous study[9] on community preferences where our team, supported by Dr. John Bridges of Johns Hopkins, found that caregivers are willing to accept risk and uncertainty when balanced with non-curative slowing or stopping of the progression of muscle weakness, even absent improvement in lifespan. Protection of muscle function, including muscle for pulmonary and cardiac function[10] are the highest priorities for patients. These preference findings are important both for regulatory review and for determining the value of a treatment for a health plan beneficiary.

We recommend you carefully consider all this information in evaluating coverage of all Duchenne therapies approved by FDA.

About Duchenne

Duchenne muscular dystrophy is a fatal genetic disorder caused by mutations in the dystrophin gene and characterized by the progressive loss of skeletal muscle and degeneration, primarily in boys. It affects one out of 5000 live male births in the US [11,12.] The primary symptoms of Duchenne muscular dystrophy are caused by a lack of dystrophin in the muscle. Children with Duchenne lose the ability to walk independently and most become reliant on wheelchairs for mobility by the age of 13[13]. Most individuals with Duchenne experience serious respiratory, orthopedic, and cardiac complications. By the age of 18, the majority of patients require ventilation support at night[14]. The average life expectancy is approximately 25 years of age, with respiratory complications and cardiomyopathy being common causes of death[14]. Dystrophin is located beneath the sarcolemma, and functions to connect the subsarcolemmal cytoskeleton to the sarcolemma. A loss of dystrophin in muscle results in inflammation, muscle degeneration and replacement of muscle with fibroadipose (fat and fibrotic) tissue and muscle cell death[15].

EXONDYS 51, VYONDYS 53, VILTEPSO, AMONDYS 45

The data contained in the NDA submissions for **EXONDYS 51[16], VYONDYS 53[17], and VILTEPSO[18], and AMONDYS 45[19]** have met the standard for accelerated approval under 21 CFR 314.510 based on the surrogate endpoint of increased dystrophin protein production, with the FDA concluding that this surrogate is *reasonably likely to predict* clinical benefit. The goal of these therapies is to slow the progression of the disease, which can be monitored through regular outcome and functional testing. We believe the totality of evidence presented by all sponsors to the FDA provide enough reason to believe these therapies are likely to benefit the majority of amenable patients, and through their own health care providers the ability to assess the potential effect and exercise judgment based on the benefit-risk profile.

Given the high unmet medical need and identified preferences of the Duchenne community, PPMD strongly believes that the data supporting approvals of **EXONDYS 51, VYONDYS 53, VILTEPSO, and AMONDYS 45** are sufficient to warrant coverage for all amendable patients as the post-approval studies are conducted to further confirm clinical benefit in real world settings.

We thank you for your dedication to the wellbeing of patients and for all you do.

Sincerely,

Pat Furlong
President & CEO
Parent Project Muscular Dystrophy

Ryan Fischer
Chief Advocacy Officer
Parent Project Muscular Dystrophy

References

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[3] FDA grants accelerated approval to first targeted treatment for rare Duchenne muscular dystrophy mutation (VYONDYS 53)https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation

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[7] VILTEPSO FDA Label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212154s000lbl.pdf

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[16] *Jerry R. Mendell, MD,1,2,3 Nathalie Goemans, MD, PhD,4 Linda P. Lowes, PhD,1,3 Lindsay N. Alfano, PT,1,3 Katherine Berry, PT,1,3 James Shao, MS,5 Edward M. Kaye, MD,5 and Eugenio Mercuri, MD, PhD,6 for the Eteplirsen Study Group and Telethon Foundation DMD Italian Network*
[17] *Cirak, Sebahattin, et al. "Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study." The Lancet 378.9791 (2011): 595-605.*
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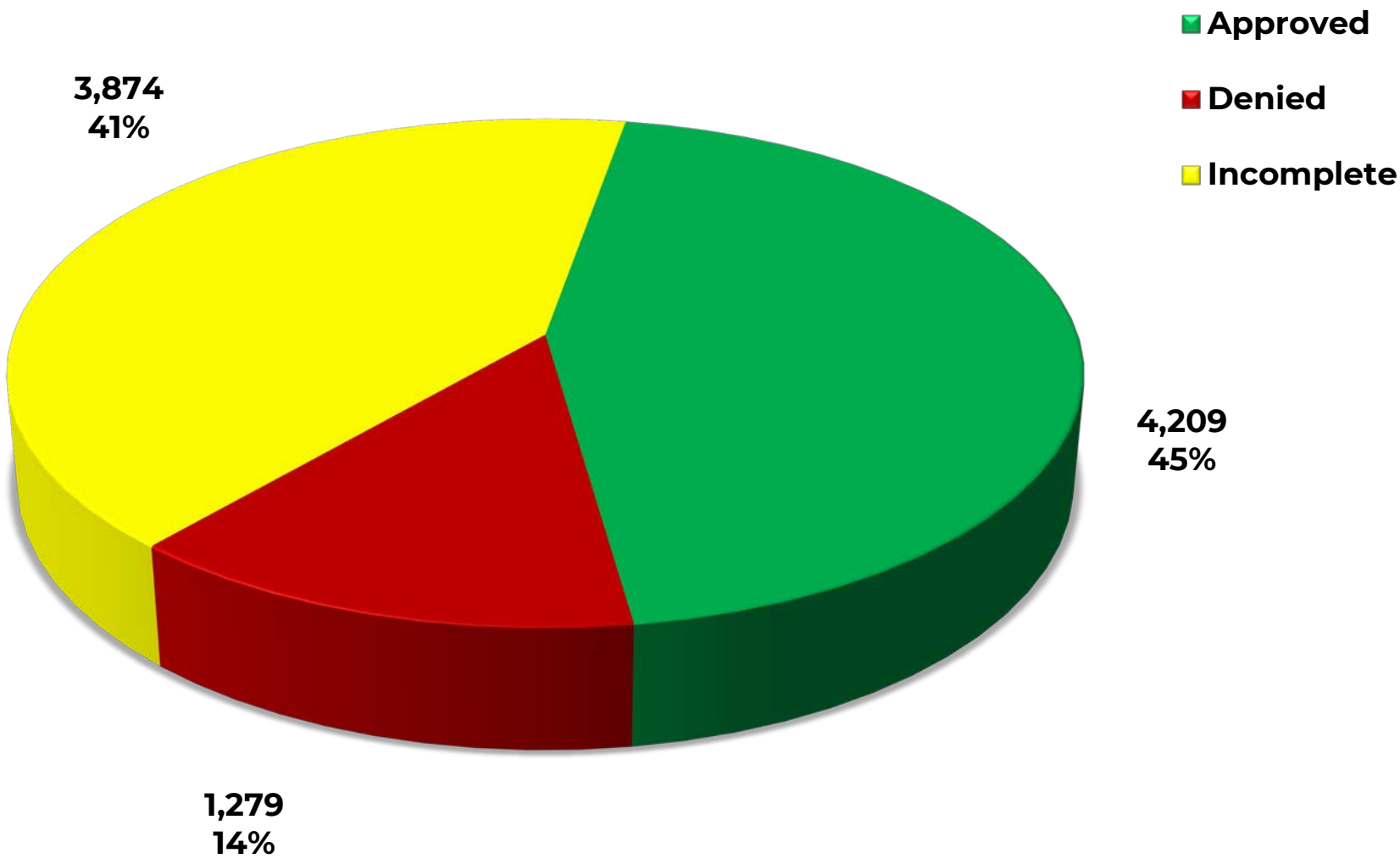
[19] *Poster Presented at the World Muscle Society Virtual Congress September 28−October 2, 2020 http://join.parentprojectmd.org/amondysposter (publication pending)*
[20] *AMONDYS 45 FDA Label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213026lbl.pdf*

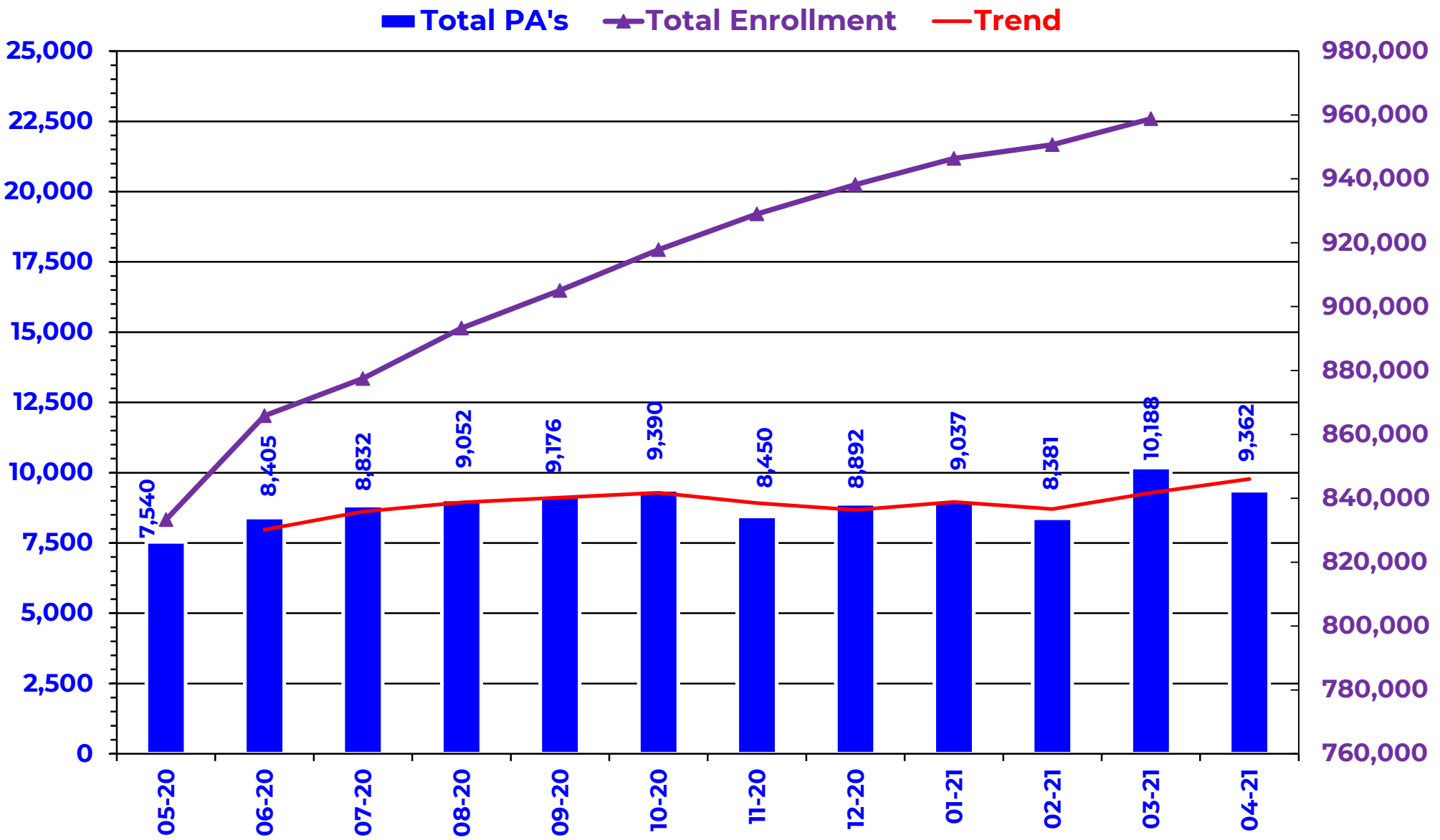
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: APRIL 2021



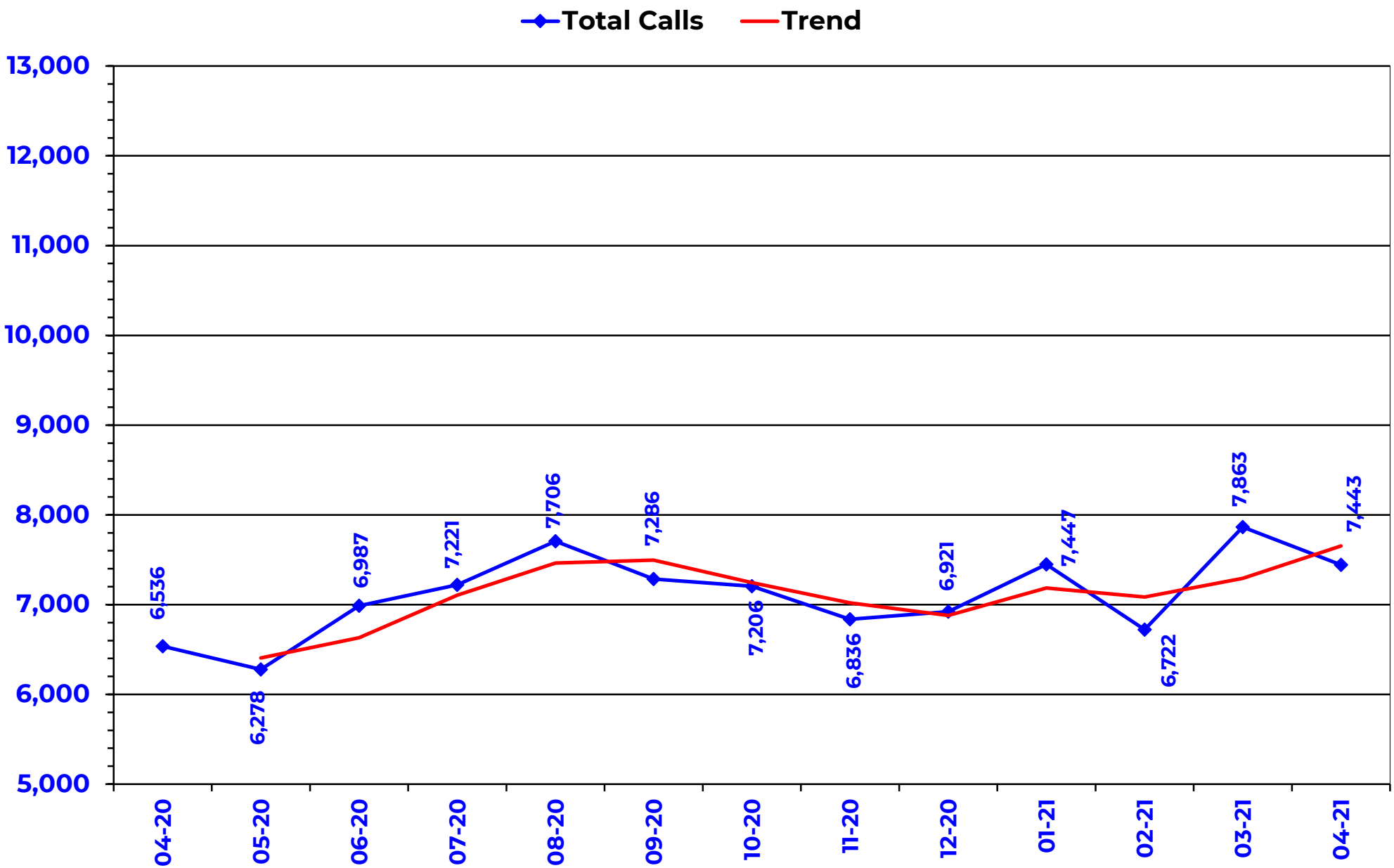
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: APRIL 2020 – APRIL 2021



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
APRIL 2020 – APRIL 2021



Prior Authorization Activity
4/1/2021 Through 4/30/2021

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	52	11	4	37	337
Analgesic - NonNarcotic	16	0	2	14	0
Analgesic, Narcotic	240	97	32	111	165
Antiasthma	67	19	16	32	217
Antibiotic	42	23	0	19	263
Anticonvulsant	189	80	14	95	342
Antidepressant	188	35	26	127	331
Antidiabetic	447	141	69	237	356
Antihistamine	53	12	14	27	290
Antimigraine	286	46	113	127	221
Antineoplastic	137	98	8	31	176
Antiulcers	80	13	16	51	131
Anxiolytic	21	0	2	19	0
Atypical Antipsychotics	311	122	42	147	339
Biologics	170	77	28	65	264
Bladder Control	42	6	15	21	319
Blood Thinners	375	224	24	127	341
Botox	63	41	15	7	308
Buprenorphine Medications	61	17	3	41	70
Cardiovascular	52	15	8	29	340
Chronic Obstructive Pulmonary Disease	179	27	46	106	341
Constipation/Diarrhea Medications	150	35	42	73	243
Contraceptive	30	12	5	13	333
Dermatological	421	123	109	189	160
Diabetic Supplies	862	470	82	310	267
Diuretic	14	9	0	5	321
Endocrine & Metabolic Drugs	84	39	9	36	164
Erythropoietin Stimulating Agents	26	17	2	7	103
Fish Oils	16	4	3	9	358
Gastrointestinal Agents	146	36	37	73	193
Genitourinary Agents	14	3	5	6	288
Glaucoma	13	5	0	8	157
Growth Hormones	109	78	8	23	152
Hematopoietic Agents	23	11	1	11	197
Hepatitis C	157	86	19	52	10
HFA Rescue Inhalers	12	1	2	9	58
Insomnia	74	4	18	52	154
Insulin	133	52	9	72	351
Miscellaneous Antibiotics	13	1	3	9	15
Multiple Sclerosis	69	32	9	28	219
Muscle Relaxant	28	3	10	15	156

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Nasal Allergy	119	15	25	79	117
Neurological Agents	120	40	18	62	249
Neuromuscular Agents	11	6	0	5	219
NSAIDs	31	2	8	21	181
Ocular Allergy	24	0	5	19	0
Ophthalmic	15	1	4	10	358
Ophthalmic Anti-infectives	20	3	2	15	138
Ophthalmic Corticosteroid	20	4	0	16	358
Osteoporosis	29	8	8	13	296
Other*	283	60	63	160	272
Otic Antibiotic	20	0	2	18	0
Pediculicide	17	3	0	14	36
Respiratory Agents	38	23	0	15	250
Statins	33	4	10	19	244
Stimulant	829	387	87	355	351
Testosterone	80	22	17	41	329
Thyroid	10	5	1	4	315
Topical Antifungal	27	3	5	19	58
Topical Corticosteroids	72	0	56	16	0
Vitamin	58	22	21	15	192
Pharmacotherapy	69	62	0	7	238
Emergency PAs	0	0	0	0	
Total	**7,390**	**2,795**	**1,202**	**3,393**	
Overrides					
Brand	43	24	3	16	339
Compound	8	6	0	2	47
Diabetic Supplies	14	11	0	3	193
Dosage Change	370	352	1	17	12
High Dose	4	3	0	1	265
Ingredient Duplication	2	2	0	0	5
Lost/Broken Rx	102	97	1	4	16
MAT Override	237	172	2	63	65
NDC vs. Age	337	214	26	97	242
NDC vs. Sex	6	4	1	1	69
Nursing Home Issue	30	26	0	4	20
Opioid MME Limit	119	42	7	70	126
Opioid Quantity	39	28	3	8	153
Other*	66	58	0	8	13
Quantity vs. Days Supply	544	332	33	179	237
Step Therapy Exception	2	1	0	1	355
Stolen	2	2	0	0	11
Third Brand Request	26	23	0	3	16
Overrides Total	**1,972**	**1,414**	**77**	**481**	
Total Regular PAs + Overrides	**9,362**	**4,209**	**1,279**	**3,874**	

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

Denial Reasons	
Unable to verify required trials.	3,254
Does not meet established criteria.	1,304
Lack required information to process request.	589
Other PA Activity	
Duplicate Requests	967
Letters	16,189
No Process	4
Changes to existing PAs	706
Helpdesk Initiated Prior Authorizations	783
PAs Missing Information	1

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

Prenatal Vitamin Utilization Update

Oklahoma Health Care Authority
May 2021

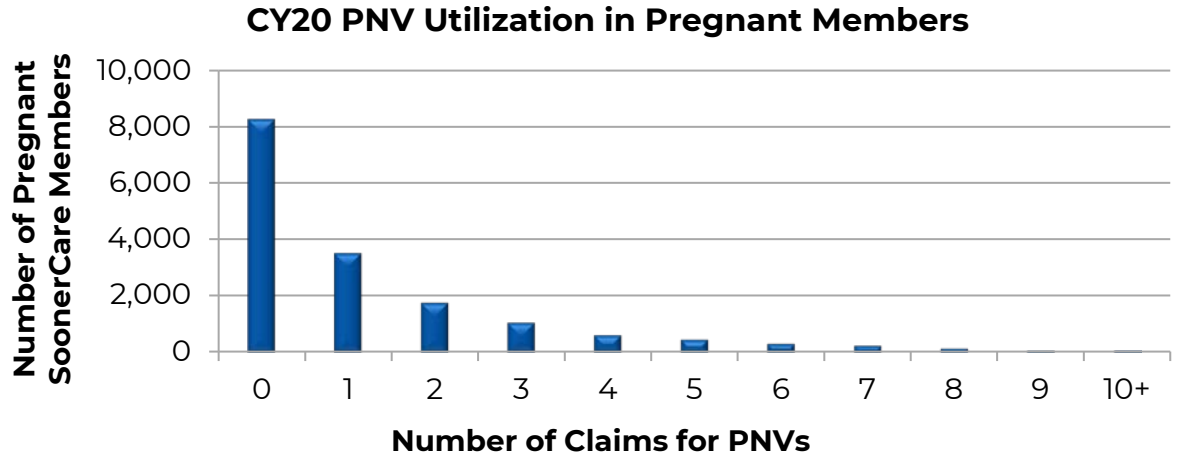
Introduction[1,2,3]

The use of prenatal vitamins (PNVs) plays a major role in optimal pregnancy outcomes. Deficiencies in folic acid, iron, calcium, and vitamin D can lead to an array of adverse outcomes that can affect both the mother and baby. The increased risk of neural tube defects due to folic acid deficiency has been well documented in the literature. Iron deficiency is the second most common cause of anemia in pregnancy, and several large studies have found correlations between maternal anemia and the risk of preterm birth and low birth weight. Insufficient calcium has been linked to the development of maternal hypertension, which can lead to maternal mortality, fetal growth restriction, and preterm birth. Vitamin D deficiency can also lead to pre-eclampsia and increase the risk of preterm birth and small-for-gestational age. The role of PNVs in reducing these possible outcomes cannot be understated.

The College of Pharmacy and the Oklahoma Health Care Authority (OHCA) are engaged in an ongoing effort to increase PNV utilization among pregnant SoonerCare members. PNVs currently have a $0 copay and do not count toward the monthly prescription limit. Prescribers also have the option to select from 35 different PNVs that are covered without a prior authorization (PA). In June 2020, prescribers and pharmacies received an educational outreach addressing the concerning decrease in PNV utilization in pregnant SoonerCare members. The educational outreach highlighted SoonerCare's preferred PNVs and included NDC numbers to encourage increased prescribing of PNVs. The College of Pharmacy also incorporates prenatal education into its workflow to increase PNV utilization. When a PA for any non-PNV medication is received for a member in the Soon-To-Be-Sooners (STBS) program, the member's claims history is reviewed for PNV paid claims. If the member does not have a paid claim for a PNV, a reminder is included in the PA response to the prescriber and the pharmacy. The STBS program began in April 2008 and provides health care benefits for pregnancy-related medical services for pregnant women who would not otherwise qualify for SoonerCare benefits due to their citizenship status. There is a similar program, the STBS-Maintenance (STBS-M) program, which began in 2014 to provide health care benefits for pregnancy-related medical services for pregnant women who do not otherwise qualify for SoonerCare; PAs for a

member in the STBS-M program are evaluated in a similar manner to review for PNV utilization.

Utilization of PNV: Calendar Year 2020 (CY20)



In CY20, there was a total of 27,034 members with an outcome of delivery, based on mother's paid claims with delivery ICD-10 diagnosis codes, which may include non-live births. Mothers with multiple delivery ICD-10 diagnosis codes occurring on multiple dates were only included once. In CY20, only 31% of these members had at least 1 claim for a PNV. Of the 8,244 pregnant members that received a PNV in CY20, 64% of these members had only 1 to 2 fills of a PNV. Although preferred PNVs may be filled for greater than a 30-day supply, this number is very concerning since the maximum benefits of PNVs requires continued use throughout pregnancy. However, it is important to note that PNV utilization may be falsely low due to the large number of over-the-counter (OTC) products available. Data for the use of OTC products in SoonerCare members is not obtainable and is not included in this analysis.

Recommendations

Based on the low percentage of pregnant members utilizing PNV in CY20, further education efforts are warranted. The College of Pharmacy will continue to promote PNV use in pregnant members by continuing educational outreach initiatives through prescriber letters, pharmacy fax blasts, provider and member newsletters, and other platforms as appropriate.

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Appendix C

Vote to Prior Authorize Lyumjev™ (Insulin Lispro-aabc)

Oklahoma Health Care Authority
May 2021

New U.S. Food and Drug Administration (FDA) Approval(s)[1,2,3,4,5]

- **Lyumjev™ (Insulin Lispro-aabc) Injection:** In June 2020, the FDA approved Lyumjev™ injection, a new rapid-acting insulin indicated to improve glycemic control in adults with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM). The approval of Lyumjev™ was based on data from the Phase 3 trials, PRONTO-T1D and PRONTO-T2D, which were randomized, active controlled, treat-to-target comparisons of Lyumjev™ and Humalog® (insulin lispro injection) in adults with T1DM or T2DM, respectively. Both trials met the primary endpoint of non-inferior hemoglobin A1c (HbA1c) reduction from baseline compared to Humalog® at 26 weeks, when Lyumjev™ and Humalog® were dosed at mealtime. In both trials, Lyumjev™ demonstrated superior reduction in blood glucose spikes at both 1 hour and 2 hours after a test meal when compared to Humalog®. In the Lyumjev™ formulation, microdoses of treprostinil are used as an excipient to induce a local vasodilation effect for quicker absorption. Lyumjev™ is supplied in 2 strengths, 100 units/mL (U-100) and 200 units/mL (U-200). Lyumjev™ dosing should be individualized and adjusted based on the patient's metabolic needs, glucose monitoring results, and glycemic control goal. For subcutaneous (sub-Q) administration, Lyumjev™ should be administered into the abdomen, upper arm, thigh, or buttocks at the start of a meal or within 20 minutes after starting a meal. For intravenous administration, the U-100 strength should be diluted to a concentration of 1 unit/mL and only administered under medical supervision. The Wholesale Acquisition Cost (WAC) per mL of Lyumjev™ U-100 KwikPen® is $35.36 and $70.72 for the U-200 strength. Lyumjev™ will be included in the Lilly Insulin Value Program, allowing patients with commercial insurance and those without insurance to fill their monthly prescription of Lyumjev™ for $35.
- **Farxiga® (Dapagliflozin):** The FDA approved Farxiga® to reduce the risk of cardiovascular (CV) death and hospitalization for heart failure (HF) in adults with HF [New York Heart Association (NYHA) class II-IV] with reduced ejection fraction (HFrEF) with and without T2DM. Farxiga® is the first sodium-glucose co-transporter-2 (SGLT-2) inhibitor approved by the FDA to treat patients with HFrEF [left ventricular ejection fraction (LVEF) ≤40%]. The FDA approval was based on positive results from the landmark Phase 3 DAPA-HF trial, which showed Farxiga®

achieving a statistically significant and clinically meaningful reduction of CV death or hospitalization for HF, compared to placebo. The decision follows the Priority Review designation granted by the FDA earlier in 2020 and the Fast Track designation granted in September 2019. The DAPA-HF trial showed that Farxiga®, in addition to standard of care, reduced the risk of the composite outcome of CV death or the worsening of HF versus placebo by 26% [absolute risk reduction (ARR)= 5% (event rate/100 patient years: 11.6 vs 15.6, respectively); P<0.0001] in patients with HFrEF. During the trial duration, 1 CV death, hospitalization, or urgent visit associated with HF could be avoided for every 21 patients treated with Farxiga®. The safety profile of Farxiga® in the DAPA-HF trial was consistent with the well-established safety profile of the medication. The data from the DAPA-HF trial was published in *The New England Journal of Medicine*. In October 2019, the FDA approved Farxiga® to reduce the risk of hospitalization for HF in adult patients with T2DM and established CV disease or multiple CV risk factors. The approval was based on the DECLARE-TIMI 58 trial. Farxiga® is also indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

News[6,7]

- **Bydureon® (Exenatide) Pen:** In September 2020, AstraZeneca announced that Bydureon® pen will be discontinued as of March 2021 due to business reasons. Bydureon BCise® (exenatide) autoinjector pen will continue to be available. Bydureon® and Bydureon BCise® pens are both indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM. Bydureon BCise® pen is an autoinjector that does not need to be titrated or reconstituted. Bydureon® 2mg single-dose vial was previously discontinued from the market in September 2018.

Recommendations

The College of Pharmacy recommends the prior authorization of Lyumjev™ (insulin lispro-aabc) with the following criteria (changes shown in red):

Insulin Lispro (Generic Humalog® U-100), Admelog® (Insulin Lispro), and Lyumjev™ (Insulin Lispro-aabc 100 Units/mL) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use the brand formulation (Humalog®) must be provided (the brand formulation of Humalog® U-100 is preferred).

Humalog® KwikPen® U-200 (Insulin Lispro 200 Units/mL) and Lyumjev™ (Insulin Lispro-aabc 200 Units/mL) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. Authorization of the 200 units/mL strength requires a patient-specific, clinically significant reason why the member cannot use the 100 units/mL strength (the brand formulation of Humalog® U-100 is preferred).

Additionally, the College of Pharmacy recommends updating the anti-diabetic medications Tier-2 and Tier-3 approval criteria to provide a clinical exception for FDA approved indications for higher tiered medications not covered by lower tiered medications (changes shown in red):

Anti-Diabetic Medications Tier-2 Approval Criteria:

1. A trial of 1 Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate must be provided.
2. For initiation with dual or triple therapy, additional Tier-2 medications may be approved based on current American Association of Clinical Endocrinologists (AACE) or American Diabetes Association (ADA) guidelines.
3. A clinical exception will apply for medications with a unique FDA approved indication not covered by all Tier-1 medications. Tier structure rules for unique FDA approved indications will apply.
4. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (T2DM) and CV disease for patients with the diagnosis of T2DM at high risk for CV events. Tier structure rules for this indication will apply.~~
5. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of end-stage kidney disease, worsening of kidney function, CV death, and heart failure (HF) hospitalization in adults with T2DM and diabetic kidney disease. Tier structure rules for this indication will apply.~~
6. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of hospitalization for HF in adults with T2DM and other CV risk factors. Tier structure rules for this indication will apply.~~

Anti-Diabetic Medications Tier-3 Approval Criteria:

1. Member must have tried 1 Tier-2 medication in the same category and have a documented clinical reason why the Tier-2 medication is not appropriate (for Tier-3 medications that do not have a similar category in Tier-2, a medication from any category in Tier-2 may be used).

2. A clinical exception will apply for medications with a unique FDA approved indication not covered by all Tier-1 and Tier-2 medications. Tier structure rules for unique FDA approved indications will apply.
3. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (T2DM) and CV disease for patients with the diagnosis of T2DM at high risk for CV events. Tier structure rules for this indication will apply.~~
4. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of end-stage kidney disease, worsening of kidney function, CV death, and heart failure (HF) hospitalization in adults with T2DM and diabetic kidney disease. Tier structure rules for this indication will apply.~~
5. ~~A clinical exception will apply for medications with an FDA approved indication to reduce the risk of hospitalization for HF in adults with T2DM and other CV risk factors. Tier structure rules for this indication will apply.~~

Finally, the College of Pharmacy recommends moving Adlyxin® (lixisenatide) and Rybelsus® (semaglutide) from Tier-3 to the Special Prior Authorization (PA) Tier of the Anti-Diabetic Medications Product Based Prior Authorization (PBPA) Tier Chart based on net cost, removing Bydureon® pen from the Tier Chart based on product discontinuation, and updating the Special PA criteria (changes shown in red):

Anti-Diabetic Medications Special Prior Authorization (PA) Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least 3 other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member; and
2. Use of Invokamet® XR [canagliflozin/metformin extended-release (ER)] or Jentadueto® XR (linagliptin/metformin ER) will require a patient-specific, clinically significant reason why the member cannot take the immediate-release formulation(s); and
3. Use of Adlyxin® (lixisenatide), Bydureon® BCise™ (exenatide ER autoinjector pen), or Rybelsus® (semaglutide) will require a patient-specific, clinically significant reason (other than convenience) why the member cannot use ~~the vial or pen formulation~~ all available lower-tiered glucagon-like peptide 1 receptor agonists (GLP-1 agonists).

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors			
acarbose (Precose®)		miglitol (Glyset®)	
Amylinomimetics			
			pramlintide (Symlin®)
Biguanides			
metformin (Glucophage®)			metformin ER (Fortamet®, Glumetza®)
metformin SR (Glucophage XR®)			metformin soln (Riomet®)
metformin/glipizide (Metaglip®)			metformin ER susp (Riomet ER™)
metformin/ glyburide (Glucovance®)			
DPP-4 Inhibitors			
	linagliptin (Tradjenta®)	alogliptin (Nesina®)	linagliptin/metformin ER (Jentadueto® XR)
	linagliptin/metformin (Jentadueto®)	alogliptin/metformin (Kazano®)	
	sitagliptin (Januvia®)	alogliptin/ pioglitazone (Oseni®)	
	sitagliptin/metformin (Janumet®)	saxagliptin (Onglyza®)	
	sitagliptin/ metformin ER (Janumet XR®)	saxagliptin/ metformin (Kombiglyze®)	
		saxagliptin/ metformin ER (Kombiglyze XR®)	
DPP-4 Inhibitors/SGLT-2 Inhibitors			
	empagliflozin/ linagliptin (Glyxambi®)	dapagliflozin/ saxagliptin (Qtern®)	
		ertugliflozin/ sitagliptin (Steglujan™)	
Dopamine Agonists			
		bromocriptine (Cycloset®)	
Glinides			
repaglinide (Prandin®)	nateglinide (Starlix®)		
	repaglinide/ metformin (Prandimet®)		
GLP-1 Agonists			

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
	dulaglutide (Trulicity®)	~~**lixisenatide (Adlyxin®)**~~	exenatide ER autoinjector (Bydureon® BCise™)
	exenatide (Byetta®)	semaglutide (Ozempic®)	**lixisenatide (Adlyxin®)**
	~~**exenatide ER (Bydureon®)**~~	~~**semaglutide (Rybelsus®)**~~	**semaglutide (Rybelsus®)**
	liraglutide (Victoza®)		
GLP-1 Agonists/Insulin			
		insulin degludec/ liraglutide (Xultophy® 100/3.6)+	
		insulin glargine/ lixisenatide (Soliqua® 100/33)+	
SGLT-2 Inhibitors			
	dapagliflozin (Farxiga®)	canagliflozin (Invokana®)	canagliflozin/metformin ER (Invokamet® XR)
	dapagliflozin/ metformin ER (Xigduo® XR)	canagliflozin/ metformin (Invokamet®)	
	empagliflozin (Jardiance®)	ertugliflozin (Steglatro™)	
	empagliflozin/ metformin (Synjardy®)	ertugliflozin/ metformin (Segluromet™)	
	empagliflozin/ metformin ER (Synjardy® XR)		
SGLT-2 Inhibitors/DPP-4 Inhibitors/Biguanides			
			dapagliflozin/ saxagliptin/metformin ER (Qternmet® XR)
			empagliflozin/ linagliptin/metformin ER (Trijardy® XR)
Sulfonylureas			
chlorpropamide (Diabinese®)			
glimepiride (Amaryl®)			
glipizide (Glucotrol®)			
glipizide SR (Glucotrol XL®)			
glyburide (Diabeta®)			

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
glyburide micronized (Micronase®)			
tolbutamide (Orinase®)			
Thiazolidinediones			
pioglitazone (Actos®)		pioglitazone/ glimepiride (Duetact®)	
		pioglitazone/ metformin (Actoplus Met®, Actoplus Met XR®)	
		rosiglitazone (Avandia®)	
		rosiglitazone/ glimepiride (Avandaryl®)	
		rosiglitazone/ metformin (Avandamet®)	

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

[1] Eli Lilly and Company. FDA Approves Lyumjev™ (Insulin Lispro-aabc Injection), Lilly's New Rapid-Acting Insulin. *PR Newswire*. Available online at: https://investor.lilly.com/news-releases/news-release-details/fda-approves-lyumjevtm-insulin-lispro-aabc-injection-lillys-new. Issued 06/15/2020. Last accessed 04/19/2021.
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[3] AstraZeneca. Farxiga is the First SGLT2 Inhibitor Proven to Significantly Reduce the Risk of Cardiovascular Death and Hospitalization for Heart Failure. Available online at: https://www.astrazeneca.com/media-centre/press-releases/2020/farxiga-approved-in-the-us-for-the-treatment-of-heart-failure-in-patients-with-heart-failure-with-reduced-ejection-fraction.html. Issued 05/06/2020. Last accessed 04/19/2021.
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Appendix D

Vote to Prior Authorize Amondys 45™ (Casimersen), Viltepso® (Viltolarsen), and Vyondys 53™ (Golodirsen)

Oklahoma Health Care Authority
May 2021

Introduction[1,2,3]

Amondys 45™ (casimersen) is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping. Approximately 8% of patients with DMD have a mutation that is amendable to exon 45 skipping. This indication was approved by the U.S. Food and Drug Administration (FDA) in February 2021 under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Amondys 45™. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory studies. Amondys 45™ is supplied as a 100mg/2mL preservative-free concentrated solution in single-dose vials (SDVs). The recommended dose of Amondys 45™ is 30mg/kg administered once weekly as a 35 to 60 minute intravenous (IV) infusion. Due to the kidney toxicity observed in animals who received casimersen, serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio (UPCR) should be measured prior to starting treatment with casimersen. During treatment, urine dipstick should be monitored monthly, and serum cystatin C and UPCR should be monitored every 3 months. Interim efficacy from an ongoing, double-blind, placebo-controlled, multicenter study was assessed based on change from baseline in the dystrophin protein level at week 48. Interim results from patients who had a muscle biopsy at week 48 of the double-blind period showed a statistically significant change from baseline to week 48 ($P<0.001$) in the casimersen-treated group.

Viltepso® (viltolarsen) is an antisense oligonucleotide indicated for the treatment of DMD in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Approximately 8% of patients with DMD have a mutation that is amendable to exon 53 skipping. This indication was approved by the FDA in August 2020 under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Viltepso®. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory studies. Viltepso® is supplied as a 250mg/5mL preservative-free solution in SDVs. The recommended dose of Viltepso® is 80mg/kg administered once weekly as a 60 minute IV infusion. Due to the kidney toxicity observed in animals who received viltolarsen, serum cystatin C, urine dipstick, and UPCR should be

measured prior to starting treatment with viltolarsen. During treatment, urine dipstick should be monitored monthly, and serum cystatin C and UPCR should be monitored every 3 months. The effect of viltolarsen on dystrophin production was evaluated in a multicenter, 2-period, dose-finding study. Efficacy was assessed based on change from baseline in dystrophin protein level at week 25. Muscle biopsies were obtained from patients at baseline and following 24 weeks of viltolarsen treatment. The viltolarsen-treated patients showed a statistically significant change from baseline to week 25 (P=0.01).

Vyondys 53™ (golodirsen) is an antisense oligonucleotide indicated for the treatment of DMD in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. This indication was approved by the FDA in December 2019 under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53™. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory studies. Vyondys 53™ is supplied as a 100mg/2mL preservative-free concentrated solution in SDVs. The recommended dose of Vyondys 53™ is 30mg/kg administered once weekly as a 35 to 60 minute IV infusion. Due to the kidney toxicity observed in animals who received golodirsen, serum cystatin C, urine dipstick, and UPCR should be measured prior to starting treatment with golodirsen. During treatment, urine dipstick should be monitored monthly, and serum cystatin C and UPCR should be monitored every 3 months. The effect of golodirsen on dystrophin production was evaluated in a 2-part study. Part 2 of study 1 was a 168-week, open-label study assessing the efficacy and safety of golodirsen at a dose of 30mg/kg/week. Efficacy was assessed based on change from baseline in the dystrophin protein level at week 48 of part 2. Muscle biopsies were obtained at baseline prior to treatment and at week 48 in all golodirsen-treated patients, and were analyzed for dystrophin protein level. The golodirsen-treated patients showed a statistically significant change from baseline to week 48 (P<0.001) in dystrophin protein level.

Cost Comparison: DMD Exon-Skipping Therapies

Medication	Cost Per SDV	Cost Per 28 Days*	Cost Per Year*
Amondys 45™ (casimersen) 100mg/2mL	**$1,600**	**$48,000**	**$624,000**
Viltepso® (viltolarsen) 250mg/5mL	**$1,410**	**$45,120**	**$586,560**
Vyondys 53™ (golodirsen) 100mg/2mL	**$1,600**	**$48,000**	**$624,000**
Exondys 51® (eteplirsen) 100mg/2mL	$1,600	$48,000	$624,000

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
DMD = Duchenne muscular dystrophy; SDV = single-dose vial
*Cost per 28 days and cost per year based on FDA recommended dosing for a 25kg patient. Costs will vary due to weight-based dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Amondys 45™ (casimersen), Viltepso® (viltolarsen), and Vyondys 53™ (golodirsen) and updating the current Exondys 51® (eteplirsen) criteria with the following changes shown in red:

Amondys 45™ (Casimersen), Exondys 51® (Eteplirsen), Viltepso® (Viltolarsen), and Vyondys 53™ (Golodirsen) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD); and
2. Member must have a confirmed mutation of the *DMD* gene that is amenable to exon skipping for the requested medication (results of genetic testing must be submitted); and
3. Must be prescribed by a neurologist or specialist with expertise in the treatment of DMD (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of DMD); and
4. Prescriber must verify the member's renal function will be appropriately assessed prior to initiation of therapy and monitored during treatment; and
5. Member must be on a stable dose of a corticosteroid (at least 3 months in duration) or a patient-specific, clinically significant reason why corticosteroids are not appropriate for the member must be provided; and
6. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
   a. 6-minute walk test (6MWT); or
   b. Forced vital capacity percent predicted (FVCpp); and
7. The requested exon-skipping therapy will not be approved for concurrent use with any other exon-skipping therapies for DMD; and
8. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically significant improvement or maintenance of function from pretreatment baseline status using the same exam as performed at baseline assessment; and
9. Subsequent approvals will be for the duration of 1 year. For yearly approvals, the prescriber must verify the member is responding to the medication as demonstrated by clinically significant improvement or maintenance of function from pretreatment baseline status using the same exam as performed at baseline assessment; and
10. 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.

[1] Amondys 45™ Prescribing Information. Sarepta Therapeutics, Inc. Available online at: https://www.amondys45.com/Amondys45_(casimersen)_Prescribing_Information.pdf. Last revised 02/2021. Last accessed 04/13/2021.
[2] Viltepso® Prescribing Information. NS Pharma, Inc. Available online at: https://www.viltepso.com/prescribing-information. Last revised 03/2021. Last accessed 04/13/2021.
[3] Vyondys 53™ Prescribing Information. Sarepta Therapeutics, Inc. Available online at: https://www.vyondys53.com/static/patient/assets/Vyondys53_(golodirsen)_Prescribing_Information.pdf. Last revised 02/2021. Last accessed 04/13/2021.

Appendix E

Vote to Prior Authorize Verquvo™ (Vericiguat)

Oklahoma Health Care Authority
May 2021

New U.S. Food and Drug Administration (FDA) Approval(s)[1,2,3]

Verquvo™ (vericiguat) was approved by the FDA in January 2021 to reduce the risk of cardiovascular (CV) death and hospitalization for heart failure (HF) following a hospitalization for HF or need for outpatient intravenous (IV) diuretics in adult patients with symptomatic chronic HF and left ventricular ejection fraction (LVEF) <45%. Vericiguat is an oral soluble guanylate cyclase (sGC) stimulator which was studied as an addition to standard guideline-based medical therapy for HF in adults with evidence of worsening HF. Verquvo™ is the first sGC stimulator approved by the FDA for the treatment of HF. Verquvo™ is available as 2.5mg, 5mg, and 10mg oral tablets. The recommended starting dose is 2.5mg orally once daily with food. The dose should be doubled approximately every 2 weeks to reach the target maintenance dose of 10mg once daily, as tolerated by the patient.

The FDA approval of Verquvo™ was based on data from the Phase 3 VICTORIA study, a randomized, parallel-group, placebo-controlled, double-blind, multi-center study comparing Verquvo™ to placebo. The study included 5,050 adult patients with symptomatic chronic HF [New York Heart Association (NYHA) Class II, III, or IV] and LVEF <45% with worsening HF, defined as a hospitalization for HF within the previous 6 months or the need for IV diuretics within the previous 3 months before randomization. All patients included in the study received guideline-based medical therapy for HF. At baseline, 93% of patients were receiving a beta blocker, 73% were receiving an angiotensin converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), 70% of patients were receiving a mineralocorticoid receptor antagonist (MRA), and 15% were receiving a combination angiotensin receptor and neprilysin inhibitor (ARNI). Of the patients included in the study, 91% were receiving 2 or more HF medications and 60% of patients were receiving triple combination therapy with a beta blocker, an ACEI or ARB, and a MRA. The median dose of vericiguat used in the study was 9.2mg, with 90.3% of patients receiving the 10mg target dose after approximately 12 months. The primary efficacy endpoint was the composite of time to first event of CV death or hospitalization for HF. The results of the study showed a statistically significantly lower risk of the composite endpoint of CV death or HF hospitalization with vericiguat vs. placebo [hazard ratio (HR): 0.90; 95% confidence interval (CI): 0.82, 0.98; P=0.019]. Additionally, there

was a 4.2% annualized absolute risk reduction (ARR) with vericiguat compared to placebo.

Verquvo™ has a *Boxed Warning* for embryo-fetal toxicity and is contraindicated in pregnancy because it may cause fetal harm. Females of reproductive potential should not be breastfeeding, should have pregnancy excluded before the start of treatment, and should use effective forms of contraception during treatment and for 1 month after discontinuing treatment with vericiguat. Additionally, the use of Verquvo™ is contraindicated with concomitant use of other sGC stimulators (e.g., riociguat). In a Phase 3 study, the most common adverse reactions (occurring in ≥5% of patients treated with vericiguat and more commonly than with placebo) were hypotension and anemia.

Cost Comparison:

Product	Cost Per Tablet	Cost Per Month*	Cost Per Year*
Verquvo™ (vericiguat) 2.5mg, 5mg, or 10mg tablet	**$19.43**	**$582.90**	**$6,994.80**
Entresto® (sacubitril/valsartan) 49mg/51mg tablet	$9.32	$559.20	$6,710.40
Corlanor® (ivabradine) 7.5mg tablet	$7.94	$476.40	$5,716.80

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per month and cost per year based on 1 tablet daily for Verquvo™ and 1 tablet twice daily for Entresto® and Corlanor®.

Recommendations

The College of Pharmacy recommends the prior authorization of Verquvo™ (vericiguat) with the following criteria:

Verquvo™ (Vericiguat) Approval Criteria:

1. An FDA approved indication to reduce the risk of cardiovascular death and hospitalization for heart failure (HF) in adults with all of the following:
    a. Chronic symptomatic HF [New York Heart Association (NYHA) Class II, III, or IV]; and
    b. Reduced left ventricular ejection fraction (LVEF) <45%; and
    c. Already receiving guideline-directed medical therapy for HF, as documented in member's pharmacy claims history; and
2. Member has evidence of worsening HF (decompensation) demonstrated by at least 1 of the following:
    a. Hospitalization for HF within the past 6 months; or
    b. Received outpatient intravenous (IV) diuretics within the past 3 months; and
3. Member must be 18 years of age or older; and

4. Member must not be taking concomitant soluble guanylate cyclase (sGC) stimulators (e.g., riociguat); and
5. Female members of reproductive potential must not be breastfeeding, must have a negative pregnancy test prior to initiation of therapy, and must agree to use effective contraception during treatment and for 1 month after the final dose of Verquvo™; and
6. Prescriber must agree to titrate to the target maintenance dose according to package labeling, as tolerated by the member; and
7. Initial approvals will be for the duration of 6 months. Compliance will be checked for continued approval every 6 months; and
8. A quantity limit of 30 tablets per 30 days will apply.

[1] Merck. Merck Announces U.S. Approval of Verquvo™ (Vericiguat). Available online at: https://www.merck.com/news/merck-announces-u-s-fda-approval-of-verquvo-vericiguat/. Issued 01/20/2021. Last accessed 03/15/2021.
[2] Verquvo™ (Vericiguat) Prescribing Information. Merck. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214377s000lbl.pdf. Last revised 01/2021. Last accessed 03/15/2021.
[3] Armstrong PW, Pieske B, Anstrom KJ, et al. Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med* 2020; 382(20):1883-1893.

Appendix F

Vote to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel)

Oklahoma Health Care Authority
May 2021

New U.S. Food and Drug Administration (FDA) Approval(s)[1]

- **February 2021:** The FDA approved Breyanzi® (lisocabtagene maraleucel) for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma (FL) grade 3B.

Breyanzi® (Lisocabtagene Maraleucel) Product Summary[2]

- **Therapeutic Class:** CD19-directed genetically modified autologous T-cell immunotherapy
- **Indication(s):** Treatment of adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and FL grade 3B
- **How Supplied:** Cell suspension for intravenous (IV) infusion with a patient-specific concentration [each mL contains 1.5×10^6 to 70×10^6 chimeric antigen receptor (CAR)-positive viable T-cells]
- **Dose:** Based on the number of CAR-positive viable T-cells, the dose is 50 to 110×10^6 CAR-positive viable T-cells
- **Cost:** The Wholesale Acquisition Cost (WAC) is $410,300 per one-time treatment

Cost Comparison: CAR T-Cell Therapies for Lymphoma

Medication	Cost Per One-Time Treatment*
Breyanzi® (lisocabtagene maraleucel)	**$410,300**
Yescarta® (axicabtagene ciloleucel)	$399,000
Kymriah® (tisagenlecleucel)	$373,000
Tecartus® (brexucabtagene autoleucel)	$399,000

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per one-time treatment based on recommended dosing for adult patients.
CAR = chimeric antigen receptor

Recommendations

The College of Pharmacy recommends the prior authorization of Breyanzi® (lisocabtagene maraleucel) with the following criteria, including an update based on net cost in comparison to other available CAR T-cell therapies indicated for large B-cell lymphoma [items shown in red are changes from what was included in the March 2021 Drug Utilization Review (DUR) Board packet]:

Breyanzi® (Lisocabtagene Maraleucel) Approval Criteria [Lymphoma Diagnosis]:

1. Diagnosis of large B-cell lymphoma; and
2. Relapsed or refractory disease; and
3. Member must have received at least 2 lines of systemic therapy; and
4. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategy (REMS) requirements; and
5. A patient-specific, clinically significant reason why Kymriah® (tisagenlecleucel) or Yescarta® (axicabtagene) is not appropriate for the member must be provided.

[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 04/16/2021. Last accessed 04/19/2021.

[2] Breyanzi® Prescribing Information. Bristol Myers Squibb. Available online at: https://packageinserts.bms.com/pi/pi_breyanzi.pdf. Last revised 02/2021. Last accessed 04/19/2021.

Appendix G

Vote to Prior Authorize Cosela™ (Trilaciclib), Gavreto™ (Pralsetinib), Retevmo® (Selpercatinib), Tabrecta™ (Capmatinib), Tepmetko® (Tepotinib), and Zepzelca™ (Lurbinectedin)

Oklahoma Health Care Authority
May 2021

New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)[1,2,3,4,5,6]

- **March 2020:** The FDA approved Imfinzi® (durvalumab) in combination with etoposide and either carboplatin or cisplatin as first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).
- **May 2020:** The FDA granted accelerated approval to Tabrecta™ (capmatinib) for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping.
- **May 2020:** The FDA granted accelerated approval to Retevmo® (selpercatinib) for the following indications:
  - Adult patients with metastatic rearranged during transfection (RET) fusion-positive NSCLC; and
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy; and
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
- **May 2020:** The FDA approved Alunbrig® (brigatinib) for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic NSCLC.
- **May 2020:** The FDA approved Cyramza® (ramucirumab) in combination with erlotinib for first-line treatment of adult patients with metastatic NSCLC with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations.
- **May 2020:** The FDA approved Tecentriq® (atezolizumab) in combination with bevacizumab for the treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

- **June 2020:** The FDA granted accelerated approval to Zepzelca™ (lurbinectedin) for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy.
- **September 2020:** The FDA granted accelerated approval to Gavreto™ (pralsetinib) for the treatment of adult patients with metastatic RET fusion-positive NSCLC.
- **December 2020:** The FDA approved Gavreto™ (pralsetinib) for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who require systemic therapy or RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
- **December 2020:** The FDA approved Tagrisso® (osimertinib) for adjuvant therapy after tumor resection in adult patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.
- **February 2021:** The FDA granted accelerated approval to Tepmetko® (tepotinib) for the treatment of adult patients with metastatic NSCLC harboring MET exon 14 skipping alterations.
- **February 2021:** The FDA approved Libtayo® (cemiplimab-rwlc) as the first immunotherapy indicated for adult patients with advanced basal cell carcinoma (BCC) previously treated with a hedgehog pathway inhibitor (HHI) or for whom an HHI is not appropriate. Full approval was granted for patients with locally advanced BCC and accelerated approval was granted for patients with metastatic BCC.
- **February 2021:** The FDA approved Cosela™ (trilaciclib) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. It is the first and only therapy designed to help protect bone marrow when administered prior to treatment with chemotherapy.
- **February 2021:** The FDA approved Libtayo® (cemiplimab-rwlc) for the first-line treatment of adult patients with advanced NSCLC (locally advanced who are not candidates for surgical resection or definitive chemoradiation or metastatic) whose tumors have high programmed death ligand 1 (PD-L1) expression [tumor proportion score (TPS) >50%], with no EGFR, ALK, or *ROS1* aberrations.
- **March 2021:** The FDA granted regular approval to Lorbrena® (lorlatinib) for the treatment of adult patients with metastatic NSCLC whose tumors are ALK-positive. The FDA previously granted Lorbrena® accelerated approval in November 2018 for the second- or third-line treatment of ALK-positive metastatic NSCLC.
- **March 2021:** The FDA approved Keytruda® (pembrolizumab) in combination with platinum- and fluoropyrimidine-based

chemotherapy for the treatment of adult patients with metastatic or locally advanced esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma who are not candidates for surgical resection or definitive chemoradiation.

Guideline Update(s):

- Following an FDA approval, the National Comprehensive Cancer Network (NCCN) Compendium guideline recommendations were updated to include use of Tecentriq® (atezolizumab) for advanced, unresectable, or metastatic HCC in combination with Avastin® (bevacizumab) in patients who have not received prior systemic therapy. The IMbrave150 trial showed the atezolizumab-bevacizumab combination reduced the risk of death by 42% and the risk of disease progression or death by 41% compared with Nexavar® (sorafenib).
- Per NCCN Compendium guideline recommendations, Keytruda® (pembrolizumab) can be used for esophageal carcinoma as first-line therapy. In the Phase 3 KEYNOTE-590 trial, Keytruda® plus chemotherapy significantly improved overall survival (OS), progression-free survival (PFS), and objective response rates (ORR) compared with chemotherapy alone as first-line therapy in patients with locally advanced, unresectable, or metastatic esophageal cancer.

News:

- **February 2021:** AstraZeneca announced the voluntary withdrawal of the Imfinzi® (durvalumab) indication in the United States for previously treated adult patients with locally advanced or metastatic bladder cancer. This decision was made in consultation with the FDA based on results from the DANUBE Phase 3 trial in the 1st-line metastatic bladder cancer setting, which did not meet its primary endpoints in 2020. This withdrawal does not impact other approved Imfinzi® indications.

Recommendations

The College of Pharmacy recommends the prior authorization of Cosela™ (trilaciclib), Gavreto™ (pralsetinib), Retevmo® (selpercatinib), Tabrecta™ (capmatinib), Tepmetko® (tepotinib), and Zepzelca™ (lurbinectedin) with the following criteria (shown in red):

Cosela™ (Trilaciclib) Approval Criteria:

1. Diagnosis of extensive-stage small cell lung cancer (ES-SCLC); and
2. Member is undergoing myelosuppressive chemotherapy with 1 of the following:
   a. Platinum (carboplatin or cisplatin) and etoposide-containing regimen; or

   b. Topotecan-containing regimen; and
3. Cosela™ will not be approved for concomitant use with colony-stimulating factors (CSF) [e.g., granulocyte CSF (G-CSF), pegylated G-CSF (peg-G-CSF), granulocyte-macrophage CSF (GM-CSF)] for primary prophylaxis of febrile neutropenia prior to day 1 cycle 1 of chemotherapy.

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

1. Diagnosis of NSCLC in adults; and
2. Recurrent, advanced, or metastatic disease; and
3. Rearranged during transfection (RET) fusion-positive tumor.

Gavreto™ (Pralsetinib) Approval Criteria [Thyroid Cancer Diagnosis]:

1. Adult and pediatric members 12 years of age and older; and
2. Diagnosis of advanced or metastatic disease with either:
   a. Rearranged during transfection (RET)-mutant medullary thyroid cancer (MTC) requiring systemic therapy; or
   b. RET fusion-positive thyroid cancer requiring systemic therapy and member is radioactive iodine-refractory (if radioactive iodine is appropriate).

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC; and
2. Rearranged during transfection (RET) fusion-positive tumor; and
3. As a single-agent.

Retevmo® (Selpercatinib) Approval Criteria [Thyroid Cancer Diagnosis]:

1. Adult and pediatric members 12 years of age and older; and
2. As a single-agent; and
3. Diagnosis of advanced or metastatic disease with either:
   a. Rearranged during transfection (RET)-mutant medullary thyroid cancer (MTC) requiring systemic therapy; or
   b. RET fusion-positive thyroid cancer requiring systemic therapy and member is radioactive iodine-refractory (if radioactive iodine is appropriate).

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC; and
2. Mesenchymal-epithelial transition (MET) exon 14 skipping positive tumor; and
3. As a single-agent.

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

1. Diagnosis of advanced, metastatic, or unresectable NSCLC; and
2. Mesenchymal-epithelial transition (MET) exon 14 skipping positive tumor.

Zepzelca™ (Lurbinectedin) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of metastatic SCLC; and
2. Used following disease progression on or after platinum-based chemotherapy.

Additionally, the College of Pharmacy recommends updating the approval criteria for Alunbrig® (brigatinib), Cyramza® (ramucirumab), Imfinzi® (durvalumab), Keytruda® (pembrolizumab), Libtayo® (cemiplimab-rwlc), Lorbrena® (lorlatinib), Tagrisso® (osimertinib), and Tecentriq® (atezolizumab) based on recent FDA approvals (changes noted in red):

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

1. Diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity~~.; and~~
~~3. Progressed on or intolerant to crizotinib; and~~
~~4. Brigatinib must be used as a single-agent only.~~

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

1. Diagnosis of metastatic NSCLC; and
2. First-line in combination with erlotinib; and
   a. Epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R mutation; or
3. Subsequent therapy for metastatic disease; and
   a. In combination with docetaxel.

Imfinzi® (Durvalumab) Approval Criteria [Extensive-Stage Small Cell Lung Cancer (ES-SCLC) Diagnosis]:

1. Diagnosis of ES-SCLC; and
2. In combination with etoposide and either cisplatin or carboplatin followed by single-agent maintenance.

Libtayo® (Cemiplimab-rwlc) Approval Criteria [Basal Cell Carcinoma (BCC) Diagnosis]:

1. Diagnosis of locally advanced or metastatic BCC; and
2. Member has previously been treated with a hedgehog pathway inhibitor (HHI); or
3. Treatment with a HHI is not appropriate for the member.

Libtayo® (Cemiplimab-rwlc) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Diagnosis of advanced, unresectable, or metastatic NSCLC; and
2. High programmed death ligand 1 (PD-L1) expression [tumor proportion score (TPS) ≥50%]; and
3. No epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), or *ROS1* mutations.

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

1. Diagnosis of metastatic NSCLC; and
2. Tumor expresses anaplastic lymphoma kinase (ALK) translocation; and
3. As a single-agent as first-line therapy; or
4. As a single-agent as second-line therapy following disease progression on either alectinib or ceritinib; or
5. As a single-agent as third-line or greater therapy following disease progression on crizotinib and 1 other ALK inhibitor (i.e., ceritinib, alectinib).

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

1. As adjuvant therapy following tumor resection in members with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations; or
2. Diagnosis of metastatic NSCLC; and
    a. EGFR T790M mutation-positive disease and following progression on erlotinib, afatinib, or gefitinib for asymptomatic disease, symptomatic brain lesions, or multiple symptomatic systemic lesions; or
    b. First-line treatment of members with EGFR exon 19 deletions or exon 21 L858R mutations.

Tecentriq® (Atezolizumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Diagnosis of advanced, unresectable, or metastatic HCC; and
2. Used in combination with bevacizumab; and
3. Member has not received prior systemic therapy.

The College of Pharmacy also recommends the removal of the Imfinzi® (durvalumab) approval criteria for the indication of locally advanced or metastatic bladder cancer based on FDA guided voluntary withdrawal of this indication by the manufacturer.

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

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

Finally, the College of Pharmacy recommends updating the approval criteria for Keytruda® (pembrolizumab) based on NCCN Compendium approval and the recent FDA approved indication (changes and new criteria noted in red; only criteria with updates are listed):

Keytruda® (Pembrolizumab) Approval Criteria [Esophageal, Gastric, or Gastroesophageal Junction (GEJ) Carcinoma Diagnosis]:

1. Diagnosis of locally advanced, recurrent, or metastatic esophageal, gastric, or GEJ carcinoma; and
2. Tumor must have positive programmed death ligand 1 (PD-L1) expression [combined positive score (CPS) ≥10]; and
3. For first-line therapy:
    a. Must be used in combination with either oxaliplatin or cisplatin plus a fluoropyrimidine; or
4. For second-line or greater therapy:
    a. Must be used following disease progression after 1 or more prior lines of systemic therapy; and
    b. Tumor must be squamous cell histology; and
    c. Must be used as monotherapy; and
5. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo (nivolumab)].

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Appendix H

Calendar Year 2020 Annual Review of Balversa® (Erdafitinib) and 30-Day Notice to Prior Authorize Cabometyx® (Cabozantinib), Fotivda® (Tivozanib), Jelmyto® (Mitomycin), and Padcev® (Enfortumab Vedotin-ejfv)

Oklahoma Health Care Authority
May 2021

Introduction[1]

Bladder cancers are a heterogeneous group of malignancies each with its own behavior, prognosis, and treatment. Urothelial carcinoma is the most common histologic type in the United States, accounting for 90% of all bladder cancers. Approximately 25% of patients will have muscle-invasive disease and either present with or later develop metastases. The traditional standard of care involves systemic chemotherapy which is associated with an approximately 15-month survival rate. In recent years, new targeted agents have been developed aimed at increasing efficacy outcomes.

Current Prior Authorization Criteria

Balversa® (Erdafitinib) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. Diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Tumor positive for *FGFR2* or *FGFR3* genetic mutation; and
3. Used as second-line or greater therapy including:
    a. Following at least 1 line of platinum-containing chemotherapy; and
    b. Within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Utilization of Balversa® (Erdafitinib): Calendar Year 2020

There was no SoonerCare utilization of Balversa® (erdafitinib) during calendar year 2020.

Prior Authorization of Balversa® (Erdafitinib)

There were no prior authorization requests submitted for Balversa® (erdafitinib) during calendar year 2020.

Market News and Updates[2,3]

Anticipated Patent Expiration(s):

- Fotivda® (tivozanib): November 2023

- Jelmyto® (mitomycin): January 2031
- Cabometyx® (cabozantinib): July 2033
- Balversa® (erdafitinib): February 2036

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

- **December 2019:** The FDA granted accelerated approval to Padcev® (enfortumab vedotin-ejfv) for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced, or metastatic setting.
- **April 2020:** The FDA approved Jelmyto® (mitomycin) for the treatment of adult patients with low-grade upper tract urothelial cancer (LG-UTUC).
- **January 2021:** The FDA approved the combination of Opdivo® (nivolumab) and Cabometyx® (cabozantinib) as first-line treatment for adult patients with advanced renal cell carcinoma (RCC). Cabometyx® was originally approved by the FDA in April 2016 for the treatment of adult patients with advanced RCC who have received prior antiangiogenic therapy. Additionally, in January 2019, Cabometyx® was FDA approved for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with Nexavar® (sorafenib).
- **March 2021:** The FDA approved Fotivda® (tivozanib) for the treatment of adult patients with relapsed or refractory advanced RCC following 2 or more prior systemic therapies.

Product Summaries[4,5,6,7]

Cabometyx® (Cabozantinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Advanced RCC
  - Advanced RCC as a first-line treatment in combination with nivolumab
  - HCC in patients previously treated with sorafenib
- **How Supplied:** 20mg, 40mg, and 60mg oral tablets
- **Dose:**
  - Advanced RCC as a single-agent: 60mg once daily
  - Advanced RCC in combination with nivolumab: 40mg once daily with nivolumab 240mg every 2 weeks or 480mg every 4 weeks for up to 2 years
  - HCC: 60mg once daily

- **Cost:** The Wholesale Acquisition Cost (WAC) is $722.09 per 60mg tablet, resulting in a cost per 30 days of $21,662.70 for the recommended dose of 60mg daily

Fotivda® (Tivozanib):
- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Relapsed or refractory advanced RCC following 2 or more prior systemic therapies
- **How Supplied:** 1.34mg and 0.89mg oral capsules
- **Dose:** 1.34mg once daily for 21 days followed by 7 days off treatment (28-day cycle)
  - For moderate hepatic impairment, dose reduction to 0.89mg once daily for 21 days on and 7 days off (28-day cycle) is recommended
- **Cost:** The WAC is $1,150 for the 1.34mg capsule, resulting in a cost per 21 days of $24,150 for the recommended dose of 1.34mg daily

Jelmyto® (Mitomycin):
- **Therapeutic Class:** Alkylating drug
- **Indication(s):** LG-UTUC
- **How Supplied:** A single-dose carton containing the following:
  - (2) 40mg single-dose vials (SDVs) of mitomycin for pyelocalyceal solution
  - (1) 20mL vial of sterile hydrogel for reconstitution
- **Dose:**
  - 4mg/mL instilled once weekly for 6 weeks via ureteral catheter or nephrostomy tube, with total instillation volume not to exceed 15mL (60mg of mitomycin)
  - For patients with a complete response 3 months after therapy initiation, instillations may be administered once a month for a maximum of 11 additional instillations
- **Cost:** The WAC is $21,376 per single-dose carton containing (2) 40mg SDVs of mitomycin, resulting in a cost per 6 weeks of $128,256 based on the recommended once weekly dosing

Padcev® (Enfortumab Vedotin-ejfv):
- **Therapeutic Class:** Nectin-4-directed antibody and microtubule inhibitor conjugate
- **Indication(s):** Locally advanced or metastatic urothelial cancer after previous treatment with PD-1 or PD-L1 inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced, or metastatic setting
- **How Supplied:** 20mg and 30mg lyophilized powder for reconstitution in SDVs
- **Dose:** 1.25mg/kg (up to a maximum dose of 125mg) via intravenous (IV) infusion on days 1, 8, and 15 of a 28-day cycle

- **Cost:** The WAC is $2,277.00 per 20mg vial and $3,415.50 per 30mg vial, resulting in a cost per 28 days of $30,739.50 for an adult patient weighing 70kg

Recommendations

The College of Pharmacy recommends the prior authorization of Cabometyx® (cabozantinib), Fotivda® (tivozanib), Jelmyto® (mitomycin), and Padcev® (enfortumab vedotin-ejfv) with the following criteria:

Cabometyx® (Cabozantinib) Approval Criteria:

1. For cabozantinib monotherapy:
    a. Diagnosis of advanced renal cell carcinoma (RCC); or
    b. Diagnosis of advanced hepatocellular carcinoma (HCC); and
        i. The patient has previously received sorafenib.
2. For cabozantinib in combination with nivolumab:
    a. Diagnosis of relapsed or surgically unresectable stage 4 disease in the initial treatment of members with advanced RCC; and
    b. Nivolumab, when used in combination with cabozantinib for RCC, will be approved for a maximum duration of 2 years.

Fotivda® (Tivozanib) Approval Criteria:

1. Diagnosis of relapsed or refractory advanced renal cell carcinoma (RCC); and
2. Member has received at least 2 prior systemic therapies; and
3. As a single-agent.

Jelmyto® (Mitomycin) Approval Criteria [Urothelial Cancer Diagnosis]:

1. Diagnosis of non-metastatic upper urinary tract tumor; and
2. Must be a single, residual, low-grade, low-volume (5 to 15mm) tumor; and
3. Member is not a candidate for nephroureterectomy; and
4. Initial approvals will be for the duration of 6 weeks. With documentation from the prescriber of complete response 3 months after initial treatment, subsequent approvals may be authorized for once monthly use for up to 11 additional instillations.

Padcev® (Enfortumab) Approval Criteria [Urothelial Cancer Diagnosis]:

1. Diagnosis of locally advanced or metastatic urothelial cancer; and
2. Previously received a programmed death 1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced, or metastatic setting.

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Appendix I

Calendar Year 2020 Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Gemtesa® (Vibegron)

Oklahoma Health Care Authority
May 2021

Current Prior Authorization Criteria

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

ER, XL, XR = extended-release; LA = long-acting; PA = prior authorization; SL = sublingual
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).
+Unique criteria specific to Oxytrol® (oxybutynin patch), Noctiva™ (desmopressin acetate nasal spray), and Nocdurna® (desmopressin acetate SL tablets) applies.
ΔUnique criteria specific to use of Myrbetriq® (mirabegron) in combination with VESIcare® (solifenacin) applies.

Bladder Control Medications Tier-2 Approval Criteria:

1. A trial of all Tier-1 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-1 medications lack.

Bladder Control Medications Tier-3 Approval Criteria:

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

Nocdurna® (Desmopressin Acetate Sublingual Tablet) Approval Criteria:

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adult members who awaken at least 2 times per night to void; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and
3. The prescriber must confirm the member has a 6-month history of at least 2 nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and
5. Member must have failed a trial of DDAVP® (desmopressin acetate tablets) or have a patient-specific, clinically significant reason why the standard tablet formulation of desmopressin cannot be used; and
6. The prescriber must be willing to measure serum sodium levels prior to starting treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within the first week and approximately 1 month after starting treatment, and periodically during treatment; and
8. The prescriber must confirm the member is not taking loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m^2; and
10. Initial approvals will be for the duration of 3 months. For continued authorization, the prescriber must provide the following:
    a. Documentation that serum sodium levels are acceptable to the prescriber; and
    b. Documentation that the member is responding to treatment; and
11. Approvals will be limited to the 27.7mcg dose for female members; and
12. A quantity limit of 30 tablets per 30 days will apply.

Noctiva™ (Desmopressin Acetate Nasal Spray) Approval Criteria:

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults; 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 2 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 of desmopressin cannot be used; and

6. The prescriber must be willing to measure serum sodium levels within 7 days of anticipated start of treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within 1 month of starting treatment or increasing the dose; and
8. The prescriber must confirm the member is not taking any of the following:
    a. Other medications via the nasal route; or
    b. Loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m^2; and
10. Initial approvals will be for the duration of 3 months. For continued authorization, the prescriber must provide the following:
    a. Documentation that serum sodium levels are acceptable to the prescriber; and
    b. Documentation that the member is responding to treatment; and
11. A quantity limit of 1 bottle (3.8g) per 30 days will apply.

Oxytrol® (Oxybutynin 3.9mg/Day Patch) Approval Criteria:

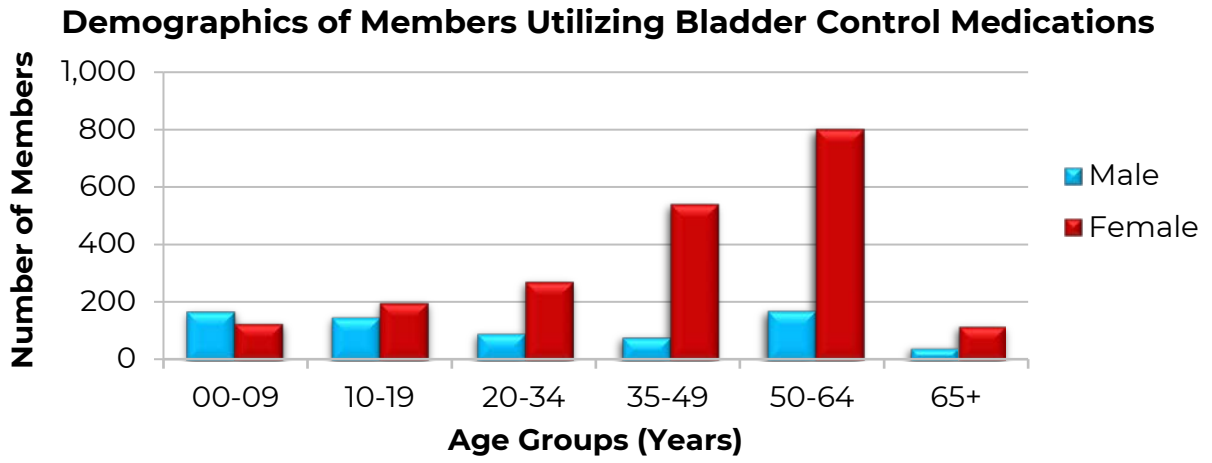
1. An FDA approved diagnosis of overactive bladder; and
2. A patient-specific, clinically significant reason why all lower tiered medications are not appropriate for the member must be provided; and
3. A quantity limit of 8 patches per 30 days will apply.

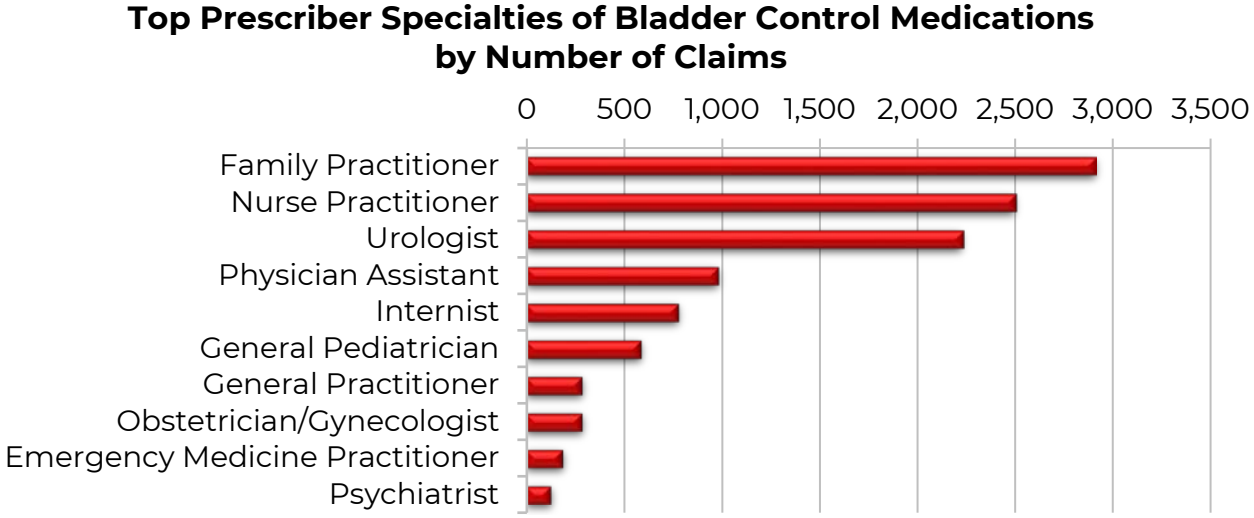
Utilization of Bladder Control Medications: Calendar Year 2020

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	2,742	12,119	$668,588.37	$55.17	$1.67	804,221	401,272
2020	2,749	11,397	$654,140.20	$57.40	$1.52	839,845	429,784
% Change	**0.30%**	**-6.00%**	**-2.20%**	**4.00%**	**-9.00%**	**4.40%**	**7.10%**
Change	**7**	**-722**	**-$14,448.17**	**$2.23**	**-$0.15**	**35,624**	**28,512**

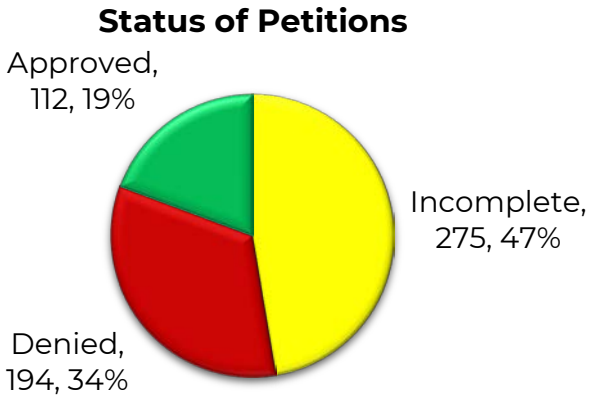
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Bladder Control Medications

There were 581 prior authorization requests submitted for bladder control medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.



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

Anticipated Patent Expiration(s):

- Toviaz® (fesoterodine tablet): June 2027
- Myrbetriq® (mirabegron tablet): March 2030
- Nocdurna® (desmopressin acetate sublingual tablet): April 2030
- Gemtesa® (vibegron tablet): December 2030
- Gelnique® (oxybutynin gel): March 2031
- VESIcare LS™ (solifenacin oral suspension): May 2031

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

- **May 2020:** The FDA approved VESIcare LS™ (solifenacin oral suspension) for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 2 years of age and older. VESIcare LS™ is available as a 5mg/5mL oral suspension. The recommended dose for NDO is based on weight and ranges from 2mg to 10mg per day (refer to the full *Prescribing Information* for the complete weight-based dosing recommendations for this indication, including the starting dose and maximum dose by weight range). VESIcare LS™ should be taken once daily followed by a liquid such as water or milk. The efficacy and safety of solifenacin oral suspension for pediatric NDO were determined based on data from (2) 52-week, open-label, baseline-controlled, sequential dose titration studies in a total of 95 pediatric patients with NDO. Study 1 enrolled patients 2 years of age to younger than 5 years of age. Study 2 enrolled patients 5 years of age to 17 years of age. The primary efficacy endpoint in both studies was the change from baseline in maximum cystometric (bladder) capacity (MCC) after 24 weeks of treatment. In study 1, there was an average 39mL increase in MCC from baseline [95% confidence interval (CI): 21, 57]. In study 2, there was an average 57mL increase in MCC from baseline (95% CI: 26, 88). Additionally, the number of daily incontinence episodes decreased by 1.6 episodes per day in both studies after 24 weeks of treatment. The Wholesale Acquisition Cost (WAC) of VESIcare LS™ is $1.71 per mL.
- **December 2020:** The FDA approved Gemtesa® (vibegron) for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence (UUI), urgency, and urinary frequency in adults. Vibegron is a selective beta-3 adrenergic agonist. When activated, beta-3 receptors in the bladder increase the bladder's capacity by causing a relaxation of the detrusor smooth muscle during bladder filling. Gemtesa® does not require dose titration and was not associated with an increased incidence of hypertension (HTN) relative to placebo in the Phase 3 EMPOWUR study.
- **March 2021:** The FDA approved Myrbetriq® (mirabegron tablets) for a new indication for the treatment of NDO in pediatric patients 3 years of age and older weighing ≥35kg. Additionally, the FDA approved a new

formulation of Myrbetriq® (mirabegron granules for oral suspension) which can be used in pediatric patients with NDO 3 years of age or older weighing <35kg. The tablet and granule formulations of Myrbetriq® are not substitutable on a milligram-per-milligram basis. Myrbetriq® granules will be available in bottles containing 830mg of mirabegron, resulting in an 8mg/mL oral suspension after reconstitution with 100mL of water. The recommended dose for NDO in patients weighing <35kg is weight-based and ranges from 24mg to 64mg per day. For patients weighing ≥35kg, either formulation of mirabegron may be used, but the recommended dosing varies depending on which formulation is selected (refer to the full *Prescribing Information* for the complete dosing recommendations for this indication, including the starting dose and maximum dose by weight range and formulation). The efficacy and safety of mirabegron for the new indication were determined based on data from a Phase 3 pivotal study in children and adolescents from 3 years of age to younger than 18 years of age with NDO. A total of 86 patients received mirabegron tablets or granules and 70 patients completed 52 weeks of treatment. The primary efficacy endpoint was the change from baseline in MCC after 24 weeks of treatment. In patients 3 years of age to younger than 12 years of age, there was an average 72mL increase in MCC from baseline (95% CI: 45, 99). In patients 12 years of age to 17 years of age, there was an average 113mL increase in MCC from baseline (95% CI: 79, 147). The FDA has granted a 6-month pediatric exclusivity period for Myrbetriq®. Astellas plans to launch the new granule formulation of Myrbetriq® in the United States by the end of 2021. Cost information for the granule formulation is not yet available.

Pipeline:

- **URO-902:** Urovant Sciences is currently in Phase 2 development of URO-902, a novel gene therapy product for patients with OAB who have failed oral pharmacologic therapy. URO-902 is administered as an intradetrusor injection into the bladder wall under local anesthesia. In February 2021, Urovant announced a Phase 2A study is proceeding with cohort 2 after the independent Data and Safety Monitoring Board recommended continuation of the study. The Phase 2A study is evaluating the efficacy, safety, and tolerability of a single administration of URO-902 and plans to enroll approximately 80 female patients with OAB. The primary efficacy outcome is the change in average daily number of UUI episodes from baseline to week 12. If approved, URO-902 would be the first gene therapy available for patients with OAB.
- **Vibegron:** Urovant Sciences is also evaluating vibegron for the treatment of OAB in men with benign prostatic hyperplasia (BPH). Phase 3 studies are ongoing for this potential new indication.

Additionally, in November 2020, Urovant announced that a Phase 2A study evaluating vibegron for the treatment of abdominal pain due to irritable bowel syndrome (IBS) did not meet its primary endpoint of at least a 30% improvement in average worst abdominal pain over the week 12 period relative to placebo. Urovant will continue to evaluate the use of vibegron for OAB in men with BPH.

Gemtesa® (Vibegron) Product Summary[10,11]

Indication: Gemtesa® (vibegron) is a beta-3 adrenergic agonist indicated for the treatment of OAB with symptoms of UUI, urgency, and urinary frequency in adults.

How Supplied: 75mg oral tablet

Dosing and Administration:

- 75mg once daily with or without food, swallowed whole with a glass of water
- In adults, tablets may be crushed, mixed with approximately 15mL of applesauce, and taken immediately with a glass of water

Contraindication(s):

- Known hypersensitivity to vibegron or any components of the product

Safety:

- Urinary Retention: Urinary retention has been reported with the use of vibegron and the risk may be increased for patients with bladder outlet obstruction or concomitant use of muscarinic antagonist medications for the treatment of OAB. Patients should be monitored for signs and symptoms of urinary retention and vibegron should be discontinued if urinary retention develops.
- Pregnancy: There is no data available on the use of vibegron in pregnant women to evaluate the risk of birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal studies, no effects on embryofetal development were observed with vibegron exposures approximately 275-fold greater in rats and 285-fold greater in rabbits than the recommended daily dose of vibegron. At exposures approximately 898-fold greater than clinical exposure, delayed fetal skeletal ossification was observed in rabbits.
- Lactation: There is no data available on the presence of vibegron in human milk, the effects on the breastfed infant, or the effects on milk production. When radiolabeled vibegron was administered to postnatal nursing rats, radioactivity was observed in milk.
- Pediatric Use: The safety and effectiveness of vibegron have not been established in pediatric patients.

- Geriatric Use: In clinical studies of vibegron for OAB, 242 patients (46%) were 65 years of age or older and 75 patients (14%) were 75 years of age or older. No overall differences in the safety or efficacy of vibegron have been observed between younger adult patients and patients 65 years of age or older.
- Renal Impairment: No dosage adjustment is recommended in patients with mild, moderate, or severe renal impairment [estimated glomerular filtration rate (eGFR) 15 to <90mL/min/1.73m^2]. Vibegron has not been studied in patients with eGFR <15mL/min/1.73m^2, with or without dialysis, and is not recommended in these patients.
- Hepatic Impairment: No dosage adjustment is recommended for patients with mild or moderate hepatic impairment (Child-Pugh class A or B). Vibegron has not been studied in patients with severe hepatic impairment (Child-Pugh class C) and is not recommended in these patients.

Adverse Reactions: The most common adverse reactions (occurring in ≥2% of patients treated with vibegron and more commonly than with placebo) were headache, nasopharyngitis, diarrhea, nausea, and upper respiratory tract infection. Other adverse reactions (occurring in <2% of patients) were dry mouth, constipation, residual urine volume increased, urinary retention, and hot flush.

Efficacy: The efficacy of Gemtesa® for the treatment of OAB was established in the Phase 3 EMPOWUR study, a 12-week, double-blind, randomized, placebo- and active-controlled study in adult patients 18 years of age or older with OAB. Patients were randomized 5:5:4 to receive vibegron 75mg, placebo, or tolterodine extended-release (ER) 4mg once daily for 12 weeks. Tolterodine ER was included as an active control in the study, but no formal statistical comparisons were conducted between vibegron and tolterodine ER. The co-primary endpoints were change from baseline in average daily number of micturitions and average daily number of UUI episodes at week 12. After 12 weeks of treatment, the average daily number of micturitions was reduced by 1.8 for patients receiving vibegron and 1.3 for patients receiving placebo (treatment difference: -0.5; P<0.001; 95% CI: -0.8, -0.2). The average daily number of UUI episodes was reduced by 2 for patients receiving vibegron and 1.4 for patients receiving placebo (treatment difference: -0.6; P<0.0001; 95% CI: -0.9, -0.3).

Cost Comparison:

Product	Cost Per Unit*	Cost Per Month+
Gemtesa® (vibegron) 75mg tablet	**$15.28**	**$458.40**
Myrbetriq® (mirabegron) 50mg tablet	$13.34	$400.20
tolterodine 4mg ER capsule	$1.31	$39.30
oxybutynin 15mg ER tablet	$0.26	$15.60

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Unit = 1 capsule or tablet
+Cost per month based on the maximum FDA approved dose for each product.
ER = extended-release

Recommendations

The College of Pharmacy recommends the placement of Gemtesa® (vibegron) into the Special Prior Authorization (PA) Tier of the bladder control medications Product Based Prior Authorization (PBPA) category, based on net costs, with the following additional criteria:

Gemtesa® (Vibegron) Approval Criteria:

1. An FDA approved indication of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why all lower tiered medications are not appropriate for the member must be provided; and
4. A quantity limit of 30 tablets per 30 days will apply.

Additionally, the College of Pharmacy recommends the placement of VESIcare LS™ (solifenacin oral suspension) into Tier-1 of the bladder control medications PBPA category, based on net costs, with an age restriction of 2 to 10 years of age. Members older than 10 years of age will require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

The College of Pharmacy also recommends the placement of Myrbetriq® (mirabegron granules for oral suspension) into Tier-3 of the bladder control medications PBPA category with an age restriction of 3 years of age and older in members weighing <35kg. Members weighing ≥35kg would require a patient-specific, clinically significant reason why the granule formulation of mirabegron is needed in place of the regular tablet formulation. Current Tier-3 criteria will also apply.

Finally, the College of Pharmacy recommends removing Noctiva™ (desmopressin acetate nasal spray) from the Tier chart based on product discontinuation (additions and changes shown in red):

Bladder Control Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
fesoterodine (Toviaz®)	tolterodine (Detrol®)	darifenacin (Enablex®)	~~**desmopressin acetate nasal spray (Noctiva™)⁺**~~
oxybutynin (Ditropan®)	tolterodine ER (Detrol LA®)	mirabegron (Myrbetriq®)Δ **tablets and granulesβ**	desmopressin acetate SL tablets (Nocdurna®)⁺
oxybutynin ER (Ditropan XL®)		oxybutynin gel (Gelnique®)	oxybutynin patch (Oxytrol®)⁺
solifenacin (VESIcare®)Δ		trospium ER (Sanctura XR®)	**vibegron (Gemtesa®)⁺**
solifenacin oral susp (VESIcare LS™)α			
trospium (Sanctura®)			

ER, XL, XR = extended-release; LA = long-acting; PA = prior authorization; SL = sublingual; susp = suspension

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).

⁺Unique criteria specific to Gemtesa® (vibegron), Oxytrol® (oxybutynin patch)~~, Noctiva™ (desmopressin acetate nasal spray),~~ and Nocdurna® (desmopressin acetate SL tablets) applies.

ΔUnique criteria specific to use of Myrbetriq® (mirabegron) in combination with VESIcare® (solifenacin) applies.

αAn age restriction of 2 to 10 years of age will apply for VESIcare LS™. Members older than 10 years of age will require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

βThe Myrbetriq® granule formulation is covered for members 3 years of age or older weighing <35kg. Members weighing ≥35kg will require a patient-specific, clinically significant reason why the granule formulation is needed in place of the regular tablet formulation.

Utilization Details of Bladder Control Medications: Calendar Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-1 PRODUCTS						
OXYBUTYNIN PRODUCTS						
OXYBUTYNIN 5MG TAB	3,931	1,062	$65,731.05	$16.72	3.7	10.05%
OXYBUTYNIN 10MG ER TAB	2,141	591	$46,698.22	$21.81	3.62	7.14%
OXYBUTYNIN 5MG ER TAB	1,493	432	$32,378.08	$21.69	3.46	4.95%
OXYBUTYNIN 5MG/5ML SYP	834	250	$14,028.66	$16.82	3.34	2.14%
OXYBUTYNIN 15MG ER TAB	798	201	$17,443.02	$21.86	3.97	2.67%
SUBTOTAL	**9,197**	**2,536**	**$176,279.03**	**$19.17**	**3.63**	**26.95%**
FESOTERODINE PRODUCTS						
TOVIAZ 8MG TAB	391	99	$171,554.98	$438.76	3.95	26.23%
TOVIAZ 4MG TAB	377	109	$155,096.39	$411.40	3.46	23.71%
SUBTOTAL	**768**	**208**	**$326,651.37**	**$425.33**	**3.69**	**49.94%**
SOLIFENACIN PRODUCTS						
SOLIFENACIN 10MG TAB	282	85	$5,717.65	$20.28	3.32	0.87%
SOLIFENACIN 5MG TAB	207	92	$4,472.99	$21.61	2.25	0.68%
VESICARE 5MG TAB	12	8	$12,665.53	$1,055.46	1.5	1.94%
VESICARE 10MG TAB	9	4	$5,630.80	$625.64	2.25	0.86%
SUBTOTAL	**510**	**189**	**$28,486.97**	**$55.86**	**2.7**	**4.35%**
TROSPIUM PRODUCTS						
TROSPIUM CHL 20MG TAB	179	49	$5,488.85	$30.66	3.65	0.84%
SUBTOTAL	**179**	**49**	**$5,488.85**	**$30.66**	**3.65**	**0.84%**
TIER-1 SUBTOTAL	**10,654**	**2,682***	**$536,906.22**	**$50.39**	**3.97**	**82.08%**
TIER-2 PRODUCTS						
TOLTERODINE PRODUCTS						
TOLTERODINE 2MG TAB	179	27	$8,766.70	$48.98	6.63	1.34%
TOLTERODINE 4MG ER CAP	143	22	$6,898.31	$48.24	6.5	1.05%
TOLTERODINE 2MG ER CAP	43	3	$1,604.06	$37.30	14.33	0.25%
TOLTERODINE 1MG TAB	18	2	$421.35	$23.41	9	0.06%
SUBTOTAL	**383**	**54**	**$17,690.42**	**$46.19**	**7.09**	**2.70%**
TIER-2 SUBTOTAL	**383**	**53***	**$17,690.42**	**$46.19**	**7.23**	**2.70%**
TIER-3 PRODUCTS						
MIRABEGRON PRODUCTS						
MYRBETRIQ 50MG TAB	123	22	$48,688.29	$395.84	5.59	7.44%
MYRBETRIQ 25MG TAB	81	13	$29,686.64	$366.50	6.23	4.54%
SUBTOTAL	**204**	**35**	**$78,374.93**	**$384.19**	**5.83**	**11.98%**
TROSPIUM PRODUCTS						
TROSPIUM CHL 60MG ER CAP	115	19	$15,039.63	$130.78	6.05	2.30%
SUBTOTAL	**115**	**19**	**$15,039.63**	**$130.78**	**6.05**	**2.30%**
DARIFENACIN PRODUCTS						
DARIFENACIN 15MG TAB	30	3	$2,904.33	$96.81	10	0.44%
DARIFENACIN 7.5MG TAB	4	1	$376.09	$94.02	4	0.06%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SUBTOTAL	**34**	**4**	**$3,280.42**	**$96.48**	**8.5**	**0.50%**
OXYBUTYNIN PRODUCTS						
GELNIQUE 10% GEL	7	1	$2,848.58	$406.94	7	0.44%
SUBTOTAL	**7**	**1**	**$2,848.58**	**$406.94**	**7**	**0.44%**
TIER-3 SUBTOTAL	**360**	**56***	**$99,543.56**	**$276.51**	**6.43**	**15.22%**
TOTAL	**11,397**	**2,749***	**$654,140.20**	**$57.40**	**4.15**	**100.00%**

CAP = capsule; CHL = chloride; ER = extended-release; SYP = syrup; TAB = tablet
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

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Appendix J

Calendar Year 2020 Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Zilxi® (Minocycline 1.5% Topical Foam)

Oklahoma Health Care Authority
May 2021

Current Prior Authorization Criteria

Aczone® (Dapsone Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. Member must be 20 years of age or younger; and
3. A previous trial of benzoyl peroxide or a patient-specific, clinically significant reason why benzoyl peroxide is not appropriate for the member must be provided; and
4. A previous trial of a topical antibiotic, such as clindamycin or erythromycin, or a patient-specific, clinically significant reason why a topical antibiotic is not appropriate for the member must be provided.

Amzeeq® (Minocycline 4% Topical Foam) Approval Criteria:

1. An FDA approved indication of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris; and
2. Member must be 9 years of age or older; and
3. Amzeeq® is not covered for members older than 20 years of age; and
4. A patient-specific, clinically significant reason why the member cannot use erythromycin 2% topical solution or clindamycin 1% topical solution, which are available without prior authorization, must be provided; and
5. A quantity limit of 30 grams per 30 days will apply.

Clindagel® (Clindamycin 1% Topical Gel) and Evoclin® (Clindamycin 1% Topical Foam) Approval Criteria:

1. Member must have failed a trial of a different formulation of topical clindamycin such as lotion, solution, swabs, or the preferred generic clindamycin gel (generic for Cleocin-T®; this generic medication is not interchangeable with Clindagel®); and
2. Member must be 20 years of age or younger.

Erythromycin 2% Swabs and 2% Topical Gel Approval Criteria:

1. A patient specific, clinically significant reason why the member cannot use erythromycin 2% topical solution must be provided; and
2. Member must be 20 years of age or younger.

MetroGel® (Metronidazole 1% Gel) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use metronidazole 0.75% gel, which is available without prior authorization, must be provided; and
2. Metronidazole 1% gel is not covered for members older than 20 years of age.

Noritate® (Metronidazole 1% Cream) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use metronidazole 0.75% cream, which is available without prior authorization for members 20 years of age or younger, must be provided; and
2. Noritate® is not covered for members older than 20 years of age.

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. Authorization of tazarotene 0.1% cream will require a patient-specific, clinically significant reason why the member cannot use the other formulations of tazarotene (brand Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel are preferred); and
4. For the diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and
    b. Based on current net costs, Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel will not require prior authorization for members 20 years of age or younger; and
5. A quantity limit of 100 grams per 30 days will apply.

Utilization of Topical Acne and Rosacea Products: Calendar Year 2020

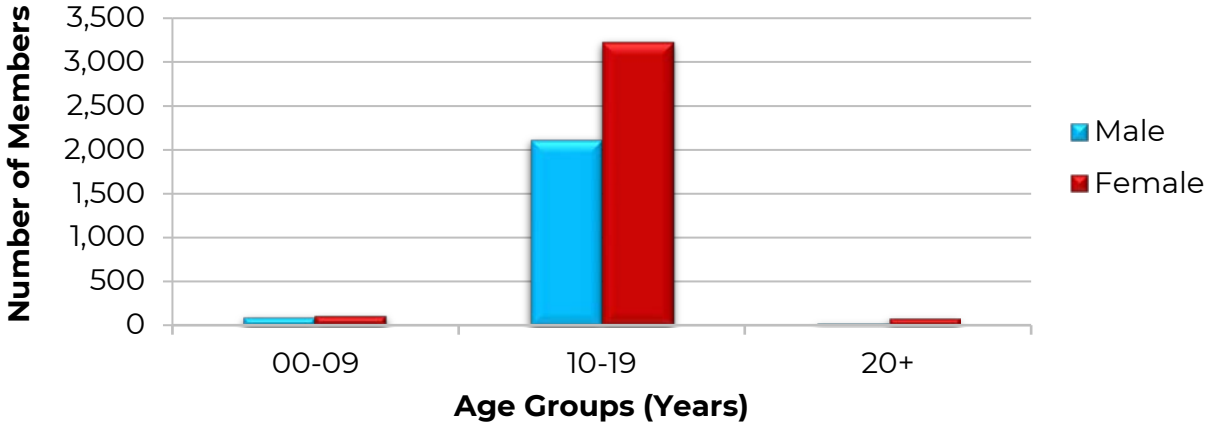
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	5,962	11,771	$1,751,982.54	$148.84	$5.92	581,276	295,973
2020	5,656	11,788	$1,743,700.02	$147.92	$5.69	598,083	306,240
% Change	**-5.10%**	**0.10%**	**-0.50%**	**-0.60%**	**-3.90%**	**2.90%**	**3.50%**
Change	**-306**	**17**	**-$8,282.52**	**-$0.92**	**-$0.23**	**16,807**	**10,267**

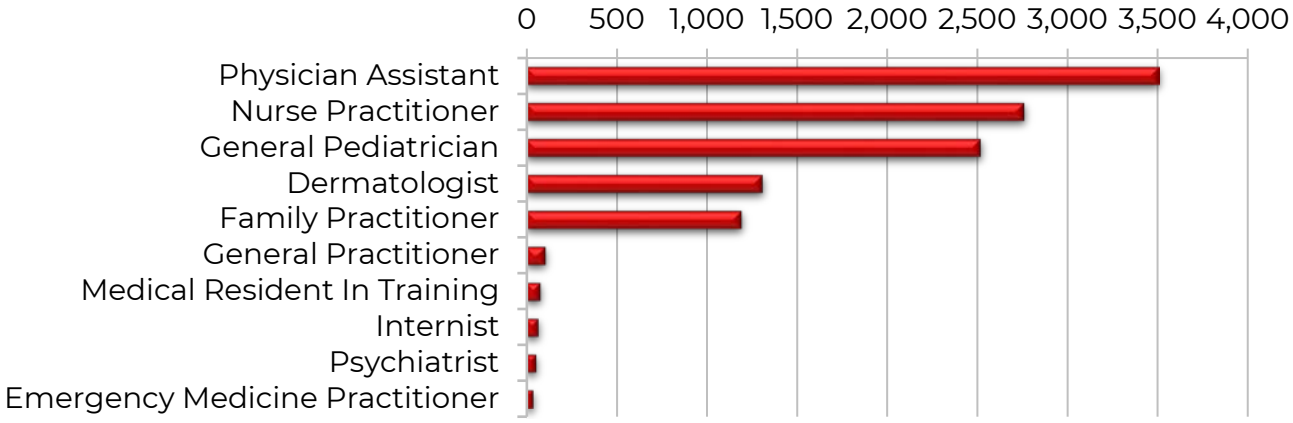
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

- Please note: Aczone® and Tazorac® both have significant federal rebates and costs included in this report do not reflect rebated prices or net costs.

Demographics of Members Utilizing Topical Acne and Rosacea Products



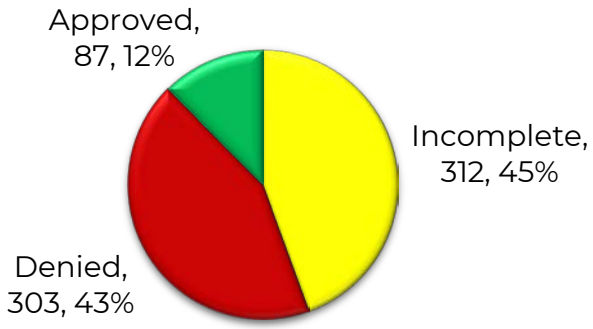
Top Prescriber Specialties of Topical Acne and Rosacea Products by Number of Claims



Prior Authorization of Topical Acne and Rosacea Products

There were 702 prior authorization requests submitted for topical acne and rosacea products during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Evoclin® (clindamycin 1% foam): February 2024
- Zilxi® (minocycline 1.5% foam): October 2030
- Aczone® (dapsone 7.5% gel): November 2033
- Amzeeq® (minocycline 4% foam): September 2037

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

- **September 2019:** The FDA approved Aczone® (dapsone) 7.5% gel for an expanded indication to include patients 9 to 11 years of age. Aczone® 7.5% gel was previously FDA approved in February 2016 for patients 12 years of age and older for the treatment of inflammatory and non-inflammatory acne. The expanded approval was based on data from an open-label safety study to assess safety, pharmacokinetics, and treatment effect of Aczone® 7.5% gel in 101 patients 9 to 11 years of age with acne vulgaris. Based on the results of the study, Aczone® 7.5% gel was determined to be safe and effective in this age range.
- **May 2020:** The FDA approved Zilxi® (minocycline 1.5% topical foam) for the treatment of inflammatory lesions of rosacea in adults. Zilxi® is the first minocycline-containing product approved by the FDA for rosacea. The FDA approval was based on data from (2) 12-week, multicenter, double-blind, vehicle-controlled Phase 3 studies in 1,522 adult patients with moderate-to-severe facial papulopustular rosacea. The co-primary endpoints were absolute change from baseline in inflammatory lesion count and Investigator Global Assessment (IGA) treatment success at week 12. Both studies met the co-primary endpoints, demonstrating significantly greater reduction in inflammatory lesions and a higher proportion of patients with IGA treatment success at week 12 with Zilxi® compared to vehicle.

Pipeline:

- **BPX-01:** BioPharmX is in Phase 2 development of BPX-01, a novel, proprietary topical minocycline gel formulation for the treatment of patients with inflammatory lesions of acne vulgaris. BPX-01 uses an anhydrous hydrophilic topical delivery system to completely solubilize the minocycline, resulting in a formulation that is stable and able to penetrate into the region of the skin where *Propionibacterium acnes (P. acnes)* reside. A Phase 2A study showed a statistically significant reduction in facial *P. acnes* after 4 weeks of once daily treatment with BPX-01. Additionally, no measurable systemic levels of minocycline or adverse drug effects were observed. BioPharmX has received feedback from the FDA regarding its planned Phase 3 study of BPX-01 and is seeking a strategic partnership to assist with funding the study.

- **BPX-04:** BioPharmX is also conducting Phase 2 studies of BPX-04, a fully solubilized formulation of minocycline 1% topical gel, for the treatment of moderate-to-severe papulopustular rosacea. In a Phase 2B study, treatment with BPX-04 resulted in a statistically significant reduction in the number of facial inflammatory lesions, with no treatment-related adverse events reported. The results of the study support progression of BPX-04 into Phase 3 studies.

Zilxi® (Minocycline 1.5% Topical Foam) Product Summary[8]

Indication: Zilxi® (minocycline 1.5% topical foam) is a topical tetracycline-class antibiotic indicated for the treatment of inflammatory lesions of rosacea in adults.

- Limitations of Use: This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Zilxi® should be used only as indicated.

How Supplied: 1.5% topical foam (containing 15mg minocycline per gram) in a 30g pressurized aluminum aerosol can

Dosing and Administration:

- After shaking the can well, patients should apply a small amount of topical foam onto the fingertips and then apply the foam as a thin layer over all areas of the face.
- Additional foam may be used as needed to ensure the entire face is treated.
- The foam should be applied at approximately the same time each day at least 1 hour before bedtime.
- Patients should not bathe, shower, or swim for at least 1 hour after application of the product.

Cost Comparison:

Product	Cost Per Unit*	Cost Per Package⁺
Zilxi® (minocycline) 1.5% topical foam	**$16.17**	**$970.20**
Amzeeq® (minocycline) 4% topical foam	$15.51	$465.30
metronidazole 0.75% topical cream (generic)	$0.99	$44.55
metronidazole 0.75% topical gel (generic)	$0.73	$32.85
clindamycin 1% topical solution (generic)	$0.22	$13.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Unit = 1 gram or mL
⁺Cost per package based on the largest package size available for each product listed (60g for Zilxi®, 30g for Amzeeq®, 45g for metronidazole 0.75% cream and metronidazole 0.75% gel, and 60mL for clindamycin 1% topical solution)

Recommendations

The College of Pharmacy recommends the prior authorization of Zilxi® (minocycline 1.5% topical foam) with the following criteria:

Zilxi® (Minocycline 1.5% Topical Foam) Approval Criteria:

1. An FDA approved diagnosis of inflammatory lesions of rosacea in adults; and
2. Member must be 18 to 20 years of age; and
3. A patient-specific, clinically significant reason why the member cannot utilize clindamycin topical solution (generic), metronidazole topical gel and cream 0.75%, erythromycin topical 2% solution, oral isotretinoin medications, and other generically available preferred oral or topical antibiotic products must be provided; and
4. A quantity limit of 30 grams per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the Aczone® (dapsone gel) approval criteria based on the FDA approved age expansion for the 7.5% gel with the following changes shown in red:

Aczone® (Dapsone Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. For Aczone® 7.5% gel, the member must be 9 years of age or older; and
3. Aczone® will not be covered for members older than 20 years of age; and
4. A previous trial of benzoyl peroxide or a patient-specific, clinically significant reason why benzoyl peroxide is not appropriate for the member must be provided; and
5. A previous trial of a topical antibiotic, such as clindamycin or erythromycin, or a patient-specific, clinically significant reason why a topical antibiotic is not appropriate for the member must be provided.

Finally, the College of Pharmacy recommends updating the Tazorac® (tazarotene) approval criteria based on net costs and current product availability with the following changes in red:

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. ~~Authorization of tazarotene 0.1% cream will require a patient-specific, clinically significant reason why the member cannot use the other formulations of tazarotene (brand Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel are preferred); and~~
4. For the diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and

b. ~~Based on current net costs,~~ Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel and tazarotene 0.1% cream will not require prior authorization for members 20 years of age or younger; and

5. A quantity limit of 100 grams per 30 days will apply.

Utilization Details of Topical Acne and Rosacea Products: Calendar Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CLINDAMYCIN PRODUCTS						
CLINDAMYCIN GEL 1%	4,531	2,494	$239,381.03	$52.83	1.82	13.73%
CLINDAMYCIN SOL 1%	1,708	976	$38,794.50	$22.71	1.75	2.22%
CLINDAMYCIN LOT 10MG/ML	1,091	633	$88,620.03	$81.23	1.72	5.08%
CLINDAMYCIN SWAB 1%	852	308	$26,168.55	$30.71	2.77	1.50%
CLINDAMYCIN LOT 1%	837	488	$67,942.95	$81.17	1.72	3.90%
CLINDACIN-P SWAB 1%	9	6	$325.80	$36.20	1.5	0.02%
CLINDAGEL GEL 1%	5	1	$8,943.35	$1,788.67	5	0.51%
CLINDACIN ETZ SWAB 1%	2	1	$65.94	$32.97	2	0.00%
SUBTOTAL	**9,035**	**4,700***	**$470,242.15**	**$52.05**	**1.92**	**26.97%**
TAZAROTENE PRODUCTS						
TAZORAC GEL 0.05%	1,038	706	$564,998.96	$544.31	1.47	32.40%
TAZORAC CRE 0.05%	728	550	$409,897.43	$563.05	1.32	23.51%
TAZORAC GEL 0.1%	417	273	$221,664.04	$531.57	1.53	12.71%
TAZAROTENE CRE 0.1%	116	103	$23,059.36	$198.79	1.13	1.32%
TAZORAC CRE 0.1%	36	31	$20,581.87	$571.72	1.16	1.18%
SUBTOTAL	**2,335**	**1,482***	**$1,240,201.66**	**$531.14**	**1.58**	**71.12%**
ERYTHROMYCIN PRODUCTS						
ERYTHROMYCIN SOL 2%	257	149	$9,923.78	$38.61	1.72	0.57%
SUBTOTAL	**257**	**149***	**$9,923.78**	**$38.61**	**1.72**	**0.57%**
METRONIDAZOLE PRODUCTS						
METRONIDAZOLE CRE 0.75%	70	54	$3,999.81	$57.14	1.3	0.23%
METRONIDAZOLE GEL 0.75%	41	34	$2,136.83	$52.12	1.21	0.12%
METRONIDAZOLE LOT 0.75%	3	3	$245.49	$81.83	1	0.01%
SUBTOTAL	**114**	**91***	**$245.49**	**$2.15**	**1.25**	**0.01%**
DAPSONE PRODUCTS						
DAPSONE GEL 5%	30	18	$9,812.73	$327.09	1.67	0.56%
DAPSONE GEL 7.5%	2	2	$997.90	$498.95	1	0.06%
ACZONE GEL 7.5%	2	2	$1,344.26	$672.13	1	0.08%
ACZONE GEL 5%	1	1	$880.09	$880.09	1	0.05%
SUBTOTAL	**35**	**23***	**$13,034.98**	**$372.43**	**1.52**	**0.75%**
MINOCYCLINE PRODUCTS						
AMZEEQ AER 4%	7	5	$3,354.12	$479.16	1.4	0.19%
SUBTOTAL	**7**	**5***	**$3,354.12**	**$479.16**	**1.4**	**0.19%**
SULFACETAMIDE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SULFACETAMIDE LOT 10%	5	5	$561.20	$112.24	1	0.03%
SUBTOTAL	**5**	**5***	**$561.20**	**$112.24**	**1**	**0.03%**
TOTAL	**11,788**	**5,656***	**$1,743,700.02**	**$147.92**	**2.08**	**100.00%**

AER = foam; CRE = cream; ETZ = pledgets; LOT = lotion; SOL = solution
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Aczone® and Tazorac® both have significant federal rebates and costs included in this report 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: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 04/2021. Last accessed 04/13/2021.
[2] Almirall LLC. Aczone® (Dapsone) Gel, 7.5% Now Approved for the Topical Treatment of Acne Vulgaris in Patients 9 Years of Age and Older. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/aczone-dapsone-gel-7-5-now-approved-for-the-topical-treatment-of-acne-vulgaris-in-patients-9-years-of-age-and-older-300915589.html. Issued 09/10/2019. Last accessed 04/13/2021.
[3] Menlo Therapeutics, Inc. Menlo Therapeutics Receives FDA Approval of Zilxi® (Minocycline) Topical Foam, 1.5%, the First Topical Minocycline Treatment for Rosacea. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/05/29/2041047/0/en/Menlo-Therapeutics-Receives-FDA-Approval-of-ZILXI-minocycline-topical-foam-1-5-the-First-Topical-Minocycline-Treatment-for-Rosacea.html. Issued 05/29/2020. Last accessed 04/13/2021.
[4] BioPharmX Corporation. BioPharmX Pipeline: BPX-01. Available online at: https://www.biopharmx.com/pipeline/bpx-01-acne/. Last accessed 04/19/2021.
[5] BioPharmX Corporation. BioPharmX Receives Concurrence from FDA on Phase 3 Acne Study Plans. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/biopharmx-receives-concurrence-from-fda-on-phase-3-acne-study-plans-300551723.html. Issued 11/08/2017. Last accessed 04/19/2021.
[6] BioPharmX Corporation. BioPharmX Pipeline: BPX-04. Available online at: https://www.biopharmx.com/pipeline/bpx-04-rosacea/. Last accessed 04/19/2021.
[7] BioPharmX Corporation. BioPharmX Announces Positive Topline Results from Phase 2B Trial of BPX-04 for Papulopustular Rosacea. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/biopharmx-announces-positive-topline-results-from-phase-2b-trial-of-bpx-04-for-papulopustular-rosacea-300874090.html. Issued 06/25/2019. Last accessed 04/19/2021.
[8] Zilxi® (Minocycline Topical Foam) Prescribing Information. Vyne Therapeutics, Inc. Available online at: https://zilxi.com/sites/default/files/documents/prescribing-information.pdf. Last revised 01/2021. Last accessed 04/13/2021.

Appendix K

Calendar Year 2020 Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Fetroja® (Cefiderocol) and Kimyrsa™ (Oritavancin)

Oklahoma Health Care Authority
May 2021

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®)
   - Cephalexin 250mg and 500mg tablets
   - Cephalexin 750mg capsules
   - Doxycycline hyclate 75mg and 150mg tablets (Acticlate®)
   - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
   - Doxycycline monohydrate 150mg capsules and tablets
   - Doxycycline monohydrate DR 40mg capsules (Oracea®)
   - Minocycline ER capsules (Ximino®)
   - Minocycline ER tablets (Minolira™)
   - Minocycline ER tablets (Solodyn®)

Arikayce® (Amikacin Liposome Inhalation Suspension) Approval Criteria:

1. An FDA approved indication for the treatment of *Mycobacterium avium* complex (MAC) lung disease in adult members who have limited or no alternative treatment options; and
2. Member must have had a minimum of 6 consecutive months of a multidrug background regimen therapy used compliantly and not achieved negative sputum cultures within the last 12 months. Dates of previous treatments and regimens must be listed on the prior authorization request; and
   a. If claims for a multidrug background regimen are not in the member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the prescriber; and
3. Member must continue a multidrug background regimen therapy while on Arikayce®, unless contraindicated, or provide reasoning why

continuation of a multidrug background regimen is not appropriate for the member; and
4. A patient-specific, clinically significant reason why the member requires an inhaled aminoglycoside in place of an intravenous or intramuscular aminoglycoside (e.g., amikacin, streptomycin) must be provided; and
5. Arikayce® will not be approved for patients with non-refractory MAC lung disease; and
6. Arikayce® must be prescribed by or in consultation with a pulmonary disease or infectious disease specialist (or an advanced care practitioner with a supervising physician who is a pulmonary disease or infectious disease specialist); and
7. Initial approvals will be for the duration of 6 months after which time the prescriber must document the member is responding to treatment for continued approval.
8. A quantity limit of 28 vials per 28 days will apply.

Avycaz® (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infection (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infection (cUTI), including pyelonephritis; or
    c. Hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP); and
2. Member must be 3 months of age or older; and
3. For the diagnosis of cIAI, Avycaz® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. Approval quantity will be based on Avycaz® *Prescribing Information* and FDA approved dosing regimen(s).

Baxdela® (Delafloxacin) Tablet and Vial Approval Criteria [Acute Bacterial Skin and Skin Structure Infection (ABSSSI) Diagnosis]:

1. An FDA approved diagnosis of 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) must be provided; and
3. Approval quantity will be based on Baxdela® *Prescribing Information* and FDA approved dosing regimen(s); and
    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.

Baxdela® (Delafloxacin) Tablet and Vial Approval Criteria [Community-Acquired Bacterial Pneumonia (CABP) Diagnosis]:

1. An FDA approved diagnosis of CABP caused by designated susceptible bacteria; and
2. A patient-specific, clinically significant reason why the member cannot use an appropriate beta-lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin/sulbactam) in combination with a macrolide (e.g., azithromycin, clarithromycin) or doxycycline, monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin, gemifloxacin), or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. Approval quantity will be based on Baxdela® *Prescribing Information* and FDA approved dosing regimen(s); and
    a. For Baxdela® vials, an initial quantity limit of 6 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

Ciprofloxacin 100mg Tablet Approval Criteria:

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

Ciprofloxacin 500mg and 1,000mg Extended-Release (ER) Tablet Approval Criteria:

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

Dalvance® (Dalbavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and

2. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, or other cost effective therapeutic equivalent medication(s) must be provided.
3. A quantity limit of 3 vials per 7 days will apply.

Levofloxacin 25mg/mL Oral Solution, Ciprofloxacin 250mg/mL Oral Suspension, and Ciprofloxacin 500mg/mL Oral Suspension:

1. Members older than 6 years of age require a patient-specific, clinically significant reason why the oral tablet formulations cannot be used.

Minocycline (50, 75, 100mg) Immediate-Release (IR) Tablet:

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

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

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

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

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

clinically significant reason why the member cannot switch to the oral tablet formulation for the remainder of therapy.

Ofloxacin 300mg and 400mg Tablet Approval Criteria:

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

Recarbrio™ (Imipenem/Cilastatin/Relebactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infection (cIAI); or
    b. Complicated urinary tract infection (cUTI), including pyelonephritis; and
2. Member must be 18 years of age or older; and
3. The prescriber must verify that limited or no alternative treatment options are available; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. A quantity limit of 56 vials per 14 days will apply.

Seysara® (Sarecycline) Approval Criteria:

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

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 linezolid or other cost effective therapeutic equivalent medication(s) must be provided; and
3. A quantity limit of 6 tablets or vials per 6 days will apply.

Solosec® (Secnidazole Oral Granules) Approval Criteria:

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

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

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

Tetracycline 250mg and 500mg Capsule Approval Criteria:

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

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) must be provided; and
3. Approval quantity will be based on Vabomere® *Prescribing Information* and FDA approved dosing regimen(s).

Xenleta® (Lefamulin) Approval Criteria:

1. An FDA approved diagnosis of community-acquired bacterial pneumonia (CABP) caused by designated susceptible microorganisms; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use an appropriate beta-lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin/sulbactam) in combination with a macrolide (e.g., azithromycin, clarithromycin) or doxycycline, or other cost-effective therapeutic equivalent alternative(s) must be provided; and

4. Approval quantity will be based on Xenleta® *Prescribing Information* and FDA approved dosing regimen(s).

Xerava™ (Eravacycline) Approval Criteria:

1. An FDA approved diagnosis of complicated intra-abdominal infection (cIAI) caused by designated susceptible microorganisms; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; 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.

Zemdri® (Plazomicin) Approval Criteria:

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

Zerbaxa® (Ceftolozane/Tazobactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infection (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infection (cUTI), including pyelonephritis; or
    c. Hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP); and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Zerbaxa® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone,

ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and

5. Approval quantity will be based on Zerbaxa® *Prescribing Information* and FDA approved dosing regimen(s).

Utilization of Various Systemic Antibiotics: Calendar Year 2020

Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	261	391	$181,608.68	$464.47	$38.06	44,028	4,772
2020	222	328	$447,983.61	$1,365.80	$100.81	37,647	4,444
% Change	**-14.9%**	**-16.1%**	**146.7%**	**194.1%**	**164.9%**	**-14.5%**	**-6.9%**
Change	**-39**	**-63**	**$266,374.93**	**$901.33**	**$62.75**	**-6,381**	**-328**

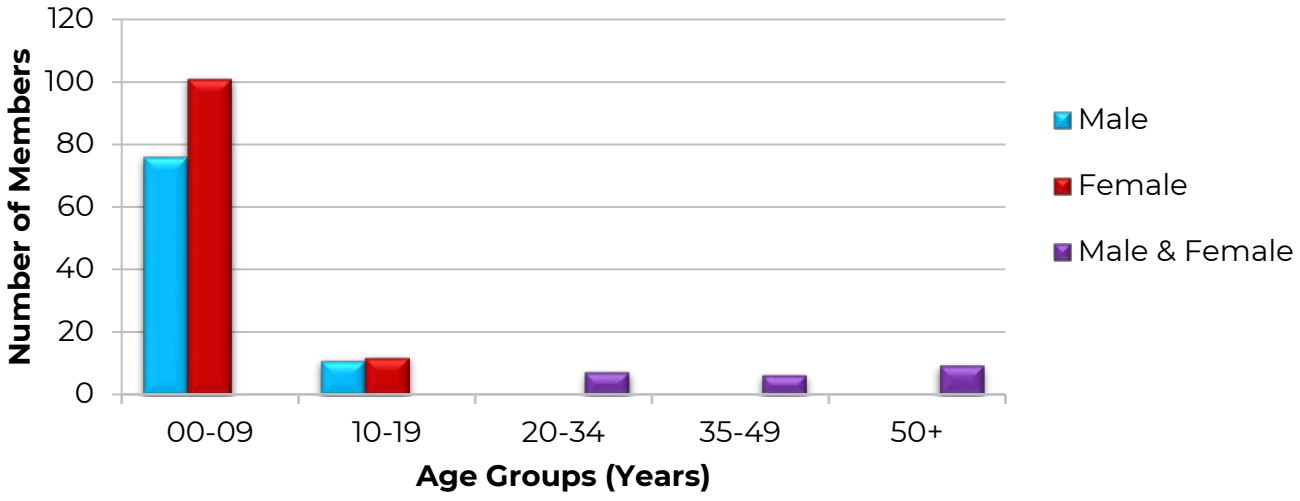
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

Calendar Year 2020 Utilization: Medical Claims

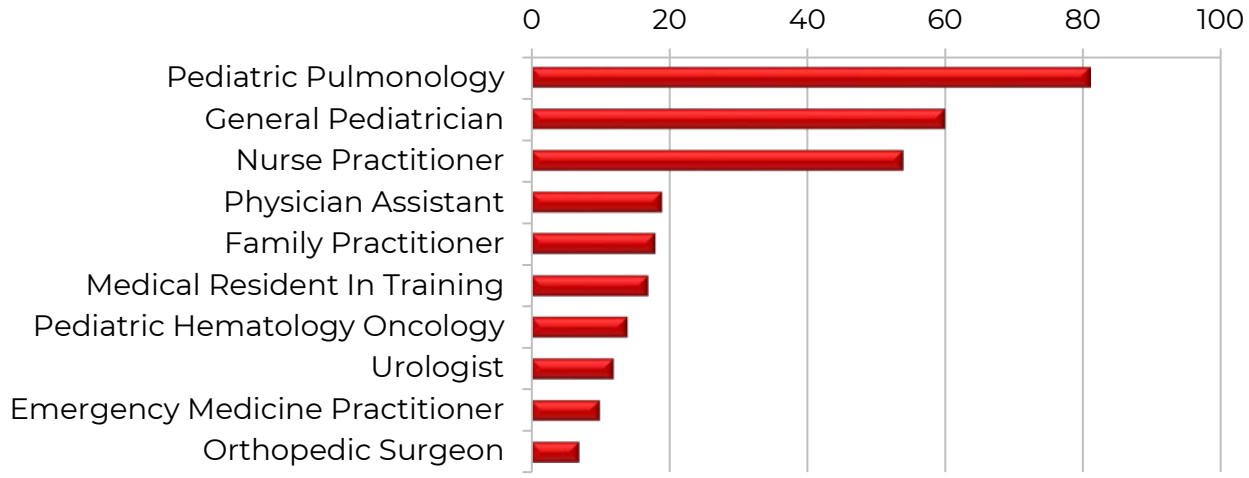
Calendar Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2020	3	3	$13,653.00	$4,551.00	1

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

Demographics of Members Utilizing Various Systemic Antibiotics



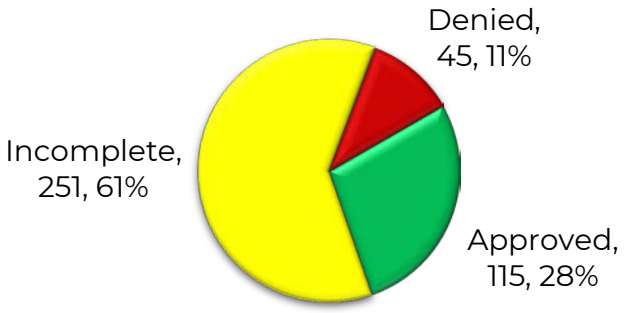
Top Prescriber Specialties of Various Systemic Antibiotics by Number of Claims



Prior Authorization of Various Systemic Antibiotics

There were 411 prior authorization requests submitted for various systemic antibiotics during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Dalvance® [dalbavancin vial for intravenous (IV) infusion]: December 2023
- Ximino® [minocycline extended-release (ER) capsule]: April 2027
- Doryx® [doxycycline hyclate delayed-release (DR) tablet]: February 2028
- Suprax® (cefixime 500mg/5mL oral suspension): December 2028
- Xenleta® (lefamulin vial for IV infusion): January 2029
- Recarbrio (imipenem/cilastatin/relebactam): November 2029
- Baxdela® (delafloxacin tablet): December 2029
- Sivextro® (tedizolid tablet and vial for IV infusion): February 2030

- Xerava™ (eravacycline vial for IV infusion): December 2030
- Xenleta® (lefamulin tablet): May 2031
- Zemdri® (plazomicin vial for IV infusion): June 2031
- Vabomere® (meropenem/vaborbactam vial for IV infusion): August 2031
- Solodyn® (minocycline ER tablet): November 2031
- Avycaz® (ceftazidime/avibactam vial for IV infusion): June 2032
- Baxdela® (delafloxacin vial for IV infusion): February 2033
- Seysara® (sarecycline tablet): February 2033
- Orbactiv® (oritavancin vial for IV infusion): July 2035
- Zerbaxa® (ceftolozane/tazobactam vial for IV infusion): August 2035
- Fetroja® (cefiderocol): September 2035
- Nuzyra® (omadacycline tablet and vial for IV infusion): October 2037

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

- **November 2019:** The FDA approved Fetroja® (cefiderocol) for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by susceptible gram-negative microorganisms. The safety and efficacy of Fetroja® was assessed in a trial of 448 patients with cUTI. Of the patients receiving Fetroja®, 72.6% had resolution of symptoms and eradication of the bacteria 7 days after completing treatment, compared to 54.6% of patients receiving imipenem/ cilastatin.
- **September 2020:** The FDA approved an expanded indication for Fetroja® (cefiderocol) for the treatment of hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) caused by susceptible gram-negative microorganisms. This expanded indication was based on results from the Phase 3 APEKS-NP trial, which showed Fetroja® was non-inferior to meropenem in all-cause mortality 14 days after initiation of the study drug in hospitalized patients with HABP and VABP.
- **March 2021:** The FDA approved Kimyrsa™ (oritavancin) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of designated gram-positive microorganisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) in adult patients. The safety and efficacy of Kimyrsa™ were established in previous trials done with another oritavancin product, Orbactiv®. Kimyrsa™ has a shorter infusion time when compared to Orbactiv® (1 hour vs. 3 hours). Melinta Therapeutics is planning to launch Kimyrsa™ in summer of 2021.

News:

- **December 2019:** In September 2019, the Centers for Medicare and Medicaid Services (CMS) released a final rule requiring all acute care

hospitals that participate in Medicare or Medicaid to develop and implement an antibiotic stewardship program (ASP) by March 30, 2020 as part of their infection control efforts. In response to this requirement, the Centers for Disease Control and Prevention (CDC) provided an update to their Core Elements for *Hospital Antibiotic Stewardship Programs* that was originally created in 2014. The 2019 revised version provided major updates to each of 7 core elements of ASP, which include hospital leadership commitment, accountability, pharmacy expertise, action, reporting, education, and tracking. The 2019 update highlights the effectiveness of the physician and pharmacy co-leadership, the vital importance of pharmacists in the ASP, and how to implement antibiotic interventions (including prospective audit and feedback). The updated recommendations also mention the development of a facility-specific treatment guideline that is focused on the 3 most common types of infections seen, which include urinary tract infections, lower respiratory infections, and skin and soft tissue infections. Antibiotic use and resistance reporting should be communicated regularly to prescribers, pharmacists, nurses, and hospital leadership. This information should also be shared among different types of hospitals. The new recommendations also advise on teaching adverse reactions, resistance, and optimal prescribing to prescribers, pharmacists, and nurses. Lastly, the updates address the need for tracking prescription monitoring, intervention impact, disease resistance patterns, outcome measures, and adherence to treatment guidelines.

Guideline Updates:

- **Community Acquired Pneumonia (CAP):** In October 2019, the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) updated the current practice guidelines for CAP. The update focuses on 16 specific areas for recommendations in regards to diagnostic testing, determination of site care, selection of initial empiric antibiotic therapy, and subsequent management decisions. The following is a summary of changes between the 2019 and 2007 ATS/IDSA CAP guidelines in regards to treatment recommendations:

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of corticosteroids	Not covered	Not recommended; may be considered in patients with refractory septic shock

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Standard empiric therapy for severe community acquired pneumonia (CAP)	β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β-lactam /macrolide combination
Use of health care-associated pneumonia (HCAP)	Accepted as per 2005 hospital-acquired pneumonia guidelines	Remove HCAP and focus on local epidemiology and validated risk factors for methicillin-resistant *Staphylococcus aureus (MRSA)* and *Pseudomonas aeruginosa*

Fetroja® (Cefiderocol) Product Summary[9,10,11]

Indication(s): Fetroja® (cefiderocol) is a cephalosporin antibiotic indicated in patients 18 years of age and older for the treatment of the following infections caused by susceptible gram-negative microorganisms:

- cUTI, including pyelonephritis
- HABP/VABP

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

- **cUTI, including pyelonephritis:** *Escherichia coli, Enterobacter cloacae* complex, *Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa*
- **HABP/VABP:** *Acinetobacter baumannii* complex, *Escherichia coli, Enterobacter cloacae* complex, *Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens*

Dosing:

- Fetroja® is supplied as a 1 gram lyophilized powder for reconstitution in a single-dose vial (SDV).
- The recommended dosing of Fetroja® is 2 grams every 8 hours via IV infusion over 3 hours in patients with a creatine clearance (CrCl) between 60 to 119mL/min.
- Dose adjustments are required for patients with a CrCl of <60mL/min, (including patients received intermittent hemodialysis or continuous renal replacement therapy) and patients with a CrCl >120mL/min.

Mechanism of Action: Cefiderocol is a cephalosporin antibacterial with activity against gram-negative aerobic bacteria. Cefiderocol functions as a siderophore and binds to extracellular free (ferric) iron. In addition to passive diffusion via porin channels, cefiderocol is actively transported across the outer cell membrane of bacteria into the periplasmic space using the bacterial siderophore iron uptake mechanism. Cefiderocol exerts bactericidal

action by inhibiting cell wall biosynthesis through binding to penicillin-binding proteins (PBPs).

Adverse Reactions:

- The most common adverse reactions seen in the clinical trials (incidence ≥2% and > placebo) were diarrhea, infusion site reactions, constipation, rash, candidiasis, cough, elevated liver tests, headache, hypokalemia, nausea, vomiting, hypomagnesemia, and atrial fibrillation.

Efficacy: The safety and efficacy of cefiderocol for cUTI, including pyelonephritis, and HABP/VABP were assessed in 2 active-controlled, double-blind, randomized, Phase 3 trials in hospitalized patients 18 years of age and older.

- Trial 1: A total of 448 hospitalized adults with cUTI (including pyelonephritis) were randomized in a 2:1 ratio to receive either cefiderocol 2 grams IV every 8 hours or imipenem/cilastatin 1 gram/ 1 gram IV every 8 hours for 7 to 14 days. No switch from IV to oral antibacterial therapy was permitted.
    - Primary Endpoint: The primary endpoint was the composite outcome of clinical response and microbiological response at the test of cure (TOC) assessment, defined as 7 days (±2 days) after the end of antibiotic treatment. Clinical response was based on the investigator's evaluation of the patient's clinical signs and symptoms of cUTI and the microbiological outcome was based on urine cultures.
    - Results: The composite response at TOC for the cefiderocol group was 72.6% compared to imipenem/cilastatin at 54.6% with a treatment difference of 18.6% [95% confidence interval (CI): 8.2, 28.9].
- Trial 2: A total of 298 hospitalized adults with HABP/VABP were randomized in a 1:1 ratio to receive either cefiderocol 2 grams IV every 8 hours or meropenem 2 grams IV every 8 hours for 7 to 14 days. Dosing was adjusted for renal function and both arms received linezolid 600mg every 12 hours for at least 5 days for empiric treatment of gram-positive organisms.
    - Primary Endpoint: The primary endpoint was the rate of all-cause mortality (ACM) at day 14, which was calculated as the percentage of patients in each treatment group who experienced mortality, regardless of cause, from the first infusion through day 14.
    - Results: The ACM rate at day 14 for the cefiderocol group was 12.4% compared to 12.2% in the meropenem group with a treatment difference of 0.2% (95% CI: -12.5, 8.5). Cefiderocol

showed non-inferiority to meropenem in regards to the primary outcome measure.

Cost: The Wholesale Acquisition Cost (WAC) of Fetroja® is $189.75 per SDV, resulting in a cost of $1,138.50 per day of therapy at the recommended dose of 2 grams every 8 hours.

Kimyrsa™ (Oritavancin) Product Summary[12]

Indication(s): Kimyrsa™ (oritavancin) is a lipoglycopeptide antibacterial drug indicated for the treatment of adult patients with ABSSSI caused or suspected to be caused by susceptible isolates of designated gram-positive microorganisms.

Microbiology: Oritavancin has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections:

- *Staphylococcus aureus* (including methicillin-resistant isolates), *Streptococcus agalactiae, Streptococcus anginosus group (*includes *S. anginosus, S. intermedius,* and *S. constellatus), Streptococcus dysgalactiae, Streptococcus pyogenes,* and *Enterococcus faecalis* (vancomycin-susceptible isolates only)

Dosing:

- Kimyrsa™ is supplied as a 1,200mg lyophilized powder for reconstitution in a SDV.
- The recommended dosing of Kimyrsa™ is 1,200mg as a single dose given by IV infusion over 1 hour.

Mechanism of Action: Oritavancin exerts concentration-dependent bactericidal activity via inhibition of the transglycosylation (polymerization) step of cell wall biosynthesis, inhibition of the transpeptidation (crosslinking) step of cell wall biosynthesis, and disruption of bacterial membrane integrity which lead to depolarization, permeabilization, and cell death.

Warnings and Precautions:

- Concomitant Warfarin Use: Oritavancin has been shown to artificially prolong PT/INR for up to 12 hours. Patients should be monitored for signs of bleeding if using warfarin and oritavancin concomitantly.

Adverse Reactions:

- The most common adverse reactions seen in the clinical trials (incidence ≥3% and >placebo) were headache, nausea, vomiting, limb and subcutaneous abscesses, and diarrhea.

Efficacy: The safety and efficacy of Kimyrsa™ for ABSSSI were established in the SOLO clinical trials with another oritavancin product, Orbactiv®. The approval of Kimyrsa™ was based on an open-label, pharmacokinetic study

which compared Kimyrsa™ infused over 1 hour to Orbactiv® infused over 3 hours. Kimyrsa™ was shown to be comparable to Orbactiv® with a favorable safety profile.

Cost: Pricing information for Kimyrsa™ is not available at this time.

Recommendations

The College of Pharmacy recommends the prior authorization of Fetroja® (cefiderocol) and Kimyrsa™ (oritavancin) with the following criteria:

Fetroja® (Cefiderocol) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
    a. Complicated urinary tract infection (cUTI), including pyelonephritis; or
    b. Hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP); and
2. Member must be 18 years of age or older; and
3. The prescriber must verify that limited or no alternative treatment options are available; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime), or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. Approval quantity will be based on Fetroja® *Prescribing Information* and FDA approved dosing regimen(s).

Kimyrsa™ (Oritavancin) Approval Criteria:

1. An FDA approved indication for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused or suspected to be caused by susceptible isolates of designated gram-positive microorganisms; and
2. Member must be 18 years of age or older; and
3. The prescriber must verify that limited or no alternative treatment options are available; and
4. A patient-specific, clinically significant reason why the member cannot use Orbactiv® (oritavancin) or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. Approval quantity will be based on Kimyrsa™ *Prescribing Information* and FDA approved dosing regimen(s).

Utilization Details of Various Systemic Antibiotics: Calendar Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
LEVOFLOXACIN PRODUCTS					
LEVOFLOXACIN SOL 25MG/ML	119	78	$16,884.74	$141.89	1.53
SUBTOTAL	**119**	**78**	**$16,884.74**	**$141.89**	**1.53**
CIPROFLOXACIN PRODUCTS					
CIPRO (5%) SUS 250MG/5ML	78	66	$12,634.27	$161.98	1.18
CIPRO (10%) SUS 500MG/5ML	53	47	$9,251.62	$174.56	1.13
CIPROFLOXACIN SUS 500MG/5ML	1	1	$239.73	$239.73	1
CIPROFLOXACIN SUS 250MG/5ML	1	1	$59.15	$59.15	1
SUBTOTAL	**133**	**115**	**$22,184.77**	**$166.80**	**1.16**
OMADACYCLINE PRODUCTS					
NUZYRA TAB 150MG	18	2	$222,686.44	$12,371.47	9
SUBTOTAL	**18**	**2**	**$222,686.44**	**$12,371.47**	**9**
AMIKACIN PRODUCTS					
ARIKAYCE SUS 590MG/8.4ML	8	2	$93,099.20	$11,637.40	4
SUBTOTAL	**8**	**2**	**$93,099.20**	**$11,637.40**	**4**
DALBAVANCIN PRODUCTS					
DALVANCE SOL 500MG	7	1	$27,737.77	$3,962.54	7
SUBTOTAL	**7**	**1**	**$27,737.77**	**$3,962.54**	**7**
AMOXICILLIN/CLAVULANATE POTASSIUM PRODUCTS					
AMOX-POT CLA TAB ER 1000/62.5MG	7	1	$1,023.90	$146.27	7
SUBTOTAL	**7**	**1**	**$1,023.90**	**$146.27**	**7**
CEFIXIME PRODUCTS					
CEFIXIME SUS 100MG/5ML	6	5	$1,653.53	$275.59	1.2
CEFIXIME CAP 400MG	6	6	$595.69	$99.28	1
CEFIXIME SUS 200MG/5ML	4	4	$835.84	$208.96	1
SUPRAX CHW 200MG	1	1	$323.88	$323.88	1
SUBTOTAL	**17**	**16**	**$3,408.94**	**$200.53**	**1.06**
TETRACYCLINE PRODUCTS					
TETRACYCLINE CAP 500MG	5	5	$543.19	$108.64	1
TETRACYCLINE CAP 250MG	4	4	$233.30	$58.33	1
SUBTOTAL	**9**	**9**	**$776.49**	**$86.28**	**1**
CEFTAZIDIME/AVIBACTAM PRODUCTS					
AVYCAZ INJ 2.5GM	3	2	$46,317.09	$15,439.03	1.5
SUBTOTAL	**3**	**2**	**$46,317.09**	**$15,439.03**	**1.5**
SECNIDAZOLE PRODUCTS					
SOLOSEC GRA 2GM	2	2	$565.90	$282.95	1
SUBTOTAL	**2**	**2**	**$565.90**	**$282.95**	**1**
DELAFLOXACIN PRODUCTS					
BAXDELA TAB 450MG	2	2	$2,996.08	$1,498.04	1
SUBTOTAL	**2**	**2**	**$2,996.08**	**$1,498.04**	**1**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TEDIZOLID PRODUCTS					
SIVEXTRO TAB 200MG	1	1	$2,329.39	$2,329.39	1
SUBTOTAL	**1**	**1**	**$2,329.39**	**$2,329.39**	**1**
MINOCYCLINE PRODUCTS					
MINOCYCLINE TAB 100MG	1	1	$124.19	$124.19	1
SUBTOTAL	**1**	**1**	**$124.19**	**$124.19**	**1**
MEROPENEM/VABORBACTAM PRODUCTS					
VABOMERE INJ 2GM	1	1	$7,848.71	$7,848.71	1
SUBTOTAL	**1**	**1**	**$7,848.71**	**$7,848.71**	**1**
TOTAL	**328**	**222***	**$447,983.61**	**$1,365.80**	**1.48**

AMOX-POT CLA = amoxicillin/clavulanate potassium; CAP = capsule; CHW = chewable; ER = extended-release GRA = granules; INJ = injection; SOL = solution; SUS = suspension; TAB = tablet
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
DALBAVANCIN (J0875)	3	3	$13,653.00	$4,551.00	1
SUBTOTAL	**3**	**3**	**$13,653.00**	**$4,551.00**	**1**
TOTAL	**3†**	**3***	**$13,653.00**	**$4,551.00**	**1**

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

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[3] Shionogi Announces FDA Approval of Fetroja® (Cefiderocol) for the Treatment of Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20200928005181/en/Shionogi-Announces-FDA-Approval-of-FETROJA%C2%AE-cefiderocol-for-the-Treatment-of-Hospital-acquired-Bacterial-Pneumonia-and-Ventilator-associated-Bacterial-Pneumonia. Issued 09/28/2020. Last accessed 04/16/2021.
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[10] A Study of Efficacy and Safety of Intravenous Cefiderocol (S-649266) Versus Imipenem/Cilastatin in Complicated Urinary Tract Infections (APEKS-cUTI). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02321800. Last revised 12/12/2019. Last accessed 04/16/2021.
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Appendix L

Calendar Year 2020 Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Kynmobi™ (Apomorphine) and Ongentys® (Opicapone)

Oklahoma Health Care Authority
May 2021

Current Prior Authorization Criteria

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

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

Gocovri® [Amantadine Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication for the treatment of dyskinesia in members with Parkinson's disease (PD) receiving levodopa-based therapy; and
2. Member must use Gocovri® concomitantly with levodopa therapy; and
3. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m^2]; and
4. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
5. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
6. A patient-specific, clinically significant reason why Osmolex® ER (amantadine ER) cannot be used must be provided; and
7. A quantity limit of (1) 68.5mg capsule or (2) 137mg capsules per day will apply.

Inbrija® (Levodopa Inhalation Powder) Approval Criteria:

1. An FDA approved indication for the treatment of "off" episodes in members with Parkinson's disease (PD) treated with carbidopa/levodopa; and

2. Member must be taking carbidopa/levodopa in combination with Inbrija®. Inbrija® has been shown to be effective only in combination with carbidopa/levodopa; and
3. Member must be experiencing motor fluctuations with a minimum of 2 hours of "off" time and demonstrate levodopa responsiveness; and
4. Member must not be taking nonselective monoamine oxidase inhibitors (MAOIs) concomitantly with Inbrija® or within 2 weeks prior to initiating Inbrija® and
5. A previous failed trial of immediate-release (IR) carbidopa/levodopa formulations alone or in combination with long-acting carbidopa/levodopa formulations or a reason why supplementation with IR carbidopa/levodopa formulations is not appropriate for the member must be provided; and
6. A quantity limit of 10 capsules for inhalation per day will apply.

Neupro® (Rotigotine Transdermal System) Approval Criteria:

1. For the diagnosis of Parkinson's disease (PD) the following criteria apply:
    a. An FDA approved indication for the treatment of signs and symptoms of PD; and
    b. Member must be 18 years of age or older; and
    c. Failed treatment, intolerance, or a patient-specific, clinically significant reason why the member cannot use oral dopamine agonists must be provided.
2. For the diagnosis of restless leg syndrome (RLS) the following criteria apply:
    a. An FDA approved indication of RLS; and
    b. Member must be 18 years of age or older; and
    c. Documented treatment attempts at the recommended dose with at least 2 of the following that did not yield adequate relief:
        i. carbidopa/levodopa; or
        ii. pramipexole; or
        iii. ropinirole.

Nourianz® (Istradefylline) Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease (PD); and
2. Member must be taking carbidopa/levodopa in combination with istradefylline (istradefylline has not been shown to be effective as monotherapy for the treatment of PD); and
3. Prescriber must verify that the dose is appropriate for the member based on degree of hepatic impairment, concomitant strong CYP3A4 inhibitors, and smoking status of the member; and
4. Member must be experiencing at least 2 hours of "off" time per day; and
5. A quantity limit of 1 tablet per day will apply.

Nuplazid® (Pimavanserin) Approval Criteria:

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease (PD) psychosis; and
2. Member must have a concomitant diagnosis of PD; and
3. Member must not be taking concomitant medications known to prolong the QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin); and
4. Member must not have a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia, hypomagnesemia, and the presence of congenital prolongation of the QT interval; and
5. Nuplazid® will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD psychosis; and
6. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
7. A quantity limit of 1 tablet per day will apply.

Osmolex® ER [Amantadine Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication for the treatment of Parkinson's disease (PD) or drug-induced extrapyramidal reactions in adult members; and
2. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m^2]; and
3. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
4. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
5. A quantity limit will apply based on FDA approved dosing regimen(s).

Requip XL® [Ropinirole Extended-Release (ER)] and Mirapex ER® (Pramipexole ER) Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease (PD); and
2. A patient-specific, clinically significant reason why the immediate-release products cannot be used must be provided.

Rytary® [Carbidopa/Levodopa Extended-Release (ER) Capsule] Approval Criteria:

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

Xadago® (Safinamide) Approval Criteria:

1. An FDA approved indication as adjunctive treatment to carbidopa/levodopa in members with Parkinson's disease (PD) experiencing "off" episodes; and
2. Member must be taking carbidopa/levodopa in combination with safinamide (safinamide has not been shown to be effective as monotherapy for the treatment of PD); and
3. A patient-specific, clinically significant reason why the member cannot use rasagiline or other lower cost monoamine oxidase type B (MAO-B) inhibitors must be provided; and
4. Member must not have severe hepatic impairment; and
5. Member must not be taking any of the following medications concomitantly with safinamide:
    a. Monoamine oxidase inhibitors (MAOIs); or
    b. Linezolid; or
    c. Opioid analgesics (including tramadol); or
    d. Selective norepinephrine reuptake inhibitors (SNRIs); or
    e. Tri- or tetra-cyclic or triazolopyridine antidepressants; or
    f. St. John's wort; or
    g. Cyclobenzaprine; or
    h. Methylphenidate and its derivatives; or
    i. Amphetamine and its derivatives; or
    j. Dextromethorphan; and
6. Prescriber must verify member has been counseled on avoiding foods that contain a large amount of tyramine while taking safinamide; and
7. A quantity limit of 1 tablet per day will apply.

Utilization of PD Medications: Calendar Year 2020

The following utilization data includes PD medications used for all diagnoses and does not differentiate between PD diagnoses and other diagnoses, for which use may be appropriate.

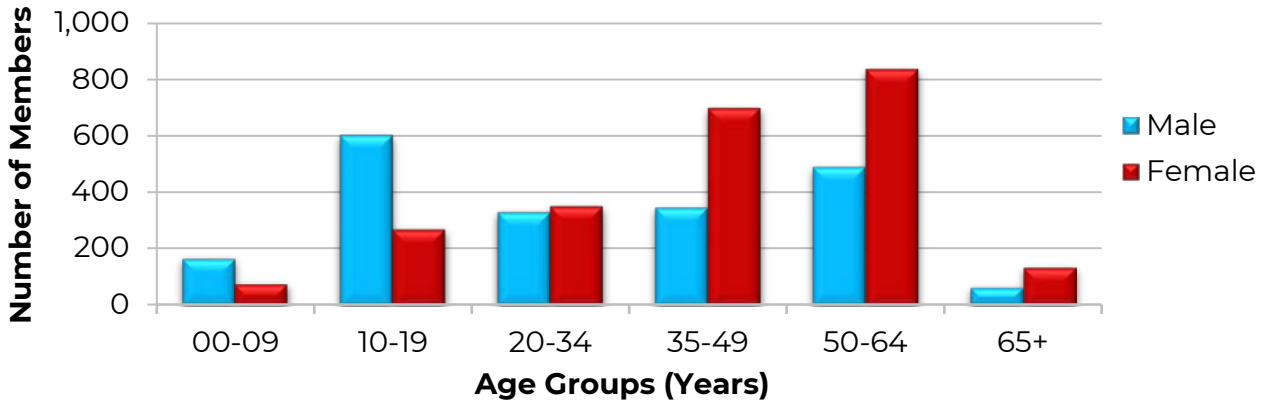
Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	4,498	25,839	$884,385.74	$34.23	$1.07	1,628,229	823,139
2020	4,354	26,065	$871,401.51	$33.43	$1.02	1,722,886	853,928
% Change	**-3.20%**	**0.90%**	**-1.50%**	**-2.30%**	**-4.70%**	**5.80%**	**3.70%**
Change	**-144**	**226**	**-$12,984.23**	**-$0.80**	**-$0.05**	**94,657**	**30,789**

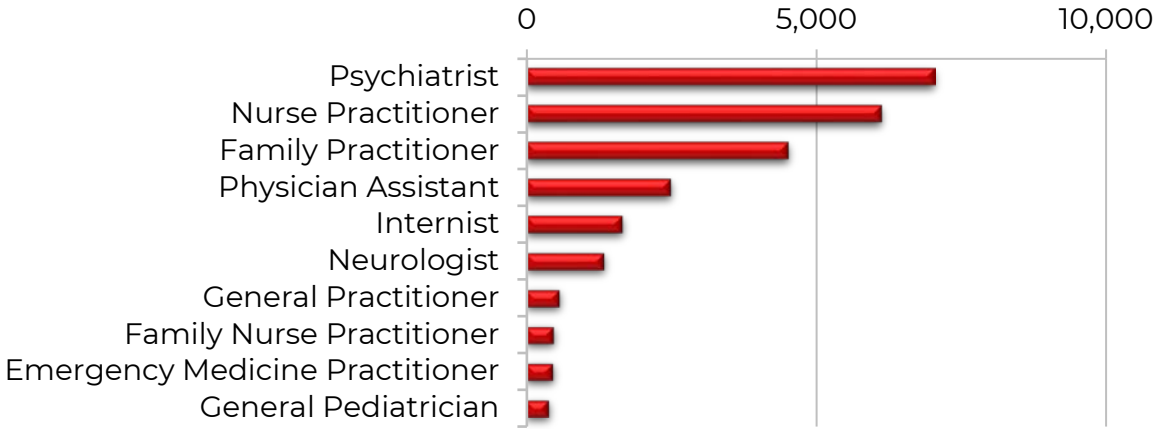
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

- There were no SoonerCare paid medical claims for Duopa® (carbidopa/levodopa enteral suspension) during calendar year 2020.

Demographics of Members Utilizing PD Medications



Top Prescriber Specialties of PD Medications by Number of Claims



Prior Authorization of PD Medications

There were 166 prior authorization requests submitted for PD medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

Status of Petitions

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

Anticipated Patent Expiration(s):

- Duopa® (carbidopa/levodopa enteral suspension): There are no unexpired patents for Duopa®; however, the anticipated exclusivity expiration is January 2022
- Azilect® (rasagiline tablet): August 2027
- Nourianz® (istradefylline tablet): September 2027
- Rytary® [carbidopa/levodopa extended-release (ER) capsule]: December 2028
- Xadago® (safinamide tablet): December 2028
- Neupro® (rotigotine transdermal patch): March 2032
- Inbrija® (levodopa inhalation powder): November 2032
- Gocovri® (amantadine ER capsule): December 2034
- Ongentys® (opicapone capsule): May 2035
- Kynmobi™ [apomorphine sublingual (SL) film]: April 2036
- Osmolex® ER (amantadine ER tablet): February 2038
- Nuplazid® (pimavanserin tablet): August 2038

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

- **April 2020:** The FDA approved Ongentys® (opicapone) 25mg and 50mg capsules as an add-on treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes. As the disease progresses, patients taking levodopa/carbidopa may begin to experience "off" time between treatment doses, during which an increase in PD motor symptoms such as tremor, slowed movement, and difficulty walking occur. Ongentys® increases "on" time without troublesome dyskinesia, the time when the motor symptoms of a patient with PD are better controlled. Ongentys® is an oral, selective catechol-O-methyltransferase (COMT) inhibitor that helps block the COMT enzyme which breaks down levodopa, the gold standard therapy for controlling motor symptoms in patients with PD. Ongentys® protects levodopa by reducing its breakdown in the blood, making more levodopa available to reach the brain, prolonging its clinical effects and helping patients achieve motor symptom control. The FDA

approval of Ongentys® is supported by data from 38 clinical studies, including 2 multinational Phase 3 clinical studies (BIPARK-1 and BIPARK-2), with >1,000 PD patients treated with Ongentys®. Both studies included a 1-year, open-label extension. Data from both studies showed that Ongentys® 50mg significantly reduced "off" time from baseline to week 14 or 15 compared to placebo. "On" time without troublesome dyskinesia also increased from baseline to week 14 or 15 compared to placebo.

- **May 2020:** The FDA approved Kynmobi™ (apomorphine) SL film for the acute, intermittent treatment of "off" episodes in patients with PD. Kynmobi™ SL film, a novel formulation of apomorphine (a dopamine agonist) is the first and only SL therapy for the fast-acting, on-demand treatment of "off" episodes associated with PD. Kynmobi™ may be used up to 5 times a day. Phase 3 clinical study results, published in *Lancet Neurology,* demonstrated that patients with PD receiving Kynmobi™ experienced significant improvements in motor symptoms at 30 minutes after dosing at week 12, with a mean reduction of 7.6 points, compared to placebo, on the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score. Higher scores indicate increased severity. Initial clinical improvements were seen at 15 minutes post-administration. Additionally, a significantly higher percentage of patients treated with Kynmobi™ had a patient-rated full "on" response within 30 minutes at week 12, compared with patients receiving placebo.

Pipeline:

- **Nuplazid® (Pimavanserin):** In April 2021, Acadia Pharmaceuticals announced the receipt of a Complete Response Letter (CRL) from the FDA regarding its supplemental New Drug Application (sNDA) for Nuplazid® for the treatment of hallucinations and delusions associated with dementia-related psychosis. The CRL cited a lack of statistical significance from the Phase 3 HARMONY study in some of the subgroups of dementia, and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. Pimavanserin is a selective serotonin inverse agonist and antagonist preferentially targeting 5-HT_{2A} receptors. These receptors are thought to play an important role in neuropsychiatric disorders. In vitro, pimavanserin demonstrated no appreciable binding affinity for dopamine (including D_2), histamine, muscarinic, or adrenergic receptors. Pimavanserin was approved for the treatment of hallucinations and delusions associated with PD psychosis by the FDA in April 2016. Nuplazid® is not approved for dementia-related psychosis. In addition, Acadia is developing pimavanserin in other neuropsychiatric conditions. In July 2020, the

company announced top-line results from the 293-patient Phase 3 CLARITY study which combined 2 identical, double-blind, placebo-controlled studies evaluating the efficacy, safety, and tolerability of pimavanserin as an adjunctive treatment for major depressive disorder. The study did not achieve statistical significance on the primary endpoint which was the 17-item Hamilton Depression Rating Scale (HAMD-17) total score change from baseline to week 5.

Kynmobi™ (Apomorphine) Product Summary[6,7]

Indication(s): Kynmobi™ (apomorphine) a non-ergoline dopamine agonist indicated for the acute, intermittent treatment of "off" episodes in patients with PD.

Dosing:

- Kynmobi™ is supplied as a SL film in the following strengths: 10mg, 15mg, 20mg, 25mg, and 30mg of apomorphine.
- Dose initiation should be supervised by a health care provider.
- The dose range for Kynmobi™ is 10mg to 30mg per dose administered as needed.
- Kynmobi™ doses should be separated by at least 2 hours. If a single dose of Kynmobi™ is ineffective for a particular "off" episode, a second dose should not be given for that "off" episode. The efficacy or safety of administering a second dose for a single "off" episode has not been studied.
- The maximum single dose of Kynmobi™ is 30mg.
- Kynmobi™ administration should not exceed >5 doses per day.
- Kynmobi™ should be administered whole and will disintegrate in about 3 minutes. Kynmobi™ should not be cut, chewed, or swallowed.
- Due to the high incidence of nausea and vomiting with Kynmobi™ administration at recommended doses, treatment with a concomitant antiemetic (e.g., trimethobenzamide) is recommended, beginning 3 days prior to the initial dose of Kynmobi™. Treatment with the antiemetic should only be continued as long as necessary to control nausea and vomiting, and generally no longer than 2 months after initiation of treatment with Kynmobi™.

Mechanism of Action: Kynmobi™ is a non-ergoline dopamine agonist with high in vitro binding affinity for the dopamine D_4 receptor, and moderate affinity for the dopamine D_2, D_3, and D_5, and adrenergic α_1D, α_2B, α_2C receptors. The precise mechanism of action of Kynmobi™ as a treatment for "off" episodes associated with PD is unknown, although it is believed to be due to stimulation of post-synaptic dopamine D_2-type receptors within the caudate-putamen in the brain.

Contraindication(s):

- Concomitant use of Kynmobi™ with $5HT_3$ antagonists, including antiemetics (e.g., ondansetron, granisetron, dolasetron, palonosetron) and alosetron, is contraindicated due to reports of profound hypotension and loss of consciousness when subcutaneous (sub-Q) apomorphine was administered with a $5HT_3$ antagonist.
- Kynmobi™ is contraindicated in patients with hypersensitivity to apomorphine or any of its ingredients including sodium metabisulfite, as angioedema or anaphylaxis may occur. Oral soft tissue swelling (lips, tongue, gingiva, and mouth) was reported as an adverse reaction in 15% of patients treated with Kynmobi™ during the maintenance phase of study 1, compared with 0% of patients who received placebo; 11% of patients discontinued Kynmobi™ because of this event. Swelling of the face, oral allergy syndrome, hypersensitivity, or urticaria were reported as an adverse reaction in 6% of patients treated with Kynmobi™ during the maintenance phase of study 1, compared with 0% of patients who received placebo; 4% of patients discontinued Kynmobi™ because of this event. It is not known whether these events are related to apomorphine, sodium metabisulfite, or another Kynmobi™ excipient. Kynmobi™ rechallenge is not generally recommended after discontinuation as oral adverse reactions may recur and may be more severe than the initial reaction.

Warnings and Precautions:

- Nausea and Vomiting: Kynmobi™ may cause nausea and vomiting when administered at recommended doses. Because of the high incidence of nausea and vomiting with Kynmobi™ when administered at recommended doses, an antiemetic (e.g., trimethobenzamide 300mg 3 times a day) is recommended beginning 3 days prior to the initial dose of Kynmobi™. Treatment with the antiemetic should only be continued as long as necessary to control nausea and vomiting, and generally no longer than 2 months after initiation of treatment with Kynmobi™. Concomitantly administered antiemetic drugs other than trimethobenzamide have not been studied. $5HT_3$ antagonist antiemetics are contraindicated. Antiemetics with anti-dopaminergic actions (e.g., haloperidol, chlorpromazine, promethazine, prochlorperazine, metoclopramide) have the potential to worsen symptoms in patients with PD and should be avoided.
- Daytime Somnolence/Falling Asleep During Activities of Daily Living: Patients treated with dopaminergic medications, including apomorphine, have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes has resulted in accidents. During the titration phase of study 1, somnolence was reported as an adverse reaction in 11% of

patients treated with Kynmobi™. During the maintenance phase of study 1, somnolence was reported as an adverse reaction in 13% of patients treated with Kynmobi™, compared with 2% of patients who received placebo. Before initiating treatment with Kynmobi™, patients should be advised of the risk of drowsiness and asked about factors that could increase the risk with Kynmobi™, such as concomitant sedating medications and the presence of sleep disorders. If a patient develops significant daytime sleepiness or falls asleep during activities that require active participation (e.g., conversations, eating, etc.), Kynmobi™ should ordinarily be discontinued. If a decision is made to continue Kynmobi™, patients should be advised not to drive and to avoid other potentially dangerous activities. There is insufficient information to determine whether dose reduction will eliminate episodes of falling asleep while engaged in activities of daily living.

- Syncope and Hypotension/Orthostatic Hypotension: Kynmobi™ may cause syncope, hypotension, or orthostatic hypotension. Blood pressure should be monitored.
- Oral Mucosal Irritation: Kynmobi™ may cause oral mucosal irritation. In general, oral mucosal irritation reactions were mild-to-moderate in severity, and usually resolved with treatment discontinuation. Kynmobi™ rechallenge is not generally recommended after discontinuation as oral adverse reactions may recur and be more severe than the initial reaction. Hypersensitivity adverse reactions may also occur during treatment with Kynmobi™.
- Hallucinations/Psychotic-Like Behavior: Kynmobi™ may cause hallucinations and psychotic-like behavior. During the maintenance phase of study 1, hallucinations, delusions, disorientation, or confusion were reported as adverse reactions in 6% of patients treated with Kynmobi™, compared with 2% of patients who received placebo. No patient developed hallucinations or psychotic-like behavior during the titration phase. A total of 4% of patients treated with Kynmobi™ discontinued treatment because of disorientation, confusional state, or delusions, compared with 2% of patients who received placebo. Postmarketing reports with sub-Q apomorphine indicate that patients may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior after starting or increasing the dose of apomorphine. Other drugs prescribed to improve the symptoms of PD can have similar effects on thinking and behavior. This abnormal thinking and behavior can consist of 1 or more of a variety of manifestations, including paranoid ideation, delusions, hallucinations, confusion, disorientation, aggressive behavior, agitation, and delirium.
- Impulse Control/Compulsive Behaviors: Kynmobi™ may cause impulse control and impulsive behaviors; dose reduction or discontinuing

Kynmobi™ should be considered if this occurs. Case reports suggest that patients taking 1 or more medications that increase central dopaminergic tone, including Kynmobi™, can experience intense urges to gamble, increased sexual urges, intense urges to spend money uncontrollably, other intense urges, and the inability to control these urges. In some cases, although not all, these urges were reported to have stopped when the dose was reduced, or the medication was discontinued.

- Withdrawal-Emergent Hyperpyrexia and Confusion: Withdrawal-emergent hyperpyrexia and confusion may occur with rapid dose reduction or withdrawal of Kynmobi™. A symptom complex resembling the neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, elevated serum creatine kinase, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in antiparkinsonian therapy.
- QTc Prolongation and Potential for Proarrhythmic Effects: Kynmobi™ may prolong QTc and cause torsades de pointes or sudden death; risks and benefits of Kynmobi™ treatment should be considered prior to initiating treatment with Kynmobi™ in patients with risk factors for prolonged QTc.

Adverse Reactions: The most common adverse reactions (incidence ≥10% in patients treated with Kynmobi™ and with an incidence >placebo) were nausea, oral/pharyngeal soft tissue swelling, oral/pharyngeal soft tissue pain and paresthesia, dizziness, and somnolence.

Efficacy: The efficacy of Kynmobi™ was established in a randomized, double-blind, placebo-controlled study in 109 patients with PD. Patients received Kynmobi™ or placebo. The primary endpoint of the study was the mean change from pre-dose to 30 minutes post dose in the MDS-UPDRS at the 12-week visit of the maintenance phase.

- The study enrolled patients with a mean duration of PD of approximately 9 years (range: 2 years to 22 years) who were Hoehn and Yahr Stage III or less in the “on” state, and who were all receiving concomitant levodopa with a stable dose for at least 4 weeks before screening. The Hoehn and Yahr scale rates the progression of PD stage 1 through 5 with 5 being the most severe symptoms including confinement to a bed or wheelchair. The most commonly used concomitant PD medications in addition to levodopa were oral dopaminergic agonists (51%), MAO-B inhibitors (41%), amantadine derivatives (21%), and other dopaminergic agents (8%). At baseline, the mean number of daily “off” episodes was 4 and the mean duration of “off” episodes was slightly over an hour in both groups.

- The study included a titration phase and a 12-week maintenance phase. Patients were titrated to the dose that achieved a full "on" response and was tolerated during the titration phase. Patients were treated with an oral antiemetic starting 3 days before the titration phase. In the titration phase, patients (N=141) arrived at the study site in an "off" state having not taken their regular morning dose of carbidopa/levodopa or any other adjunctive PD medications, as well as having taken their last dose of carbidopa/levodopa and any other adjunctive PD medications no later than midnight the night before.
- Treatment was initiated in the clinic with a 10mg dose of Kynmobi™. If the patient responded to treatment and tolerated the 10mg Kynmobi™ dose, the patient was randomized in a blinded fashion to Kynmobi™ or placebo in a 1:1 ratio.
- If the patient tolerated the dose but did not adequately respond, the patient was asked to return to the clinic within 3 days and the dose was increased by 5mg. The titration process was continued up to a maximum Kynmobi™ dose of 35mg or until a full "on" response was achieved as determined by the investigator and the patient.
- Dose administration was permitted up to 5 times per day in the maintenance phase.
- The MDS-UPDRS III (motor examination) was measured pre-dose, and at 15, 30, 45, 60, and 90 minutes post dose.
- The primary endpoint of the study was the mean change from pre-dose to 30 minutes post dose in the MDS-UPDRS III at the 12-week visit of the maintenance phase.
- A total of 54 patients were randomized to Kynmobi™ and 55 patients to placebo. The Kynmobi™ treatment group showed a least-square mean improvement (i.e., reduction in score) of -11.1 points (95% CI: -14.0, -8.2), versus -3.5 points for the placebo group (95% CI: -6.1, -0.9). The least-square mean treatment difference between Kynmobi™ and placebo was -7.6 (95% CI: -11.5, -3.7; P=0.0002).

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Kynmobi™ (apomorphine) 30mg sublingual film	**$26.25/film**	**$3,937.50⁺**	**$47,250.00⁺**
Apokyn® (apomorphine) 10mg/mL cartridge	$331.67/mL	$17,910.18¥	$214,922.16¥
pramipexole 1.5mg oral tablet	$0.08/tablet	$7.20‡	$86.40‡

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
⁺Kynmobi™ cost per month and year based on maximum dose of 30mg 5 times daily.
¥Apokyn® cost per month and year based on maximum dose of 0.6mL per dose, at 3 times daily dosing, which was the average frequency of dosing in the development program.
‡Pramipexole cost per year based on maximum dose of 1.5mg 3 times a day.

Ongentys® (Opicapone) Product Summary[8,9]

Indication(s): Ongentys® (opicapone) is a catechol-O-methyltransferase (COMT) inhibitor indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

Dosing:

- Ongentys® is supplied as a 25mg and 50mg oral capsule.
- The recommended dosage is 50mg administered orally once daily at bedtime.
- Patients should not eat food 1 hour before and at least 1 hour after taking Ongentys®.
- The recommended dosage in patients with moderate hepatic impairment is 25mg orally once daily at bedtime.
- Ongentys® should be avoided in patients with severe hepatic impairment.

Mechanism of Action: Opicapone is a selective and reversible inhibitor of COMT. COMT catalyzes the transfer of the methyl group of S-adenosyl-L-methionine to the phenolic group of substrates that contain a catechol structure. Physiological substrates of COMT include dihydroxyphenylalanine (DOPA), catecholamines (dopamine, norepinephrine, and epinephrine), and their hydroxylated metabolites. When decarboxylation of levodopa is prevented by carbidopa, COMT becomes the major metabolizing enzyme for levodopa, catalyzing its metabolism to 3-methoxy-4-hydroxy-L-phenylalanine (3-OMD).

Contraindication(s):

- Concomitant use of non-selective monoamine oxidase inhibitors (MAOIs)
- History of pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms

Warnings and Precautions:

- Cardiovascular Effects with Concomitant Use of Drugs Metabolized by COMT: Ongentys® may cause arrhythmias, increased heart rate, and excessive changes in blood pressure. Patients should be monitored when treated concomitantly with products metabolized by COMT (e.g., isoproterenol, epinephrine, norepinephrine, dopamine, dobutamine).
- Falling Asleep During Activities of Daily Living: Prior to starting treatment with Ongentys®, patients should be advised of the risks of falling asleep during activities of daily living.
- Hypotension/Syncope: If hypotension or syncope occurs, discontinuing Ongentys® should be considered or adjusting the dosage of other medications that can lower blood pressure.

- Dyskinesia: Ongentys® may cause or exacerbate dyskinesia; dose reduction of levodopa or dopaminergic medication should be considered.
- Hallucinations and Psychosis: Stopping Ongentys® should be considered if hallucinations or psychosis occurs.
- Impulse Control/Compulsive Disorders: Discontinuing Ongentys® should be considered if impulse control or compulsive disorders occur.
- Withdrawal-Emergent Hyperpyrexia and Confusion: When discontinuing Ongentys®, patients should be monitored and adjustment of other dopaminergic therapies as needed should be considered.

Adverse Reactions: The most common adverse reactions (≥4% and >placebo) were dyskinesia, constipation, blood creatine kinase increase, hypotension/syncope, and weight decrease.

Efficacy: The efficacy of Ongentys® as adjunctive treatment to levodopa/carbidopa in patients with PD experiencing "off" episodes was evaluated in 2 double-blind, randomized, placebo- and active-controlled studies, BIPARK-1 and BIPARK-2.

- In study 1 (BIPARK-1), 600 patients with PD and motor fluctuations were randomized to treatment with 1 of 3 doses of Ongentys® (5mg, 25mg, or 50mg), placebo, or 200mg doses of COMT inhibitor entacapone for 14 or 15 weeks. In both groups, 82% of patients used concomitant PD medications in addition to levodopa; the most commonly used were dopamine agonists (68%), amantadine (23%), MAO-B inhibitors (20%), and anticholinergics (5%).
- In study 2 (BIPARK-2), 427 patients were randomized to treatment with either 1 of 2 doses of Ongentys® (25mg or 50mg) or placebo for 14 or 15 weeks. In the Ongentys® 50mg treatment group, 85% of patients compared to 81% of patients who received placebo used concomitant PD medications in addition to levodopa; the most commonly used were dopamine agonists (70%), amantadine (21%), MAO-B inhibitors (20%), and anticholinergics (12%).
- The primary efficacy endpoint was the change in mean absolute "off"-time based on 24-hour patient diaries completed 3 days prior to each of the scheduled visits.
- In both studies, Ongentys® 50mg significantly reduced mean absolute "off"-time compared to placebo from baseline to week 14 or 15.
- In study 1, the placebo-subtracted difference was -1.01 hours [95% confidence interval (CI): -1.620, -0.407; P=0.002].
- In study 2, the placebo-subtracted difference was -0.91 hours (95% CI: -1.523, -0.287; P=0.008).

Cost Comparison:

Medication	Cost Per Tablet	Cost Per Month	Cost Per Year
Ongentys® (opicapone) 50mg tablet	**$19.67**	**$590.10⁺**	**$7,081.20⁺**
entacapone 200mg tablet	$0.41	$98.40*	$1,180.80*

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
⁺Ongentys® cost per month and cost per year based on the recommended maintenance/maximum dosage of 50mg once daily.
*Entacapone cost per month and cost per year based on the recommended maintenance dosage of 200mg up to a maximum of 8 times daily (maximum daily dose of 1,600mg).

Recommendations

The College of Pharmacy recommends the prior authorization of Kynmobi™ (apomorphine) and Ongentys® (opicapone) with the following criteria:

Kynmobi™ [Apomorphine Sublingual (SL) Film] Approval Criteria:

1. An FDA approved diagnosis of acute, intermittent treatment of "off" episodes in patients with Parkinson's disease (PD); and
2. Member must be taking carbidopa/levodopa in combination with Kynmobi™; and
3. Member should be experiencing at least 1 well defined "off" episode per day with a total daily "off" time duration of ≥2 hours during the waking day; and
4. Initial dose titration should occur in an "off" state and in a setting supervised by a health care provider to monitor blood pressure and heart rate; and
5. Member should not use apomorphine concomitantly with $5HT_3$ antagonists (e.g., ondansetron, granisetron, dolasetron, palonosetron, alosetron); and
6. Prescriber must verify the member has been counseled on separating doses by at least 2 hours; and
7. The maximum single dose approvable is 30mg; and
8. A quantity limit of 5 doses per day will apply.

Ongentys® (Opicapone) Approval Criteria:

1. An FDA approved diagnosis of adjunctive treatment to levodopa/carbidopa in members with Parkinson's disease (PD) experiencing "off" episodes; and
2. Member must be taking levodopa/carbidopa in combination with Ongentys® and
3. Member must not use non-selective monoamine-oxidase inhibitors (MAOIs) concomitantly with Ongentys®, and
4. Member must not have a history of pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms; and

5. Prescriber must verify member has been counseled to avoid eating food 1 hour before and at least 1 hour after taking Ongentys®; and
6. For members with moderate hepatic impairment, the prescriber must verify the dose of Ongentys® will be reduced in accordance with package labeling; and
7. Prescriber must agree to monitor member for changes in heart rate, heart rhythm, and blood pressure in members concurrently taking medications known to be metabolized by catechol-O-methyltransferase (COMT); and
8. A patient-specific, clinically significant reason why the member cannot use entacapone must be provided; and
9. A quantity limit of 30 capsules per 30 days will apply.

Utilization Details of PD Medications: Calendar Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AMANTADINE PRODUCTS						
AMANTADINE CAP 100MG	3,051	500	$87,977.84	$0.96	$28.84	10.10%
AMANTADINE TAB 100MG	2,046	341	$116,364.04	$1.88	$56.87	13.35%
AMANTADINE SYP 50MG/5ML	245	51	$4,410.29	$0.62	$18.00	0.51%
GOCOVRI CAP 137MG	12	1	$25,178.92	$69.94	$2,098.24	2.89%
SUBTOTAL	**5,354**	**893**	**$233,931.09**	**$1.46**	**$43.69**	**26.85%**
BENZTROPINE PRODUCTS						
BENZTROPINE TAB 1MG	5,925	1,108	$80,116.88	$0.44	$13.52	9.19%
BENZTROPINE TAB 2MG	2,218	376	$35,313.73	$0.51	$15.92	4.05%
BENZTROPINE TAB 0.5MG	2,141	390	$29,924.14	$0.46	$13.98	3.43%
BENZTROPINE INJ 1MG/ML	1	1	$58.41	$58.41	$58.41	0.01%
SUBTOTAL	**10,285**	**1,875**	**$145,413.16**	**$0.46**	**$14.14**	**16.68%**
ROPINIROLE PRODUCTS						
ROPINIROLE TAB 1MG	1,301	350	$16,692.59	$0.32	$12.83	1.92%
ROPINIROLE TAB 0.5MG	1,200	361	$15,300.92	$0.33	$12.75	1.76%
ROPINIROLE TAB 0.25MG	724	240	$9,153.41	$0.37	$12.64	1.05%
ROPINIROLE TAB 2MG	676	164	$8,411.39	$0.32	$12.44	0.97%
ROPINIROLE TAB 4MG	301	70	$4,263.83	$0.33	$14.17	0.49%
ROPINIROLE TAB 3MG	254	65	$3,336.92	$0.33	$13.14	0.38%
ROPINIROLE TAB 5MG	132	28	$2,376.65	$0.44	$18.00	0.27%
ROPINIROLE TAB 12MG ER	4	1	$818.15	$6.82	$204.54	0.09%
SUBTOTAL	**4,592**	**1,279**	**$60,353.86**	**$0.34**	**$13.14**	**6.93%**
TRIHEXYPHENIDYL PRODUCTS						
TRIHEXYPHENIDYL TAB 5MG	1,088	163	$14,941.60	$0.45	$13.73	1.71%
TRIHEXYPHENIDYL TAB 2MG	914	183	$10,916.14	$0.39	$11.94	1.25%
TRIHEXYPHENIDYL ELX 0.4MG/ML	205	29	$6,196.78	$1.05	$30.23	0.71%
SUBTOTAL	**2,207**	**375**	**$32,054.52**	**$0.48**	**$14.52**	**3.67%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
CARBIDOPA/LEVODOPA PRODUCTS						
CARB/LEVO TAB 25-100MG	777	152	$15,455.02	$0.59	$19.89	1.77%
CARB/LEVO TAB 25-250MG	200	31	$5,023.52	$0.74	$25.12	0.58%
CARB/LEVO TAB 10-100MG	139	34	$2,772.32	$0.58	$19.94	0.32%
CARB/LEVO ER TAB 50-200MG	119	21	$5,009.74	$1.25	$42.10	0.57%
CARB/LEVO ER TAB 25-100MG	52	10	$1,555.04	$0.98	$29.90	0.18%
CARB/LEVO ODT 25-100MG	11	1	$568.38	$1.72	$51.67	0.07%
CARB/LEVO ODT 25-250MG	9	2	$897.82	$3.73	$99.76	0.10%
CARB/LEVO ODT 10-100MG	5	3	$313.64	$1.05	$62.73	0.04%
RYTARY CAP 95MG	1	1	$462.83	$15.43	$462.83	0.05%
RYTARY CAP 245MG	1	1	$586.43	$19.55	$586.43	0.07%
SUBTOTAL	**1,314**	**256**	**$32,644.74**	**$0.74**	**$24.84**	**3.75%**
CARBIDOPA/LEVODOPA/ENTACAPONE PRODUCTS						
CARB/LEVO/EN 25-100-200MG	34	4	$3,532.34	$3.70	$103.89	0.41%
CARB/LEVO/EN 50-200-200MG	27	3	$2,125.14	$2.76	$78.71	0.24%
CARB/LEVO/EN 37.5-150-200MG	14	1	$1,850.61	$4.65	$132.19	0.21%
CARB/LEVO/EN 12.5-50-200MG	4	1	$596.91	$4.97	$149.23	0.07%
SUBTOTAL	**79**	**9**	**$8,105.00**	**$3.61**	**$102.59**	**0.93%**
PRAMIPEXOLE PRODUCTS						
PRAMIPEXOLE TAB 0.5MG	385	110	$4,811.73	$0.29	$12.50	0.55%
PRAMIPEXOLE TAB 1MG	341	78	$4,411.46	$0.29	$12.94	0.51%
PRAMIPEXOLE TAB 0.125MG	329	99	$3,909.54	$0.32	$11.88	0.45%
PRAMIPEXOLE TAB 0.25MG	315	91	$3,812.57	$0.29	$12.10	0.44%
PRAMIPEXOLE TAB 1.5MG	67	15	$915.67	$0.32	$13.67	0.11%
PRAMIPEXOLE TAB 0.75MG	38	7	$553.14	$0.34	$14.56	0.06%
SUBTOTAL	**1,475**	**400**	**$18,414.11**	**$0.30**	**$12.48**	**2.12%**
BROMOCRIPTINE PRODUCTS						
BROMOCRIPTINE TAB 2.5MG	393	88	$42,810.18	$3.50	$108.93	4.91%
BROMOCRIPTINE CAP 5MG	232	34	$56,077.05	$8.09	$241.71	6.44%
SUBTOTAL	**625**	**122**	**$98,887.23**	**$5.16**	**$158.22**	**11.35%**
ENTACAPONE PRODUCTS						
ENTACAPONE TAB 200MG	15	4	$664.50	$1.48	$44.30	0.08%
SUBTOTAL	**15**	**4**	**$664.50**	**$1.48**	**$44.30**	**0.08%**
RASAGILINE PRODUCTS						
RASAGILINE TAB 0.5MG	12	2	$1,591.19	$4.42	$132.60	0.18%
RASAGILINE TAB 1MG	8	2	$974.40	$4.06	$121.80	0.11%
SUBTOTAL	**20**	**4**	**$2,565.59**	**$4.28**	**$128.28**	**0.29%**
ROTIGOTINE PRODUCTS						
NEUPRO 4MG/24 HOUR PATCH	11	2	$7,541.75	$22.85	$685.61	0.87%
NEUPRO 8MG/24 HOUR PATCH	1	1	$680.58	$22.69	$680.58	0.08%
SUBTOTAL	**12**	**3**	**$8,222.33**	**$22.84**	**$685.19**	**0.95%**
SELEGILINE PRODUCTS						
SELEGILINE CAP 5MG	9	2	$686.10	4.5	$2.54	$76.23

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SELEGILINE TAB 5MG	4	1	$321.86	4	$2.68	$80.47
SUBTOTAL	**13**	**3**	**$1,007.96**	**4.33**	**$2.58**	**$77.54**
PIMAVANSERIN PRODUCTS						
NUPLAZID TAB 34MG	70	8	$228,865.42	$116.06	$3,269.51	26.26%
SUBTOTAL	**70**	**8**	**$228,865.42**	**$116.06**	**$3,269.51**	**26.26%**
TOTAL	**26,065**	**4,354***	**$871,401.51**	**$1.02**	**$33.43**	**100%**

*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
CAP = capsule; TAB = tablet; SYP = syrup; INJ = injection; CARB = carbidopa; LEVO = levodopa; EN = entacapone; ER = extended release; ODT = orally disintegrating tablet; ELX = elixir

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[9] Ongentys® (Opicapone) – New Drug Approval. *OptumRX®*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_ongentys_2020-0428.pdf. Issued 2020. Last accessed 04/16/2021.

Appendix M

Calendar Year 2020 Annual Review of Alzheimer's Disease Medications

Oklahoma Health Care Authority
May 2021

Current Prior Authorization Criteria

Alzheimer's Disease Medications Approval Criteria:

1. Special formulation products including oral solutions, transdermal patches, and other convenience formulations require prior authorization with the following approval criteria:
    a. A patient-specific, clinically significant reason why the special formulation is necessary in place of the standard formulation must be provided; and
2. An age restriction for ages 0 to 50 years applies to all Alzheimer's disease medications. Members older than 50 years of age can receive regular formulations without prior authorization. Members younger than 50 years of age will require prior authorization with the following criteria:
    a. An FDA approved indication; or
    b. Other patient-specific, clinically significant information supporting the use of the medication must be provided.

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

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

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

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

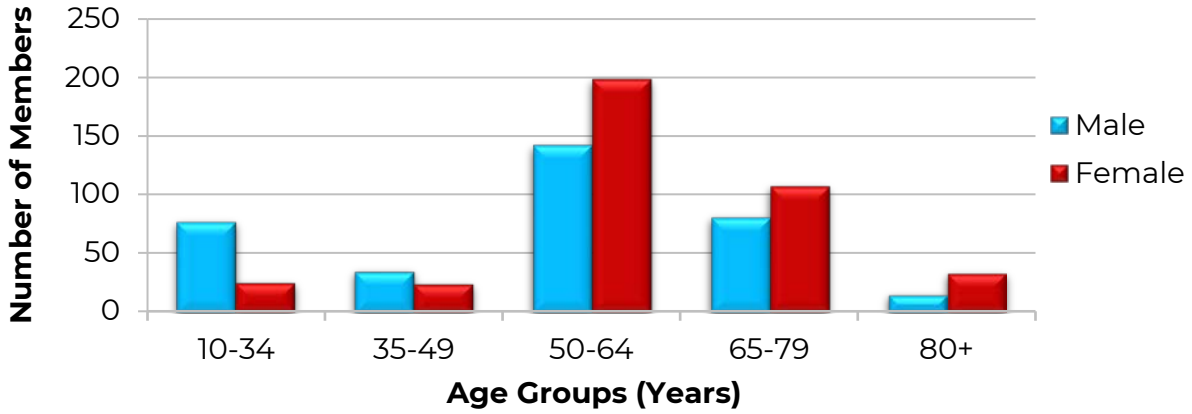
Utilization of Alzheimer's Disease Medications: Calendar Year 2020

Comparison of Calendar Years: Pharmacy Claims

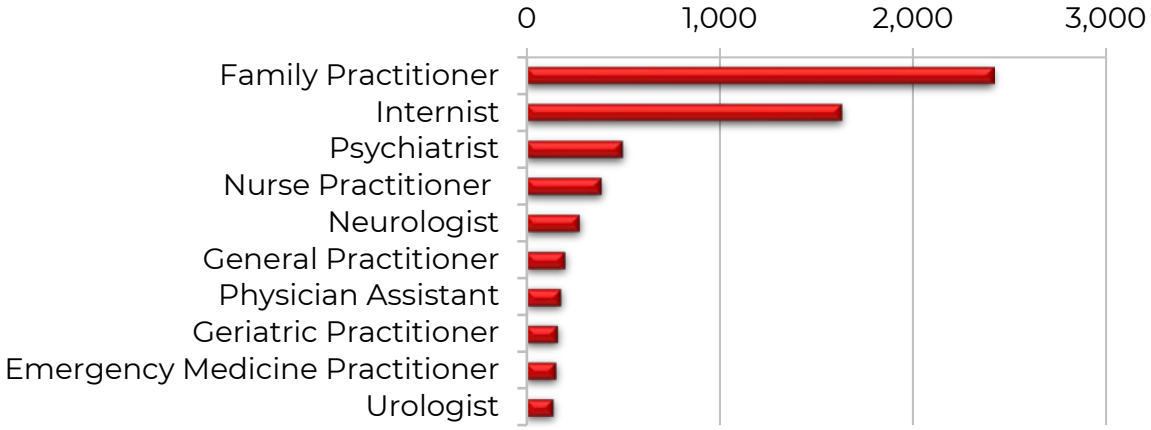
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	698	6,486	$129,395.33	$19.95	$0.65	312,352	200,516
2020	684	6,166	$114,085.37	$18.50	$0.57	313,197	200,758
% Change	**-2.00%**	**-4.90%**	**-11.80%**	**-7.30%**	**-12.30%**	**0.30%**	**0.10%**
Change	**-14**	**-320**	**-$15,309.96**	**-$1.45**	**-$0.08**	**845**	**242**

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

Demographics of Members Utilizing Alzheimer's Disease Medications



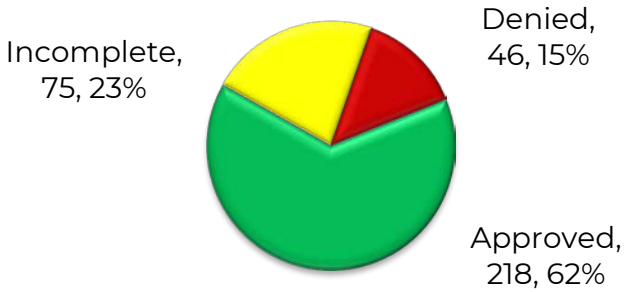
Top Prescriber Specialties of Alzheimer's Disease Medications by Number of Claims



Prior Authorization of Alzheimer's Disease Medications

There were 339 prior authorization requests submitted for Alzheimer's disease medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Namenda XR® [memantine extended-release (ER) capsules]: September 2029, however, after litigation settlements, generic versions are currently available in the United States
- Namzaric® (memantine ER/donepezil): December 2029

News:

- **April 2020:** According to a study published in April 2020 in *Nature*, the E4 variant of *apolipoprotein E* (ApoE4), the main susceptibility gene for Alzheimer's disease, leads to accelerated breakdown of the blood-brain barrier (BBB) in the hippocampus and degeneration of brain capillary pericytes, which maintain BBB integrity, and by this mechanism causes cognitive decline. Researchers reported the ApoE4 carriers had increased permeability in their hippocampal BBBs than did noncarriers, and this permeability was even worse if carriers were cognitively impaired. The cognitive impairment occurred regardless of amyloid-beta (Aβ) or tau pathology, the hallmarks of Alzheimer's disease. Markers of BBB damage soared in the cerebrospinal fluid of E4 carriers and predicted subsequent decline on cognitive tests. The findings suggest breakdown of the BBB contributes to ApoE4-associated cognitive decline independently of Alzheimer's disease pathology and might be a therapeutic target in ApoE4 carriers.
- **July 2020:** A meta-analysis published in the *Journal of Neurology, Neurosurgery & Psychiatry* suggested 10 risk factors appeared to have a significant effect on developing Alzheimer's disease, many of which could be targeted with preventive steps. From the analysis of 395 studies, 21 clinical evidence-based suggestions to reduce Alzheimer's disease risk emerged. The suggestions pinpointed 10 risk factors with Class 1 Level A strong evidence which include diabetes, reduced education, hyperhomocysteinemia, poor body mass index (BMI) management, hypertension in midlife, orthostatic hypotension, head trauma, less cognitive activity, stress, and depression. Nine additional

risk factors had Class 1 Level B weaker evidence which include obesity in midlife, weight loss in late life, amount of physical exercise, smoking, sleep, cerebrovascular disease, frailty, atrial fibrillation, and vitamin C status. Two interventions with Class 3 evidence were not recommended: estrogen replacement therapy and acetylcholinesterase inhibitors. In the review, data from 243 observational prospective studies and 152 randomized controlled studies, culled from electronic databases and relevant websites from inception until March 2019 were reviewed. A total of 104 modifiable risk factors and 11 interventions were included in the analysis. Most studies (82%) recruited people without dementia at baseline, and 17% specifically constrained the sample population to people with normal cognition. Observational studies stem bias mainly from generalizability, attrition, and misclassification. In studies, performance bias, incomplete outcome data, inadequate allocation concealment, and selective outcome reporting were considerable factors. The authors noted the suggestions that emerge from this meta-analysis should be particularly considered by non-demented but high-risk individuals, people who carry ApoE4 or who have a high polygenic score, family history of dementia, or amyloid-positive evidence, and their primary care physicians.

Pipeline:

- **Aducanumab:** In January 2021, Biogen and Eisai, announced the FDA has extended the review period by 3 months for the Biologics License Application (BLA) for aducanumab, an investigational monoclonal antibody treatment for Alzheimer's disease. The updated Prescription Drug User Fee Act (PDUFA) action date is June 7, 2021. As part of the ongoing review, Biogen submitted a response to an information request by the FDA, including additional analyses and clinical data, which the FDA considered a major amendment to the application that will require additional time for review. Based on clinical data from patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease, aducanumab has the potential to impact underlying disease pathophysiology, slow cognitive and functional decline and provide benefits on patients' ability to perform activities of daily living, including conducting personal finances, performing household chores, such as cleaning, shopping and doing laundry, and independently traveling out of the home. Biogen submitted the aducanumab BLA to the FDA in July 2020. The FDA accepted the BLA in August 2020 and granted Priority Review.
- **Donanemab:** In January 2021, Eli Lilly and Company announced donanemab, an investigational monoclonal antibody that targets a modified form of beta amyloid called N3pG, showed significant slowing

of decline in a composite measure of cognition and daily function in patients with early symptomatic Alzheimer's disease compared to placebo in the Phase 2 TRAILBLAZER-ALZ study. Donanemab met the primary endpoint of change from baseline to 76 weeks in the Integrated Alzheimer's Disease Rating Scale (iADRS), slowing decline by 32% relative to placebo, which was statistically significant. The iADRS is a clinical composite tool combining the cognitive measure Alzheimer's disease assessment scale-cognitive 13-item scale (ADAS-Cog13) and functional measure Alzheimer's disease cooperative study–instrumental activities of daily living (ADCS-iADL), 2 commonly used measures in Alzheimer's disease. Donanemab also showed consistent improvements in all pre-specified secondary endpoints measuring cognition and function compared to placebo but did not reach nominal statistical significance on every secondary endpoint. By targeting N3pG beta amyloid, donanemab treatment has been shown to rapidly result in high levels of amyloid plaque clearance, as measured by amyloid imaging. In TRAILBLAZER-ALZ, donanemab-treated patients, on average, showed an 84 centiloid reduction of amyloid plaque at 76 weeks compared to a baseline of 108 centiloids (<25 centiloids is typical of a negative amyloid scan). In this study, patients stopped receiving donanemab and switched to placebo once their plaque level was <25 centiloids for 2 consecutive measures or <11 centiloids at any 1 measure. Amyloid-related imaging abnormalities (ARIA) were observed, which is consistent with amyloid plaque clearing antibodies. In the donanemab treatment group, ARIA-edema (ARIA-E) occurred in 27% of treated patients, with an overall incidence of 6% experiencing symptomatic ARIA-E. Eli Lilly has enlarged TRAILBLAZER-ALZ 2 to become a Phase 3 registration study with 1,500 patients. The ongoing study has already enrolled some people with tau-PET above 1.46 standardized uptake value ratio (SUVR), but primary efficacy will be determined in 1,000 patients who are below this cut-off. The primary outcome will be iADRS, and effectiveness will be judged using a disease-progression model, rather than solely on change from baseline in the iADRS at the final time point. Results are expected in the first half of 2023.

Recommendations

The College of Pharmacy does not recommend any changes to the current Alzheimer's disease medications prior authorization criteria at this time.

Utilization Details of Alzheimer's Disease Medications: Calendar Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MEMANTINE PRODUCTS						
MEMANTINE TAB HCL 10MG	3,243	383	$53,751.12	$0.53	$16.57	47.11%
MEMANTINE TAB HCL 5MG	584	111	$9,939.06	$0.52	$17.02	8.71%
MEMANTINE CAP 28MG ER	249	22	$17,817.15	$2.51	$71.55	15.62%
NAMENDA XR CAP 28MG	11	1	$4,499.96	$15.20	$409.09	3.94%
MEMANTINE TITRATION 5-10MG	1	1	$23.70	$0.85	$23.70	0.02%
SUBTOTAL	**4,088**	**518**	**$86,030.99**	**$0.67**	**$21.04**	**75.40%**
DONEPEZIL PRODUCTS						
DONEPEZIL TAB 10MG	1,431	218	$17,679.81	$0.36	$12.35	15.50%
DONEPEZIL TAB 5MG	568	128	$6,722.61	$0.32	$11.84	5.89%
DONEPEZIL TAB 5MG ODT	1	1	$29.31	$0.33	$29.31	0.03%
SUBTOTAL	**2,000**	**347**	**$24,431.73**	**$0.35**	**$12.22**	**21.42%**
RIVASTIGMINE PRODUCTS						
RIVASTIGMINE CAP 3MG	24	3	$683.04	$0.95	$28.46	0.60%
RIVASTIGMINE PATCH 4.6MG/24HR	16	2	$1,844.54	$3.84	$115.28	1.62%
RIVASTIGMINE CAP 1.5MG	8	1	$197.76	$0.82	$24.72	0.17%
RIVASTIGMINE CAP 4.5MG	5	2	$123.34	$0.82	$24.67	0.11%
RIVASTIGMINE CAP 6MG	1	1	$30.90	$1.03	$30.90	0.03%
SUBTOTAL	**54**	**9**	**$2,879.58**	**$1.78**	**$53.33**	**2.53%**
GALANTAMINE PRODUCTS						
GALANTAMINE TAB 4MG	24	2	$743.07	$1.03	$30.96	0.65%
SUBTOTAL	**24**	**2**	**$743.07**	**$1.03**	**$30.96**	**0.65%**
TOTAL	**6,166**	**684***	**$114,085.37**	**$0.57**	**$18.50**	**100%**

*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
CAP = capsule; TAB = tablet; HCL = hydrochloride; ER/XR = extended release; ODT = orally disintegrating tablet; HR = hour

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 04/2021. Last accessed 04/12/2021.
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Appendix N

Calendar Year 2020 Annual Review of Allergen Immunotherapies

Oklahoma Health Care Authority
May 2021

Current Prior Authorization Criteria

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 immunoglobulin E (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 2 different products for 14 days each during a previous season; and
    b. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and
6. Treatment must begin ≥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 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 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 or immunologist (or an advanced care practitioner with a supervising physician who is an allergist or immunologist).

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 immunoglobulin E (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 2 different products for 14 days each; and
    b. **Intranasal corticosteroids:** Trials of 2 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 or immunologist (or an advanced care practitioner with a supervising physician who is an allergist or immunologist); and
10. A quantity limit of 1 tablet daily will apply; and
11. Initial approvals will be for the duration of 6 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.

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

1. Member must be 5 to 65 years of age; and
2. Member must have a positive skin test or *in vitro* testing for pollen specific immunoglobulin E (IgE) antibodies to 1 of the 5 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 2 different products for 14 days each during a previous season; and
b. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and

6. Treatment must begin ≥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 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 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 or immunologist (or an advanced care practitioner with a supervising physician who is an allergist or immunologist).

Palforzia® (Peanut Allergen Powder-dnfp) Approval Criteria:

1. Member must be 4 to 17 years of age to initiate initial dose escalation (maintenance dosing may be continued for members 4 years of age and older); and
2. Member must have a diagnosis of peanut allergy confirmed by a positive skin test, positive *in vitro* test for peanut-specific immunoglobulin E (IgE), or positive clinician-supervised oral food challenge; and
3. Prescriber must confirm member will use Palforzia® with a peanut-avoidant diet; and
4. Member must not have severe uncontrolled asthma; and
5. Member must not have a history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease; and
6. Member must not have had severe or life-threatening anaphylaxis within the previous 60 days; and
7. Member or caregiver must be trained in the use of an auto-injectable epinephrine device and have such a device available for immediate use at all times; and
8. Prescriber must be an allergist or immunologist (or an advanced care practitioner with a supervising physician who is an allergist or immunologist); and

9. Prescriber, health care setting, and pharmacy must be certified in the Palforzia® Risk Evaluation and Mitigation Strategy (REMS) program; and
10. Member must be enrolled in the Palforzia® REMS program; and
11. Palforzia® must be administered under the direct observation of a health care provider in a REMS certified health care setting with an observation duration in accordance with the Palforzia® *Prescribing Information*; and
12. After successful completion of initial dose escalation and all levels of up-dosing as documented by the prescriber, initial approvals of maintenance dosing will be for 6 months. For continued approval, the member must be compliant and prescriber must verify the member is responding well to treatment.

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 or *in vitro* testing for pollen specific immunoglobulin E (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; 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 2 different products for 14 days each during a previous season; and
    b. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and
6. Treatment must begin ≥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 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 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 or immunologist (or an advanced care practitioner with a supervising physician who is an allergist or immunologist).

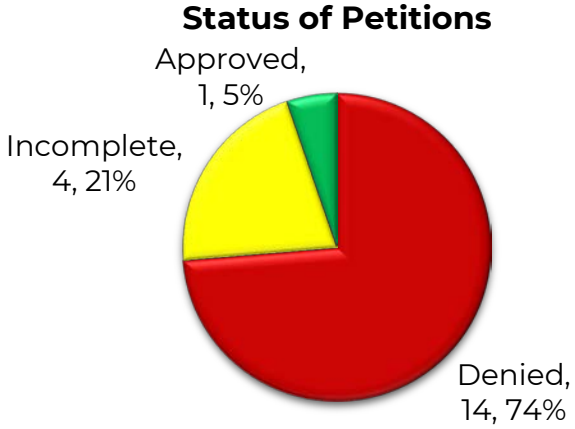
*Current prior authorization criteria is only applicable to allergen immunotherapies with a current federal drug rebate agreement. All criteria, regardless of coverage, are provided in this report for informational purposes.

Utilization of Allergen Immunotherapies: Calendar Year 2020

There was no SoonerCare utilization of allergen immunotherapies during calendar year 2020.

Prior Authorization of Allergen Immunotherapies

There were 19 prior authorization requests submitted for allergen immunotherapies during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020. While there was 1 approved prior authorization request during calendar year 2020, there were no paid claims.



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

News:

- **August 2020:** DBV Technologies announced the U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) for Viaskin® Peanut, a non-invasive epicutaneous immunotherapy patch, being studied for the treatment of peanut allergy in children 4 to 11 years of age. In its CRL, the FDA identified concerns regarding the impact of patch-site adhesion on efficacy and indicated the need for patch modifications. Additionally, the FDA indicated supplementary clinical data would need to be generated to support the modified patch as well as additional chemistry, manufacturing, and controls data. There were no safety concerns raised by the FDA for Viaskin® Peanut.

Pipeline:

- **CA002:** CA002 is a peanut protein-based biological drug for oral immunotherapy being developed by Camallergy. The regimen includes a single dose at the initial appointment and a 7-stage dose escalation period completed in 4 months or less with the goal of increasing the dose of peanut protein and then maintaining a steady dose indefinitely. A Phase 2 study showed the safety and efficacy of CA002 compared to standard of care (SOC, peanut avoidance) in children 7 to 16 years of age. In the first phase of the study, of the patients who received CA002, 62% tolerated 1,400mg of peanut protein compared to none of the SOC patients. Of the patients who received CA002, 84% tolerated 800mg. In the second phase, the SOC patients received CA002. Of the patients who received CA002, 54% and 91% tolerated 1,400mg and 800mg, respectively, of peanut protein. Mild side effects occurred in most patients, with gastrointestinal symptoms being the most common (31 patients had nausea and 31 had vomiting). A Phase 3 study is being planned to evaluate the safety and efficacy of CA002 in patients 4 years of age and older with peanut allergy.
- **Dupixent® (Dupilumab):** Dupilumab, a monoclonal antibody against the interleukin 4 (IL-4) receptor, is currently FDA-approved to treat atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyps (CRSwNP). It is also being studied for peanut allergy, grass allergy, chronic obstructive pulmonary disease (COPD), and eosinophilic esophagitis. Dupilumab is being studied with a grass pollen subcutaneous immunotherapy (SCIT) to determine if the antibody can enhance the patient's response to the SCIT. A Phase 2 study was completed with 103 patients in the United States and Canada studying dupilumab alone and as an adjunct therapy to Timothy Grass SCIT. After 16 weeks of treatment, allergic rhinitis symptoms were measured after nasal allergen challenge; however, no results have been reported.
- **Ragwitek® (Short Ragweed Pollen Allergen Extract):** In November 2019, ALK presented Phase 3 data on Ragwitek® at the American College of Allergy, Asthma & Immunology (ACAAI) 2019 Annual Scientific Meeting. The data included efficacy and safety findings from the largest allergy immunotherapy clinical trial in children with ragweed allergic rhinitis with or without conjunctivitis (AR/C). The data demonstrated that Ragwitek® sublingual allergy immunotherapy (SLIT) significantly improved AR/C symptoms in children 5 to 17 years of age and decreased medication use compared to placebo. Overall, treatment was well tolerated and discontinuation rates due to adverse events were low.
- **REGN1908-1909:** Regeneron Pharmaceuticals announced in February 2021 detailed results from a Phase 2 proof-of-concept study evaluating the investigational antibody cocktail REGN1908-1909 in cat-allergic

patients with mild asthma. The trial met the primary endpoint of preventing early asthma reactions [EAR, defined as a ≥20% decline in forced expiratory volume over 1 second (FEV_1)]. The trial also met key secondary endpoints, including improved lung function and an increased amount of cat allergen that patients could tolerate following a single dose of treatment, from as early as the first assessment conducted at week 1. A single dose of REGN1908-1909 prevented EAR in cat-allergic patients with mild asthma as early as 1 week after treatment and for up to 3 months. Cat allergy is primarily caused by exposure to Fel d 1, the major allergen in cat dander produced by all cats. REGN1908-1909 is a novel cocktail of 2 fully-human monoclonal immunoglobulin G (IgG) antibodies given as a 600mg dose subcutaneously (sub-Q). It is designed to specifically bind and block the Fel d 1 allergen, thus preventing it from binding and triggering the endogenous antibodies that cause allergies.

Recommendations

The College of Pharmacy does not recommend any changes to the current allergen immunotherapies prior authorization criteria at this time.

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[1] Keown A. FDA Issues CRL for DBV Technologies' Viaskin Peanut Allergy Patch. *BioSpace*. Available online at: https://www.biospace.com/article/dbv-technologies-craters-following-fda-crl-for-viaskin-peanut-allergy-patch. Issued 08/04/2020. Last accessed 04/13/2021.

[2] Burke CW. Insight Report: Where is the Peanut Allergy Drug Pipeline Now? *BioSpace*. Available online at: https://www.biospace.com/article/insight-report-where-is-the-peanut-allergy-drug-pipeline-now-/#drug-pipeline. Issued 11/07/2019. Last accessed 04/16/2021.

[3] Burke CW. Allergy Immunotherapy: Relief that is Nothing to Sneeze at. *BioSpace*. Available online at: https://www.biospace.com/article/allergy-immunotherapy-relief-that-is-nothing-to-sneeze-at/. Issued 02/27/2020. Last accessed 04/15/2021.

[4] ALK. ALK to Present New Phase 3 Data Demonstrating the Efficacy and Safety of Ragwitek® (Short Ragweed Pollen Allergen Extract Tablet for Sublingual Use 12 Amb a 1-U) Sublingual Allergy Immunotherapy (SLIT)-Tablets in Pediatric Patients at ACAAI 2019 Annual Scientific Meeting. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/alk-to-present-new-phase-3-data-demonstrating-the-efficacy-and-safety-of-ragwitek-short-ragweed-pollen-allergen-extract-tablet-for-sublingual-use-12-amb-a-1-u-sublingual-allergy-immunotherapy-slit-tablets-in-pediatric-patient-300954202.html. Issued 11/08/2019. Last accessed 04/15/2021.

[5] Regeneron Pharmaceuticals, Inc. Regeneron Announces Positive Phase 2 Data Evaluating Fel d 1 Antibody Cocktail in Cat-allergic Patients with Mild Asthma. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/regeneron-announces-positive-phase-2-data-evaluating-fel-d-1-antibody-cocktail-in-cat-allergic-patients-with-mild-asthma-301236868.html. Issued 02/25/2021. Last accessed 04/16/2021.

Appendix O

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: April 23, 2021

FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review

Following a thorough safety review, including 2 meetings of the U.S. Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices, the FDA and the CDC have determined that the recommended pause regarding the use of the Johnson & Johnson (Janssen) COVID-19 vaccine in the United States should be lifted and use of the vaccine should resume.

The pause was recommended after reports of 6 cases of a rare and severe type of blood clot in individuals following administration of the Janssen COVID-19 vaccine. During the pause, medical and scientific teams at the FDA and CDC examined available data to assess the risk of thrombosis involving the cerebral venous sinuses (CVST), and other sites in the body (including but not limited to the large blood vessels of the abdomen and the veins of the legs) along with thrombocytopenia, or low blood platelet counts. The teams at the FDA and CDC also conducted extensive outreach to providers and clinicians to ensure they were made aware of the potential for these adverse events and could properly manage and recognize these events due to the unique treatment required for these blood clots and low platelets, also known as thrombosis-thrombocytopenia syndrome (TTS).The 2 agencies have determined the following:

- Use of the Janssen COVID-19 Vaccine should be resumed in the United States.
- The FDA and CDC have confidence that this vaccine is safe and effective in preventing COVID-19.
- The FDA has determined that the available data show that the vaccine's known and potential benefits outweigh its known and potential risks in individuals 18 years of age and older.
- At this time, the available data suggest that the chance of TTS occurring is very low, but the FDA and CDC will remain vigilant in continuing to investigate this risk.
- Health care providers administering the vaccine and vaccine recipients or caregivers should review the Janssen COVID-19 vaccine *Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)* and *Fact Sheet for Recipients and Caregivers*, which have been revised to include information about the risk of this syndrome, which has occurred in a very small number of people who have received the Janssen COVID-19 vaccine.

The CDC's independent Advisory Committee on Immunization Practices (ACIP) met to discuss the latest data on TTS, hearing from the vaccine manufacturer Janssen and the COVID-19 Vaccine Safety Technical (VaST) subgroup, as well as a risk benefit analysis. ACIP is committed to be vigilant and responsive to additional information that could impact the risk benefit analysis of any of these vaccines. Vaccine safety monitoring will continue and any new information about TTS will be brought to ACIP as needed.

FDA NEWS RELEASE

For Immediate Release: April 22, 2021

FDA Approves Immunotherapy for Endometrial Cancer with Specific Biomarker

The FDA granted accelerated approval to Jemperli (dostarlimab) for treating patients with recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing chemotherapy and whose cancers have a specific genetic feature known as mismatch repair deficient (dMMR)(which contain abnormalities that affect the proper repair of DNA inside the cell).

Jemperli works by targeting the cellular pathway known as a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1). Jemperli helps the body's immune system in its fight against cancer cells by blocking this pathway. The safety and efficacy of Jemperli was studied in a single-arm, multi-cohort clinical study. Of the 71 patients with dMMR recurrent or advanced endometrial cancer who received Jemperli in the study, 42.3% had a complete or partial response to treatment with Jemperli. For 93% of responders, the response lasted for 6 months or more.

Common side effects of Jemperli include fatigue, nausea, diarrhea, anemia, and constipation. Jemperli can cause serious conditions known as immune-mediated side effects, including inflammation of healthy organs such as the lungs, colon, liver, endocrine glands, and kidneys.

The FDA granted Jemperli Priority Review and Breakthrough Therapy designations for this indication.

FDA NEWS RELEASE

For Immediate Release: April 16, 2021

Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Monoclonal Antibody Bamlanivimab

The FDA revoked the emergency use authorization (EUA) that allowed for the investigational monoclonal antibody therapy bamlanivimab, when administered alone, to be used for the treatment of mild-to-moderate COVID-19 in adults and certain pediatric patients. Based on its ongoing analysis of emerging scientific data, specifically the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab alone resulting in the increased risk for treatment failure, the FDA has determined that the known and potential benefits of bamlanivimab, when administered alone, no longer outweigh the known and potential risks for its authorized use. Therefore, the agency determined that the criteria for issuance of an authorization are no longer met and has revoked the EUA.

On November 9, 2020, based on the totality of scientific evidence available at the time, the FDA issued an EUA to Eli Lilly and Co. authorizing the emergency use of bamlanivimab alone for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing ≥40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Importantly, although the FDA is now revoking this EUA, alternative monoclonal antibody therapies remain available under EUA, including REGEN-COV (casirivimab and imdevimab, administered together), and bamlanivimab and etesevimab, administered together, for the same uses as previously authorized for bamlanivimab alone. The FDA believes that these alternative monoclonal antibody therapies remain appropriate to treat patients with COVID-19 when used in accordance with the authorized labeling based on information available at this time.

FDA NEWS RELEASE

For Immediate Release: April 16, 2021

FDA Approves First Immunotherapy for Initial Treatment of Gastric Cancer

The FDA approved Opdivo (nivolumab), in combination with chemotherapy, for the initial treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction (GEJ) cancer, and esophageal adenocarcinoma. This is the first FDA-approved immunotherapy for the first-line treatment of gastric cancer.

There are approximately 28,000 new diagnoses of gastric cancer each year in the United States. With currently available therapy, overall survival is generally poor; the rate of cure with resection is very low and the survival rate for all stages is 32%. The 5-year survival rate for advanced or metastatic gastric cancer is 5%.

Opdivo is a monoclonal antibody that inhibits tumor growth by enhancing T-cell function. Its efficacy was evaluated in a randomized, multicenter, open-label study of 1,581 patients with previously untreated advanced or metastatic gastric cancer, GEJ cancer, and esophageal adenocarcinoma. The 789 patients who received Opdivo in combination with chemotherapy, on average, lived longer than the 792 patients who received chemotherapy alone. Median survival was 13.8 months for patients who received Opdivo plus chemotherapy compared to 11.6 months for patients who received chemotherapy alone.

Opdivo received Priority Review and Orphan Drug designations for this indication. Review for this indication was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, the FDA collaborated with the Australian Therapeutic Goods Administration, the Brazilian Health Regulatory Agency, Health Canada, and Switzerland's Swissmedic. The application reviews are ongoing at the other regulatory agencies.

FDA NEWS RELEASE

For Immediate Release: April 13, 2021

Joint CDC and FDA Statement on Johnson & Johnson COVID-19 Vaccine

As of April 12, 2021, more than 6.8 million doses of the Johnson & Johnson (J&J, Janssen) vaccine have been administered in the United States. The centers for disease control and prevention (CDC) and the FDA are reviewing data involving 6 reported United States cases of a rare and severe type of blood clot in individuals after receiving the J&J vaccine. In these cases, cerebral venous sinus thrombosis (CVST) was seen in combination with thrombocytopenia. All 6 cases occurred among women between 18 and 48 years of age, and symptoms occurred 6 to 13 days after vaccination. Treatment of this specific type of blood clot is different from the treatment that might typically be administered. Usually, an anticoagulant drug called heparin is used to treat blood clots. In this setting, administration of heparin may be dangerous, and alternative treatments need to be given.

The CDC will convene a meeting of the Advisory Committee on Immunization Practices (ACIP) to further review these cases and assess their potential significance. The FDA will review that analysis as it also investigates these cases. Until that process is complete, the FDA recommends a pause in the use of this vaccine out of an abundance of caution. This is important, in part, to ensure that the health care provider community is aware of the potential for these adverse events and can plan for proper recognition and management due to the unique treatment required with this type of blood clot.

These adverse events appear to be extremely rare. COVID-19 vaccine safety is a top priority for the federal government, and the FDA takes all reports of health problems following COVID-19 vaccination very seriously. The FDA recommends that anyone who has received the J&J vaccine and develops severe headache, abdominal pain, leg pain, or shortness of breath within 3 weeks after vaccination should contact their health care provider. The FDA is asking that health care providers report adverse events to the Vaccine Adverse Event Reporting System at https://vaers.hhs.gov/reportevent.html.

FDA NEWS RELEASE

For Immediate Release: April 6, 2021

Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for the Symbiotica COVID-19 Self-Collected Antibody Test System

The FDA announced it has issued an emergency use authorization (EUA) for the Symbiotica COVID-19 Self-Collected Antibody Test System, the first antibody test authorized for use with home collected dried blood spot samples. Samples collected at home are then sent to a Symbiotica, Inc. laboratory for analysis.

The COVID-19 Self-Collected Antibody Test System is authorized for prescription use with a fingerstick dried blood sample that is self-collected by an individual 18 years of age or older or collected by an adult from an individual 5 years of age and older. The test is intended to aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. The COVID-19 Self-Collected Antibody Test System should not be used to diagnose or exclude acute SARS-CoV-2 infection. At this time, it is unknown how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

Antibody tests, also known as serology tests, detect antibodies present in the blood when the body is responding to a specific infection, as with SARS-CoV-2. COVID-19 antibody tests can help identify people who may have had a prior infection or who may have recovered from COVID-19. However, these tests cannot detect the presence of the SARS-CoV-2 virus to diagnose COVID-19.

FDA NEWS RELEASE

For Immediate Release: April 1, 2021

Coronavirus (COVID-19) Update: FDA Makes Two Revisions to Moderna COVID-19 Vaccine Emergency Use Authorization to Help Increase the Number of Vaccine Doses Available

The FDA announced 2 revisions regarding the number of doses per vial available for the Moderna COVID-19 vaccine. The first revision clarifies the number of doses per vial for the vials that are currently available, in that the maximum number of extractable doses is 11, with a range of 10-11 doses. The second revision authorizes the availability of an additional multi-dose vial in which each vial contains a maximum of 15 doses, with a range of 13-15 doses that can potentially be extracted.

Depending on the type of syringes and needles used to extract each dose, there may not be sufficient volume to extract >10 doses from the vial containing a maximum of 11 doses or >13 doses from the vial containing a maximum of 15 doses. To support these changes to the EUA, the FDA evaluated data showing the number of doses that could be extracted from the vials and on the fill volumes for both vials that were submitted by ModernaTX, Inc. The *Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)* and *Prescribing Information* have been revised to reflect the new

information and are intended to help frontline workers administering COVID-19 vaccines understand the number of doses that can potentially be extracted per vial.

Because the Moderna COVID-19 vaccine does not contain preservative, any further remaining product that does not constitute a full dose should not be pooled from multiple vials to create 1 full dose. If 1 vial becomes contaminated during use, pooling doses from multiple vials can spread contamination to other vials. Use of contaminated vials may cause serious bacterial infections in vaccinated individuals. The updated information in the revised *Fact Sheet for Vaccination Providers* and *Prescribing Information* provides instructions to not pool vaccine from multiple vials. The dosing regimen remains unchanged; the vaccine is administered as a 2-dose series, 0.5mL each dose, 1 month apart.

FDA NEWS RELEASE

For Immediate Release: March 27, 2021

FDA Approves First Cell-Based Gene Therapy for Adult Patients with Multiple Myeloma

The FDA approved Abecma (idecabtagene vicleucel), a cell-based gene therapy to treat adult patients with multiple myeloma who have not responded to, or whose disease has returned after, at least 4 prior lines of therapy. Abecma is the first cell-based gene therapy approved by the FDA for the treatment of multiple myeloma.

Multiple myeloma is an uncommon type of blood cancer in which abnormal plasma cells build up in the bone marrow and form tumors in bones. The exact cause of multiple myeloma is unknown. According to the National Cancer Institute, myeloma accounted for approximately 1.8% (32,000) of all new cancer cases in the United States in 2020.

Abecma is a B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy. Each dose of Abecma is a customized treatment created by using a patient's own T-cells to help fight the myeloma. The patient's T-cells are collected and genetically modified to include a new gene that facilitates targeting and killing myeloma cells. Once the cells are modified, they are infused back into the patient.

The safety and efficacy of Abecma were established in a multicenter study of 127 patients with relapsed myeloma and refractory myeloma, who received at least 3 prior anti-myeloma lines of therapy. About 88% of patients in the study group had received 4 or more prior lines of anti-myeloma therapy. Overall, 72% of patients partially or completely responded to the treatment. Of those studied, 28% of patients showed complete response to Abecma, and 65% of this group remained in complete response to the treatment for at least 12 months.

Treatment with Abecma has the potential to cause severe side effects. The label carries a *Boxed Warning* for cytokine release syndrome (CRS), hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), neurologic toxicity, and prolonged cytopenia. All of these can be fatal or life-threatening. CRS and HLH/MAS are systemic responses to the activation and proliferation of CAR T-cells causing high fever and flu-like symptom. The most common side effects of Abecma include CRS, infections, fatigue, musculoskeletal pain, and a weakened immune system. Because of the risk of CRS and neurologic toxicities, Abecma is being approved with a risk evaluation and mitigation strategy (REMS) program. To further evaluate the long-term safety, the FDA is also requiring the manufacturer to conduct a post-marketing observational study involving patients treated with Abecma.

Abecma was granted Orphan Drug and Breakthrough Therapy designations by the FDA. Breakthrough Therapy designation was granted based on sustained responses observed in patients with relapsed and refractory myeloma.

FDA NEWS RELEASE

For Immediate Release: March 26, 2021

FDA Authorizes Marketing of Device to Improve Gait in Multiple Sclerosis Patients

The FDA authorized marketing of a new device indicated for use as a short-term treatment of gait deficit due to mild-to-moderate symptoms from multiple sclerosis (MS). The device is intended to be used by prescription only as an adjunct to a supervised therapeutic exercise program in patients 22 years of age and older. The device, called the Portable Neuromodulation Stimulator (PoNS), is a neuromuscular tongue stimulator that consists of a non-implantable apparatus to generate electrical pulses for stimulation of the trigeminal and facial nerves via the tongue to provide treatment of motor deficits.

The PoNS device delivers mild neuromuscular electrical stimulation to the dorsal surface of the patient's tongue. It consists of a controller and a mouthpiece that are connected to each other by a cord. The mouthpiece is held lightly in place by the lips and teeth and the control unit is worn around the neck during a patient's visit with a therapist. The controller sends signals to the mouthpiece placed on the tongue; receptors on the tongue send millions of neural impulses to the brain through natural pathways. Additionally, the therapist can connect the control unit to a computer and view usage data via software developed specifically for the PoNS device. The usage data gives the therapist information on how to improve a patient's execution of therapy by identifying potential areas of missed or shortened sessions.

The FDA assessed the safety and effectiveness of the PoNS device through 2 clinical studies and a retrospective analysis of real-world data (RWD). In the first study, 20 patients with gait deficits due to MS participated in a randomized, double-blind controlled study where 10 patients used the PoNS device and the remaining 10 patients used a sham control device that did not deliver stimulation. The primary outcome measure was the Dynamic Gait Index (DGI) where the clinician scored an index of 8 gait tasks. The DGI was assessed for a baseline, at 2 weeks, 6 weeks, 10 weeks, and 14 weeks. The results showed that the PoNS group on average achieved improvement in their DGI score of 7.95 at the end of the study, which was statistically significant and clinically significant, while the control group did not.

In the second study, the clinicians investigated the effects of the PoNS device with cognitive rehab and physical rehab in 14 patients with MS, who did not know whether they had the PoNS device or the sham control device, in a randomized controlled study where 7 patients used the PoNS device and the other 7 used a sham device. Baseline evaluations included sensory organization tasks (SOT) and DGI scores. The PoNS device group showed a statistically significant improvement in SOT scores at 14 weeks compared to the baseline value. Analysis of DGI scores after 14 weeks showed no significant result.

The sponsor also provided a retrospective analysis of RWD collected with the PoNS device in MS patients in clinical rehabilitation settings. Patients who agreed to treatment were given 1-hour consultation, provided consent, and given baseline assessments of gait function using the Functional Gait Assessment. No serious safety adverse events were reported in the clinical studies or retrospective analysis of RWD.

The PoNS device should not be used by patients with penetrating brain injuries, neurodegenerative diseases, oral health problems, chronic infectious diseases,

unmanaged hypertension or diabetes, pacemakers, and/or a history of seizures. Because the PoNS device delivers electrical stimulation directly to the surface of the tongue, precautions for use are similar to those for transcutaneous electrical nerve stimulation. Electrical stimulation should not be used if there is an active or suspected malignant tumor; in areas of recent bleeding or open wounds; or in areas that lack normal sensation. The PoNS device has not been tested on, and thus should not be used by, individuals younger than 22 years of age or who are pregnant. The PoNS device should not be used if a patient is sensitive to nickel, gold, or copper.

The PoNS device was granted Breakthrough Device designation by the FDA. The FDA granted marketing authorization of the PoNS to Helius Medical, Inc.

FDA NEWS RELEASE

For Immediate Release: March 22, 2021

FDA Warns Companies Illegally Selling Over-the-Counter CBD Products for Pain Relief

The FDA has issued warning letters to Honest Globe, Inc. and Biolyte Laboratories, LLC for selling products labeled as containing cannabidiol (CBD) in ways that violate the Federal Food, Drug, and Cosmetic (FD&C) Act . Specifically, the warning letters address the illegal marketing of unapproved drugs labeled as containing CBD. The FDA has not approved any over-the-counter (OTC) drugs containing CBD, and none of these products meet the requirements to be legally marketed without an approved new drug application. The letters explain that, as CBD has known pharmacological effects on humans, with demonstrated risks, it cannot be legally marketed as an inactive ingredient in OTC drug products that are not reviewed and approved by the FDA. Additionally, the letters cite substandard manufacturing practices, including failure to comply with current good manufacturing practices.

The products that are the subject of the warning letters issued have not gone through the FDA drug approval process and are considered unapproved new drugs. There has been no FDA evaluation of whether these unapproved drug products are effective for the uses manufacturers claim, what an appropriate dose might be, how they could interact with FDA-approved drugs or other products or whether they have dangerous side effects or other safety concerns. The FDA has previously sent warning letters to other companies illegally selling unapproved CBD products that claimed to prevent, diagnose, mitigate, treat, or cure various diseases, in violation of the FD&C Act. The FDA has requested written responses from these companies within 15 working days stating how they will address these violations or providing their reasoning and supporting information as to why they believe these products are not in violation of the law. Failure to adequately address the violations promptly may result in legal action, including product seizure and/or injunction.

The FDA has not approved any CBD-containing drug products other than 1 prescription drug for the treatment of seizures associated with tuberous sclerosis complex, Lennox-Gastaut syndrome, and Dravet syndrome in human patients.

Current Drug Shortages Index (as of April 16, 2021):

The information provided in this section is provided voluntarily to the FDA by manufacturers and is not specific to Oklahoma.

Acetazolamide Injection	***Currently in Shortage***
Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Azacitidine for Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG/ML	***Currently in Shortage***
Calcium Disodium Versenate Injection	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Ceftazidime and Avibactam (Avycaz) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Ceftolozane and Tazobactam (Zerbaxa) Injection	***Currently in Shortage***
Chlordiazepoxide Hydrochloride USP, Capsules	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cortisone Acetate Tablets	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***
Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Desmopressin Acetate (Stimate) Nasal Spray	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Diltiazem Hydrochloride Injection	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***

Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Floxuridine for Injection, USP	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Histreline Acetate Implant	***Currently in Shortage***
Hydralazine Hydrochloride Injection, USP	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Isoniazid Injection USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Misoprostol Tablets	***Currently in Shortage***

Morphine Sulfate Injection	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifampin Injection	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Succimer (Chemet) Capsules	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Teprotumumab-trbw	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Trimethobenzamide Hydrochloride Capsules	***Currently in Shortage***
Valproate Sodium Injection, USP	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***
Zinc Acetate Capsules	***Currently in Shortage***