OKLAHOMA
Health Care Authority

Drug Utilization Review Board

OHCA Webinar
Wednesday,
November 4, 2020
4:00pm

OHCA Webinar

Register for the meeting using the following website address:
https://odot.webex.com/odot/onstage/g.php?MTID=e8f4367350ba553df91e069c0bfba1048

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – November 4, 2020 @ 4:00pm

OHCA Webinar
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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

Telephone Conference Participants

DUR Board Members:

Dr. Stephen Anderson –	participating via Webex Teleconference
Dr. Jennifer de los Angeles –	participating via Webex Teleconference
Ms. Jennifer Boyett –	participating via Webex Teleconference
Dr. Markita Broyles –	participating via Webex Teleconference
Dr. Theresa Garton –	participating via Webex Teleconference
Dr. Megan Hanner –	participating via Webex Teleconference
Dr. Lynn Mitchell –	participating via Webex Teleconference
Dr. John Muchmore –	participating via Webex Teleconference
Dr. Lee Muñoz –	participating via Webex Teleconference
Dr. James Osborne –	participating via Webex Teleconference

Public Access to Meeting via Webex:

Register at:
https://odot.webex.com/odot/onstage/g.php?MTID=e8f4367350ba553df91e069c0bfba1048

Or join by phone:

Dial: +1-415-655-0002

Event number: 133 317 0056
Event password: OHCADUR1104

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. October 14, 2020 DUR Minutes – Vote

B. October 14, 2020 DUR Recommendations Memorandum

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

4. Action Item – 2021 DUR Board Meeting Dates – See Appendix B

A. 2021 DUR Board Meeting Dates

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

5. Update on Medication Coverage Authorization Unit/U.S. Food and Drug Administration (FDA) Safety Alerts – See Appendix C

A. Pharmacy Helpdesk Activity for October 2020

B. Medication Coverage Activity for October 2020

C. U.S. Food and Drug Administration (FDA) Safety Alerts

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

6. Action Item – Vote to Prior Authorize Evrysdi™ (Risdiplam) – See Appendix D

A. Introduction

B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) – 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. Ford, Chairman:

8. Action Item – Vote to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet – See Appendix F

A. New U.S. Food and Drug Administration (FDA) Approval(s) and Label Update(s)

B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) – See Appendix G

A. Introduction

B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Mycapssa® (Octreotide) – See Appendix H

A. Introduction

B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Zejula® (Niraparib) – See Appendix I

A. Market News and Updates

B. Zejula® (Niraparib) Product Summary

C. Recommendations

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

12. Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor) – See Appendix J

A. Introduction
B. Utilization of Multiple Myeloma Medications
C. Prior Authorization of Multiple Myeloma Medications
D. Market News and Updates
E. Product Summaries
F. Recommendations
G. Utilization Details of Multiple Myeloma Medications

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

13. 30-Day Notice to Prior Authorize Lenvima® (Lenvatinib) – See Appendix K

A. Introduction
B. Lenvima® (Lenvatinib) Product Summary
C. Recommendations

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

14. Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Maintenance Asthma and COPD Medications
C. Prior Authorization of Maintenance Asthma and COPD Medications
D. Market News and Updates
E. AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol) Product Summary
F. ArmonAir® Digihaler® (Fluticasone Propionate) Product Summary
G. Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Maintenance Asthma and COPD Medications
J. Utilization Details of Inhaled Corticosteroids

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

15. Action Item – Annual Review of Atopic Dermatitis (AD) Medications – See Appendix M

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

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

16. Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Anticoagulants and Platelet Aggregation Inhibitors
C. Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Anticoagulants
G. Utilization Details of Platelet Aggregation Inhibitors

Non-presentation/Questions only:

17. Annual Review of Tepezza® (Teprotumumab-trbw) – See Appendix O

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Tepezza® (Teprotumumab-trbw)
D. Prior Authorization of Tepezza® (Teprotumumab-trbw)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Tepezza® (Teprotumumab-trbw)

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

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

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

19. Future Business

A. Nondiscrimination in Health Care Coverage Act

i. Discussion of the Nondiscrimination in Health Care Coverage Act, which became effective on November 1, 2020 (63 Okla. Stat. §§2560-2565), and the DUR Board's compliance therewith.

B. Upcoming Product and Class Reviews*

i. Targeted Immunomodulator Agents
ii. Antidepressants
iii. Ulcerative Colitis (UC) and Crohn's Disease Medications
iv. Thrombocytopenia Medications

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

20. Adjournment

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 – November 4, 2020

DATE: October 26, 2020

NOTE: In response to COVID-19, the November 2020 meeting will be held via OHCA webinar at 4:00pm. Please register for the meeting using the following website address: https://odot.webex.com/odot/onstage/g.php?MTID=e8f4367350ba553df91e069c0bfba1048

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

Call to Order

Public Comment Forum

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

2021 DUR Board Meeting Dates – Appendix B

Update on Medication Coverage Authorization Unit/U.S. Food and Drug Administration (FDA) Safety Alerts – Appendix C

Action Item – Vote to Prior Authorize Evrysdi™ (Risdiplam) – Appendix D

Action Item – Vote to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) – Appendix E

Action Item – Vote to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet – Appendix F

Action Item – Vote to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) – Appendix G

Action Item – Vote to Prior Authorize Mycapssa® (Octreotide) – Appendix H

Action Item – Vote to Prior Authorize Zejula® (Niraparib) – Appendix I

Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor) – Appendix J

30-Day Notice to Prior Authorize Lenvima® (Lenvatinib) – Appendix K

Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate) – Appendix L

Action Item – Annual Review of Atopic Dermatitis (AD) Medications – Appendix M

Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – Appendix N

Annual Review of Tepezza® (Teprotumumab-trbw) – Appendix O

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

Future Business

Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING OCTOBER 14, 2020

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, Tyler Fisher	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
Stacey Hale; Drug Rebate Manager		x
Michael Herndon, D.O.; Chief Medical Officer		x
Paula Root, M.D.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Michelle Tahah, Pharm.D.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Senior Medical Director	x	
Kerri Wade; Pharmacy Operations Manager	x	

OTHERS PRESENT:	
Greg Rasmussen, Vertex Pharmaceuticals	Robert Katz, M.D., OUHSC
Bart Vleugels, ODOT	Camille Kerr, Regeneron
John Omick, Global Blood Therapeutics	Sunil Majethia, Gilead
Jim Chapman, AbbVie	David Nathanson, Vertex Pharmaceuticals
Sieana Mackiewicz, ODOT	Jeff Mussack, BreaBurnRX
Doug Pierce, Genentech	Brent Hildebrand, Gilead Sciences
Eardie Curry, Genentech	Janie Huff, Tricida
Peter Zoob, Vertex Pharmaceuticals	Rick Andrews, Chiasma Pharmaceuticals
Eric Gardner, Vertex Pharmaceuticals	Brian Maves, Pfizer
Jeff Knappen, Spark Therapeutics	Shellie Keast, Mercer
Doug Wood, ViiV Healthcare	Bethany Holderread, Mercer
Janelle Hardisty, Novartis	Andi Stratton, Novartis
Bob Atkins, Biogen	Charlie Collins, Sanofi-Genzyme
Robert Greely, Biogen	Gina Heinen, Novo Nordisk
Melanie Curlett, Takeda	Aaron Shaw, Boehringer Ingelheim
Crystal Henderson, Global Blood Therapeutics	Nima Nabavi, Amgen
John Logan, AbbVie	Evie Knisely, Novartis
Burl Beasley, EGID-State of Oklahoma	Marc Parker, Sunovion
Ryan Crawford, Vertex Pharmaceuticals	Roxann Dominguez, AbbVie
Kristin Crouch, Vertex Pharmaceuticals	James Dick, Genentech
Frank Alvarado, Johnson & Johnson	

PRESENT FOR PUBLIC COMMENT:	
Janelle Hardisty	Novartis
Eardie Curry	Genentech
Peter Zoob	Vertex Pharmaceuticals
Sunil Majethia	Gilead

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. 5 JANELLE HARDISTY
2B: AGENDA ITEM NO. 9 EARDIE CURRY
2C: AGENDA ITEM NO. 10 PETER ZOOB
2D: AGENDA ITEM NO. 11 SUNIL MAJETHIA
ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **APPROVAL OF DUR BOARD MEETING MINUTES**
3A: SEPTEMBER 9, 2020 DUR MINUTES – VOTE
3B: SEPTEMBER 9, 2020 DUR RECOMMENDATIONS MEMORANDUM
Materials included in agenda packet; presented by Dr. Muchmore
Dr. Mitchell moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/FALL 2020 PIPELINE UPDATE**
4A: PHARMACY HELPDESK ACTIVITY FOR SEPTEMBER 2020
4B: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2020
4C: FALL 2020 PIPELINE UPDATE
Materials included in agenda packet; presented by Dr. Adams, Dr. Daniel
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE ADAKVEO® (CRIZANLIZUMAB-TMCA), OXBRYTA® (VOXELOTOR), AND REBLOZYL® (LUSPATERCEPT-AAMT)**
5A: INTRODUCTION
5B: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
5C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ENHERTU® (FAM-TRASTUZUMAB DERUXTECAN-NXKI), PHESGO™ (PERTUZUMAB/TRASTUZUMAB/ HYALURONIDASE-ZZXF), TRODELVY™ (SACITUZUMAB GOVITECAN-HZIY), AND TUKYSA™ (TUCATINIB)**
6A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND INDICATION(S)
6B: PRODUCT SUMMARIES
6C: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE RUBRACA® (RUCAPARIB)**
7A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND INDICATION(S)
7B: RUBRACA® (RUCAPARIB) PRODUCT SUMMARY
7C: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Anderson moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF OVARIAN CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZEJULA® (NIRAPARIB)**

8A: INTRODUCTION
8B: CURRENT PRIOR AUTHORIZATION CRITERIA
8C: UTILIZATION OF OVARIAN CANCER MEDICATIONS
8D: PRIOR AUTHORIZATION OF OVARIAN CANCER MEDICATIONS
8E: MARKET NEWS AND UPDATES
8F: ZEJULA® (NIRAPARIB) PRODUCT SUMMARY
8G: RECOMMENDATIONS
8H: UTILIZATION DETAILS OF OVARIAN CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Borders

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF SPINAL MUSCULAR ATROPHY (SMA) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EVRYSDI™ (RISDIPLAM)**

9A: CURRENT PRIOR AUTHORIZATION CRITERIA
9B: UTILIZATION OF SMA MEDICATIONS
9C: PRIOR AUTHORIZATION OF SMA MEDICATIONS
9D: MARKET NEWS AND UPDATES
9E: EVRYSDI™ (RISDIPLAM) PRODUCT SUMMARY
9F: COLLEGE OF PHARMACY RECOMMENDATIONS
9G: UTILIZATION DETAILS OF SMA MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) MODULATORS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TRIKAFTA® (ELEXACAFTOR/TEZACAFTOR/ IVACAFTOR AND IVACAFTOR)**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF CFTR MODULATORS
10C: PRIOR AUTHORIZATION OF CFTR MODULATORS
10D: MARKET NEWS AND UPDATES
10E: TRIKAFTA® (ELEXACAFTOR/TEZACAFTOR/IVACAFTOR AND IVACAFTOR) PRODUCT SUMMARY
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
10G: UTILIZATION DETAILS OF CFTR MODULATORS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF HEPATITIS C MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EPCLUSA® (SOFOSBUVIR/ VELPATASVIR) 200MG/50MG TABLET**

11A: INTRODUCTION
11B: CURRENT PRIOR AUTHORIZATION CRITERIA
11C: TRENDS OF HEPATITIS C MEDICATION UTILIZATION
11D: HEPATITIS C SUMMARY STATISTICS FOR TREATED MEMBERS
11E: UTILIZATION OF HEPATITIS C MEDICATIONS
11F: PRIOR AUTHORIZATION OF HEPATITIS C MEDICATIONS
11G: MARKET NEWS AND UPDATES
11H: REGIMEN COMPARISON

11I: COLLEGE OF PHARMACY RECOMMENDATIONS
11J: UTILIZATION DETAILS OF HEPATITIS C MEDICATIONS
Materials included in agenda packet; presented by Dr. Ford
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 12:</u> 30-DAY NOTICE TO PRIOR AUTHORIZE CYSTADROPS® (CYSTEAMINE 0.37% OPHTHALMIC SOLUTION) AND CYSTARAN™ (CYSTEAMINE 0.44% OPHTHALMIC SOLUTION)
12A: INTRODUCTION
12B: PRODUCT COMPARISON
12C: COLLEGE OF PHARMACY RECOMMENDATIONS
12D: UTILIZATION DETAILS OF CYSTARAN™ (CYSTEAMINE 0.44% OPHTHALMIC SOLUTION)
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 13:</u> ANNUAL REVIEW OF SIGNIFOR® LAR (PASIREOTIDE) AND 30-DAY NOTICE TO PRIOR AUTHORIZE MYCAPSSA® (OCTREOTIDE)
13A: INTRODUCTION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA
13C: UTILIZATION OF SIGNIFOR® LAR (PASIREOTIDE)
13D: PRIOR AUTHORIZATION OF SIGNIFOR® LAR (PASIREOTIDE)
13E: MARKET NEWS AND UPDATES
13F: MYCAPSSA® (OCTREOTIDE) PRODUCT SUMMARY
13G: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Daniel
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 14:</u> ANNUAL REVIEW OF LAMBERT-EATON MYASTHENIC SYNDROME (LEMS) MEDICATIONS [FIRDAPSE® (AMIFAMPRIDINE) AND RUZURGI® (AMIFAMPRIDINE)]
14A: INTRODUCTION
14B: CURRENT PRIOR AUTHORIZATION CRITERIA
14C: UTILIZATION OF LEMS MEDICATIONS
14D: PRIOR AUTHORIZATION OF LEMS MEDICATIONS
14E: MARKET NEWS AND UPDATES
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF LEMS MEDICATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 15:</u> U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 16:</u> FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
DUE TO THE VETERANS' DAY HOLIDAY, THE NOVEMBER DUR MEETING WILL BE HELD ON THE FIRST WEDNESDAY OF THE MONTH ON NOVEMBER 4, 2020.
16A: TARGETED IMMUNOMODULATOR AGENTS
16B: CONSTIPATION AND DIARRHEA MEDICATIONS

16C: ATOPIC DERMATITIS (AD) MEDICATIONS
16D: ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT
The meeting was adjourned at 5:28pm.

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

Memorandum

Date: October 15, 2020

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 of October 14, 2020

Recommendation 1: Fall 2020 Pipeline Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Adakveo® (Crizanlizumab-tmca), Oxbryta® (Voxelotor), and Reblozyl® (Luspatercept-aamt)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Adakveo® (crizanlizumab-tmca), Oxbryta® (voxelotor), and Reblozyl® (luspatercept-aamt) with the following criteria:

Adakveo® (Crizanlizumab-tmca) Approval Criteria:

1. An FDA approved indication to reduce the frequency of vaso-occlusive crises (VOCs) in adult members and in pediatric members 16 years of age and older with sickle cell disease (SCD); and
2. Member must have a history of VOCs; and
3. Adakveo® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and

4. Prescriber must verify Adakveo® will be administered by a trained health care provider. The prior authorization request must indicate how Adakveo® will be administered; and
    a. Adakveo® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Adakveo® must be shipped via cold chain supply to the member's home and administered by a home health provider, and the member or member's caregiver must be trained on the proper storage of Adakveo®; and
5. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
6. Approval quantities will be dependent on the member's weight and will include loading doses at week 0 and 2, then subsequent doses every 4 weeks in accordance with package labeling; and
7. Initial approvals will be for the duration of 3 months. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Oxbryta® (Voxelotor) Approval Criteria:

1. An FDA approved indication for the treatment of sickle cell disease (SCD) in members 12 years of age and older; and
2. Member must have a history of vaso-occlusive crises (VOCs); and
3. Member must have baseline hemoglobin ≥5.5 to ≤10.5g/dL; and
4. Oxbryta® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. The member must not be taking concomitant strong CYP3A4 inhibitors (e.g., fluconazole, ketoconazole) or the prescriber must verify the dose of Oxbryta® will be reduced during concomitant use according to package labeling; and
6. Prescriber must verify that the dose of Oxbryta® will be reduced in accordance with package labeling for members with severe hepatic impairment; and
7. The member must not be taking concomitant strong or moderate CYP3A4 inducers (e.g., rifampin) or the prescriber must verify the dose of Oxbryta® will be adjusted during concomitant use according to package labeling; and
8. A quantity limit of 3 tablets per day will apply; and
9. Initial approvals will be for the duration of 6 months. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Reblozyl® (Luspatercept-aamt) Approval Criteria [Beta Thalassemia Diagnosis]:

1. An FDA approved indication for the treatment of adult members with beta thalassemia who require regular red blood cell (RBC) transfusions; and
2. Member must require regular RBC transfusions (no transfusion-free period >35 days during the prior 6 month period); and
3. Reblozyl® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of beta thalassemia (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating beta thalassemia); and
4. The prescriber must verify the member's hemoglobin will be monitored prior to each Reblozyl® administration; and
5. Prescriber must verify Reblozyl® will be administered by a trained health care provider; and
6. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
7. Approval quantities will be dependent on member weight and every 3 week dosing in accordance with package labeling; and
8. Initial approvals will be for the duration of 4 months. Further approvals will not be granted if the member does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose of 1.25mg/kg (allows for initial dosing of 6 weeks at 1mg/kg). Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Reblozyl® (Luspatercept-aamt) Approval Criteria [Myelodysplastic Syndromes (MDS) Diagnosis]:

1. An FDA approved indication for the treatment of adult members with very low-to-intermediate risk MDS with ring sideroblasts (MDS-RS) or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) with anemia failing an erythropoiesis stimulating agent (ESA) and requiring ≥2 red blood cell (RBC) units over 8 weeks; and
2. Member must have had an inadequate response to prior treatment with an ESA, be intolerant of ESAs, or have a serum erythropoietin level >200U/L; and
3. Member must not have been previously treated with a disease modifying agent for the treatment of MDS; and
4. Prescriber must verify the member does not have deletion 5q (del 5q); and
5. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber and in accordance with package labeling; and

6. Reblozyl® must be prescribed by, or in consultation with, a hematologist, oncologist, or a specialist with expertise in treatment of MDS (or an advanced care practitioner with a supervising physician who is a hematologist, oncologist, or specialist with expertise in treating MDS); and
7. The prescriber must verify the member's hemoglobin will be monitored prior to each Reblozyl® administration; and
8. Prescriber must verify Reblozyl® will be administered by a trained health care provider; and
9. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
10. Approval quantities will be dependent on member weight and every 3 week dosing in accordance with package labeling; and
11. Initial approvals will be for the duration of 6 months. Further approvals will not be granted if the member does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose of 1.75mg/kg or if unacceptable toxicity occurs at any time. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Recommendation 3: Vote to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/ Trastuzumab/Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib)

MOTION CARRIED by unanimous approval.

- The prior authorization of Enhertu® (fam-trastuzumab deruxtecan-nxki), Phesgo™ (pertuzumab/trastuzumab/hyaluronidase-zzxf), Trodelvy™ (sacituzumab govitecan-hziy), and Tukysa™ (tucatinib) with the following criteria listed in red:

Enhertu® (Fam-Trastuzumab Deruxtecan-nxki) Approval Criteria [Breast Cancer Diagnosis]:

1. Adult members with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
2. Member has received ≥2 prior anti-HER2-based regimens in the metastatic setting.

Phesgo™ (Pertuzumab/Trastuzumab/Hyaluronidase-zzxf) Approval Criteria [Breast Cancer Diagnosis]:

1. Human epidermal growth factor receptor 2 (HER2)-positive disease; and
2. Used in 1 of the following settings:

a. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer; or
b. Adjuvant treatment of members with early stage breast cancer; or
c. In combination with docetaxel for members with metastatic disease.

Trodelvy™ (Sacituzumab Govitecan-hziy) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of triple-negative breast cancer; and
2. Metastatic disease; and
3. Member must have received ≥2 therapies for metastatic disease.

Tukysa™ (Tucatinib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced unresectable or metastatic breast cancer; and
2. Used in combination with trastuzumab and capecitabine; and
3. Disease is human epidermal growth factor receptor 2 (HER2)-positive; and
4. Following progression of ≥1 prior anti-HER2 regimen(s) in the metastatic setting.

- Update the current Herzuma® (trastuzumab-pkrb), Lynparza® (olaparib), Nerlynx® (neratinib), Perjeta® (pertuzumab), and Tecentriq® (atezolizumab) prior authorization criteria based on new FDA approved indications (changes noted in red in the following approval criteria; only criteria with changes are listed):

Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ogivri® (Trastuzumab-dkst), Ontruzant® (Trastuzumab-dttb), and Trazimera™ (Trastuzumab-qyyp) Approval Criteria [Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Diagnosis]:

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

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

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

Lynparza® (Olaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), advanced disease; and
    b. Previous treatment with ≥~~3~~ 2 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
    c. A quantity limit based on FDA approved dosing will apply; or
2. **Maintenance Treatment of Advanced Disease:**
    a. ~~Member~~ Disease must be in a complete or partial response to ~~first-line platinum-based~~ primary chemotherapy; and
        i. Used as a single-agent in members with a diagnosis of deleterious or suspected deleterious *gBRCAm* or somatic BRCA-mutated (*sBRCAm*), advanced ovarian cancer; or
        ii. Used in combination with bevacizumab following a primary therapy regimen that included bevacizumab; or
    b. Complete or partial response to second-line or greater platinum-based based chemotherapy (no mutation required); and
    c. A quantity limit based on FDA approved dosing will apply.

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

1. Diagnosis of metastatic pancreatic adenocarcinoma with known germline BRCA1/BRCA2 mutation; and
2. Maintenance therapy as a single-agent; and
3. In members who have not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

Nerlynx® (Neratinib) Approval Criteria [Recurrent or Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Member must have human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
3. Used in combination with capecitabine; or
4. Used in combination with capecitabine or paclitaxel if brain metastases are present.

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

1. Human epidermal growth factor receptor 2 (HER2)-positive; and
2. Used in 1 of the following settings:
    a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
        i. Used in combination with trastuzumab and docetaxel; or
    b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):

i. Used in combination with trastuzumab and docetaxel or paclitaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel or paclitaxel); or

c. Adjuvant systemic therapy for members with node positive, HER2-positive tumors or members with high-risk node negative tumors [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or younger than 35 years of age]:
   i. Used in combination with trastuzumab and paclitaxel following doxorubicin/cyclophosphamide (AC); or
   ii. Used in combination with trastuzumab and docetaxel following AC; or
   iii. Used in combination with docetaxel/carboplatin/trastuzumab (TCH).

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

1. Diagnosis of metastatic disease; and
2. Used in combination with bevacizumab; and
3. Member has not received prior systemic therapy.

Tecentriq® (Atezolizumab) Approval Criteria [Melanoma Diagnosis]:

1. Unresectable or metastatic disease; and
2. BRAF V600 mutation-positive; and
3. In combination with cobimetinib and vemurafenib.

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

1. **Diagnosis of Non-Squamous Non-Small Cell Lung Cancer (NSCLC):**
   a. First-line therapy for metastatic disease; and
   b. The member does not have epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF, MET exon 14 skipping, or RET mutations; and
   c. Used in combination with bevacizumab, paclitaxel, and carboplatin (maximum of 6 cycles) or in combination with paclitaxel (protein bound) and carboplatin; and
   d. Atezolizumab and bevacizumab may be continued after the above combination in members without disease progression (applies to the bevacizumab/paclitaxel/carboplatin regimen); or
2. **Diagnosis of NSCLC:**
   a. For first-line therapy for metastatic disease:
      i. Used as a single-agent; and
      ii. The member does not have EGFR, ALK, ROS1, BRAF, MET exon 14 skipping, or RET mutations; and
      iii. High programmed death ligand-1 (PD-L1) expression determined by 1 of the following:

1. PD-L1 stained ≥50% of tumor cells (TC≥50%); or
2. PD-L1 stained tumor-infiltrating immune cells (IC) covering ≥10% of the tumor area (IC≥10%); or

b. For subsequent therapy for metastatic disease:
   i. Used as a single-agent only.

Recommendation 4: Vote to Prior Authorize Rubraca® (Rucaparib)

MOTION CARRIED by unanimous approval.

- The prior authorization of Rubraca® (rucaparib) with the following criteria listed in red:

Rubraca® (Rucaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
   a. Diagnosis of recurrent or refractory disease; and
   b. Previous treatment with ≥2 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
   c. Disease is associated with a deleterious or suspected deleterious BRCA mutation; and
   d. Used as a single-agent; or
2. **Maintenance Treatment of Advanced Disease:**
   a. Diagnosis of advanced or recurrent disease; and
   b. Disease must be in a complete or partial response to platinum-based chemotherapy; and
   c. Used as a single-agent.

Rubraca® (Rucaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Member must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
   a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in BRCA1 or BRCA2.

- Update the current Lynparza® (olaparib) and Xtandi® (enzalutamide) prior authorization criteria based on new FDA approved indications (changes noted in red in the following approval criteria; only criteria with changes are listed):

Lynparza® (Olaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and

2. Members must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
    a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in a homologous recombination gene.

Xtandi® (Enzalutamide) Approval Criteria [Castration-Sensitive Prostate Cancer (CSPC) Diagnosis]:

1. Diagnosis of metastatic CSPC.

Recommendation 5: Annual Review of Ovarian Cancer Medications and 30-Day Notice to Prior Authorize Zejula® (Niraparib)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Spinal Muscular Atrophy (SMA) Medications and 30-Day Notice to Prior Authorize Evrysdi™ (Risdiplam)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Trikafta® (Elexacaftor/ Tezacaftor/Ivacaftor and Ivacaftor)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Epclusa® (Sofosbuvir/ Velpatasvir) 200mg/50mg Tablet

NO ACTION REQUIRED.

Recommendation 9: 30-Day Notice to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Signifor® LAR (Pasireotide) and 30-Day Notice to Prior Authorize Mycapssa® (Octreotide)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Lambert-Eaton Myasthenic Syndrome (LEMS) Medications [Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine)]

NO ACTION REQUIRED.

Recommendation 12: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 13: Future Business

NO ACTION REQUIRED.

Appendix B

2021 Drug Utilization Review (DUR) Board Meeting Dates

Oklahoma Health Care Authority
November 2020

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

January 13, 2021

February 10, 2021

March 10, 2021

April 14, 2021

May 12, 2021

June 9, 2021

July 14, 2021

August 11, 2021

September 8, 2021

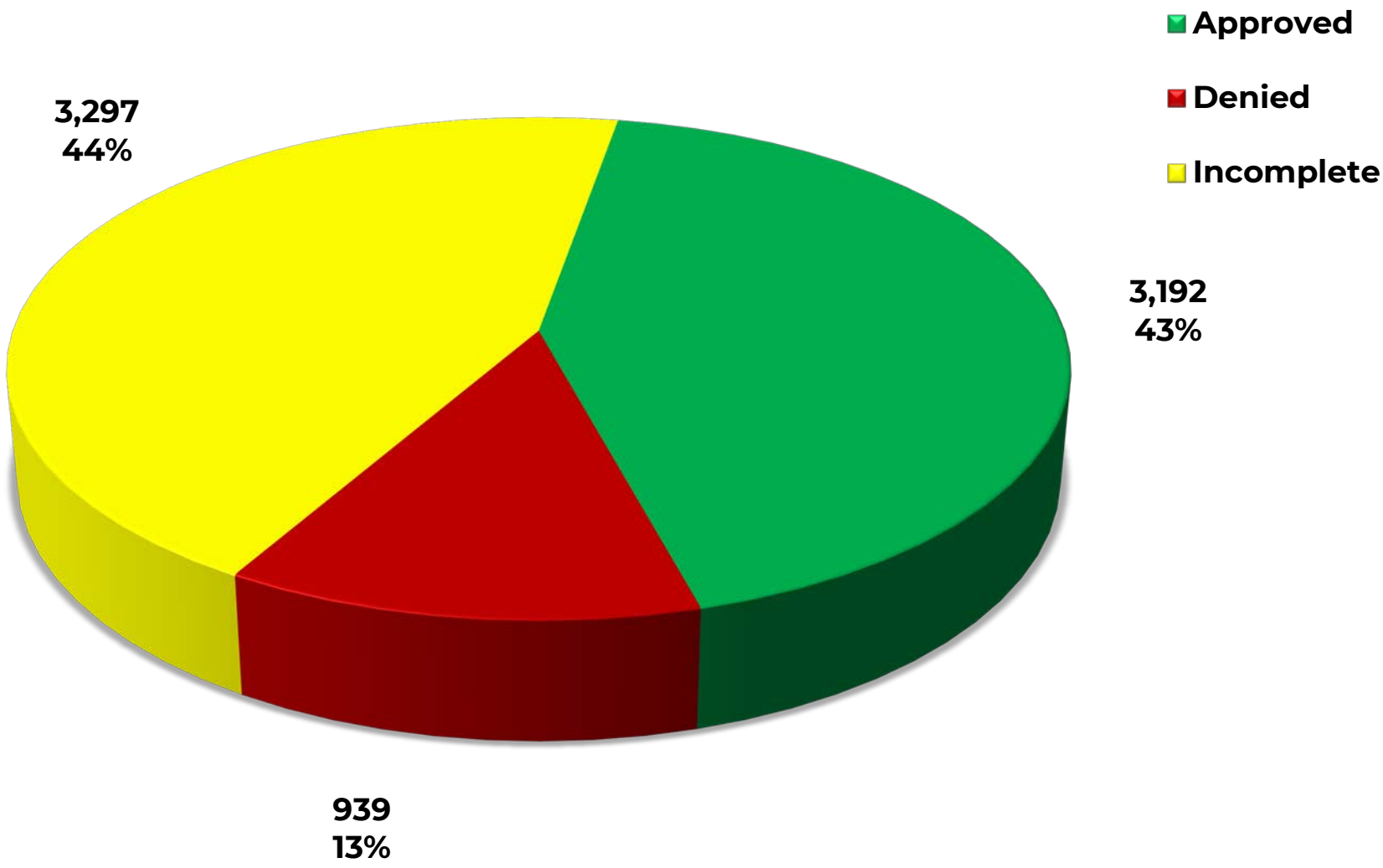
October 13, 2021

November 10, 2021

December 8, 2021

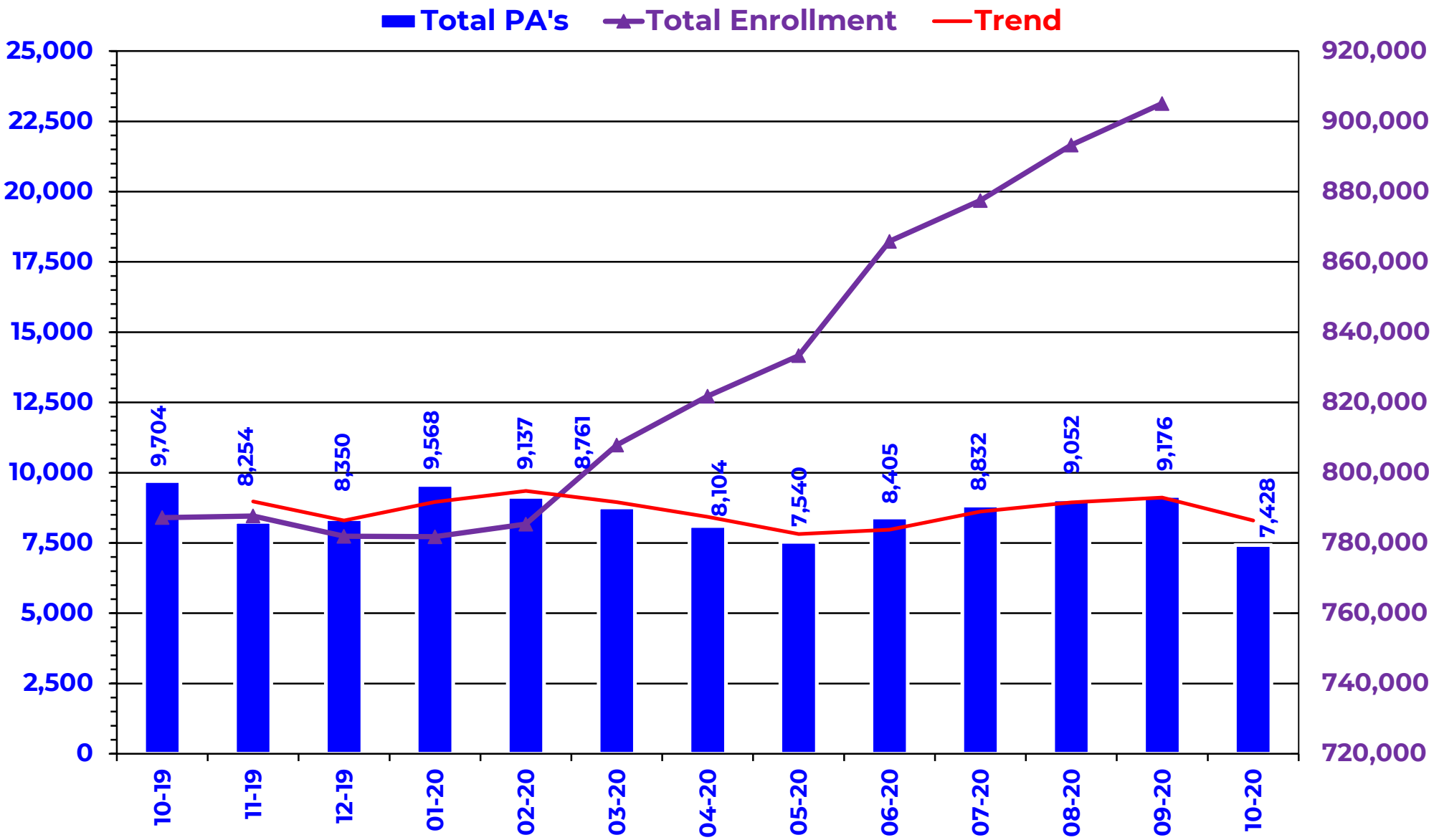
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER 2020*



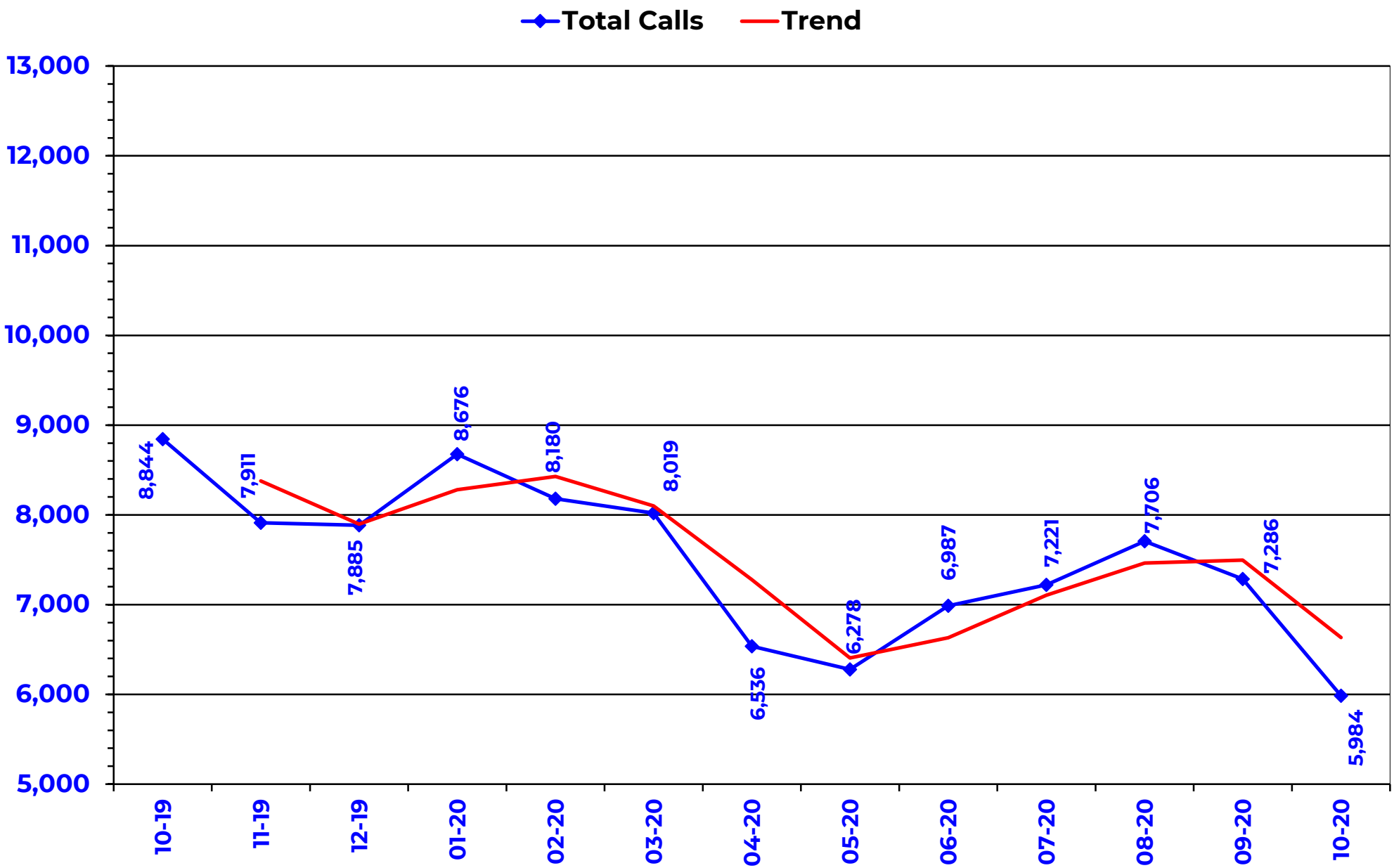
PA totals include approved/denied/incomplete/overrides
**Current as of October 23, 2020*

PRIOR AUTHORIZATION REPORT: OCTOBER 2019 – OCTOBER 2020*



PA totals include approved/denied/incomplete/overrides
**Current as of October 23, 2020*

CALL VOLUME MONTHLY REPORT: OCTOBER 2019 – OCTOBER 2020*



*Current as of October 23, 2020

Prior Authorization Activity

10/1/2020 Through 10/23/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	61	7	9	45	359
Analgesic - NonNarcotic	17	1	4	12	360
Analgesic, Narcotic	252	76	22	154	155
Antiasthma	50	13	14	23	182
Antibiotic	38	25	0	13	199
Anticonvulsant	180	79	12	89	325
Antidepressant	186	39	27	120	328
Antidiabetic	293	90	38	165	354
Antihistamine	29	4	13	12	287
Antimigraine	171	36	55	80	196
Antineoplastic	93	59	8	26	165
Antiparasitic	11	1	3	7	17
Antiulcers	48	6	13	29	168
Anxiolytic	23	1	6	16	117
Atypical Antipsychotics	225	98	25	102	345
Biologics	117	62	8	47	298
Bladder Control	41	8	9	24	359
Blood Thinners	259	146	11	102	335
Botox	31	16	14	1	312
Buprenorphine Medications	56	6	2	48	75
Calcium Channel Blockers	14	3	0	11	215
Cardiovascular	63	32	6	25	312
Chronic Obstructive Pulmonary	162	23	41	98	335
Constipation/Diarrhea Medications	112	20	31	61	192
Contraceptive	23	4	4	15	356
Dermatological	289	89	65	135	190
Diabetic Supplies	583	267	47	269	219
Endocrine & Metabolic Drugs	66	29	7	30	181
Erythropoietin Stimulating Agents	10	7	2	1	107
Fibromyalgia	16	3	6	7	248
Fish Oils	10	2	5	3	238
Gastrointestinal Agents	106	26	13	67	205
Glaucoma	11	1	1	9	56
Growth Hormones	93	58	6	29	147
Hematopoietic Agents	12	5	1	6	140
Hepatitis C	99	55	6	38	9
HFA Rescue Inhalers	15	1	0	14	10
Insomnia	57	8	13	36	197
Insulin	139	48	13	78	347
Multiple Sclerosis	35	16	4	15	241
Muscle Relaxant	29	3	13	13	135
Nasal Allergy	75	16	16	43	110
Neurological Agents	85	30	9	46	258
NSAIDs	45	2	12	31	49
Ocular Allergy	31	5	8	18	97
Ophthalmic Anti-infectives	16	5	2	9	10

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	3	3	0	0	358
Other*	303	75	38	190	241
Otic Antibiotic	12	1	2	9	24
Respiratory Agents	31	16	2	13	171
Statins	20	1	8	11	177
Stimulant	722	346	68	308	343
Synagis	158	42	66	50	150
Testosterone	71	20	14	37	325
Thyroid	10	4	2	4	292
Topical Antifungal	34	4	6	24	19
Topical Corticosteroids	59	0	40	19	0
Vitamin	70	24	25	21	156
Pharmacotherapy	26	20	1	5	274
Emergency PAs	0	0	0	0	
Total	**5,896**	**2,087**	**896**	**2,913**	
Overrides					
Brand	20	11	2	7	282
Compound	4	4	0	0	28
Diabetic Supplies	9	9	0	0	107
Dosage Change	317	286	0	31	13
High Dose	3	3	0	0	267
Ingredient Duplication	3	1	0	2	3
Lost/Broken Rx	85	74	1	10	15
MAT Override	236	170	1	65	76
NDC vs Age	231	141	15	75	256
NDC vs Sex	4	4	0	0	61
Nursing Home Issue	20	20	0	0	18
Opioid MME Limit	68	32	4	32	131
Opioid Quantity	29	21	2	6	165
Other*	43	34	2	7	24
Quantity vs. Days Supply	410	257	12	141	248
STBS/STBSM	13	7	4	2	118
Stolen	14	12	0	2	33
Third Brand Request	23	19	0	4	16
Overrides Total	**1,532**	**1,105**	**43**	**384**	
Total Regular PAs + Overrides	**7,428**	**3,192**	**939**	**3,297**	

Denial Reasons	
Unable to verify required trials.	2,746
Does not meet established criteria.	965
Lack required information to process request.	521
Other PA Activity	
Duplicate Requests	718
Letters	13,378
No Process	10
Changes to existing PAs	510
Helpdesk Initiated Prior Authorizations	648
PAs Missing Information	42

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

U.S. Food and Drug Administration (FDA) Safety Alerts

Oklahoma Health Care Authority
November 2020

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

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

Date	Drug	Issue
09/13/2019	**Palbociclib (Ibrance®), Ribociclib (Kisqali®), and Abemaciclib (Verzenio®)**	**Rare, but severe lung inflammation**
Issue Details: The FDA issued a Drug Safety Communication regarding rare, but severe lung inflammation in patients using palbociclib, ribociclib, or abemaciclib for the treatment of advanced breast cancers. The FDA reviewed completed trials, ongoing clinical trials, and their postmarket safety databases and found serious cases of interstitial lung disease and pneumonitis leading to fatalities. **FDA Recommendation(s):** The FDA recommends regular monitoring for pulmonary symptoms related to interstitial lung disease and/or pneumonitis. New warning information has been updated in the *Prescribing Information* and patient package insert for the entire class of cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors. The overall benefit of these drugs still outweighs the risk of the side effects listed. **Pharmacy Claims Evaluation:** During fiscal year (FY) 2020, a total of 50 SoonerCare members had paid claims for either palbociclib, ribociclib, or abemaciclib, accounting for 342 paid claims and an average of 6.84 claims per member. **SoonerCare Action:** Palbociclib, ribociclib, and abemaciclib all require prior authorization and may be reviewed by an Oklahoma Health Care Authority (OHCA)-consulting oncology specialist for initial authorization. For continued authorization of these medications, each prior authorization form has a section for the prescriber to indicate if the member has had any adverse drug reactions (ADRs) related to the medication. If the member has experienced ADRs, this information will be sent to the OHCA-consulting oncology specialist to review for continued approval of therapy.		

Date	Drug	Issue
12/19/2019	**Gabapentin (Neurontin®, Gralise®, Horizant®) and Pregabalin (Lyrica®, Lyrica CR®)**	**Serious breathing problems**

Issue Details: The FDA issued a Drug Safety Communication regarding serious breathing problems in patients using gabapentin or pregabalin who have respiratory risk factors. These risk factors include the use of central nervous system (CNS) depressants, such as opioids and anti-anxiety medications, and patients with conditions that reduce lung function such as chronic obstructive pulmonary disease (COPD). The FDA reviewed several sources of data, including case reports, medical literature, and clinical trials that showed serious breathing issues occurred when these medications were taken by patients with pre-existing respiratory risk factors. In 49 case reports that were submitted to the FDA between 2012 and 2017, 12 patients died from respiratory depression who were on 1 of these medications and had at least 1 respiratory risk factor.
FDA Recommendation(s): The FDA is requiring a new warning about the risk of respiratory depression be added to the *Prescribing Information* of these medications. They are also requiring the drug manufacturers to conduct clinical trials to evaluate the misuse and abuse of these medications in combination with opioids and the effects on respiratory depression. Prescribers should start these medications at the lowest dose and monitor for respiratory depression and sedation when prescribed with other opioids or CNS depressants.
Pharmacy Claims Evaluation: During FY 2020, a total of 19,914 SoonerCare members had paid claims for either gabapentin or pregabalin, accounting for 103,204 paid claims and an average of 5.18 claims per member.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations.

Date	Drug	Issue
01/28/2020	**Clozapine (Clozaril®)**	**Untreated constipation leading to serious bowel problems**

Issue Details: The FDA issued a Drug Safety Communication regarding untreated constipation leading to serious bowel problems in patients using clozapine. Constipation is a common side effect of clozapine. The risk is greater with higher doses of clozapine and when it is taken with anticholinergic medications or opioids. The FDA reviewed 10 cases between 2006 and 2016 in which patients on this medication had constipation that led to necrotizing colitis, intestinal ischemia, intestinal necrosis, and volvulus.

FDA Recommendation(s): The FDA is requiring a new warning and update about constipation risks be added to the *Prescribing Information* for all clozapine products. The FDA recommends prescribers evaluate bowel function prior to starting clozapine and avoid prescribing medications that can cause gastrointestinal hypomotility. Prophylactic laxative treatment may be considered when starting clozapine in patients with a history of constipation.
Pharmacy Claims Evaluation: During FY 2020, a total of 540 SoonerCare members had paid claims for clozapine, accounting for 9,739 paid claims and an average of 18.04 claims per member. Of the 540 SoonerCare members on clozapine, 112 of those members had a diagnosis of constipation in their SoonerCare claims history.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations.

Date	Drug	Issue
03/04/2020	**Montelukast (Singulair®)**	**Serious mental health side effects**

Issue Details: The FDA issued a Drug Safety Communication regarding serious mental health side effects in patients taking montelukast. The *Prescribing Information* for montelukast already has warnings about mental health side effects, but many health care professionals may not be aware of the risk. The FDA reviewed multiple case reports and saw increases in reporting of neuropsychiatric side effects on the FDA Adverse Event Reporting System (FAERS) database. The FDA also performed a focused evaluation on completed suicides. There were 82 cases of completed suicide associated with montelukast identified. Of those cases, 45 cases were in patients older than 17 years of age, 19 cases were in patients 17 years of age and younger, and 18 cases did not provide an age.
FDA Recommendation(s): The FDA has added a *Boxed Warning* to the *Prescribing Information* of montelukast describing the serious mental health side effects. They recommend that montelukast should be reserved to for the treatment of allergic rhinitis in patients that do not respond to other allergy medications. The FDA also recommends health care professionals counsel patients about the mental health side effects (e.g., depression, irritability, suicidal thoughts) prior to starting therapy.
Pharmacy Claims Evaluation: During FY 2020, a total of 37,559 SoonerCare members had paid claims for montelukast, accounting for 140,804 paid claims and an average of 3.75 claims per member.
SoonerCare Action: The College of Pharmacy provided an update regarding the new *Boxed Warning* for serious mental health side effects from montelukast in a provider mailing that was completed in May 2020. The mailing targeted providers who prescribed montelukast to pediatric

members who did not have a diagnosis of asthma in their SoonerCare claims history. The College of Pharmacy also plans to include an article regarding the new *Boxed Warning* in an upcoming SoonerCare provider newsletter and will continue to monitor the FDA recommendations.

Date	Drug	Issue
04/24/2020	**Hydroxychloroquine (Plaquenil®) and Chloroquine (Aralen®)**	**Risk of heart rhythm problems**

Issue Details: The FDA issued a Drug Safety Communication regarding the risk of heart rhythm problems in patients with COVID-19 who were treated with hydroxychloroquine or chloroquine, often in combination with other QT prolonging medications such as azithromycin. These heart rhythm problems include QT prolongation and ventricular tachycardia, and patients with heart and kidney disease are at an increased risk of these adverse events. On June 15, 2020, the FDA revoked the Emergency Use Authorization (EUA) of these medications for COVID-19 and provided information about the results of a recent clinical trial in hospitalized patients. In this large, randomized clinical trial of hospitalized patients with COVID-19, hydroxychloroquine and chloroquine showed no benefit for decreasing the likelihood of death or for speeding recovery time. On July 1, 2020, the FDA added an update that included reports of blood and lymph system disorders, kidney injuries, and liver problems and failure with use of these medications.
FDA Recommendation(s): The FDA recommended initial evaluation and monitoring when using this medication for COVID-19, including baseline electrocardiogram (ECG), electrolytes, and renal and hepatic function tests. The FDA advised that prescribers should be aware that hydroxychloroquine or chloroquine can cause QT prolongation and increase insulin levels, causing severe hypoglycemia and hemolysis in patients with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency. Due to the long half-life of hydroxychloroquine, there is still potential for drug interactions with other medications known to cause QT prolongation after hydroxychloroquine has been discontinued.
Pharmacy Claims Evaluation: During FY 2020, a total of 1,085 SoonerCare members had paid claims for hydroxychloroquine or chloroquine, accounting for 4,440 paid claims and an average of 4.09 claims per member.
SoonerCare Action: The College of Pharmacy added a prior authorization to hydroxychloroquine and chloroquine to follow the guidance from the FDA under the EUA issued on March 28, 2020 and ensure appropriate use. This prior authorization has been removed as of July 2, 2020 since the FDA revoked the EUA of these medications for COVID-19. The College of

Pharmacy will continue to review updated literature and make recommendations as needed.

Date	Drug	Issue
07/23/2020	**Opioid Pain Relievers and Medications to Treat Opioid Use Disorder (OUD)**	**Counseling on Naloxone for Patients Using Opioids or Medications for OUD**

Issue Details: The FDA issued a Drug Safety Communication regarding counseling on naloxone for patients on opioid pain relievers or medications to treat OUD. From 1999 to 2018, nearly 450,000 people died from an overdose involving opioids, including prescription and illicit opioids. In 2018, opioids were involved in 46,802 deaths. Due to the large number of deaths and increased access to naloxone, the FDA is committed to raising awareness of the availability of naloxone in patients currently using opioids or medications used to treat OUD.

FDA Recommendation(s): The FDA is requiring the manufacturers of all opioid pain relievers and medications used to treat OUD add new recommendations about naloxone to the *Prescribing Information*. The FDA is also requiring patient medication guides be updated with information regarding naloxone. The FDA is recommending that providers consider prescribing naloxone to patients at increased risk of an opioid overdose. This includes patients that have a history of OUD, experienced a previous opioid overdose, or are on medications that can increase the risk of opioid overdose such as benzodiazepines.

Pharmacy Claims Evaluation: During FY 2020, a total of 68,361 SoonerCare members had paid claims for an opioid analgesic medication or a medication for OUD, accounting for 241,826 paid claims and an average of 3.54 claims per member.

SoonerCare Action: The College of Pharmacy added a prior authorization for members with a daily opioid morphine milligram equivalent (MME) >90 MME per day. The Statement of Medical Necessity for Opioid Morphine Milligram Equivalent (MME) Limit Override form (Pharm-111) asks the prescriber if a prescription of naloxone was offered to the member or member's household. Naloxone injection and nasal spray are currently covered by SoonerCare without a prior authorization. Additionally, the College of Pharmacy included an article regarding the FDA's recommendations in a recent SoonerCare provider newsletter. The College of Pharmacy will continue to make recommendations on naloxone counseling to prescribers and pharmacies for members at a high risk of opioid overdose.

Date	Drug	Issue
08/26/2020	**Canagliflozin (Invokana®, Invokamet®, Invokamet XR®)**	**Removal of *Boxed Warning* about the Risk of Leg and Foot Amputations**

Issue Details: The FDA issued a Drug Safety Communication regarding the removal of the *Boxed Warning* for the risk of leg and foot amputations in patients using anti-diabetic medications that contain canagliflozin. The FDA originally required this *Boxed Warning* in 2017, but due to new clinical data received from recent clinical trials, they have decided to remove this warning. Information from these clinical trials suggest there is still an increased risk of amputation with canagliflozin, but the risk is lower than previously described especially when appropriately monitored.
FDA Recommendation(s): Although the *Boxed Warning* has been removed, the FDA still recommends health care professionals and patients recognize the importance of foot care and continue to monitor patients for new foot or leg symptoms such as pain, sores, and ulcers.
Pharmacy Claims Evaluation: During FY 2020, a total of 84 SoonerCare members had paid claims for a medication containing canagliflozin, accounting for 567 paid claims and an average of 6.75 claims per member. Of the 84 members on medications containing canagliflozin, none had a diagnosis of either a leg or foot amputation in their SoonerCare claims history.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations.

Date	Drug	Issue
09/23/2020	**Benzodiazepines**	**Risk of Abuse, Addiction, Physical Dependence, and Withdrawal Reactions**

Issue Details: The FDA issued a Drug Safety Communication regarding the risk of abuse, addiction, physical dependence, and withdrawal reactions with benzodiazepines. The FDA determined the current benzodiazepine *Prescribing Information* does not provide sufficient warnings about these risks. These risks increase when benzodiazepines are taken with other CNS depressants such as opioids, alcohol, or illicit drugs. Stopping benzodiazepines too abruptly can result in withdrawal reactions that could be life threatening.
FDA Recommendation(s): The FDA is requiring the manufacturers of all benzodiazepines update the *Boxed Warning* in the *Prescribing Information* to describe the risk of abuse, addiction, physical dependence, and withdrawal reactions. They are also requiring the patient medication guides

be updated to include these risks. The FDA recommends prescribers assess these risks before prescribing benzodiazepines and recommends limiting the dosage and duration when possible. When discontinuing benzodiazepines, a gradual taper is recommended to reduce withdrawal symptoms.

Pharmacy Claims Evaluation: During FY 2020, a total of 16,817 SoonerCare members had paid claims for a benzodiazepine, accounting for 92,449 paid claims and an average of 5.5 claims per member.

SoonerCare Action: The College of Pharmacy plans to include an article regarding the updated *Boxed Warning* in an upcoming SoonerCare provider newsletter and will continue to monitor the FDA recommendations.

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[2] U.S. FDA. 2020 Drug Safety Communications. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/2020-drug-safety-communications. Last revised 07/23/2020. Last accessed 09/25/2020.

[3] U.S. FDA. FDA Warns about Rare but Severe Lung Inflammation with Ibrance, Kisqali, and Verzenio for Breast Cancer. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-severe-lung-inflammation-ibrance-kisqali-and-verzenio-breast-cancer. Issued 09/13/2019. Last accessed 08/17/2020.

[4] U.S. FDA. FDA Warns about Serious Breathing Problems with Seizure and Nerve Pain Medicines Gabapentin (Neurontin, Gralise, Horizant) and Pregabalin (Lyrica, Lyrica CR). Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-serious-breathing-problems-seizure-and-nerve-pain-medicines-gabapentin-neurontin. Issued 12/19/2019. Last accessed 08/17/2020.

[5] U.S. FDA. FDA Strengthens Warning that Untreated Constipation Caused by Schizophrenia Medicine Clozapine (Clozaril) can lead to Serious Bowel Problems. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-strengthens-warning-untreated-constipation-caused-schizophrenia-medicine-clozapine-clozaril-can. Issued 01/28/2020. Last accessed 08/17/2020.

[6] U.S. FDA. FDA Requires *Boxed Warning* about Serious Mental Health Side Effects for Asthma and Allergy Drug Montelukast (Singulair); Advises restricting Use for Allergic Rhinitis. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-boxed-warning-about-serious-mental-health-side-effects-asthma-and-allergy-drug. Issued 03/04/2020. Last accessed 08/17/2020.

[7] U.S. FDA. FDA Cautions Against Use of Hydroxychloroquine or Chloroquine for COVID-19 Outside of the Hospital Setting or a Clinical Trial Due to Risk of Heart Rhythm Problems. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or. Issued 04/24/2020. Last accessed 08/17/2020.

[8] U.S. FDA. FDA Recommends Health Care Professionals Discuss Naloxone with All Patients When Prescribing Opioid Pain Relievers or Medicines to Treat Opioid Use Disorder. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-health-care-professionals-discuss-naloxone-all-patients-when-prescribing-opioid-pain. Issued 07/23/2020. Last accessed 08/17/2020.

[9] U.S. FDA. FDA Removes *Boxed Warning* about Risk of Leg and Foot Amputations for the Diabetes Medicine Canagliflozin (Invokana, Invokamet, Invokamet XR). Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-removes-boxed-warning-about-risk-leg-and-foot-amputations-diabetes-medicine-canagliflozin. Issued 08/26/2020. Last accessed 09/25/2020.

[10] U.S. FDA. FDA Requiring *Boxed Warning* Updated to Improve Safe Use of Benzodiazepine Drug Class. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requiring-boxed-warning-updated-improve-safe-use-benzodiazepine-drug-class. Issued 09/23/2020. Last accessed 09/25/2020.

Appendix D

Vote to Prior Authorize Evrysdi™ (Risdiplam)

Oklahoma Health Care Authority
November 2020

Introduction[1]

Evrysdi™ (risdiplam) was approved by the U.S. Food and Drug Administration (FDA) in August 2020 for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older. Risdiplam is a survival motor neuron 2 (SMN2) splicing modifier designed to treat patients with SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Evrysdi™ is supplied as a powder for oral solution. Prior to dispensing to the patient, the powder must be constituted to an oral solution by a pharmacist. The constituted oral solution should be stored refrigerated at 2°C to 8°C (36°F to 46°F) and can be stored refrigerated for 64 days once in solution form. Any unused portion should be discarded 64 days after constitution. Prior to administration of the first dose of Evrysdi™, it is recommended a health care provider discuss with the patient or caregiver how to prepare the prescribed daily dose. The recommended dose of risdiplam is 0.2mg/kg to 5mg (depending on the patient's age and weight) taken orally once daily after a meal; the maximum dose of risdiplam is 5mg per day. Evrysdi™ must be taken immediately after it is drawn up into the oral syringe. If the dose is not taken within 5 minutes, it should be discarded and a new dose should be prepared. Evrysdi™ cannot be mixed with formula or milk.

Risdiplam may cause embryofetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to initiating risdiplam. It is also recommended that female patients of reproductive potential use effective contraception during treatment with risdiplam and for at least 1 month after the last dose. Studies of risdiplam in juvenile and adult rats and in monkeys demonstrated adverse effects on the reproductive organs, including germ cells, in males at clinically-relevant plasma exposures. Male fertility may be compromised by treatment with risdiplam; therefore, it is recommended that male patients of reproductive potential be counseled on the potential effects on fertility prior to initiating risdiplam. The safety and efficacy of risdiplam in patients with hepatic impairment have not been studied. Because risdiplam is predominantly metabolized in the liver, hepatic impairment may potentially increase the exposures to risdiplam. It is recommended to avoid use of risdiplam in patients with impaired hepatic function.

The efficacy of risdiplam was evaluated in 2 studies, FIREFISH and SUNFISH.

- **Study 1 (FIREFISH):** FIREFISH was an open-label, 2-part study to investigate the efficacy, safety, pharmacokinetics (PK), and pharmacodynamics (PD) of risdiplam in patients with Type 1 SMA (symptom onset between 28 days and 3 months of age). At the time of study enrollment the patients ranged in age from 3.3 to 6.9 months. Part 1 of Study 1 (N=21) provided efficacy and safety data. Additional safety information was provided by Part 2 of Study 1. Effectiveness was measured in Part 1 of the study by the ability to sit without support for ≥5 seconds [as measured by Item 22 of the Bayley Scales of Infant and Toddler Development–Third Edition (BSID-III) gross motor scale] and on the basis of survival without permanent ventilation. Permanent ventilation was defined as requiring a tracheostomy or >21 consecutive days of either non-invasive ventilation (≥16 hours per day) or intubation, in the absence of an acute reversible event. Of the patients who were treated with the recommended dosage of risdiplam (0.2mg/kg/day), 41% (7/17) were able to sit independently for ≥5 seconds after 12 months of treatment. This is clinically meaningful as the natural history of untreated infantile-onset SMA indicates patients would not be expected to attain the ability to sit independently. After 12 months of treatment with risdiplam, 90% (19/21) of patients were alive without permanent ventilation and reached 15 months of age or older. The natural history of untreated infantile-onset SMA indicates ≤25% of these patients would be expected to survive without permanent ventilation beyond 14 months of age.
- **Study 2 (SUNFISH):** SUNFISH was a 2-part, multicenter study to investigate the efficacy, safety, PK, and PD of risdiplam in patients diagnosed with SMA Type 2 or Type 3. Part 1 of Study 2 was a dose-finding and exploratory study. The efficacy was evaluated in Part 2 of Study 2 in a randomized, double-blind, placebo-controlled study in these patients. Patients were randomized 2:1 to receive risdiplam at the recommended dosage or placebo. The age of the patients at the start of treatment ranged from 2 years to 25 years. All enrolled patients were non-ambulatory. The primary endpoint was the change from baseline to month 12 in the Motor Function Measure 32 (MFM32) score. The MFM32 measures motor function abilities that relate to daily functions. The total MFM32 score is expressed as a percentage (range: 0 to 100) of the maximum possible score, with higher scores indicating greater motor function. At month 12, a clinically meaningful and statistically significant difference between patients treated with risdiplam and placebo was shown. There was an increase of 1.36 points from the baseline MFM32 score in the risdiplam group and a decrease of 0.19 points in the placebo group (P=0.0156).

Cost Comparison:

Product	Cost Per Unit	Cost For First Year	Cost Per Year (Maintenance)
Evrysdi™ (risdiplam) 0.75mg/mL oral solution	**$139.63**	**$335,112.00***	**$335,112.00***
Spinraza® (nusinersen) 12mg/5mL intrathecal solution	$25,500.00	$892,500.00⁺	$382,500.00⁺

Unit = milliliter (mL)
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*For Evrysdi™, cost for first year and cost per year for maintenance is based on the maximum recommended dose of 5mg per day or 240mL per 36-day supply.
⁺For Spinraza®, cost for first year is based on the recommended dosing of (4) 12mg loading doses followed by 12mg every 4 months; cost per year for maintenance dosing is based on 12mg every 4 months.

Recommendations

The College of Pharmacy recommends the prior authorization of Evrysdi™ (risdiplam) with the following criteria:

Evrysdi™ (Risdiplam) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in members 2 months of age and older; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Evrysdi™ must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Prescriber must agree to monitor member's liver function prior to initiating Evrysdi™ and periodically while receiving Evrysdi™ treatment; and
6. Pharmacy must confirm Evrysdi™ will be constituted to an oral solution by a pharmacist prior to dispensing and must confirm Evrysdi™ will be shipped via cold chain supply to adhere to the storage and handling requirements in the Evrysdi™ *Prescribing Information*; and
7. Prescriber must confirm the member or caregiver has been counseled on the proper storage of Evrysdi™ and has been instructed on how to prepare the prescribed daily dose of Evrysdi™ prior to administration of the first dose; and

8. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
9. Female members of reproductive potential must be willing to use effective contraception during treatment with Evrysdi™ and for at least 1 month after the last dose; and
10. Prescriber must verify male members of reproductive potential have been counseled on the potential effects on fertility and the potential of compromised male fertility is acceptable; and
11. Member will not be approved for concomitant treatment with Spinraza® (nusinersen); and
12. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
13. A baseline assessment must be provided using a functionally appropriate exam [e.g., Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale Expanded (HFMSE), Hammersmith Infant Neurological Exam (HINE), Upper Limb Module (ULM) Test]; and
14. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is compliant with Evrysdi™ and responding to the medication as demonstrated by clinically significant improvement or maintenance of function from pre-treatment baseline status using the same exam as performed at baseline assessment; and
15. Member's recent weight must be provided to ensure accurate dosing in accordance with Evrysdi™ *Prescribing Information*; and
16. A quantity limit of 240mL per 36 days will apply.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Spinraza® (nusinersen) and Zolgensma® (onasemnogene abeparvovec-xioi) approval criteria:

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
   a. Type 1; or
   b. Type 2; or
   c. Type 3 with symptoms; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner

with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
6. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam); and
7. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing must be conducted at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
8. Spinraza® must be administered in a health care facility by a specialist experienced in performing lumbar punctures; and
    a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
9. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
    a. Hammersmith Infant Neurological Exam (HINE); or
    b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
    c. Upper Limb Module (ULM) Test; or
    d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
10. 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:
    a. HINE; or
    b. CHOP-INTEND; or
    c. ULM Test; or
    d. HFMSE; and
11. Approval quantity will be based on Spinraza® *Prescribing Information* and FDA approved dosing regimen(s).
    a. Only (1) 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

Zolgensma® (Onasemnogene Abeparvovec-xioi) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in pediatric members younger than 2 years of age; and
2. Member must have reached full-term gestational age prior to Zolgensma® infusion; and
3. Molecular genetic testing to confirm bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene; and
4. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for

>21 days in the absence of an acute, reversible illness or a perioperative state); and

5. Zolgensma® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
6. Member must have baseline anti-AAV9 antibody titers ≤1:50; and
7. Prescriber must agree to monitor liver function tests, platelet counts, and troponin-I at baseline and as directed by the Zolgensma® *Prescribing Information*; and
8. Prescriber must agree to administer systemic corticosteroids starting 1 day prior to the Zolgensma® infusion and continuing as recommended in the Zolgensma® *Prescribing Information* based on member's liver function; and
9. Zolgensma® must be shipped to the facility where the member is scheduled to receive treatment and must adhere to the storage and handling requirements in the Zolgensma® *Prescribing Information*; and
10. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam) or Spinraza® (nusinersen) following Zolgensma® infusion (current authorizations for risdiplam or nusinersen will be discontinued upon Zolgensma® approval); and
11. Member's recent weight must be provided to ensure accurate dosing in accordance with Zolgensma® *Prescribing Information*; and
12. Only 1 Zolgensma® infusion will be approved per member per lifetime.

[1] Evrysdi™ Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/evrysdi_prescribing.pdf. Last revised 08/2020. Last accessed 10/14/2020.

Appendix E

Vote to Prior Authorize Trikafta® (Elexacaftor/ Tezacaftor/Ivacaftor and Ivacaftor)

Oklahoma Health Care Authority
November 2020

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

- **Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor)** was FDA approved in October 2019 for patients 12 years of age and older with cystic fibrosis (CF) who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator (*CFTR)* gene, which is estimated to represent 90% of the CF population. Trikafta® is supplied as a fixed-dose combination tablet containing elexacaftor 100mg/ tezacaftor 50mg/ivacaftor 75mg and co-packaged with an ivacaftor 150mg tablet. The recommended regimen for Trikafta® is 2 tablets containing elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg in the morning and 1 ivacaftor 150mg tablet in the evening. The morning and evening doses should be taken approximately 12 hours apart with fat-containing food. The efficacy of Trikafta® was established in 2 randomized, double-blind trials in patients 12 years of age and older with CF. Study 1 was a 24-week, placebo-controlled study in 403 patients who had an *F508del* mutation on 1 allele and a mutation on the second allele that results in either no CFTR protein or a CFTR protein that is not responsive to ivacaftor and tezacaftor/ivacaftor. Study 2 was a 4-week, active-controlled study in 107 patients who were homozygous for the *F508del* mutation. In Study 2, patients were randomized to receive Trikafta® or Symdeko® (tezacaftor/ivacaftor and ivacaftor). The primary efficacy endpoint was the mean absolute change in percent predicted forced expiratory volume in 1 second ($ppFEV_1$).
    - In Study 1, the treatment difference between Trikafta® and placebo for the mean absolute change from baseline in $ppFEV_1$ at week 4 was 13.8 percentage points [95% confidence interval (CI): 12.1, 15.4; P<0.0001]. The treatment difference was sustained through week 24. The number of pulmonary exacerbation events (event rate per year calculated based on 48 weeks per year) from baseline through week 24 was 0.37 and 0.98 for Trikafta® and placebo, respectively (P<0.0001).
    - In Study 2, treatment with Trikafta® vs. Symdeko® resulted in a statistically significant improvement in $ppFEV_1$ of 10 percentage points (95% CI: 7.4, 12.6; P<0.0001).

The annual cost for Trikafta® at the recommended FDA approved dose is $286,755.84, based on the wholesale acquisition cost (WAC).

- **Kalydeco® (ivacaftor)** was FDA approved in September 2020 for an age expansion to include patients with CF as young as 4 months of age who have 1 mutation in the *CFTR* gene that is responsive to ivacaftor. Kalydeco® was previously approved in the United States and Europe for the treatment of CF in patients 6 months of age and older. The FDA approval is based on data from a 24-week Phase 3 open-label safety cohort (ARRIVAL) consisting of 6 children with CF ages 4 months to younger than 6 months who have 1 of 10 mutations in the *CFTR* gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D* or *R117H*). This cohort demonstrated a safety profile similar to that observed in older children and adults. The estimated annual cost, based on the WAC, for Kalydeco® 25mg granule packets twice daily (the recommended dose for patients 4 to 6 months of age and weighing ≥5kg) is $307,235.95.

Recommendations

The College of Pharmacy recommends the prior authorization of Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) and recommends updating the age restriction of Kalydeco® (ivacaftor) based on the FDA-approved age expansion with the following criteria (changes and new criteria shown in red):

Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify that member has been counseled on proper administration of Trikafta® including taking with a fat-containing food; and

7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify that the member does not have severe hepatic impairment; and
9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and
10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
11. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
12. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events than with a previous CFTR therapy must be provided for members who switched from Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor).

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) with a mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
2. Documentation must be submitted with results of *CFTR* genetic testing; and
3. Member must be 4 ~~6~~ months of age or older; and
4. A quantity limit of 2 tablets or granule packets per day or 56 tablets or granule packets per 28 days will apply; and
5. An age restriction of 4 ~~6~~ months to younger than 6 years of age will apply to Kalydeco® oral granule packets. Members 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
6. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

[1] U.S. Food and Drug Administration (FDA). FDA Approves New Breakthrough Therapy for Cystic Fibrosis. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis. Issued 10/21/2019. Last accessed 10/16/2020.
[2] Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Prescribing Information. Vertex Pharmaceuticals. Available online at: https://pi.vrtx.com/files/uspi_elexacaftor_tezacaftor_ivacaftor.pdf. Last revised 01/2020. Last accessed 10/16/2020.
[3] Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) – New Orphan Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_trikafta_2019-1021.pdf. Last revised 2020. Last accessed 10/16/2020.
[4] Vertex Pharmaceuticals. FDA Approves Kalydeco® (Ivacaftor) as First and Only CFTR Modulator to Treat Eligible Infants with CF as Early as 4 Months of Age. *Business Wire*. Available online at: https://investors.vrtx.com/news-releases/news-release-details/fda-approves-kalydecor-ivacaftor-first-and-only-cftr-modulator-0. Issued 09/25/2020. Last accessed 10/16/2020.
[5] Kalydeco® (Ivacaftor) Prescribing Information. Vertex Pharmaceuticals. Available online at: https://pi.vrtx.com/files/uspi_ivacaftor.pdf. Last revised 09/2020. Last accessed 10/16/2020.

Appendix F

Vote to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet

Oklahoma Health Care Authority
November 2020

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

- **Epclusa® (Sofosbuvir/Velpatasvir) Label Update:** In November 2019, the FDA approved Epclusa® for the treatment of chronic hepatitis C virus (HCV) infection in patients with severe renal impairment including patients with end stage renal disease (ESRD) on dialysis.
- **Harvoni® (Ledipasvir/Sofosbuvir) Label Update:** In November 2019, the FDA approved Harvoni® for the treatment of chronic HCV infection in patients with severe renal impairment including patients with ESRD on dialysis.
- **Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Label Update:** In November 2019, the FDA approved Vosevi® for the treatment of chronic HCV infection in patients with severe renal impairment including patients with ESRD on dialysis.
- **Epclusa® (Sofosbuvir/Velpatasvir) in Pediatric Patients:** In March 2020, the FDA approved Epclusa® for the treatment of chronic HCV in pediatric patients 6 years of age and older or weighing at least 17kg with genotype-1, -2, -3, -4, -5, or -6. Epclusa® was previously approved in adult patients for the same indications. Along with the expanded indication, the FDA also approved a new sofosbuvir/velpatasvir 200mg/50mg strength oral tablet. Previously, Epclusa® was only available as a sofosbuvir/velpatasvir 400mg/100mg oral tablet. The recommended dose for patients weighing 17 to <30kg is 200mg/50mg daily. The recommended dose for patients weighing ≥30kg is 400mg/100mg daily. Launch plans for the 200mg/50mg tablet strength are pending.

Recommendations

The College of Pharmacy recommends the prior authorization of Epclusa® (sofosbuvir/velpatasvir) 200mg/50mg tablets with criteria similar to the higher strength Epclusa® 400mg/100mg tablets. Additionally, the College of Pharmacy recommends updating the Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), and Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) prior authorization criteria based on new FDA label updates. The following criteria will apply (changes and additions noted in red):

Epclusa® (Sofosbuvir/Velpatasvir 400/100mg and 200/50mg Tablets)
Approval Criteria:

1. Member must be ~~18~~ 6 years of age or older or weighing at least 17kg; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-2, GT-3, GT-4, GT-5, or GT-6; and
3. Requests for the generic formulation will require a patient-specific, clinically significant reason why the member cannot use the brand formulation; and***
4. Epclusa® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
6. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1, -2, -3, -4, -5, -6:**
        i. Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A): Epclusa® for 12 weeks; or
        ii. Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C): Epclusa® + weight based ribavirin for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and

11. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
14. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine equivalent, amiodarone, omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses >10mg; and
16. If member is using antacids, they must agree to separate antacid and Epclusa® administration by 4 hours; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
18. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance. ****The brand formulation of Epclusa® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

Harvoni® (Ledipasvir/Sofosbuvir Tablets and Oral Pellets) Approval Criteria:

1. Member must be 3 years of age or older; and

2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-4, GT-5, or GT-6; and
3. Request for the generic formulation will require a patient-specific, clinically significant reason why the member cannot use the brand formulation; and***
4. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
6. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1:**
        i. Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA <6 million IU/mL: Harvoni® for 8 weeks; or
        ii. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA >6 million IU/mL: Harvoni® for 12 weeks; or
        iii. Treatment-experienced without cirrhosis: Harvoni® for 12 weeks; or
        iv. Treatment-experienced with compensated cirrhosis:
            1. Harvoni® with weight-based ribavirin for 12 weeks; or
            2. Harvoni® for 24 weeks; or
        v. Treatment-naïve or treatment-experienced with decompensated cirrhosis: Harvoni® with weight-based ribavirin for 12 weeks; or
    b. **GT-1 or GT-4:**
        i. Treatment-naïve or treatment-experienced liver transplant recipients with or without compensated cirrhosis: Harvoni® with weight-based ribavirin for 12 weeks; or
    c. **GT-4, GT-5, or GT-6:**

i. Treatment-naïve or treatment-experienced with or without compensated cirrhosis: Harvoni® for 12 weeks; or

d. New regimens will apply as approved by the FDA; and

8. For members 6 years of age or older who request the oral pellet formulation of Harvoni®, a patient-specific, clinically significant reason to support use of the oral pellet formulation in place of the tablet formulation must be provided; and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. ~~Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
18. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and

20. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
21. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.
****The brand formulation of Harvoni® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

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

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-2, GT-3, GT-4, GT-5, or GT-6; and
3. Vosevi® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
4. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
5. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
6. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **Adult patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) GT-1, -2, -3, -4, -5, -6:**
        i. **GT-1, -2, -3, -4, -5, -6 patients who were previously treated with an HCV regimen containing an NS5A inhibitor** (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir): Vosevi® for 12 weeks; or
        ii. **GT-1a or -3 patients who were previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor:** Vosevi® for 12 weeks; or

b. New regimens will apply as approved by the FDA; and
7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
10. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
13. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
~~14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine twice daily equivalent, omeprazole doses >20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses >40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and
17. If member is using antacids, they must agree to separate antacid and Vosevi® administration by 4 hours; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and

20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

[1] Gilead DAAs Safe, Effective for Adults with HCV, Severe Renal Impairment. *Healio*. Available online at: http://www.healio.com/news/hepatology/20191121/gilead-daas-safe-effective-for-adults-with-hcv-severe-renal-impairment. Issued 11/21/2019. Last accessed 10/15/2020.
[2] U.S. Food and Drug Administration (FDA). FDA Approves New Treatment for Pediatric Patients with Any Strain of Hepatitis C. Available online at: http://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-pediatric-patients-any-strain-hepatitis-c. Issued 03/19/2020. Last accessed 10/15/2020.

Appendix G

Vote to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

Oklahoma Health Care Authority
November 2020

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

Cystinosis is caused by mutations in the *CTNS* gene and affects approximately 1 in 100,000 to 200,000 newborns worldwide. Cystinosis is characterized by accumulation of the amino acid cystine within the cells, which forms crystals in the lysosomes, damaging cells in the kidneys, eyes, and other organs. The buildup of these crystals in the cornea causes eye pain and photophobia, and if untreated, may lead to permanent visual impairment or blindness. There are 2 cysteamine ophthalmic solutions approved by the U.S. Food and Drug Administration (FDA) for the treatment of corneal cystine crystal accumulation in patients with cystinosis, Cystaran™ and Cystadrops®. Cysteamine lowers the cystine content of cells by converting cystine to cysteine and cysteine-cysteamine mixed disulfides, thus reducing corneal cystine crystal accumulation.

	Cystaran™ (cysteamine 0.44%)	Cystadrops® (cysteamine 0.37%)
FDA Approval	2012	2020
Indication(s)	Treatment of corneal cystine crystal accumulation in patients with cystinosis	
Dosage Form	Oph soln; 6.5mg/mL of cysteamine HCl equivalent to 4.4mg/mL of cysteamine (0.44%)	Oph soln; 3.8mg/mL of cysteamine (0.37%)
Dosing	1 drop in each eye every waking hour	1 drop in each eye 4 times daily during waking hours
How Supplied	15mL bottle	5mL bottle
Storage	Before use, store in the freezer (-13°F to 5°F). After opening, store thawed bottle at 36°F to 77°F for up to 7 days; discard bottle after 7 days.	Before use, store in the refrigerator (36°F to 46°F). After opening, store at room temperature (68°F to 77°F); discard bottle 7 days after opening.
Wholesale Acquisition Cost (WAC)	$108.04 per mL ($1,620.60 per bottle)	$350.00 per mL ($1,750.00 per bottle)

Costs do not reflect rebated prices or net costs. Cystaran™ was first FDA approved in 2012 and has a significant federal rebate.
Oph soln = ophthalmic solution; HCl = hydrochloride

Recommendations

The College of Pharmacy recommends the prior authorization of Cystadrops® (cysteamine 0.37% ophthalmic solution) and Cystaran™ (cysteamine 0.44% ophthalmic solution) with the following criteria:

Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication for the treatment of corneal cystine crystal accumulation in members with cystinosis; and
2. The requested medication must be prescribed by, or in consultation with, an ophthalmologist; and
3. Prescriber must verify that the member has been counseled on the proper storage of the requested medication; and
4. For Cystadrops®, a patient-specific, clinically significant reason (beyond convenience) why the member cannot use Cystaran™ must be provided; and
5. A quantity limit of 4 bottles per month will apply.

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[1] National Institutes of Health (NIH) Genetics Home Reference. Cystinosis. Available online at: https://ghr.nlm.nih.gov/condition/cystinosis#. Last accessed 10/20/2020.
[2] National Organization for Rare Disorders. Cystinosis. Available online at: https://rarediseases.org/rare-diseases/cystinosis/#:~:text=Ocular%20symptoms%20of%20cystinosis%20can%20be%20treated%20with,suffering%20from%20pain%20due%20to%20repeated%20corneal%20erosions. Last accessed 10/20/2020.
[3] Park B. Cystadrops® Approved to Treat Corneal Crystal Deposits in Cystinosis. *MPR.* Available online at: https://www.empr.com/home/news/cystadrops-cysteamine-solution-fda-approved-crystal-deposits-cystinosis/#:~:text=The%20Food%20and%20Drug%20Administration%20%28FDA%29%20has%20approved,cystine%20crystals%20throughout%20the%20body%2C%20including%20the%20eyes. Issued 08/27/2020. Last accessed 10/20/2020.
[4] Cystaran™ Prescribing Information. Leadiant Biosciences. Available online at: http://www.cystaran.com/Cystaran_PI.pdf. Last revised 04/2020. Last accessed 10/20/2020.
[5] Cystadrops® Prescribing Information. Recordati Rare Diseases. Available online at: https://www.cystadrops.com/wp-content/uploads/cystadrops-prescribing-information.pdf. Last revised 08/2020. Last accessed 10/20/2020.

Appendix H

Vote to Prior Authorize Mycapssa® (Octreotide)

Oklahoma Health Care Authority
November 2020

Introduction[1]

In June 2020, the U.S. Food and Drug Administration approved Mycapssa® [octreotide delayed-release (DR) capsules] for long term maintenance treatment of patients with acromegaly who have responded to and tolerated treatment with octreotide or lanreotide. Mycapssa® is the first and only oral somatostatin analog (SSA) approved by the FDA. Mycapssa® is supplied as 20mg DR capsules and should be initiated at a dosage of 40mg daily, administered as 20mg orally twice daily. The dosage should be titrated in increments of 20mg based on the insulin-like growth factor 1 (IGF-1) levels and the patient's signs and symptoms, up to a maximum recommended dosage of 80mg daily.

Cost Comparison:

Medication	Cost Per Unit	Cost Per 28 Days	Cost Per Year
Mycapssa® (octreotide) 20mg capsule	**$92.00**	**$5,152.00**	**$66,976.00**
Sandostatin® LAR depot (octreotide) 20mg vial	$3,535.49	$3,535.49	$45,961.37
Signifor® LAR (pasireotide) 40mg vial	$13,058.40	$13,058.40	$169,759.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = capsule or vial; LAR = long-acting release

Recommendations

The College of Pharmacy recommends the prior authorization of Mycapssa® (octreotide) with the following criteria:

Mycapssa® (Octreotide) Approval Criteria:

1. An FDA approved indication for long-term maintenance treatment in members with acromegaly who have responded to and tolerated treatment with octreotide or lanreotide; and
2. Member has elevated insulin-like growth factor-1 (IGF-1) levels for age and/or gender; and
3. Member has a documented trial with injectable octreotide or lanreotide, and the prescriber must verify that the member responded to and tolerated treatment with octreotide or lanreotide; and
4. A patient-specific, clinically significant reason why the member cannot continue treatment with injectable octreotide or lanreotide must be provided; and

5. Mycapssa® must be prescribed by, or in consultation with, an endocrinologist; and
6. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and
7. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member's IGF-1 level has decreased or normalized since initiating treatment; and
8. A quantity limit of 120 capsules per 30 days will apply.

[1] Mycapssa® (Octreotide) Prescribing Information. Chiasma. Available online at: https://label.mycapssa.com/wp-content/uploads/sites/4/2020/06/prescribinginformation.pdf. Last revised 06/2020. Last accessed 10/20/2020.

Appendix I

Vote to Prior Authorize Zejula® (Niraparib)

Oklahoma Health Care Authority
November 2020

Market News and Updates[1,2,3]

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

- **April 2020:** The FDA approved Zejula® (niraparib) for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy. In 2019, niraparib received FDA approval for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer treated with ≥3 prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status. Positive HRD status is defined by either a deleterious or suspected deleterious BRCA mutation or genomic instability and disease progression after response to >6 months of platinum-based chemotherapy. Niraparib was originally FDA approved in 2017 for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in a complete or partial response to platinum-based chemotherapy.

Guideline Update(s):

- The largest changes in the National Comprehensive Cancer Network (NCCN) Ovarian Cancer Guidelines are focused on post-remission therapy (i.e., maintenance) including the role of poly [adenosine diphosphate (ADP)-ribose] polymerase (PARP) inhibitors and bevacizumab. The evidence for using post-remission therapy is greatest in patients with advanced ovarian cancers. Data is limited for patients with stage II disease.[2]
- Another change in the NCCN guidelines involves the inclusion of several oral targeted therapies for the treatment of recurrent ovarian cancer. Entrectinib and larotrectinib have been added as options for neurotrophic receptor tyrosine kinase (*NTRK*) gene-fusion positive tumors, and trametinib is now an option for patients with low-grade serous carcinomas.

Zejula® (Niraparib) Product Summary[4]

Zejula® (Niraparib):

- **Therapeutic Class:** PARP inhibitor

- **Indication(s):**
  - Maintenance treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients in a complete or partial response to first-line platinum-based chemotherapy
  - Maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients in a complete or partial response to platinum-based chemotherapy
  - Treatment of advanced ovarian, fallopian tube, or primary peritoneal cancer for patients who have been treated with ≥3 prior chemotherapy regimens and whose cancer is associated with HRD positive status
- **How Supplied:** 100mg capsules
- **Dose:**
  - First-line Maintenance Treatment of Advanced Ovarian Cancer:
    - Patients weighing <77kg (<170lbs) or a platelet count of <150,000/mcL: 200mg orally once daily
    - Patients weighing ≥77kg (≥170lbs) and a platelet count of ≥150,000/mcL: 300mg orally once daily
  - Maintenance Treatment of Recurrent Ovarian Cancer:
    - 300mg orally once daily
  - Treatment of Advanced Ovarian Cancer after ≥3 Chemotherapies:
    - 300mg orally once daily
- **Cost:** Wholesale Acquisition Cost (WAC) of $241.96 per 100mg capsule, resulting in a cost per 30 days of $21,776.40 based on the recommended dosing of 300mg [(3) 100mg capsules] once daily

Recommendations

- The prior authorization of Zejula® (niraparib) with the following criteria listed in red:

Zejula® (Niraparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Single-Agent Treatment of Advanced Recurrent/Refractory Disease:**
   a. Diagnosis of recurrent or refractory disease; and
   b. Previous treatment with ≥3 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
   c. Diagnosis is associated with homologous recombination deficiency (HRD) positive status defined by either:
      i. A deleterious or suspected deleterious BRCA mutation; or
      ii. Genomic instability and progression >6 months after response to last platinum-based chemotherapy; and
   d. Used as a single-agent; or

2. **Treatment of Advanced Recurrent/Refractory Disease in Combination with Bevacizumab:**
    a. Used in combination with bevacizumab for platinum-sensitive persistent disease or recurrence; and
    b. Meets 1 of the following:
        i. As immediate treatment for serially rising CA-125 in members who previously received chemotherapy, or
        ii. Evidence of radiographic and/or clinical relapse in members with previous complete remission and relapse ≥6 months after completing prior chemotherapy; or
3. **Maintenance Treatment of Advanced Disease:**
    a. Diagnosis of advanced or recurrent disease; and
    b. Disease must be in a complete or partial response to platinum chemotherapy; and
    c. Used as a single-agent.

- Update the current Mekinist® (trametinib) prior authorization criteria based on NCCN Compendium approval (changes noted in red in the following approval criteria; only criteria with changes are listed):

Mekinist® (Trametinib) Approval Criteria [Serous Ovarian Cancer Diagnosis]:

1. Diagnosis of persistent disease or recurrent low-grade serous carcinoma; and
2. Meets 1 of the following:
    a. Immediate treatment for serially rising CA-125 in members who previously received chemotherapy; or
    b. Progression on primary, maintenance, or recurrence therapy; or
    c. Stable or persistent disease (if not on maintenance therapy); or
    d. Complete remission and relapse <6 months after completing chemotherapy; or
    e. Complete remission and relapse ≥6 months after completing prior chemotherapy.

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Appendix J

Fiscal Year 2020 Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/ Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

Oklahoma Health Care Authority
November 2020

Introduction[1,2]

Multiple myeloma is characterized by a malignant proliferation of plasma cells that accumulate in the bone marrow eventually causing destruction and marrow failure.[1] Multiple myeloma overall is a rare cancer (1.8% of all cancers) and is frequently diagnosed at a median age of 69 years.[1] With the currently available treatment options, multiple myeloma is considered a non-curable malignancy. Early disease is often highly susceptible to chemotherapy agents and prolonged responses are attained; however, relapse is anticipated in all patients.

There has been significant growth and changes in newer agents to treat multiple myeloma in recent years. Several new classes or new generations of older drugs have been added to the treatment standard of care.[2] These agents include immunotherapy options [i.e., chimeric antigen receptor (CAR) T-cell therapy, bi-specific T-cell engager (BiTE) therapy], immunomodulatory drugs, monoclonal antibodies, histone deacetylase inhibitors, and proteasome inhibitors (PIs).

Use of evidence-based expert consensus guidelines is imperative in the treatment of cancers. The National Comprehensive Cancer Network (NCCN) Compendium contains authoritative, scientifically derived information designed to support decision making about the appropriate use of drugs and biologics in patients with cancer. These evidence-based guidelines should be used for optimal outcomes of cancer patients.[2]

Utilization of Multiple Myeloma Medications: Fiscal Year 2020

The following utilization data includes medications indicated for multiple myeloma; the data does not differentiate between multiple myeloma diagnoses and other diagnoses, for which use may be appropriate. Prior to

this review, multiple myeloma medications have not required prior authorization.

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	2	5	$49,756.35	$9,951.27	$355.40	15	140
2020	1	13	$132,983.61	$10,229.51	$365.34	39	364
% Change	**-50.00%**	**160.00%**	**167.30%**	**2.80%**	**2.80%**	**160.00%**	**160.00%**
Change	**-1**	**8**	**$83,227.26**	**$278.24**	**$9.94**	**24**	**224**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Fiscal Year 2020 Utilization: Medical Claims

Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2020	4	28	$177,398.94	$6,335.68	3,290

*Total number of unduplicated members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing Multiple Myeloma Medications: Pharmacy Claims

- Due to the small number of members utilizing multiple myeloma medications during fiscal year 2020, detailed demographic information could not be provided.

Top Prescriber Specialties of Multiple Myeloma Medications By Number of Claims: Pharmacy Claims

- The top prescriber specialty listed on multiple myeloma paid pharmacy claims during fiscal year 2020 was hematology oncology.

Prior Authorization of Multiple Myeloma Medications

There were no prior authorization requests submitted for multiple myeloma medications during fiscal year 2020. Prior to this review, multiple myeloma medications have not required prior authorization.

Market News and Updates[3,4,5]

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

- **November 2015:** The FDA approved Ninlaro® (ixazomib) for use in combination with lenalidomide and dexamethasone for the treatment

of patients with multiple myeloma who have received at least 1 prior therapy.

- **November 2015:** The FDA approved Empliciti® (elotuzumab) for use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received 1 to 3 prior therapies.
- **June 2019:** The FDA approved Darzalex® (daratumumab) for intravenous (IV) use in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).
- **July 2019:** The FDA granted accelerated approval to Xpovio® (selinexor) in combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received ≥4 prior therapies and whose disease is refractory to ≥2 PIs, ≥2 immunomodulatory agents, and an anti-cluster of differentiation 38/cyclic adenosine diphosphate ribose hydrolase (anti-CD38) monoclonal antibody.
- **September 2019:** The FDA approved Darzalex® (daratumumab) for adult patients with multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT.
- **October 2019:** The FDA approved Hemady™ (dexamethasone 20mg tablet) for use in combination with other anti-myeloma therapies for the treatment of adults with multiple myeloma.
- **March 2020:** The FDA approved Sarclisa® (isatuximab-irfc) in combination with pomalidomide and dexamethasone for adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI.
- **May 2020:** The FDA approved Darzalex Faspro™ (daratumumab/hyaluronidase-fihj) for adult patients with newly diagnosed RRMM. This new product allows for subcutaneous (sub-Q) dosing of daratumumab.
- **June 2020:** The FDA granted accelerated approval to Xpovio® (selinexor) for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy.
- **August 2020:** The FDA approved Blenrep (belantamab mafodotin-blmf) for adult patients with RRMM who have received ≥4 prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an immunomodulatory agent.
- **August 2020:** The FDA approved Kyprolis® (carfilzomib) and Darzalex® (daratumumab) in combination with dexamethasone for adult patients with RRMM who have received 1 to 3 prior therapies.

Pipeline:

- **Idecabtagene Vicleucel (ide-cel):** In September 2020, Bristol Myers Squibb and Bluebird Bio announced that the FDA had accepted their Biologics License Application (BLA) for ide-cel. This is an investigational B-cell maturation antigen (BCMA)-directed CAR T-cell immunotherapy, for the treatment of adult patients with multiple myeloma who have received ≥3 prior therapies, including an immunomodulatory agent, a PI, and an anti-CD38 antibody. The BLA is based on results from the pivotal Phase 2 KarMMa study evaluating the efficacy and safety of ide-cel in 128 adults with heavily pre-treated and highly refractory multiple myeloma exposed to an immunomodulatory agent, a PI, and an anti-CD38 antibody. The FDA has set a Prescription Drug User Fee Act (PDUFA) goal date of March 27, 2021. Ide-cel was previously granted Breakthrough Therapy designation by the FDA.

Product Summaries[6,7,8,9,10,11,12,13]

Blenrep (Belantamab Mafodotin-blmf):

- **Therapeutic Class:** BCMA-directed antibody and microtubule inhibitor conjugate

- **Boxed Warning: Ocular Toxicity**
  - In clinical trials in the pooled safety population (patients who received up to 1.4 times the recommended dose), Blenrep caused changes in the corneal epithelium resulting in severe vision loss, corneal ulcer, blurred vision, and dry eyes.
  - Ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms are recommended. Blenrep should be withheld until improvement and then resumed, or permanently discontinued, based on the severity of symptoms.
  - Blenrep is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Blenrep REMS.

- **Indication(s):** Treatment of adult patients with RRMM who have received ≥4 prior therapies
- **How Supplied:** 100mg lyophilized powder for reconstitution and further dilution in single-dose vials (SDVs)
- **Dose:** 2.5mg/kg (based on actual body weight) via IV infusion over approximately 30 minutes once every 3 weeks
- **Cost:** The Wholesale Acquisition Cost (WAC) is $8,277.00 per SDV; cost will vary due to weight-based dosing

Darzalex® (Daratumumab):

- **Therapeutic Class:** CD38-directed cytolytic antibody

- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
    - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
    - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
    - In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT
    - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
    - In combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior therapies
    - In combination with pomalidomide and dexamethasone in patients who have received ≥2 prior therapies including lenalidomide and a PI
    - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- **How Supplied:** 100mg/5mL and 400mg/20mL solution in SDVs
- **Dose:** 16mg/kg (based on actual body weight) administered via IV infusion; dosing schedule varies based on regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $111.14 per milliliter (mL), resulting in a cost of $555.70 per 100mg/5mL SDV and $2,222.80 per 400mg/20mL SDV; cost will vary due to weight-based dosing and dosing regimen

Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj):

- **Therapeutic Class:** Combination of a CD38-directed cytolytic antibody (daratumumab) and an endoglycosidase (hyaluronidase)
- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
    - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
    - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
    - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
    - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- **How Supplied:** 1,800mg daratumumab/30,000 units hyaluronidase/15mL (120mg/2,000 units/mL) solution in SDVs

- **Dose:** 1,800mg/30,000 units via sub-Q injection over 3 to 5 minutes; dosing schedule varies based on regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $504.93 per mL, resulting in a cost of $7,573.95 per 1,800mg/30,000 units/15mL SDV; cost will vary due to weight-based dosing and dosing regimen

Empliciti® (Elotuzumab):
- **Therapeutic Class:** Signaling lymphocytic activation molecule family member 7 (SLAMF7)-directed immunostimulatory antibody
- **Indication(s):**
  - For use in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received 1 to 3 prior therapies
  - For use in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI
- **How Supplied:** 300mg or 400mg lyophilized powder for reconstitution in SDVs
- **Dose:**
  - With lenalidomide and dexamethasone: 10mg/kg (based on actual body weight) administered IV every week for the first 2 cycles, followed by every 2 weeks thereafter
  - With pomalidomide and dexamethasone: 10mg/kg administered IV every week for the first 2 cycles, followed by 20mg/kg every 4 weeks thereafter
- **Cost:** The WAC is $1,941.96 per 300mg vial and $2,589.27 per 400mg vial; cost will vary due to weight-based dosing and dosing regimen

Hemady™ (Dexamethasone 20mg Tablet):
- **Therapeutic Class:** Glucocorticoid
- **Indication(s):** For use in combination with other anti-myeloma therapies for the treatment of adults with multiple myeloma
- **How Supplied:** 20mg oral tablets
- **Dose:** 20mg or 40mg once daily, on specific days depending on the protocol regimen
- **Cost Comparison:**

Product	Cost Per Unit	Cost Per 20mg Dose	Cost Per 40mg Dose
Hemady™ (dexamethasone) 20mg tablet	**$24.85**	**$24.85**	**$49.70**
dexamethasone 4mg tablet	$0.62	$3.10	$6.20

Unit = tablet; costs will vary due to variable dosing regimens
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Ninlaro® (Ixazomib):

- **Therapeutic Class:** PI
- **Indication(s):** For use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least 1 prior therapy
- **How Supplied:** 2.3mg, 3mg, and 4mg oral capsules
- **Dose:** 4mg once a week on days 1, 8, and 15 of a 28-day treatment cycle; alternative strengths available for dose reductions/modifications if needed
- **Cost:** The WAC is $3,491.67 per capsule for all available strengths, resulting in a cost of $10,475.01 per 28 days based on the recommended dosing of 4mg on days 1, 8, and 15 of a 28-day cycle

Sarclisa® (Isatuximab-irfc):

- **Therapeutic Class:** CD38-directed cytolytic antibody
- **Indication(s):** For use in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI
- **How Supplied:** 100mg/5mL and 500mg/25mL (20mg/mL) solution in SDVs
- **Dose:** 10mg/kg (based on actual body weight) via IV infusion every week for 4 weeks followed by 10mg/kg every 2 weeks in combination with pomalidomide and dexamethasone
- **Cost:** The WAC is $130.00 per mL, resulting in a cost of $650.00 per 100mg/5mL SDV and $3,250.00 per 500mg/25mL SDV; cost will vary due to weight-based dosing

Xpovio® (Selinexor):

- **Therapeutic Class:** Nuclear export inhibitor
- **Indication(s):**
  - For use in combination with dexamethasone for the treatment of adult patients with RRMM who have received ≥4 prior therapies and whose disease is refractory to ≥2 PIs, ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody
  - For the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy
- **How Supplied:** 20mg oral tablets packaged in 7 dose presentations (allowing for dose reduction based on adverse effects and diagnosis being treated); each dosing option is available in a 28-day supply carton containing 4 weekly blister packs

- **Dose:**
  - RRMM: 80mg [(4) 20mg tablets] in combination with 20mg dexamethasone taken on days 1 and 3 of each week
  - DLBCL: 60mg [(3) 20mg tablets] taken on days 1 and 3 of each week
- **Cost:** The WAC per tablet ranges from $687.50 to $2,750.00, resulting in an approximate cost of $22,000.00 per 28-day supply carton

Recommendations

- The prior authorization of Blenrep (belantamab mafodotin-blmf), Darzalex® (daratumumab), Darzalex Faspro™ (daratumumab/ hyaluronidase-fihj), Empliciti® (elotuzumab), Hemady™ (dexamethasone 20mg tablet), Ninlaro® (ixazomib), Sarclisa® (isatuximab-irfc), and Xpovio® (selinexor) with the following criteria (shown in red):

Blenrep (Belantamab Mafodotin-blmf) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM) in adults; and
2. Member has received ≥4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor (PI), and an immunomodulatory agent; and
3. Prescriber must verify the member will receive eye exams, including visual acuity and slit lamp ophthalmic examinations, with each cycle (every 3 weeks).

Darzalex® (Daratumumab) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. Used in combination with lenalidomide and dexamethasone; and
   a. Member is not a candidate for autologous stem cell transplant (ASCT) and the regimen will be used as primary therapy; or
   b. Member has received at least 1 prior therapy; or
3. Used in 1 of the following settings:
   a. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
   b. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or
   c. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or
   d. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or

e. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or
f. As a single-agent in members who have received ≥3 prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.

Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. Used in combination with lenalidomide and dexamethasone; and
3. Must meet 1 of the following:
   a. Member is not a candidate for autologous stem cell transplant (ASCT) and the regimen will be used as primary therapy; or
   b. Member has received at least 1 prior therapy; or
4. Used in 1 of the following settings:
   a. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
   b. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or
   c. As a single-agent in members who have received ≥3 prior therapies, including a proteasome inhibitor (PI) and an immunomodulatory agent, or in members who are double refractory to a PI and an immunomodulatory agent.

Empliciti® (Elotuzumab) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of previously treated multiple myeloma with relapsed or progressive disease; and
2. Used in combination with 1 of the following regimens:
   a. Lenalidomide and dexamethasone in members who have received 1 to 3 prior therapies; or
   b. Bortezomib and dexamethasone; or
   c. Pomalidomide and dexamethasone in members who have received ≥2 prior therapies, including an immunomodulatory agent and a proteasome inhibitor (PI).

Hemady™ (Dexamethasone 20mg Tablet) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use dexamethasone 4mg tablets to achieve the required dose in place of Hemady™ must be provided.

Ninlaro® (Ixazomib) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of symptomatic multiple myeloma; and

2. Used as primary therapy; or
3. Used following disease relapse after 6 months following primary induction therapy with the same regimen; and
4. Used in combination with 1 of the following regimens:
    a. Lenalidomide and dexamethasone; or
    b. Cyclophosphamide and dexamethasone for transplant candidates only; or
    c. Pomalidomide and dexamethasone if member has failed ≥2 prior therapies and demonstrated disease progression within 60 days; or
5. Used as a single-agent for the maintenance treatment of disease.

Sarclisa® (Isatuximab-irfc) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM) after ≥2 prior therapies; and
2. Previous treatment must have included lenalidomide and a proteasome inhibitor (PI); and
3. Used in combination with pomalidomide and dexamethasone.

Xpovio® (Selinexor) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Member has received ≥4 prior therapies including refractory disease to ≥2 proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody; and
3. Used in combination with dexamethasone.

Xpovio® (Selinexor) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. Treatment of adult members with relapsed/refractory DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma; and
2. Member has received ≥2 prior lines of systemic therapy.

Utilization Details of Multiple Myeloma Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
IXAZOMIB PRODUCTS					
NINLARO CAP 3MG	13	1	$132,983.61	13	$10,229.51
SUBTOTAL	**13**	**1**	**$132,983.61**	**13**	**$10,229.51**
TOTAL	**13**	**1***	**$132,983.61**	**13**	**$10,229.51**

CAP = capsule
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS[+]	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J9145 DARATUMUMAB INJ	28	4	$177,398.94	$6,335.68
TOTAL	**28**	**4**	**$177,398.94**	**$6,335.68**

INJ = injection
[+]Total number of unduplicated claims.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix K

30-Day Notice to Prior Authorize Lenvima® (Lenvatinib)

Oklahoma Health Care Authority
November 2020

Introduction[1,2,3]

Thyroid carcinomas are uncommon cancers in the United States with approximately 52,890 new cases estimated for 2020.[1] The clinical course of the disease depends on the histology of the tumor. Differentiated thyroid carcinomas account for >90% of all thyroid cancer diagnoses and are typically associated with 90 to 95% 10-year survival rates.[2] Treatment plans typically involve surgery, radioactive iodine ablation, and thyroxine therapy.[2] Treatment options are limited in the rare cases of metastatic and relapsed diseases. Newer targeted agents, such as lenvatinib, are emerging for these unique clinical cases.

Lenvima® (lenvatinib) was approved by the U.S. Food and Drug Administration (FDA) in 2015 for locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC). Following its approval for thyroid cancer, lenvatinib quickly gained approval in the treatment of additional solid tumors. In 2016, the FDA approved Lenvima® for renal cell carcinoma (RCC) for use in combination with everolimus, for patients with advanced RCC following 1 prior anti-angiogenic therapy. The indication was expanded further in 2018 with an FDA approval for first-line treatment of patients with unresectable hepatocellular carcinoma (HCC). Most recently, in September 2019, Lenvima® received FDA approval for use in combination with pembrolizumab for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), with disease progression following prior systemic therapy, and who are not candidates for curative surgery or radiation.

Lenvima® (Lenvatinib) Product Summary[4]

Lenvima® (Lenvatinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory DTC
  - In combination with everolimus, for the treatment of patients with advanced RCC following 1 prior anti-angiogenic therapy
  - First-line treatment of patients with unresectable HCC

- In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, with disease progression following prior systemic therapy, and who are not candidates for curative surgery or radiation

- **How Supplied:** 4mg and 10mg oral capsules supplied in cartons of (6) 5-day blister cards as follows:
  - 24mg/day: (10) 10mg capsules and (5) 4mg capsules per card
  - 20mg/day: (10) 10mg capsules per card
  - 18mg/day: (5) 10mg capsules and (10) 4mg capsules per card
  - 14mg/day: (5) 10mg capsules and (5) 4mg capsules per card
  - 12mg/day: (15) 4mg capsules per card
  - 10mg/day: (5) 10mg capsules per card
  - 8mg/day: (10) 4mg capsules per card
  - 4mg/day: (5) 4mg capsules per card
- **Dose:**
  - DTC: 24mg once daily
  - RCC: 18mg once daily with everolimus 5mg once daily
  - HCC: Based on actual body weight:
    - 8mg once daily for patients <60kg
    - 12mg once daily for patients ≥60kg
  - Endometrial carcinoma: 20mg once daily with pembrolizumab 200mg via intravenous (IV) infusion every 3 weeks
- **Cost:** The Wholesale Acquisition Cost (WAC) ranges from $211.34 to $634.03 per capsule, resulting in an approximate cost of $19,000.00 per 30-day supply dose pack

Recommendations

- The prior authorization of Lenvima® (lenvatinib) with the following criteria shown in red:

Lenvima® (Lenvatinib) Approval Criteria [Differentiated Thyroid Cancer (DTC) Diagnosis]:

1. Locally recurrent or metastatic disease; and
2. Disease progression on prior treatment; and
3. Radioactive iodine-refractory disease.

Lenvima® (Lenvatinib) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Advanced disease; and
2. Following 1 prior anti-angiogenic therapy; and
3. Used in combination with everolimus.

Lenvima® (Lenvatinib) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Unresectable disease; and
2. First-line treatment.

Lenvima® (Lenvatinib) Approval Criteria [Endometrial Carcinoma Diagnosis]:

1. Advanced disease with progression on prior systemic therapy; and
2. Member is not a candidate for curative surgery or radiation; and
3. Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
4. Used in combination with pembrolizumab.

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[1] National Institutes of Health (NIH). Surveillance, Epidemiology, and End Results (SEER) Program Populations. Cancer Stat Facts: Thyroid Cancer. *National Cancer Institute, DCCPS, Surveillance Research Program*. Available online at: https://seer.cancer.gov/statfacts/html/thyro.html. Last accessed 10/12/2020.

[2] National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Thyroid Carcinoma Version 2.2020. *National Comprehensive Cancer Network*. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Issued 07/15/2020. Last accessed 10/12/2020.

[3] U.S. Food and Drug Administration (FDA). Drugs@FDA: FDA-Approved Drugs. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Last accessed 10/08/2020.

[4] Lenvima® Prescribing Information. Eisai, Inc. Available online at: http://www.lenvima.com/pdfs/prescribing-information.pdf. Last revised 09/2020. Last accessed 10/08/2020.

Appendix L

Fiscal Year 2020 Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

Oklahoma Health Care Authority
November 2020

Current Prior Authorization Criteria

Inhaled Corticosteroids (ICS) and Combination Products	
Tier-1	**Tier-2***
budesonide (Pulmicort®)	beclomethasone dipropionate (QVAR® RediHaler™)
budesonide/formoterol (Symbicort®)+	fluticasone furoate (Arnuity® Ellipta®)
ciclesonide (Alvesco®)	fluticasone furoate/vilanterol (Breo® Ellipta®)
flunisolide (Aerospan®)	fluticasone propionate (ArmonAir™ RespiClick®)
fluticasone propionate (Flovent®)	fluticasone propionate/salmeterol (AirDuo RespiClick®)
fluticasone/salmeterol (Advair®)	
mometasone furoate (Asmanex®)	
mometasone furoate/formoterol (Dulera®)	

Tier-1 products indicated for the member's age are covered with no prior authorization required.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Brand name preferred.
*Unique criteria applies to each medication.

AirDuo RespiClick® (Fluticasone Propionate/Salmeterol) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be at or above the minimum age indicated; and
3. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member; and
4. Member must have used an inhaled corticosteroid for at least 1 month immediately prior; and

5. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
6. A clinical situation warranting initiation with combination therapy due to severity of asthma.

ArmonAir™ RespiClick® (Fluticasone Propionate) and Arnuity® Ellipta® (Fluticasone Furoate) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be at or above the minimum age indicated, and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) is not an option for the member must be provided.

Breo® Ellipta® (Fluticasone Furoate/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD) or chronic bronchitis and/or emphysema associated with COPD; and
   a. For a diagnosis of COPD or chronic bronchitis and/or emphysema associated with COPD, trials of Advair® and Symbicort®, consisting of at least 30 days each within the last 90 days that did not adequately control COPD symptoms; or
2. An FDA approved diagnosis of asthma in members 18 years of age and older; and
   a. For a diagnosis of asthma, trials of Advair®, Dulera®, and Symbicort® consisting of at least 30 days each within the last 120 days that did not adequately control asthma symptoms.

QVAR® RediHaler™ (Beclomethasone Dipropionate) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 4 years of age or older; and
3. A trial of all available Tier-1 inhaled corticosteroids or a patient-specific, clinically significant reason why they are not appropriate for the member must be provided.

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA)	
Tier-1*	**Tier-2**
LABA Products*	
salmeterol inhalation powder (Serevent®)	arformoterol nebulizer solution (Brovana®)
	formoterol nebulizer solution (Perforomist®)
	indacaterol inhalation powder (Arcapta® Neohaler®)
	olodaterol inhalation spray (Striverdi® Respimat®)

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA)	
Tier-1*	**Tier-2**
LAMA Products	
tiotropium inhalation powder (Spiriva® HandiHaler®)	aclidinium inhalation powder (Tudorza® PressAir®)
tiotropium soft mist inhaler (Spiriva® Respimat®)	glycopyrrloate inhalation powder (Seebri® Neohaler®)
	glycopyrrolate inhalation solution (Lonhala® Magnair®)
	revefenacin inhalation solution (Yupelri®)
	umeclidinium inhalation powder (Incruse® Ellipta®)

*Combination agents that contain a Tier-1 ingredient qualify as Tier-1 agents.
Tier-1 medications do not require prior authorization.
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Long-Acting Beta$_2$ Agonist (LABA) and Long-Acting Muscarinic Antagonist (LAMA) Tier-2 Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), chronic bronchitis, or emphysema; and
3. A 4-week trial of at least 1 LABA and a 4-week trial of 1 LAMA within the past 90 days; or
4. A documented adverse effect, drug interaction, or contraindication to all available Tier-1 products; or
5. A clinical exception may apply for members who are unable to effectively use hand-actuated devices, such as Spiriva® HandiHaler®, or who are stable on nebulized therapy.

Anoro® Ellipta® (Umeclidinium/Vilanterol), Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate), Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate), Stiolto® Respimat® (Tiotropium/ Olodaterol), and Utibron® Neohaler® (Indacaterol/Glycopyrrolate) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components must be provided.

Trelegy® Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in members with a history of exacerbations; and
2. A 4-week trial of at least 1 long-acting beta$_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
3. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA must be provided.

Daliresp® (Roflumilast) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD) with history of chronic bronchitis; and
2. Forced expiratory volume (FEV) ≤50% of predicted; and
3. Member is inadequately controlled on long-acting bronchodilator therapy (must have 3 or more claims for long-acting bronchodilators in the previous 6 months).

Cinqair® (Reslizumab) Approval Criteria:

1. An FDA approved indication of add-on maintenance treatment of severe eosinophilic phenotype asthma; and
2. Member must be 18 years of age or older; and
3. Member must have a blood eosinophil count ≥400 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. Cinqair® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
8. Cinqair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an

allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Member's weight should be provided on prior authorization requests. Weights should have been taken within the last 4 weeks to provide accurate weight-based dosing.

Dupixent® (Dupilumab Injection) Approval Criteria⁺ [Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of moderate-to-severe eosinophilic phenotype asthma or oral corticosteroid-dependent asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count of ≥150 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. The prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
8. Dupixent® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Quantities approved must not exceed FDA recommended dosing requirements.

⁺ The current prior authorization criteria and recommendations for Dupixent® for indications other than asthma will be provided in the Fiscal Year 2020

Annual Review of Atopic Dermatitis (AD) Medications report, which is also being presented at the November 2020 DUR Board meeting.

Fasenra® (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of severe eosinophilic phenotype asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count of ≥150 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Fasenra® prefilled syringe, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Fasenra® prefilled autoinjector pen, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Fasenra®; and
9. Fasenra® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 prefilled syringe or prefilled autoinjector pen per 56 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Severe Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of severe eosinophilic phenotype asthma; and
2. Member must be 6 years of age or older; and

3. Member must have a blood eosinophil count of 150 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
9. Nucala® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 vial, prefilled autoinjector, or prefilled syringe per 28 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Eosinophilic Granulomatosis with Polyangiitis (EGPA) Diagnosis]:

1. An FDA approved diagnosis of EGPA; and
2. Member meets 1 of the following:
    a. Member must have a past history of at least 1 confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] within the past 12 months; or
    b. Member must have refractory disease within the last 6 months following induction of a standard treatment regimen administered compliantly for at least 3 months; and

3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
7. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
8. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by a Birmingham Vasculitis Activity Score (BVAS) of 0 (zero), fewer EGPA relapses from baseline, or a decrease in daily OCS dosing from baseline.

Xolair® (Omalizumab Injection) Approval Criteria [Asthma Diagnosis]:

1. A diagnosis of severe persistent asthma; and
2. Member must be between 6 and 75 years of age; and
3. Member must have a positive skin test to at least 1 perennial aeroallergen [positive perennial aeroallergen(s) must be listed on the prior authorization request]; and
4. Member must have a pretreatment serum IgE level between 30 and 1,300 IU/mL (depending on member age); and
5. Member's weight must be between 20kg and 150kg; and
6. Member must have been on a medium-to-high-dose inhaled corticosteroid (ICS) (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose) for at minimum the past 3 months; and
7. Prescribed Xolair® dose must be an FDA approved regimen per Xolair® *Prescribing Information*; and
8. Xolair® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and

9. Xolair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the past 12 months, or member must have been determined to be dependent on systemic corticosteroids to prevent serious exacerbations; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval.

Xolair® (Omalizumab Injection) Approval Criteria [Chronic Idiopathic Urticaria (CIU) Diagnosis]:

1. An FDA approved diagnosis of CIU; and
2. Member must be 12 years of age or older; and
3. Other forms of urticaria must be ruled out; and
4. Other potential causes of urticaria must be ruled out; and
5. Member must have an Urticaria Activity Score (UAS) ≥16; and
6. Prescriber must be an allergist, immunologist, or dermatologist (or an advanced care practitioner with a supervising physician that is an allergist, immunologist, or dermatologist); and
7. A trial of a second generation antihistamine dosed at 4 times the maximum FDA dose within the last 3 months for at least 4 weeks (or less if symptoms are intolerable); and
8. Initial dosing will only be approved for 150mg every 4 weeks. If the member has inadequate results at this dose, then the dose may be increased to 300mg every 4 weeks; and
9. Initial approvals will be for the duration of 3 months at which time compliance will be evaluated for continued approval.

Utilization of Maintenance Asthma and COPD Medications: Fiscal Year 2020

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	10,316	43,000	$15,853,739.12	$368.69	$11.95	1,352,902	1,326,414
2020	11,220	47,623	$17,605,724.24	$369.69	$11.28	1,458,186	1,561,172
% Change	**8.8%**	**10.8%**	**11.1%**	**0.3%**	**-5.6%**	**7.8%**	**17.7%**
Change	**904**	**4,623**	**$1,751,985.12**	**$1.00**	**-$0.67**	**105,284**	**234,758**

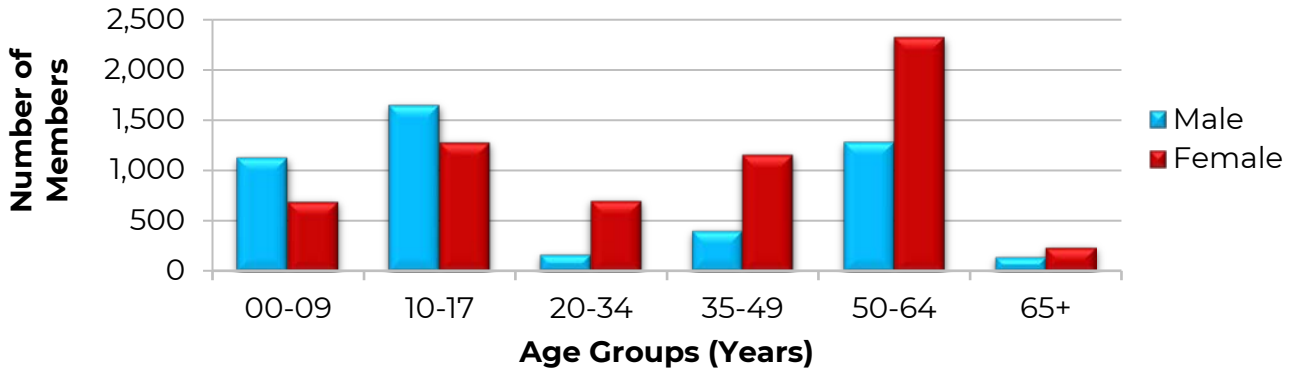
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020
Please note, the above utilization data does not include asthma-indicated monoclonal antibodies or medications that contain an inhaled corticosteroid alone. Please refer to the following table and utilization details at the end of this report for asthma-indicated monoclonal antibodies.

Comparison of Fiscal Years: Asthma-Indicated Monoclonal Antibodies¥

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	70	470	$1,400,762.99	$2,980.35	$108.87	1,640	12,866
2020	153	1,094	$3,218,523.73	$2,941.98	$106.73	3,455	30,157
% Change	**118.60%**	**132.80%**	**129.80%**	**-1.30%**	**-2.00%**	**110.70%**	**134.40%**
Change	**83**	**624**	**$1,817,760.74**	**-$38.37**	**-$2.14**	**1,815**	**17,291**

¥Pharmacy claims data only.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020
Please note, the above utilization data includes pharmacy claims for Xolair® (omalizumab), Nucala® (mepolizumab), and Dupixent® (dupilumab) used for all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate. Cinqair® (reslizumab) is billed by medical claims only and not reflected in the above pharmacy claims data; however, there were no SoonerCare medical claims for Cinqair® (reslizumab) during fiscal year 2020. Fasenra® (benralizumab), Xolair® (omalizumab), and Nucala® (mepolizumab) medical claims utilization details for fiscal year 2020 can be found at the end of this report.

Demographics of Members Utilizing Maintenance Asthma and COPD Medications

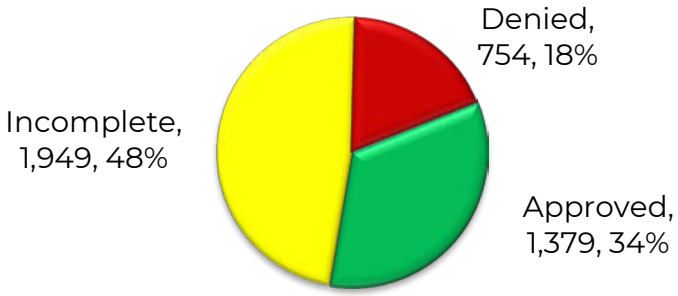


Top Prescriber Specialties of Maintenance Asthma and COPD Medications by Number of Claims

Prior Authorization of Maintenance Asthma and COPD Medications

There were 4,082 prior authorization requests submitted for maintenance asthma and COPD medications during fiscal year 2020. Of those prior authorization requests, 752 were submitted for monoclonal antibody medications. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Dulera® (mometasone/formoterol inhalation aerosol): November 2020; patent expires November 21, 2020 and exclusivity expires June 20, 2021. There are no generic equivalents to Dulera® available at this time.
- Perforomist® (formoterol nebulizer solution): June 2021
- Brovana® (arformoterol nebulizer solution): November 2021
- Daliresp® (roflumilast oral tablet): March 2024
- Arcapta® Neohaler® (indacaterol inhalation powder): October 2028; discontinued.

- Seebri® Neohaler® (glycopyrrolate inhalation powder): October 2028; discontinued.
- Utibron® Neohaler® (indacaterol/glycopyrrolate inhalation powder): October 2028; discontinued.
- Tudorza® Pressair® (aclidinium inhalation powder): March 2029
- Duaklir® Pressair® (aclidinium/formoterol inhalation powder): March 2029
- Symbicort® (budesonide/formoterol inhalation aerosol): October 2029
- Spiriva® HandiHaler® (tiotropium inhalation powder): April 2030
- Striverdi® Respimat® (olodaterol inhalation spray): October 2030
- Stiolto® Respimat® (tiotropium/olodaterol inhalation spray): October 2030
- Breo® Ellipta® (fluticasone furoate/vilanterol inhalation powder): October 2030
- Incruse® Ellipta® (umeclidinium inhalation powder): October 2030
- Arnuity® Ellipta® (fluticasone furoate inhalation powder): October 2030
- Anoro® Ellipta® (umeclidinium/vilanterol inhalation powder): November 2030
- Trelegy® Ellipta® (fluticasone furoate/umeclidinium/vilanterol inhalation powder): November 2030
- Bevespi Aerosphere® (glycopyrrolate/formoterol inhalation aerosol): March 2031
- Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol): March 2031
- Spiriva® Respimat® (tiotropium soft mist inhaler): April 2031
- QVAR® RediHaler™ (beclomethasone inhalation aerosol): January 2032
- ArmonAir™ RespiClick® (fluticasone propionate inhalation powder): February 2032; discontinued.
- AirDuo RespiClick® (fluticasone propionate/salmeterol inhalation powder): October 2034
- AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder): August 2036
- ArmonAir® Digihaler® (fluticasone propionate inhalation powder): August 2036

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

- **July 2019:** The FDA approved AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder), a combination therapy digital inhaler with built-in sensors that connects to a companion mobile application to provide information on inhaler use to patients with asthma. AirDuo® Digihaler® is indicated for the treatment of asthma in patients 12 years of age and older. AirDuo® Digihaler® is not indicated for the relief of acute bronchospasm and shouldn't replace a rescue inhaler. AirDuo® Digihaler® contains built-in sensors that detect

when the inhaler is used and measure inspiratory flow rates. This data is then sent to a companion mobile application (app) using Bluetooth® Wireless Technology so patients can review their data over time, and if desired, share it with their health care providers. Patients can also schedule reminders on their smartphone to take their AirDuo® Digihaler® as prescribed. The approval of AirDuo® Digihaler® was based on the review of the supplemental New Drug Application (sNDA) submitted by Teva to the FDA. AirDuo® Digihaler® was approved in a low, medium, and high dose: 55/14mcg, 113/14mcg, and 232/14mcg administered as 1 inhalation twice daily. As a fixed dose combination asthma therapy containing an inhaled corticosteroid (ICS) and a long-acting beta$_2$ agonist (LABA), AirDuo® Digihaler® contains the same active ingredients as Advair Diskus®, which is also approved in low, medium, and high doses: 100/50mcg, 250/50mcg, and 500/50mcg.

- **February 2020:** The FDA approved ArmonAir® Digihaler® (fluticasone propionate inhalation powder), an ICS delivered via Teva's Digihaler® device, which contains built-in sensors and connects to a companion mobile application that provides information on inhaler use to patients with asthma (*refer to AirDuo® Digihaler® above for additional information on the Digihaler® device*). ArmonAir® Digihaler® is indicated for the maintenance treatment of asthma in patients 12 years of age and older and is not indicated for the relief of acute bronchospasm. The approval of ArmonAir® Digihaler® was based on the review of the sNDA submitted by Teva to the FDA. ArmonAir® Digihaler® was approved in a low, medium, and high dose: 55mcg, 113mcg, and 232mcg administered as 1 inhalation twice daily.
- **July 2020:** The FDA approved Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) for the maintenance treatment of patients with COPD. The FDA approval was based on positive results from the Phase 3 ETHOS trial in which Breztri Aerosphere™, a triple-combination therapy, showed a statistically significant reduction in the rate of moderate or severe exacerbations compared with dual-combination therapies glycopyrrolate/formoterol fumarate and PT009 (budesonide/formoterol fumarate). The approval was also supported by efficacy and safety data from the Phase 3 KRONOS trial. Results from the Phase 3 ETHOS trial were published in *The New England Journal of Medicine* in June 2020 and results from the Phase 3 KRONOS trial were published in *The Lancet Respiratory Medicine* in September 2018. In both trials, the safety and tolerability of Breztri Aerosphere™ were consistent with the profiles of the dual comparators. Breztri Aerosphere™ is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

New FDA Expanded Indication(s) and/or Formulation(s):

- **August 2019:** Dulera® (mometasone/formoterol inhalation aerosol) was approved by the FDA for a new strength, 50mcg/5mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on findings from a trial evaluating the efficacy of Dulera® 50mcg/5mcg in pediatric patients 5 years to younger than 12 years of age compared with mometasone furoate metered dose inhaler (MDI) 50mcg; patients had been adequately controlled on an ICS/LABA for at least 4 weeks and had no symptoms of asthma worsening during a 2-week run-in on mometasone furoate MDI 50mcg. Results showed patients on Dulera® 50mcg/5mcg had a statistically significant change from baseline to week 12 in 60-minute morning post-dose percent predicted forced expiratory volume per 1 second ($ppFEV_1$) compared with mometasone furoate MDI 50mcg [primary end point: 5.21; 95% confidence interval (CI): 3.22, 7.20]. With regard to safety, patients in this age group demonstrated safety results similar to those seen in patients 12 years of age and older. Dulera® was previously approved for patients 12 years of age and older and is also available as 100mcg/5mcg and 200mcg/5mcg strengths.
- **August 2019:** Asmanex® HFA (mometasone furoate) was approved by the FDA for a new strength, 50mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on data from a 12-week, double-blind, placebo-controlled study in 583 patients 5 years to younger than 12 years of age with persistent asthma (mean baseline FEV_1: 79% of predicted) who had been using a low-to-medium dose of an ICS with or without a LABA for at least 12 weeks prior to study entry. After an approximate 2-week run-in period, patients were randomized to receive Asmanex® HFA 50mcg, 2 other doses of Asmanex® HFA, Asmanex® dry-powder inhaler (DPI), or placebo. Results showed after 12 weeks of treatment, Asmanex® HFA 50mcg was statistically superior to placebo as measured by improvement from baseline in morning pre-dose $ppFEV_1$ at the end of the dosing interval (primary end point: 6.29%; 95% CI: 3.05, 9.53). The safety profile and overall effectiveness in this age group were consistent with that observed in patients 12 years of age and older who also received Asmanex® HFA. Asmanex® HFA was previously approved for patients 12 years of age and older and is also available as 100mcg and 200mcg mometasone furoate strengths.
- **September 2020:** The FDA approved Nucala® (mepolizumab) for adults and children 12 years of age and older with hypereosinophilic syndrome (HES) for 6 months or longer without another identifiable non-blood related cause of the disease. The new indication for Nucala® is the first approval for HES patients in nearly 14 years. HES is a heterogeneous group of rare disorders associated with persistent eosinophilia with

evidence of organ damage. Symptoms include skin rashes, itching, asthma, difficulty breathing, abdominal pain, vomiting, diarrhea, arthritis, muscle inflammation, congestive heart failure, deep venous thrombosis (DVT), and anemia. Nucala® was evaluated in a randomized, double-blind, multicenter, placebo-controlled trial in 108 patients with HES. In the trial, patients were randomly assigned to receive Nucala® or placebo by injection every 4 weeks. An HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils on at least 2 occasions. The trial compared the proportion of patients who experienced at least 1 HES flare over a 32-week treatment period, as well as the time to the first flare. Fewer patients in the Nucala® treatment group (28%) had HES flares compared to patients in the placebo group (56%), with a 50% relative reduction. In addition, the time to the first HES flare was later, on average, for patients treated with Nucala® vs. placebo. Nucala® is also FDA approved for patients 6 years of age and older with severe asthma with an eosinophilic phenotype and for adult patients with eosinophilic granulomatosis with polyangiitis (EGPA), a rare autoimmune condition that causes blood vessel inflammation.

- **September 2020:** The FDA approved a new indication for Trelegy® Ellipta® (fluticasone furoate/umeclidinium/vilanterol) for the treatment of asthma in patients 18 years of age and older, adding to its current indication for the treatment of patients with COPD. Trelegy® Ellipta® is not indicated for relief of acute bronchospasm. The FDA approved strength for both COPD and asthma is fluticasone furoate/umeclidinium/vilanterol 100/62.5/25mcg. There is an additional strength for asthma alone, which is fluticasone furoate/umeclidinium/vilanterol 200/62.5/25mcg.

Guideline Update(s):

- **November 2019:** The Global Initiative for Chronic Obstructive Lung Disease (GOLD) published the 2020 update of its report on the management of COPD. In the GOLD 2020 revision, the most relevant changes include refinement of the use of non-pharmacological treatments, additional information regarding the role of eosinophils as a biomarker for the efficacy of ICS, and clarification on the diagnosis of exacerbations by describing relevant alternative diagnoses. Additionally, there is no longer a reference to an asthma and COPD overlap (ACO), instead it is emphasized asthma and COPD are different disorders, although they may share some common traits and clinical features (e.g., eosinophilia, some degree of reversibility).
- **August 2020:** The 2020 update of the Global Initiative on Asthma (GINA) Report, the *Global Strategy for Asthma Management and Prevention,* incorporates new scientific information about

asthma based on a review of recent scientific literature by an international panel of experts on the GINA Science Committee. It includes an interim guidance on asthma management during the COVID-19 pandemic advising patients with asthma to continue taking their prescribed asthma medications, particularly ICS-containing medications and oral corticosteroids (OCS) if prescribed, among other recommendations. GINA no longer recommends short-acting beta$_2$-agonists (SABA) for first-line therapy in asthma. All patients with asthma should be treated with an ICS either regularly or as needed, and children younger than 5 years of age should be treated with an ICS as a therapeutic trial with review after 3 months. For as needed relief of symptoms, GINA's preferred choice of reliever is an ICS in combination with formoterol (a LABA with rapid action) for adults and adolescents older than 12 years of age, and an ICS taken as needed together with a SABA in children 6 to 11 years of age. In patients with mild asthma, defined as needing relief treatment no more than twice per month, the preferred treatment is as needed ICS/formoterol in combination. Regular asthma review should include assessment (including diagnosis and patient preference for treatment), adjustment (including increasing or decreasing doses), and review of response to any changes.

Pipeline:

- **Benralizumab (Fasenra®):** In September 2020, AstraZeneca announced Fasenra® met both co-primary endpoints of reduced nasal polyp size and blockage in the OSTRO Phase 3 trial for patients with chronic rhinosinusitis with nasal polyps. Fasenra® demonstrated a statistically significant improvement in the endoscopic total nasal polyp score (NPS) and the nasal blockage score (NBS) compared to placebo, in patients with severe bilateral nasal polyposis who were still symptomatic despite continued treatment with standard of care (SoC). SoC consists of intranasal corticosteroids (INCS), surgery, and/or use of systemic corticosteroids. Evaluation of NPS was based on a physician assessment of polyp size during endoscopy. NBS evaluation was based on a patient-reported symptoms diary. Fasenra® is currently FDA approved for self-administration as an add-on maintenance treatment for severe eosinophilic asthma. Fasenra® is in development for multiple eosinophilic diseases and COPD. The FDA granted Orphan Drug designation to Fasenra® for the treatment of EGPA in 2018 and for the treatment of HES and eosinophilic esophagitis in 2019.
- **Ensifentrine:** In September 2020, Verona Pharma announced the initiation of ENHANCE ("Ensifentrine as a Novel inHAled Nebulized COPD thErapy") Phase 3 trials to evaluate the efficacy and safety of nebulized ensifentrine in patients with moderate-to-severe COPD. Ensifentrine is a first-in-class product candidate that combines

bronchodilator and anti-inflammatory activities in 1 compound. Ensifentrine is a long-acting inhibitor of both phosphodiesterase (PDE)3 and PDE4, 2 enzymes implicated in the development and progression of immunological respiratory diseases, particularly rhinitis and asthma, and this action makes it a potential treatment for respiratory diseases. As a PDE3 inhibitor, this drug is expected to result in bronchodilator actions, whilst the PDE4 component is expected to be anti-inflammatory. In prior clinical trials in COPD, ensifentrine has shown significant and clinically meaningful improvements in lung function, symptoms, and quality of life as monotherapy or when added onto a maintenance bronchodilator. Ensifentrine has been well tolerated in clinical trials involving >1,300 patients to date. The 2 randomized, double-blind, placebo-controlled Phase 3 trials (ENHANCE-1 and ENHANCE-2) will evaluate the efficacy and safety of nebulized ensifentrine as monotherapy and added onto a single bronchodilator, either a LAMA or a LABA, compared to placebo. The 2 trial designs will replicate measurements of efficacy and safety data over 24 weeks, and ENHANCE-1 will also evaluate longer-term safety over 48 weeks.

- **Tezepelumab:** In September 2018, the FDA granted Breakthrough Therapy designation (BTD) to tezepelumab for patients with severe asthma, without an eosinophilic phenotype, who are receiving an ICS/LABA with or without OCS and additional asthma controllers. The BTD was based on the tezepelumab Phase 2b PATHWAY data, which showed a significant reduction in the annual asthma exacerbation rate compared with placebo in a broad population of severe asthma patients irrespective of patient phenotype including T2 biomarker status. Currently available biologic therapies only target T2-driven inflammation. Tezepelumab is a potential first-in-class new therapy that blocks thymic stromal lymphopoietin (TSLP), an upstream modulator of multiple inflammatory pathways. Tezepelumab is currently in development in the Phase 3 PATHFINDER clinical trial program and data is anticipated in 2021.

AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol Inhalation Powder) Product Summary[17]

Indication(s): AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder) is a combination of fluticasone propionate, an ICS, and salmeterol, a LABA, indicated for treatment of asthma in patients 12 years of age and older. AirDuo® Digihaler® should be used for patients not adequately controlled on a long term asthma control medication such as an ICS or whose disease warrants initiation of treatment with both an ICS and a LABA.

- Limitation of Use: AirDuo® Digihaler® is not indicated for the relief of acute bronchospasm.

Dosing:

- AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder) is supplied as a multi-dose dry powder for inhalation in 3 strengths: 55/14mcg, 113/14mcg, and 232/14mcg.
- AirDuo® Digihaler® contains a built-in electronic module which detects, records, and stores data on inhaler events for transmission to a mobile app. Use of the mobile app is not required for administration of medication to the patient.
- The starting dosage is based on prior asthma therapy and disease severity. The recommended dose is 1 inhalation of AirDuo® Digihaler® 55/14mcg, 113/14mcg, or 232/14mcg twice daily.
- AirDuo® Digihaler® is for oral inhalation only and should not be used with a spacer or volume holding chamber.

Contraindication(s):

- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures
- Severe hypersensitivity to milk proteins or any ingredients of AirDuo® Digihaler®

Adverse Reactions: The most common adverse reactions (reported in ≥3% of patients treated with AirDuo® Digihaler®) include nasopharyngitis, oral candidiasis, headache, cough, and back pain.

Efficacy: The efficacy of AirDuo® Digihaler® was based primarily on the dose-ranging trials and the confirmatory trials for AirDuo RespiClick®.

Cost Comparison:

Medication	Cost Per Inhaler	Cost Per Year
AirDuo® Digihaler® (fluticasone propionate/ salmeterol inhalation powder) all strengths	**$449.00**	**$5,388.00**
AirDuo RespiClick® (fluticasone propionate/salmeterol inhalation powder) all strengths	$320.23	$3,842.76
fluticasone propionate/salmeterol inhalation powder 250/50mcg diskus	$149.96	$1,799.52

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

ArmonAir® Digihaler® (Fluticasone Propionate Inhalation Powder) Product Summary[18]

Indication(s): ArmonAir® Digihaler® (fluticasone propionate inhalation powder) is indicated for the maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.

- Limitations of Use: ArmonAir® Digihaler® is not indicated for the relief of acute bronchospasm.

Dosing:

- ArmonAir® Digihaler® (fluticasone propionate inhalation powder) is supplied as an inhalation powder in 3 strengths: 55mcg, 113mcg, and 232mcg.
- ArmonAir® Digihaler® contains a built-in electronic module which detects, records, and stores data on inhaler events for transmission to the mobile app. Use of the mobile app is not required for administration of medication to the patient.
- The starting dosage of ArmonAir® Digihaler® is based on prior asthma therapy and disease severity. The recommended dose is 1 inhalation of ArmonAir® Digihaler® 55mcg, 113mcg, or 232mcg twice daily.
- ArmonAir® Digihaler® should not be used with a spacer or volume holding chamber.

Contraindication(s):

- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures
- Severe hypersensitivity to milk proteins or any ingredients of ArmonAir® Digihaler®

Adverse Reactions: The most common adverse reactions (reported in ≥3% of patients treated with ArmonAir® Digihaler®) include upper respiratory tract infection, nasopharyngitis, oral candidiasis, headache, and cough.

Efficacy: The efficacy of ArmonAir® Digihaler® was based primarily on the dose-ranging trials and the confirmatory trials for ArmonAir™ RespiClick®.

Cost Comparison:

Medication	Cost Per Inhaler	Cost Per Year
ArmonAir® Digihaler® (fluticasone propionate inhalation powder) 232mcg	**$299.00**	**$3,588.00**
Arnuity® Ellipta® (fluticasone furoate inhalation powder) 200mcg	$229.55	$2,754.60
Flovent® Diskus® (fluticasone propionate inhalation powder) 250mcg	$247.60	$2,971.20

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

Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Aerosol) Product Summary[19,20]

Indication(s): Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) is a combination of budesonide (an ICS), glycopyrrolate (an anticholinergic), and formoterol fumarate (a LABA), indicated for the maintenance treatment of adult patients with COPD.

- Limitations of Use: Breztri Aerosphere™ is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Dosing:

- Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) is supplied as an inhalation aerosol pressurized MDI containing a combination of 160mcg budesonide, 9mcg glycopyrrolate, and 4.8mcg formoterol fumarate per actuation.
- Breztri Aerosphere™ is for oral inhalation only.
- The recommended dosage of Breztri Aerosphere™ for the maintenance treatment of COPD is 2 inhalations twice daily.

Contraindication(s):

- Hypersensitivity to budesonide, glycopyrrolate, formoterol fumarate, or to any of the excipients

Adverse Reactions: The most common adverse reactions (incidence ≥2%) in patients treated with Breztri Aerosphere™ include upper respiratory tract infection, pneumonia, back pain, oral candidiasis, influenza, muscle spasm, urinary tract infection, cough, sinusitis, and diarrhea.

Efficacy: The efficacy of Breztri Aerosphere™ was demonstrated in 2 parallel-group trials of 10,484 patients with moderate to very severe COPD.

- In Study 1, patients were randomized to Breztri Aerosphere™, BGF MDI (same ingredients as Breztri Aerosphere™, but different strengths), GFF MDI (glycopyrrolate/formoterol), or BFF MDI (budesonide/formoterol) for a total of 52 weeks. The primary endpoint was the rate of moderate-to-severe COPD exacerbations of Breztri Aerosphere™ vs. GFF MDI and BFF MDI.
  - Breztri Aerosphere™ demonstrated a 24% reduction in exacerbation rate vs. GFF MDI ($P<0.0001$) and demonstrated a 13% reduction in exacerbation rate vs. BFF MDI ($P=0.0027$).
- In Study 2, patients were randomized to Breztri Aerosphere™, GFF MDI, BFF MDI, or open-label active comparator for a total of 24 weeks. The primary endpoints were first second of forced expiration area under the curve from 0 to 4 hours (FEV_1 AUC_{0-4}) for Breztri Aerosphere™ vs. BFF MDI and change in baseline for morning pre-dose trough FEV_1 for Breztri Aerosphere™ vs. GFF MDI.

- The difference in FEV_1 AUC_{0-4} was 116mL (95% CI: 80, 152) for Breztri Aerosphere™ vs. BFF MDI.
- The change in baseline for morning pre-dose trough FEV_1 was 13mL (95% CI: -9, 36) for Breztri Aerosphere™ vs. GFF MDI, which was not statistically significant.

Cost Comparison:

Medication	Cost Per Inhaler	Cost Per Year
Breztri Aerosphere™ (budesonide/glycopyrrolate/ formoterol aerosol) 160/9/4.8mcg	**$590.40**	**$7,084.80**
Trelegy® Ellipta® (fluticasone furoate/umeclidinium/ vilanterol inhalation powder) 100/62.5/25mcg	$551.16	$6,613.92

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

Recommendations

The College of Pharmacy recommends the prior authorization of AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder) and ArmonAir® Digihaler® (fluticasone propionate inhalation powder) with the following criteria (new criteria is shown in red):

AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol Inhalation Powder) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why the member requires AirDuo® Digihaler® over AirDuo RespiClick® and all preferred Tier-1 inhaled corticosteroid and long-acting $beta_2$-agonist (ICS/LABA) products (Advair®, Dulera®, and Symbicort®) must be provided; and
4. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member must be provided; and
5. Member must have used an ICS for at least 1 month immediately prior; and
6. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
7. A clinical situation warranting initiation with combination therapy due to severity of asthma; and
8. The prescriber agrees to closely monitor member adherence; and
9. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must

ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
10. The member's phone camera must be functional and able to scan the inhaler QR code and register the AirDuo® Digihaler® inhaler; and
11. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

ArmonAir® Digihaler® (Fluticasone Propionate Inhalation Powder) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) or other preferred monotherapy inhaled corticosteroid (ICS) is not appropriate for the member must be provided; and
4. The prescriber agrees to closely monitor member adherence; and
5. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
6. The member's phone camera must be functional and able to scan the inhaler QR code and register the ArmonAir® Digihaler® inhaler; and
7. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

Additionally, the College of Pharmacy recommends the prior authorization of Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) and recommends updating the current approval criteria for Trelegy® Ellipta® (fluticasone furoate/umeclidinium/vilanterol) and Nucala® (mepolizumab) based on the newly FDA approved indications, with the following criteria (new criteria and changes are shown in red):

Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Aerosol) and Trelegy® Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis ~~of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in patients with a history of exacerbations~~; and

2. Member must be 18 years of age or older; and
3. A 4-week trial of at least 1 long-acting beta$_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
4. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA must be provided.

Nucala® (Mepolizumab Injection) Approval Criteria [Hypereosinophilic Syndrome (HES) Diagnosis]:

1. An FDA approved diagnosis of hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause; and
2. Member must be 12 years of age or older; and
3. Member must have a past history of at least 2 confirmed HES flares [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of cytotoxic or immunosuppressive therapy, or hospitalization] within the past 12 months; and
4. Member must have a baseline blood eosinophil count of 1,000 cells/mcL or higher in the last 4 weeks prior to initiating Nucala®; and
5. Diagnosis of FIP1L1-PDGFRα kinase-positive HES will not be approved; and
6. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥10mg/day) for a minimum of 4 weeks duration or member is unable to tolerate corticosteroid therapy due to significant side effects; and
7. Nucala® must be prescribed by a hematologist or a specialist with expertise in treatment of HES (or an advanced care practitioner with a supervising physician who is a hematologist or a specialist with expertise in treatment of HES); and
8. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
9. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
10. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the

member is responding to Nucala® as demonstrated by fewer HES flares from baseline or a decrease in daily OCS dosing from baseline.

Lastly, the College of Pharmacy recommends the prior authorization of Asmanex® HFA (mometasone furoate) 50mcg and Dulera® (mometasone/formoterol) 50mcg/5mcg based on net costs with the following criteria (new criteria and changes are shown in red):

Inhaled Corticosteroids (ICS) and Combination Products	
Tier-1	**Tier-2***
budesonide (Pulmicort®)	beclomethasone dipropionate (QVAR® RediHaler™)
budesonide/formoterol (Symbicort®)+	fluticasone furoate (Arnuity® Ellipta®)
ciclesonide (Alvesco®)	fluticasone furoate/vilanterol (Breo® Ellipta®)
flunisolide (Aerospan®)	fluticasone propionate (ArmonAir™ RespiClick®)
fluticasone propionate (Flovent®)	fluticasone propionate/salmeterol (AirDuo RespiClick®)
fluticasone/salmeterol (Advair®)	**mometasone furoate 50mcg (Asmanex® HFA)**
mometasone furoate (Asmanex®)¥	**mometasone furoate/formoterol 50mcg/5mcg (Dulera®)**
mometasone furoate/formoterol (Dulera®)◊	

Tier-1 products indicated for the member's age are covered with no prior authorization required.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Brand name preferred.
¥Includes all strengths and formulations other than Asmanex® HFA 50mcg.
◊ Includes all strengths other than Dulera® 50mcg/5mcg.
*Unique criteria applies to each medication.

Asmanex® HFA (Mometasone Furoate) 50mcg and QVAR® RediHaler™ (Beclomethasone Dipropionate) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be ~~4 years of age or older~~ at the indicated age for the requested product:
   a. Asmanex® 50mcg: Member must be between 5 and 11 years of age; or
   b. QVAR® RediHaler™: Member must be 4 years of age or older; and
3. A trial of all available Tier-1 inhaled corticosteroids or a patient-specific, clinically significant reason why they are not appropriate for the member must be provided.

Dulera® (Mometasone Furoate/Formoterol) 50mcg/5mcg Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be between 5 and 11 years of age ; and
3. Failure of Advair® and Symbicort® or a reason why Advair® and Symbicort® are not appropriate for the member must be provided; and
4. Member must have used an inhaled corticosteroid for at least 1 month immediately prior; and
5. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
6. A clinical situation warranting initiation with combination therapy due to severity of asthma.

Utilization Details of Maintenance Asthma and COPD Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
ICS/LABA COMBINATION PRODUCTS					
TIER-1 ICS/LABA					
ADVAIR HFA AER 115/21MCG	7,466	2,041	$2,749,892.27	$368.32	15.62%
SYMBICORT AER 160/4.5MCG	6,805	2,013	$2,429,076.96	$356.95	13.80%
ADVAIR DISKUS AER 250/50MCG	3,765	1,296	$1,479,462.26	$392.95	8.40%
FLUTIC/SALME AER 250/50MCG	3,486	1,143	$496,153.62	$142.33	2.82%
DULERA AER 200/5MCG	2,958	740	$917,849.56	$310.29	5.21%
SYMBICORT AER 80/4.5MCG	2,274	867	$674,912.24	$296.80	3.83%
ADVAIR HFA AER 230/21MCG	2,069	524	$1,009,376.91	$487.86	5.73%
ADVAIR HFA AER 45/21MCG	1,651	507	$490,154.50	$296.88	2.78%
ADVAIR DISKUS AER 100/50MCG	1,527	592	$467,798.27	$306.35	2.66%
DULERA AER 100/5MCG	1,502	476	$460,142.06	$306.35	2.61%
ADVAIR DISKUS AER 500/50MCG	1,491	448	$779,134.07	$522.56	4.43%
FLUTIC/SALME AER 500/50MCG	1,237	356	$226,206.45	$182.87	1.28%
FLUTIC/SALME AER 100/50MCG	900	362	$101,970.37	$113.30	0.58%
BUDES/FORM AER 160/4.5MCG	302	268	$87,861.09	$290.93	0.50%
BUDES/FORM AER 80/4.5MCG	82	79	$19,513.47	$237.97	0.11%
DULERA AER 50-5MCGMCG	1	1	$322.76	$322.76	0.00%
SUBTOTAL	**37,516**	**11,713**	**$12,389,826.86**	**$330.25**	**70.36%**
TIER-2 ICS/LABA					
BREO ELLIPTA 100/25MCG	110	27	$38,259.18	$347.81	0.22%
WIXELA INHUB AER 250/50MCG	4	1	$511.40	$127.85	0.00%
SUBTOTAL	**114**	**28**	**$38,770.58**	**$340.09**	**0.22%**
INDIVIDUAL COMPONENT LABA PRODUCTS					
TIER-1 LABA					
SEREVENT DISKUS AER 50MCG	585	223	$237,632.17	$406.21	1.35%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
SUBTOTAL	**585**	**223**	**$237,632.17**	**$406.21**	**1.35%**
TIER-2 LABA					
BROVANA NEB 15MCG	88	19	$78,850.87	$896.03	0.45%
PERFOROMIST NEB 20MCG	33	9	$44,851.29	$1,359.13	0.25%
SUBTOTAL	**121**	**28**	**$123,702.16**	**$1,022.33**	**0.70%**
INDIVIDUAL COMPONENT LAMA PRODUCTS					
TIER-1 LAMA					
SPIRIVA CAP HANDIHALER 18MCG	6,521	1,773	$3,494,771.93	$535.93	19.85%
SPIRIVA AER 2.5MCG	824	308	$361,089.21	$438.22	2.05%
SPIRIVA AER 1.25MCG	531	202	$220,048.57	$414.40	1.25%
SUBTOTAL	**7,876**	**2,283**	**$4,075,909.71**	**$517.51**	**23.15%**
TIER-2 LAMA					
LONHALA MAGNAIR SOL 25MCG	97	24	$120,220.03	$1,239.38	0.68%
INCRUSE ELIPTA INH 62.5MCG	93	19	$31,243.71	$335.95	0.18%
TUDORZA PRES AER 400MCG/ACT	31	8	$14,947.70	$482.18	0.08%
YUPELRI SOL 175MG/3ML	24	8	$28,544.70	$1,189.36	0.16%
SUBTOTAL	**245**	**59**	**$194,956.14**	**$24.75**	**1.1%**
LABA/LAMA COMBINATION PRODUCTS					
UTIBRON 27.5/15.36MCG	27	12	$10,053.59	$372.36	0.06%
BEVESPI AER 9/4.8MCG	54	14	$19,428.36	$359.78	0.11%
SUBTOTAL	**81**	**26**	**$29,481.95**	**$363.97**	**0.17%**
ICS/LABA/LAMA COMBINATION PRODUCTS					
TRELEGY ELLIPTA 100/62.5/25MCG	476	93	$269,883.83	$566.98	1.53%
SUBTOTAL	**476**	**93**	**$269,883.83**	**$566.98**	**1.53%**
PDE4 ENZYME INHIBITOR PRODUCTS					
DALIRESP TABLET 500MCG	145	26	$51,274.28	$353.62	0.29%
DALIRESP TABLET 250MCG	36	7	$16,685.04	$463.47	0.09%
SUBTOTAL	**181**	**33**	**$67,959.32**	**$375.47**	**0.38%**
TOTAL	**47,623**	**11,220***	**$17,605,724.24**	**$369.69**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
LABA = long-acting beta$_2$-agonist; LAMA = long-acting muscarinic antagonist; ICS = inhaled corticosteroid; PDE4 = phosphodiesterase-4; HFA = hydrofluoroalkane; AER = aerosol; FLUTIC = fluticasone; SALME = salmeterol; BUDES = budesonide; FORM = formoterol; NEB = nebulizer; CAP = capsule; SOL = solution; PRES = Pressair

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: PHARMACY CLAIMS					
DUPIXENT INJ 300/2ML	608	84	$1,827,571.56	$3,005.87	56.78%
DUPIXENT INJ 200/1.14ML	274	37	$838,504.34	$3,060.23	26.05%
XOLAIR INJ 150MG/ML	76	15	$170,688.29	$2,245.90	5.30%
XOLAIR SOL 150MG	51	9	$121,664.11	$2,385.57	3.78%
NUCALA INJ 100MG	34	8	$102,508.60	$3,014.96	3.18%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
FASENRA INJ 30MG/ML	28	7	$128,654.39	$4,594.80	4.00%
XOLAIR INJ 75MG/0.5ML	22	5	$23,951.85	$1,088.72	0.74%
FASENRA PEN 30MG/ML	1	1	$4,980.59	$4,980.59	0.15%
TOTAL	**1,094**	**153***	**$3,218,523.73 .99**	**$2,941.98**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
INJ = injection; SOL = solution
Please note, the above utilization data includes pharmacy claims for Xolair® (omalizumab), Nucala® (mepolizumab), and Dupixent® (dupilumab) used for all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: MEDICAL CLAIMS					
OMALIZUMAB INJ (J2357)	117	13	$285,763.32	$2,442.42	70.55%
MEPOLIZUMAB INJ (J2182)	24	5	$68,498.56	$2,854.11	17.04%
BENRALIZUMAB (J0517)	11	3	$47,770.10	$4,342.74	11.88%
TOTAL	**152⁺**	**21***	**$402,031.98**	**$2,644.95**	**100%**

⁺Total number of unduplicated claims.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
INJ = injection
Please note the above medical utilization data for omalizumab (J2357) includes all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.

Utilization Details of Inhaled Corticosteroids: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
INHALED CORTICOSTEROID (ICS) PRODUCTS					
TIER-1 ICS					
FLOVENT HFA AER 44MCG	19,879	7,743	$3,776,952.80	$190.00	33.18%
FLOVENT HFA AER 110MCG	19,751	7,635	$4,950,801.73	$250.66	43.50%
BUDESONIDE SUS 0.5MG/2	3,131	1,413	$281,834.90	$90.01	2.48%
BUDESONIDE SUS 0.25MG/2	3,103	1,914	$244,559.85	$78.81	2.15%
FLOVENT HFA AER 220MCG	2,371	990	$925,419.37	$390.31	8.13%
PULMICORT INH 90MCG	811	315	$161,994.23	$199.75	1.42%
ASMANEX HFA AER 100MCG	659	253	$122,052.01	$185.21	1.07%
PULMICORT INH 180MCG	595	286	$145,457.43	$244.47	1.28%
FLOVENT DISKUS AER 100MCG	513	235	$106,348.68	$207.31	0.93%
ASMANEX HFA AER 200MCG	492	183	$111,057.09	$225.73	0.98%
ALVESCO AER 80MCG	431	159	$115,911.34	$268.94	1.02%
FLOVENT DISKUS AER 250MCG	398	115	$111,282.84	$279.61	0.98%
FLOVENT DISKUS AER 50MCG	369	138	$74,102.75	$200.82	0.65%
ASMANEX 60 AER 220MCG	293	96	$64,560.35	$220.34	0.57%
ASMANEX 30 AER 220MCG	211	67	$38,893.45	$184.33	0.34%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
ALVESCO AER 160MCG	194	58	$53,138.11	$273.91	0.47%
BUDESONIDE SUS 1MG/2ML	189	79	$73,410.82	$388.42	0.64%
ASMANEX 30 AER 110MCG	43	21	$7,520.53	$174.90	0.07%
ASMANEX 120 AER 220MCG	39	24	$11,437.95	$293.28	0.10%
QVAR AER 40MCG	3	2	$403.99	$134.66	0.00%
SUBTOTAL	**53,475**	**21,726**	**$11,377,140.22**	**$212.76**	**99.96%**
TIER-2 ICS					
QVAR REDIHALER AER 40MCG	9	3	$1,704.02	$189.34	0.01%
QVAR REDIHALER AER 80MCG	8	3	$1,988.58	$248.57	0.02%
ARNUITY ELIPTA INH 100MCG	4	1	$697.98	$174.50	0.01%
SUBTOTAL	**21**	**7**	**$4,390.58**	**$209.08**	**0.04%**
TOTAL	**53,496**	**20,032***	**$11,381,530.80**	**$212.75**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
SUS = suspension; INH = inhaler; AER = aerosol; HFA = hydrofluoroalkane

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Appendix M

Fiscal Year 2020 Annual Review of Atopic Dermatitis (AD) Medications

Oklahoma Health Care Authority
November 2020

Current Prior Authorization Criteria

Dupixent® (Dupilumab Injection) Approval Criteria [Atopic Dermatitis Diagnosis]:

1. An FDA approved diagnosis of moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies; and
2. Member must be 12 years of age or older; and
3. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
   a. 1 medium potency to very-high potency Tier-1 topical corticosteroid; and
   b. 1 topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. Dupixent® must be prescribed by a dermatologist, allergist, or immunologist or the member must have been evaluated by a dermatologist, allergist, or immunologist within the last 12 months (or an advanced care practitioner with a supervising physician who is a dermatologist, allergist, or immunologist); and
5. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use (Dupixent® has not been studied in combination with other biologic therapies); and
6. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Dupixent® (Dupilumab Injection) Approval Criteria [Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment in adult members with inadequately controlled CRSwNP; and
2. Member must be 18 years of age or older; and
3. Member must have a documented trial with an intranasal corticosteroid that resulted in failure (or have a contraindication or documented intolerance); and
4. Member must meet 1 of the following:

    a. Member has required prior sino-nasal surgery; or
    b. Member has previously been treated with systemic corticosteroids in the past 2 years (or has a contraindication or documented intolerance); and
5. Dupixent® must be prescribed by an otolaryngologist, allergist, immunologist, or pulmonologist or the member must have been evaluated by an otolaryngologist, allergist, immunologist, or pulmonologist within the last 12 months (or an advanced care practitioner with a supervising physician who is an otolaryngologist, allergist, immunologist, or pulmonologist); and
6. Member has symptoms of chronic rhinosinusitis (e.g., facial pain/pressure, reduction or loss of smell, nasal blockade/obstruction/ congestion, nasal discharge) for 12 weeks or longer despite attempts at medical management; and
7. Member has evidence of nasal polyposis by direct examination, sinus CT scan, or endoscopy; and
8. Member will continue to receive intranasal corticosteroid therapy, unless contraindicated; and
9. Prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
10. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use; and
11. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval; and
12. A quantity limit of 2 syringes every 28 days will apply.

Dupixent® (Dupilumab Injection) Approval Criteria [Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of moderate-to-severe eosinophilic phenotype asthma or oral corticosteroid-dependent asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a baseline blood eosinophil count of ≥150 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and

5. Member must have failed a high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the highest FDA approved dose meets this criteria); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past 3 months; and
7. The prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
8. Dupixent® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Quantities approved must not exceed FDA recommended dosing requirements.

Elidel® (Pimecrolimus Topical) and Protopic® (Tacrolimus Topical) Approval Criteria:

1. The first 90 days of a 12-month period will be covered without prior authorization; and
2. After the initial period, authorization may be granted with documentation of 1 trial at least 6 weeks in duration within the past 90 days of a Tier-1 topical corticosteroid; and
3. Therapy will be approved only once each 90-day period to ensure appropriate short-term and intermittent utilization as advised by the FDA; and
4. Quantities will be limited to 30 grams for use on the face, neck, and groin, and 100 grams for all other areas; and
5. Authorizations will be restricted to those members who are not immunocompromised; and
6. Members must meet all of the following criteria:
    a. An FDA approved indication:
        i. Elidel®: Short-term and intermittent treatment for mild-to-moderate atopic dermatitis (eczema); or
        ii. Protopic®: Short-term and intermittent treatment for moderate-to-severe atopic dermatitis (eczema); and
    b. Age restrictions:
        i. Elidel® 1% is restricted to 2 years of age and older; and
        ii. Protopic® 0.03% is restricted to 2 years of age and older; and
        iii. Protopic® 0.1% is restricted to 15 years of age and older; or
7. Clinical exceptions for children meeting the age restriction for Elidel® (pimecrolimus topical) or Protopic® (tacrolimus topical):

   a. Documented adverse effect, drug interaction, or contraindication to Tier-1 topical corticosteroids; or
   b. Atopic dermatitis of the face or groin where prescriber does not want to use topical corticosteroids; or
   c. Prescribed by a dermatologist; or
8. Clinical exceptions for children not meeting the age restriction for Elidel® (pimecrolimus topical) or Protopic® (tacrolimus topical):
   a. Prescribed by a dermatologist.

Eucrisa® (Crisaborole Ointment) Approval Criteria:

1. An FDA approved indication for treatment of mild-to-moderate atopic dermatitis (eczema); and
2. Member must be at least 2 years of age or older; and
3. Member must have a documented trial within the last 6 months for a minimum of 2 weeks that resulted in failure with a topical corticosteroid (or have a contraindication or documented intolerance); and
4. A quantity limit of 1 tube per 30 days will apply; and
5. Initial approvals will be for the duration of 1 month. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
6. Clinical exceptions for children not meeting the age restriction for Eucrisa® (crisaborole ointment):
   a. Documented adverse effect, drug interaction, or contraindication to topical corticosteroids; or
   b. Atopic dermatitis of the face or groin where prescriber does not want to use topical corticosteroids; or
   c. Prescribed by a dermatologist.

Prudoxin™ and Zonalon® (Doxepin Cream) Approval Criteria:

1. An FDA approved indication for the short-term (up to 8 days) management of moderate pruritus in members with atopic dermatitis or lichen simplex chronicus; and
2. Requests for longer use than 8 days will not generally be approved. Chronic use beyond 8 days may result in higher systemic levels and should be avoided.

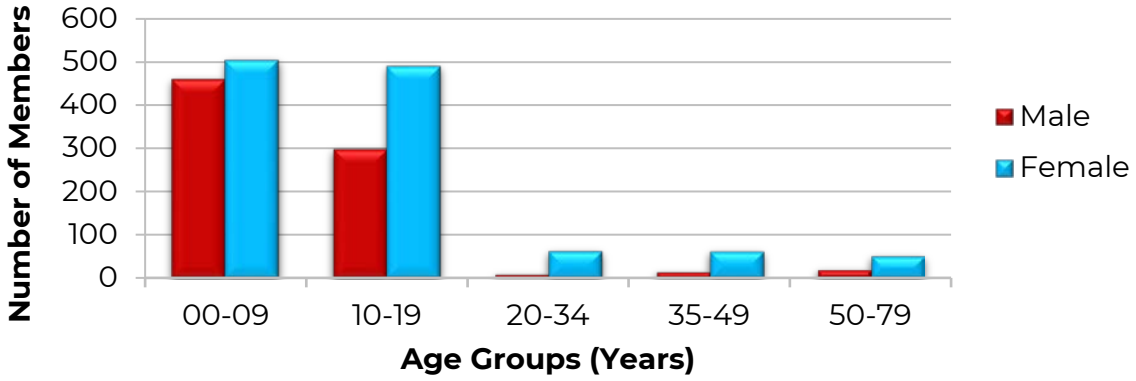
Utilization of AD Medications: Fiscal Year 2020

Comparison of Fiscal Years

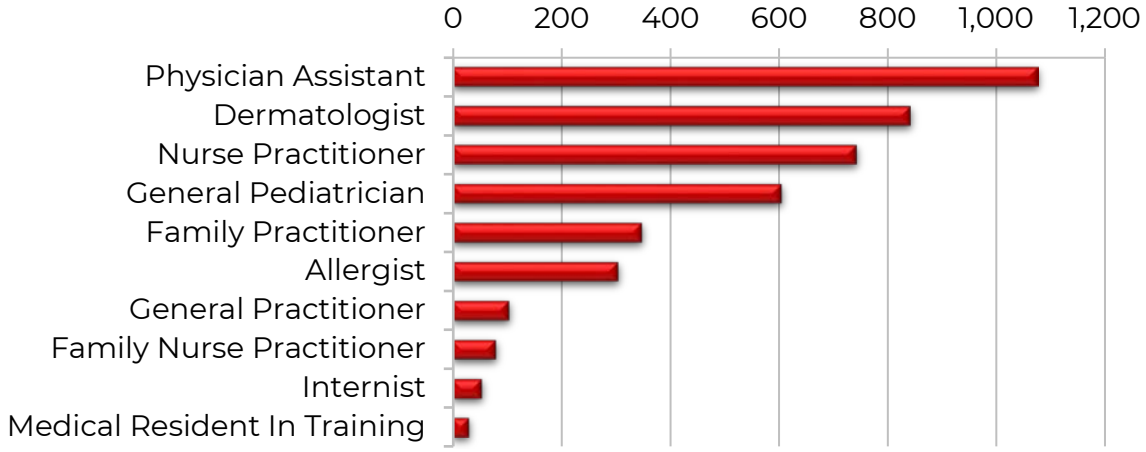
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	2,872	4,717	$3,377,452.25	$716.02	$23.49	248,484	143,802
2020	1,972	4,244	$4,202,201.62	$990.15	$33.10	190,990	126,955
% Change	**-31.30%**	**-10.00%**	**24.40%**	**38.30%**	**40.90%**	**-23.10%**	**-11.70%**
Change	**-900**	**-473**	**$824,749.37**	**$274.13**	**$9.61**	**-57,494**	**-16,847**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing AD Medications

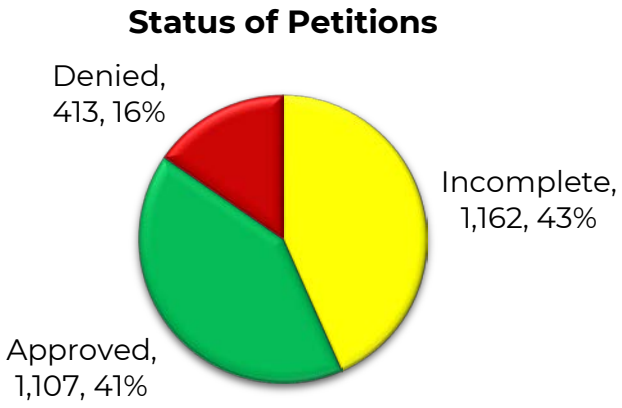


Top Prescriber Specialties of AD Medications by Number of Claims



Prior Authorization of AD Medications

There were 2,682 prior authorization requests submitted for 1,356 unique members for AD medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25]

Anticipated Patent Expiration(s):

- Eucrisa® (crisaborole): July 2030

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

- **March 2020:** The FDA approved Pfizer's supplemental New Drug Application (sNDA) for Eucrisa® (crisaborole) in March 2020, allowing for an expanded age range for the treatment of mild-to-moderate AD in patients 3 months of age and older. Previously, Eucrisa® was FDA approved for use in patients 2 years of age and older. With this approval, Eucrisa® is the only non-corticosteroid topical prescription medication for this indication for use in patients as young as 3 months of age. Support for this expanded age range came from data from the Phase 4 CrisADe CARE 1 study, an open-label, clinical study designed to assess safety in patients 3 months of age to younger than 24 months of age. A total of 137 pediatric patients within this age range were enrolled in the study which also assessed effectiveness as an exploratory endpoint. The results of the study showed Eucrisa® was well-tolerated and demonstrated effectiveness for patients in this age range, with no new safety signals identified.
- **May 2020:** The FDA approved Dupixent® (dupilumab) in May 2020 for an expanded age range of 6 to 11 years of age for the treatment of children with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Previously, Dupixent® had been approved for this indication in children 12 years of age and older. Dupixent® is the only biologic medication approved for this patient population. The approval was based on data from a Phase 3 study in children with severe AD evaluating Dupixent® in combination with topical corticosteroids (TCS) compared with TCS alone. Results of the study at 16 weeks showed an 84% improvement in average Eczema Area and Severity Index (EASI) from baseline in the patients treated with TCS + Dupixent® every 4

weeks and an 80% improvement in patients treated with TCS + Dupixent® every 2 weeks, compared to 49% and 48% for TCS alone, respectively. The safety profile in this population was similar to what has been observed in adults and adolescents with AD. Sanofi and Regeneron are also currently conducting Phase 2/3 studies of Dupixent® in pediatric patients with AD from 6 months to 5 years of age.

- **June 2020:** In June 2020, the FDA approved a new 300mg single-dose pre-filled pen formulation of Dupixent® (dupilumab) for use in patients 12 years of age and older for all Dupixent® indications for at-home administration. Features of the pre-filled pen include a hidden needle and single-press auto-injection, with visual and audio feedback to assist in the administration process. The current pre-filled syringe formulation is available in 200mg and 300mg strengths for use in clinics or for self-administration at home. The syringe and pen formulations both require training by a health care professional prior to self-administration. The 300mg pre-filled pen is expected to be available in the 3rd quarter of 2020. In addition, the FDA is currently reviewing data for a 200mg pre-filled pen.

News:

- **November 2019:** The results of a study evaluating fracture risk in adult patients with AD were published in *The Journal of Allergy and Clinical Immunology* in November 2019. The study was a population-based cohort study conducted in the United Kingdom from January 1998 through March 2016 using anonymized electronic medical records. A total of 526,808 individuals with AD and 2,569,030 individuals without AD were identified and included in the analysis. Individuals with AD were matched with up to 5 individuals without AD according to age, sex, general practice, and date of cohort entry. In addition, hazard ratios (HR) were adjusted for possible covariates and confounders including the quintile of the Index of Multiple Deprivation (IMD; a proxy for socioeconomic deprivation), asthma, body mass index (BMI), smoking status, harmful alcohol use, and oral glucocorticoid use. Median follow-up was 5 years for individuals with AD and 4.4 years for individuals without AD. The results showed a statistically significant increased risk of fractures for individuals with AD compared to those individuals without AD, with a HR of 1.07 in the fully-adjusted model [99% confidence interval (CI): 1.05, 1.09], and the highest risk was seen for spinal fractures in patients with AD (HR: 1.14; 99% CI: 1.06, 1.23). The study also evaluated whether or not the risk of fractures varied with the severity of AD and found evidence that the risk of fractures did increase as AD severity increased. In the fully adjusted model, the risk of spinal fractures was increased 2% in mild AD, 18% in moderate AD, and 98% in

severe AD compared to individuals without AD. This is the largest study to date to evaluate the risk of fractures with AD. Because AD is a common condition and fractures are associated with increases in morbidity and mortality, a potential association between AD and increased fracture risk is of significant concern. The biological mechanism linking AD with increased fractures has not been determined. The authors suggest additional research on this topic as well as the inclusion of AD in predictions of fracture risk and bone density screening guidelines, particularly for people with severe AD.

- **November 2019:** The Skin Infection Group of the International Eczema Council published "The Role of Bacterial Skin Infections in Atopic Dermatitis: Expert Statement and Review from the International Eczema Council Skin Infection Group" in the *British Journal of Dermatology*. The article is a product of a newly-created task force to define the role of bacterial skin infections and their management in AD through expert consensus statements. The article reviews the current literature regarding clinical features of bacterial skin infections in AD, host factors related to bacterial infections in AD, and bacterial factors which affect colonization and virulence in AD. Patients with AD are at an increased risk of bacterial skin infections, most commonly from *Staphylococcus aureus,* which can lead to systemic infections such as sepsis, endocarditis, or bone and joint infections if not treated. However, common features of an AD flare are similar to signs of infection, including erythema, edema, papulation, oozing, and excoriation, making the diagnosis of infection challenging. In addition, *S. aureus* is known to commonly colonize unaffected AD skin, which limits the diagnostic utility of bacterial cultures. Currently, there are no validated diagnostic criteria for skin infections in AD. A Cochrane review published in 2010 found no evidence to support routine use of topical or systemic antibacterial medications in non-infected AD. However, another study demonstrated a significant clinical benefit of antibiotic therapy for patients with infected AD lesions with a *S. aureus* density $>10^6$ colony-forming units per cm^2, suggesting the density of the bacteria may be more relevant than merely its presence or absence. The International Eczema Council plans to continue releasing expert consensus statements with the goal of providing guidance on the practical use of antimicrobials in AD.

Pipeline:

- **Abrocitinib:** Pfizer is conducting Phase 3 studies of abrocitinib, an investigational, small molecule Janus Kinase 1 (JAK1) inhibitor for the treatment of AD. Abrocitinib is thought to modulate several important cytokines in AD pathophysiology, including interleukin (IL)-4, IL-13, IL-31, and IL-22. In June 2020, Pfizer announced positive top-line results from

the JADE TEEN study in 285 patients 12 years to younger than 18 years of age with moderate-to-severe AD who were also on background topical therapy. At week 12, both strengths of abrocitinib (100mg or 200mg) demonstrated statistical significance compared to placebo for the 2 co-primary endpoints. The co-primary endpoints included a change from baseline in the Investigator's Global Assessment (IGA) score of 0 or 1 plus a reduction from baseline of at least 2 points and a change from baseline in the Eczema Area and Severity Index of >75% (EASI-75) improvement. Pfizer plans to release additional data from other studies in the JADE program later in 2020.

- **Baricitinib:** Phase 3 studies of baricitinib for the treatment of AD are currently being conducted. Baricitinib is an oral JAK1 and JAK2 inhibitor currently FDA approved for the treatment of rheumatoid arthritis (RA) under the brand name Olumiant®. In January 2020, Lilly and Incyte announced top-line results from the BREEZE-AD5 study evaluating baricitinib in adult patients with moderate-to-severe AD. The 2mg dose of baricitinib met the study's primary endpoint, demonstrating at least a 75% or greater change from baseline in EASI at week 16. Lilly plans to submit for FDA approval in 2020. If approved, baricitinib would become the first oral JAK inhibitor approved for the treatment of AD.
- **Bermekimab:** In November 2019, XBiotech announced the first patient had been enrolled into the Phase 2 placebo-controlled clinical study evaluating bermekimab for the treatment of moderate-to-severe AD. Bermekimab is an anti-IL-1α monoclonal antibody currently in Phase 2 development for AD and hidradenitis suppurativa. The study was designed to compare weekly and bi-weekly doses of bermekimab against placebo over 16 weeks of treatment. The primary outcome is a 75% or greater reduction in skin disease at week 16, as measured by EASI. In December 2019, it was announced Janssen Pharmaceutical Companies of Johnson and Johnson completed the acquisition of all rights to bermekimab from XBiotech for $750 million. Janssen will continue with the development of bermekimab.
- **Delgocitinib:** In August 2020, LEO Pharma announced the FDA had granted Fast Track designation to topical delgocitinib cream for the treatment of adults with moderate-to-severe chronic hand eczema. Delgocitinib is topical pan-JAK inhibitor. Two Phase 2b studies were recently completed which investigated the efficacy and safety of delgocitinib applied topically twice daily for chronic hand eczema and AD. Currently, no treatment options have been specifically approved for chronic hand eczema, which is a potentially disabling skin disease that can impair the ability to work and be self-sufficient. LEO Pharma plans to submit the results of the Phase 2b studies for publication later in 2020.

- **KY1005:** Kymab is developing KY1005, a human monoclonal antibody targeting OX40L, a key regulator of the immune system. Kymab believes KY1005 can help rebalance the immune system by blocking inappropriate activation and proliferation of pro-inflammatory effector T cells while also promoting expansion of anti-inflammatory regulatory T cells, without broad suppression of the immune system. In August 2020, Kymab announced positive results from the Phase 2a study of KY1005 in moderate-to-severe AD. The study compared low dose and high dose KY1005 against placebo and was administered every 28 days for 12 weeks in patients inadequately controlled by TCS. KY1005 met both of the primary endpoints, which consisted of change in EASI from baseline and the incidence of treatment emergent adverse events (TEAE) from baseline to week 16. With these primary endpoints met, KY1005 demonstrated clinically meaningful improvement in disease activity compared to placebo as well as safety and an acceptable adverse event and tolerability profile.
- **Lebrikizumab:** In December 2019, the FDA granted Fast Track designation to lebrikizumab for the treatment of moderate-to-severe AD. Lebrikizumab is an investigational monoclonal antibody designed to bind IL-13 with high affinity, resulting in inhibition of signaling pathways thought to be responsible for multiple aspects of the pathophysiology of AD, including skin barrier dysfunction, itching, skin thickening, and infection. In June 2020, Lilly and Dermira announced positive results from a Phase 2b study of lebrikizumab in patients with moderate-to-severe AD, suggesting the drug led to rapid and clinically meaningful improvement in itch, sleep, and overall quality of life. Phase 3 studies of lebrikizumab are currently underway. Approximately 800 adult and adolescent patients 12 years of age and older are expected to be enrolled in the Phase 3 studies, which will evaluate the efficacy and safety of lebrikizumab as monotherapy for moderate-to-severe AD. In addition, a Phase 3 study evaluating lebrikizumab in combination with TCS is planned. Topline results from the Phase 3 studies are expected in the first half of 2021.
- **Nemolizumab:** Maruho and Galderma are currently conducting Phase 3 studies of nemolizumab for the treatment of AD. Nemolizumab is a humanized monoclonal antibody which targets IL-31, a cytokine which is thought play a role in the development of pruritus experienced by individuals with AD. In July 2020, Maruho announced nemolizumab had achieved its primary endpoint of change from baseline pruritus visual analogue scale (VAS) at 16 weeks compared to placebo. The results of this Phase 3 study were published in *The New England Journal of Medicine*. The study enrolled a total of 215 Japanese patients randomized in a 2:1 ratio to receive subcutaneous nemolizumab or placebo. Participants were required to be at least 13 years of age with

an inadequate pruritic response to medium-potency TCS or topical calcineurin inhibitors administered at a stable dose for at least 4 weeks and to oral antihistamines for at least 2 weeks, or be unable to receive such therapies. At week 16, the percent change in pruritus VAS was -42.8% in the nemolizumab group and -21.4% in the placebo group, a statistically significant difference in favor of nemolizumab. This study did not assess the safety or efficacy of nemolizumab beyond 16 weeks of treatment. In August 2020, Galderma announced patient recruitment had started for the ARCADIA studies, which will be a series of 3 Phase 3 studies evaluating nemolizumab for the treatment of moderate-to-severe AD not adequately controlled by topical treatments in adult and adolescent patients 12 years of age and older. They plan to enroll up to 1,500 patients from approximately 300 centers in Europe, North America, and Asia.

- **Ruxolitinib:** Ruxolitinib in an investigational topical cream formulation is currently being evaluated in Phase 3 studies for the treatment of mild-to-moderate AD. In April 2020, Incyte announced the first data from the Phase 3 TRuE-AD program comprising 2 studies of 0.75% and 1.5% ruxolitinib cream administered twice daily. In both studies, the primary endpoint was the proportion of patients achieving an (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-point improvement from baseline at week 8. The primary endpoint was met in both studies. Incyte plans to submit a New Drug Application (NDA) to the FDA for topical ruxolitinib for AD later in 2020. Ruxolitinib in an oral tablet formulation was previously approved by the FDA for the treatment of myelofibrosis, polycythemia vera, and steroid-refractory acute graft-versus-host disease and is marketed under the brand name Jakafi®.
- **Tradipitant:** Tradipitant is a neurokinin-1 receptor antagonist being evaluated for the treatment of pruritus in AD. In February 2020, Vanda Pharmaceuticals announced tradipitant failed to meet the primary endpoint of reduction of the Worst Itch-Numerical Rating Scale (WI-NRS) compared with placebo in the Phase 3 EPIONE study. Although the primary endpoint was not met, tradipitant did show improvement in WI-NRS when baseline disease severity and treatment were taken into account, with the largest improvement seen in patients with mild disease severity. Vanda plans to further evaluate tradipitant for the treatment of AD using additional data from the EPIONE study, and a second study, EPIONE 2, is still ongoing.
- **Tralokinumab:** In July 2020, LEO Pharma announced the FDA accepted their Biologics License Application (BLA) for tralokinumab for the treatment of adults with moderate-to-severe AD. Tralokinumab, a fully human monoclonal antibody, binds to IL-13 and inhibits downstream signaling associated with AD. The BLA includes data from the Phase 3 ECZTRA 1-3 studies evaluating the safety and efficacy of the

drug in adults with moderate-to-severe AD. Two of the 3 studies assessed tralokinumab as monotherapy for 52 weeks, and 1 study assessed tralokinumab in combination with TCS for 32 weeks. The primary endpoint in all 3 studies was an IGA score of 0 (clear) or 1 (almost clear) at week 16 and a ≥75% change from baseline in the EASI score at week 16. The primary endpoint was met in all 3 studies with an overall safety profile that was comparable to placebo. The Prescription Drug User Fee Act (PDUFA) action date has been set for the second quarter of 2021.

- **Upadacitinib:** AbbVie is currently conducting Phase 3 studies evaluating upadacitinib for the treatment of AD. Upadacitinib is a once-daily, oral, selective JAK1 inhibitor. In July 2020, AbbVie announced upadacitinib monotherapy met both primary and all secondary endpoints in the Phase 3 Measure Up 2 study in patients with moderate-to-severe AD. Co-primary endpoints were EASI-75 and a validated IGA score of 0 (clear) or 1 (almost clear) at week 16. The EASI-75 endpoint was achieved in 60% of patients taking upadacitinib 15mg and 73% of patients taking upadacitinib 30mg, compared with 13% of patients in the placebo group. This was a statistically significant difference compared with placebo for participants taking either strength of upadacitinib. AbbVie plans to submit the full results from the Measure Up 2 study for publication in a peer-reviewed journal. Upadacitinib was previously approved by the FDA for the treatment of moderately-to-severely active RA in patients who have had an inadequate response or intolerance to methotrexate and is marketed under the brand name Rinvoq®.

Recommendations

The College of Pharmacy recommends updating the approval criteria for Eucrisa® (crisaborole) and Dupixent® (dupilumab injection) for atopic dermatitis diagnosis based on the FDA approved age expansions, with the following changes shown in red:

Eucrisa® (Crisaborole Ointment) Approval Criteria:

1. An FDA approved indication for treatment of mild-to-moderate atopic dermatitis (eczema); and
2. Member must be at least ~~2 years~~ 3 months of age or older; and
3. Member must have a documented trial within the last 6 months for a minimum of 2 weeks that resulted in failure with a topical corticosteroid (or have a contraindication or documented intolerance); and
4. A quantity limit of 1 tube per 30 days will apply; and

5. Initial approvals will be for the duration of 1 month. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
6. Clinical exceptions for children not meeting the age restriction for Eucrisa® (crisaborole ointment):
    a. Documented adverse effect, drug interaction, or contraindication to topical corticosteroids; or
    b. Atopic dermatitis of the face or groin where prescriber does not want to use topical corticosteroids; or
    c. Prescribed by a dermatologist.

Dupixent® (Dupilumab Injection) Approval Criteria [Atopic Dermatitis Diagnosis]:

1. An FDA approved diagnosis of moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
    a. 1 medium potency to very-high potency Tier-1 topical corticosteroid; and
    b. 1 topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. Dupixent® must be prescribed by a dermatologist, allergist, or immunologist or the member must have been evaluated by a dermatologist, allergist, or immunologist within the last 12 months (or an advanced care practitioner with a supervising physician who is a dermatologist, allergist, or immunologist); and
5. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use (Dupixent® has not been studied in combination with other biologic therapies); and
6. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Utilization Details of AD Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
EUCRISA OINT 2%	2,001	1,029	$1,228,574.30	$613.98	1.94	29.24%
DUPIXENT INJ 300MG/2ML	608	84	$1,827,571.56	$3,005.87	7.24	43.49%
PIMECROLIMUS CREAM 1%	602	427	$166,623.92	$276.78	1.41	3.97%
TACROLIMUS OINT 0.03%	518	347	$90,318.59	$174.36	1.49	2.15%
DUPIXENT INJ 200MG/1.14ML	274	37	$838,504.34	$3,060.23	7.41	19.95%
TACROLIMUS OINT 0.1%	239	173	$49,685.55	$207.89	1.38	1.18%
DOXEPIN HCL CREAM 5%	1	1	$376.49	$376.49	1	0.01%
PROTOPIC OINT 0.03%	1	1	$546.87	$546.87	1	0.01%
TOTAL	**4,244**	**1,972***	**$4,202,201.62**	**$990.15**	**2.15**	**100%**

INJ = injection; OINT = ointment; HCL = hydrochloride
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
Utilization data includes Dupixent® used for all diagnoses and does not differentiate between AD diagnoses and other diagnoses, for which use may be appropriate.

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Appendix N

Fiscal Year 2020 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

Oklahoma Health Care Authority
November 2020

Current Prior Authorization Criteria

Aggrenox® (Aspirin/Dipyridamole Extended-Release) Approval Criteria:

1. An FDA approved indication for the prophylaxis of recurrent thromboembolic stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use immediate-release dipyridamole and over-the-counter (OTC) aspirin in place of Aggrenox® must be provided; and
4. A quantity limit of 60 capsules per 30 days will apply.

Bevyxxa® (Betrixaban) Approval Criteria:

1. An FDA approved indication for the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE; and
2. If the member started on the medication in the hospital, the number of days of treatment with betrixaban in the hospital must be provided; and
3. Approvals will be for a maximum duration of 42 days (including use accounted for while in the hospital); and
4. A quantity limit of 43 capsules per 42 days will apply.

Brilinta® (Ticagrelor) Approval Criteria:

1. The first 365 days of therapy with Brilinta® 90mg twice daily does not require prior authorization; and
2. After the first 365 days, a patient-specific, clinically significant reason for continuing the 90mg twice daily dosage must be provided, or the member should be switched to the 60mg twice daily dosage; and
3. Approvals will be for the duration of 1 year.

Eliquis® (Apixaban) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Non-valvular atrial fibrillation; or

b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and PE following initial therapy; or
c. PE or DVT prophylaxis in members who have had hip or knee replacement surgery.

Pradaxa® (Dabigatran) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Non-valvular atrial fibrillation; or
   b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with a parenteral anticoagulant for 5 to 10 days; or
   c. To reduce the risk of recurrent DVT or PE in members who have been previously treated; or
   d. For the prophylaxis of DVT or PE in members who have undergone hip replacement surgery.

Savaysa® (Edoxaban) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. To reduce the risk of stroke and systemic embolism (SE) in members with non-valvular atrial fibrillation; or
   b. For the treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant; and
2. For the treatment of DVT or PE, the prescriber must verify that the member has undergone 5 to 10 days of initial therapy with a parenteral anticoagulant; and
3. For the diagnosis of non-valvular atrial fibrillation, the member must not have a creatinine clearance (CrCl) >95mL/min due to an increased risk of ischemic stroke compared to warfarin at the highest dose studied (60mg); and
4. A quantity limit of 30 tablets per 30 days will apply.

Xarelto® (Rivaroxaban) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Non-valvular atrial fibrillation; or
   b. Treatment of deep vein thrombosis (DVT), pulmonary embolism, or to reduce the risk of recurrent DVT and PE; or
   c. Prophylaxis of DVT, which may lead to PE in members undergoing knee or hip replacement surgery; or
   d. In combination with aspirin, to reduce the risk of major cardiovascular events [cardiovascular (CV) death, myocardial infarction (MI), and stroke] in members with chronic coronary artery disease (CAD) or peripheral artery disease (PAD); or

e. Prophylaxis of venous thromboembolism (VTE) in acutely ill medical members at risk for thromboembolic complications not at high risk of bleeding; and

2. For Xarelto® (rivaroxaban) 15mg and 20mg:
   a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. For Xarelto® (rivaroxaban) 10mg:
   a. 1 prescription for up to 39 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis in members following hip or knee replacement surgery or for prophylaxis of VTE in acutely ill medical members at risk for thromboembolic complications not at high risk of bleeding; or
4. For Xarelto® (rivaroxaban) 2.5mg:
   a. Must be used in combination with aspirin 75 to 100mg to reduce the risk of major CV events in members with chronic CAD or PAD.

Zontivity® (Vorapaxar) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. History of myocardial infarction (MI); or
   b. Peripheral arterial disease (PAD); and
2. Zontivity® must be used in combination with aspirin and/or clopidogrel (not monotherapy); and
3. Zontivity® will not be approved for members with the following conditions:
   a. History of transient ischemic attack (TIA); or
   b. Stroke; or
   c. Intracranial hemorrhage (ICH); or
   d. Active pathological bleeding; and
4. A quantity limit of 30 tablets per 30 days will apply.

Utilization of Anticoagulants and Platelet Aggregation Inhibitors: Fiscal Year 2020

Comparison of Fiscal Years: Anticoagulants

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	2,498	13,878	$3,627,155.66	$261.36	$8.15	636,297	444,785
2020	2,662	15,599	$4,864,611.30	$311.85	$9.57	761,447	508,445
% Change	**6.60%**	**12.40%**	**34.10%**	**19.30%**	**17.40%**	**19.70%**	**14.30%**
Change	**164**	**1,721**	**$1,237,455.64**	**$50.49**	**$1.42**	**125,150**	**63,660**

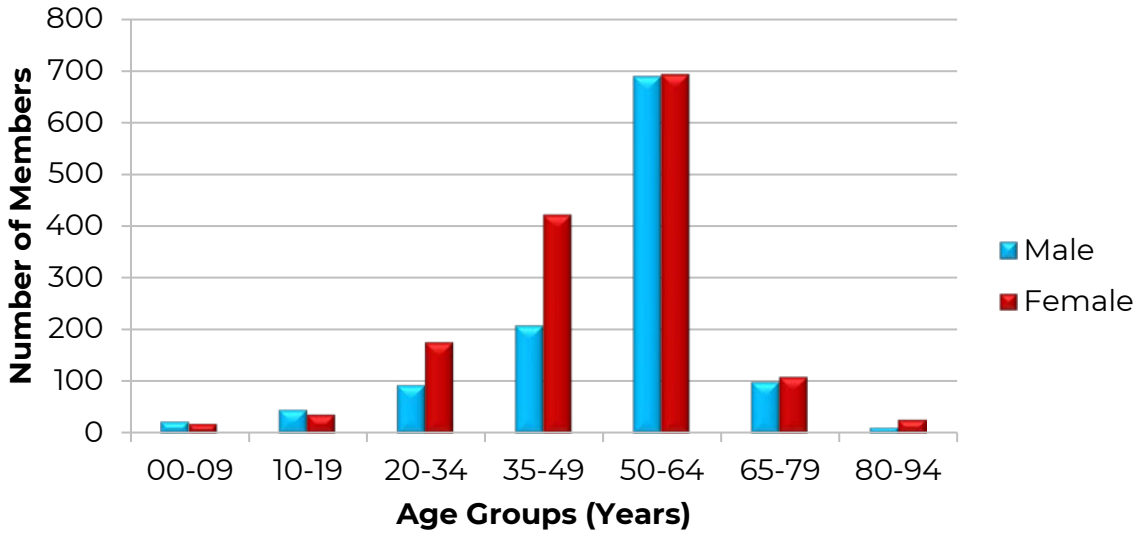
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Comparison of Fiscal Years: Platelet Aggregation Inhibitors

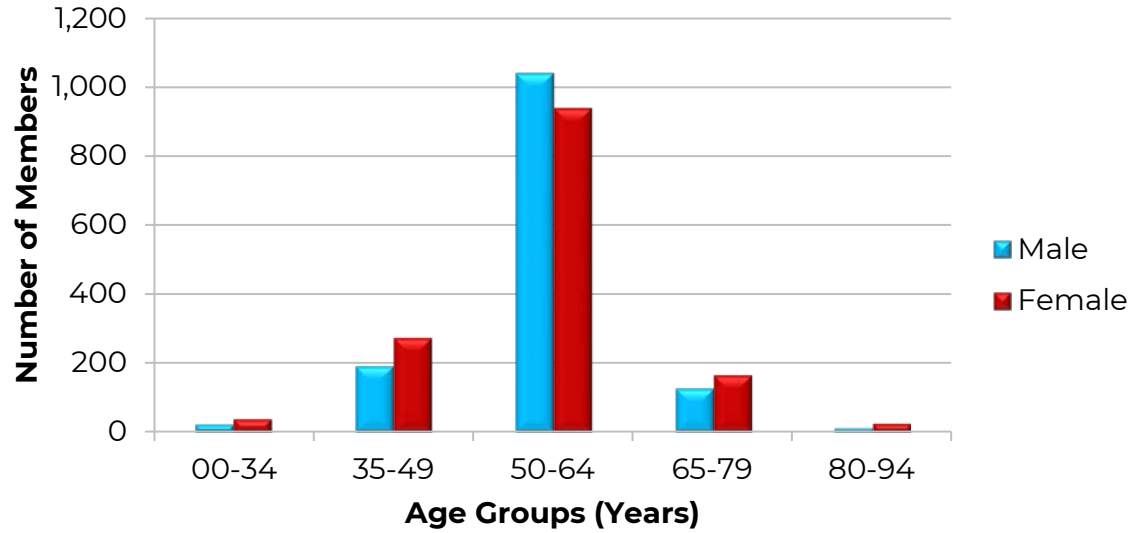
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	2,856	11,850	$654,255.90	$55.21	$1.18	597,649	554,134
2020	2,844	11,583	$724,878.85	$62.58	$1.28	615,128	567,382
% Change	**-0.40%**	**-2.30%**	**10.80%**	**13.30%**	**8.50%**	**2.90%**	**2.40%**
Change	**-12**	**-267**	**$70,622.95**	**$7.37**	**$0.10**	**17,479**	**13,248**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

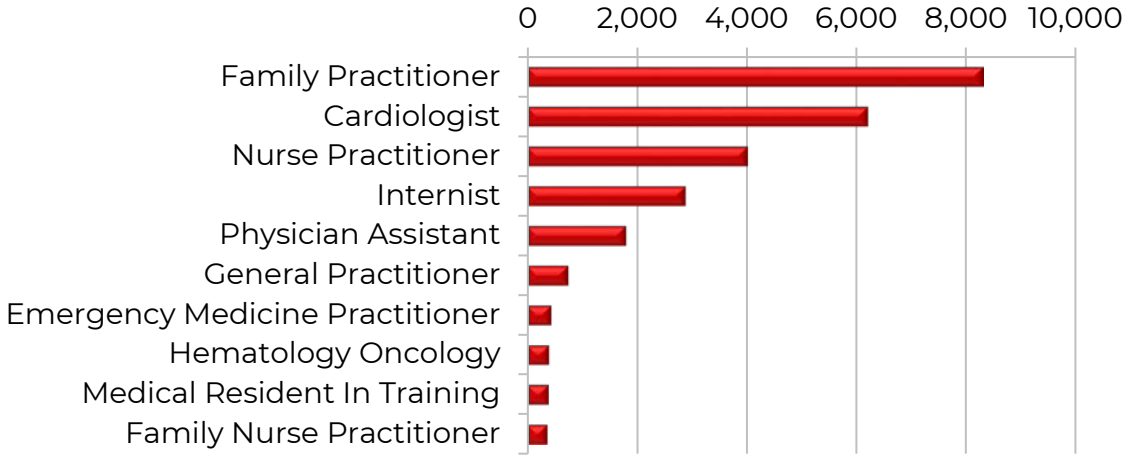
Demographics of Members Utilizing Anticoagulants



Demographics of Members Utilizing Platelet Aggregation Inhibitors



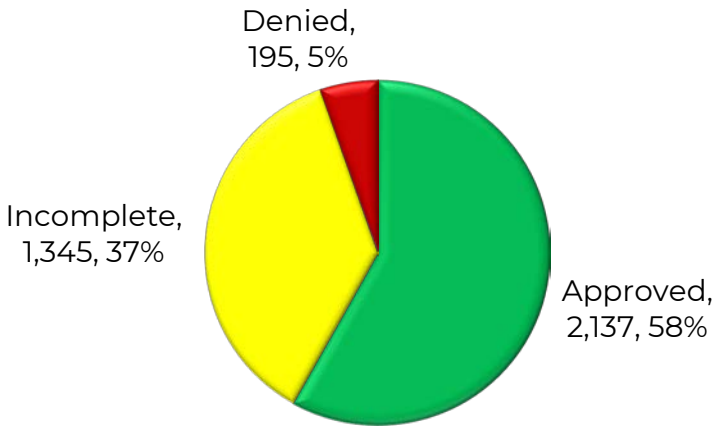
Top Prescriber Specialties of Anticoagulants and Platelet Aggregation Inhibitors by Number of Claims



Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

There were 3,677 prior authorization requests submitted for anticoagulants and platelet aggregation inhibitors during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Zontivity® (vorapaxar): May 2024
- Savaysa® (edoxaban): March 2028
- Pradaxa® (dabigatran): January 2031
- Eliquis® (apixaban): February 2031
- Bevyxxa® (betrixaban): March 2031
- Xarelto® (rivaroxaban): November 2034
- Brilinta® (ticagrelor): January 2036

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

- **June 2020:** Brilinta® (ticagrelor) has been approved by the FDA to reduce the risk of a first heart attack or stroke in high risk patients with coronary artery disease (CAD). This indication expansion was largely based on results from the Phase 3 THEMIS study. Results showed a statistically significant reduction in the primary composite endpoint of major adverse cardiovascular (CV) events at 36 months with aspirin plus Brilinta® 60mg versus aspirin alone in patients with CAD and type 2 diabetes (T2D) at high risk of a first heart attack or stroke. The THEMIS study showed a relative risk reduction of the composite endpoint of heart attack, stroke, and CV death by 10% (absolute risk reduction: 0.8%; 7.7% vs. 8.5%) with aspirin plus long-term Brilinta® compared to aspirin alone in patients who had CAD and T2D without a history of heart attack or stroke. The safety profile for Brilinta® was similar with the known profile of an increased risk of bleeding events.

News:

- **July 2020:** The THALES study showed the early treatment with Brilinta® (ticagrelor) 90mg and aspirin was better than aspirin alone for secondary prevention of acute ischemic strokes. The composite outcome of stroke or death in the 30 days after randomization in patients with mild-to-moderate acute ischemic stroke or transient ischemic attack (TIA) favored a 30-day regimen of ticagrelor plus aspirin over aspirin alone [5.5% vs. 6.6%; hazard ratio (HR): 0.83; 95% confidence interval (CI): 0.71, 0.96]. The dual antiplatelet group did experience more severe bleeding (0.5% vs. 0.1%; HR: 3.99; 95% CI: 1.74, 9.14) and more intracranial hemorrhage (0.4% vs. 0.1%; HR: 3.33; 95% CI: 1.34, 8.28) compared to the aspirin alone group. Researchers concluded the combination of ticagrelor with aspirin, when compared with aspirin alone, would result in number needed to treat of 92 to prevent 1 primary-outcome event and a number needed to harm of 263 for severe bleeding.

Guideline Update(s):

- **August 2020:** *The Journal of American College of Cardiology* released the "2020 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants" which endorsed Andexxa® [coagulation factor XI (recombinant), inactivated-zhzo] as a factor Xa (FXa) inhibitor reversal strategy. Andexanet alfa is the first reversal agent approved by the FDA to treat life-threatening bleeding in patients on apixaban and rivaroxaban. Andexanet alfa has a structure similar to endogenous FXa that binds FXa inhibitors, but is not enzymatically active. Efficacy was shown in the ANNEXA-4 study in

which 352 patients with major bleeding [primarily intracranial or gastrointestinal (GI)] had taken an FXa inhibitor within 18 hours. The study showed andexanet alfa decreased the median anti-FXa activity by 92% for both apixaban and rivaroxaban. In patients with rivaroxaban- or apixaban-associated critical site or life-threatening major bleeding, the guidelines recommend it is reasonable to use andexanet alfa for reversal (Class of Recommendation IIA; Level of Evidence B).

Pipeline:

- **Ciraparantag:** Ciraparantag is in clinical development as a reversal agent for various anticoagulants including non-vitamin K oral anticoagulants (NOACs). Two Phase 2 studies have been completed evaluating the safety and efficacy of ciraparantag in reversing anticoagulation induced by apixaban or rivaroxaban in healthy adults 50 to 75 years of age. Both studies were randomized, placebo-controlled, and dose-ranging with participants in the first study receiving apixaban 10mg orally twice daily for 3.5 days and participants in the second study receiving rivaroxaban 20mg orally once daily for 3 days. In both studies, participants were randomized 3:1 to receive a single intravenous (IV) dose of ciraparantag ranging from 30 to 180mg or placebo. Efficacy was based on whole blood clotting time (WBCT). Across both studies, preliminary data showed participants anticoagulated to ≥120% of baseline WBCT. Reversal to WBCT to ≤110% of baseline within 1 hour post-dose and sustained through 5 hours was observed in 83%, 100%, and 0% of participants receiving ciraparantag 60mg, 120mg, or placebo, respectively, in Study 1 and in 92%, 92%, 100%, and 0% in participants receiving ciraparantag 60mg, 120mg, 180mg, or placebo, respectively, in Study 2.

Recommendations

The College of Pharmacy does not recommend any changes to the current anticoagulants and platelet aggregation inhibitors prior authorization criteria at this time.

Utilization Details of Anticoagulants: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
WARFARIN PRODUCTS						
WARFARIN TAB 5MG	1,516	403	$17,278.21	$11.40	3.76	0.36%
WARFARIN TAB 1MG	606	159	$8,274.37	$13.65	3.81	0.17%
WARFARIN TAB 4MG	511	126	$6,382.09	$12.49	4.06	0.13%
WARFARIN TAB 3MG	394	114	$5,184.80	$13.16	3.46	0.11%
WARFARIN TAB 6MG	376	100	$4,964.43	$13.20	3.76	0.10%
WARFARIN TAB 2MG	371	110	$4,903.27	$13.22	3.37	0.10%
WARFARIN TAB 7.5MG	314	106	$3,696.81	$11.77	2.96	0.08%
WARFARIN TAB 2.5MG	257	80	$3,266.18	$12.71	3.21	0.07%
WARFARIN TAB 10MG	247	78	$2,892.95	$11.71	3.17	0.06%
JANTOVEN TAB 1MG	31	5	$457.94	$14.77	6.2	0.01%
JANTOVEN TAB 5MG	30	8	$413.93	$13.80	3.75	0.01%
COUMADIN TAB 5MG	25	6	$3,043.00	$121.72	4.17	0.06%
JANTOVEN TAB 2MG	24	4	$370.60	$15.44	6	0.01%
JANTOVEN TAB 3MG	13	2	$217.48	$16.73	6.5	0.00%
JANTOVEN TAB 2.5MG	12	2	$169.24	$14.10	6	0.00%
JANTOVEN TAB 4MG	12	2	$115.52	$9.63	6	0.00%
COUMADIN TAB 1MG	8	3	$1,762.84	$220.36	2.67	0.04%
COUMADIN TAB 2.5MG	7	2	$558.11	$79.73	3.5	0.01%
COUMADIN TAB 6MG	4	1	$965.02	$241.26	4	0.02%
COUMADIN TAB 2MG	4	1	$443.06	$110.77	4	0.01%
COUMADIN TAB 3MG	2	2	$253.95	$126.98	1	0.01%
JANTOVEN TAB 6MG	1	1	$19.28	$19.28	1	0.00%
JANTOVEN TAB 7.5MG	1	1	$19.19	$19.19	1	0.00%
SUBTOTAL	**4,766**	**1,316**	**$65,652.33**	**$13.54**	**3.62**	**1.36%**
DABIGATRAN PRODUCTS						
PRADAXA CAP 150MG	118	20	$54,289.25	$460.08	5.9	1.12%
PRADAXA CAP 75MG	22	3	$9,408.13	$427.64	7.33	0.19%
PRADAXA CAP 110MG	5	1	$2,093.89	$418.78	5	0.04%
SUBTOTAL	**145**	**24**	**$65,791.27**	**$453.73**	**6.04**	**1.35%**
RIVAROXABAN PRODUCTS						
XARELTO TAB 20MG	2,621	423	$1,208,455.87	$461.07	6.2	24.84%
XARELTO TAB 10MG	408	138	$166,784.36	$408.79	2.96	3.43%
XARELTO TAB 15MG	288	66	$124,757.64	$433.19	4.36	2.56%
XARELTO TAB 2.5MG	154	33	$69,835.61	$453.48	4.67	1.44%
XARELTO STAR TAB	15	15	$11,334.48	$755.63	1	0.23%
SUBTOTAL	**3,486**	**675**	**$1,581,167.96**	**$453.58**	**5.16**	**32.50%**
APIXABAN PRODUCTS						
ELIQUIS TAB 5MG	6,373	1,203	$2,808,915.33	$440.75	5.3	57.74%
ELIQUIS TAB 2.5MG	797	154	$329,584.40	$413.53	5.18	6.78%
ELIQUIS ST P TAB 5MG	9	9	$5,022.47	$558.05	1	0.10%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SUBTOTAL	**7,179**	**1,366**	**$3,143,522.20**	**$437.88**	**5.26**	**64.62%**
EDOXABAN PRODUCTS						
SAVAYSA TAB 30MG	12	1	$4,457.99	$371.50	12	0.09%
SAVAYSA TAB 60MG	11	1	$4,019.55	$365.41	11	0.08%
SUBTOTAL	**23**	**2**	**$8,477.54**	**$368.59**	**6.67**	**3.40%**
TOTAL	**15,599**	**2,662***	**$4,854,611.30**	**$311.85**	**5.86**	**100%**

TAB = tablet; CAP = capsule; STAR = starter; ST P = starter pack
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Utilization Details of Platelet Aggregation Inhibitors: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CLOPIDOGREL PRODUCTS						
CLOPIDOGREL TAB 75MG	9,311	2,480	$110.906.54	$11.91	3.75	15.30%
SUBTOTAL	**9,311**	**2,480**	**$110,906.54**	**$11.91**	**3.75**	**15.30%**
PRASUGREL PRODUCTS						
PRASUGREL TAB 10MG	574	100	$12,098.24	$21.08	5.74	1.67%
PRASUGREL TAB 5MG	28	4	$687.22	$24.54	7.0	0.09%
SUBTOTAL	**602**	**104**	**$12,785.46**	**$21.24**	**5.79**	**1.76%**
TICAGRELOR PRODUCTS						
BRILINTA TAB 90MG	1,493	301	$538,762.86	$360.86	4.96	74.32%
BRILINTA TAB 60MG	154	30	$56,994.12	$370.09	5.13	7.86%
SUBTOTAL	**1,647**	**331**	**$595,756.98**	**$361.72**	**10.09**	**82.18%**
VORAPAXAR PRODUCTS						
ZONTIVITY TAB 2.08MG	12	1	$3,615.28	$301.27	12	0.50%
SUBTOTAL	**12**	**1**	**$3,615.28**	**$301.27**	**12**	**0.50%**
ASPIRIN/DIPYRIDAMOLE PRODUCTS						
ASA/DIPYRIDA CAP	11	1	$1,814.59	$164.96	11	0.25%
SUBTOTAL	**11**	**1**	**$1,814.59**	**$164.96**	**11**	**0.25%**
TOTAL	**11,583**	**2,844***	**$724,878.85**	**$62.58**	**4.07**	**100%**

TAB = tablet; CAP = capsule; ASA = aspirin; DIPYRIDA = dipyridamole
*Total number of unduplicated member
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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[4] Tomaselli GF, et al. 2020 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants. *J Am Coll Cardiol* 2020. doi: 10.1016/j.jacc.2020.04.053.
[5] Ansell J, Bakhru S, Villano S, et al. Efficacy and Safety of Ciraparantag in Reversing Apixaban and Rivaroxaban as Measured by Whole Blood Clotting Time in Healthy Adults [abstract]. *Res Pract Haemost* 2020; 4(1).

Appendix O

Fiscal Year 2020 Annual Review of Tepezza® (Teprotumumab-trbw)

Oklahoma Health Care Authority
November 2020

Introduction[1,2,3,4]

Thyroid eye disease (TED), also known as Graves' Orbitopathy, is a rare autoimmune disease where the muscles and fatty tissues behind the eyes become inflamed. This inflammation causes the eyes to be pushed forward and bulge outwards, causing a variety of issues that include eye pain, double vision, and difficulty closing the eyes.

The particular causes of TED are not fully understood. Orbital fibroblast activation is a key contributor to this disease, and fibroblast activation is presumed to occur secondary to stimulatory auto-antibodies [anti-thyroid stimulating hormone (TSH) receptor (anti-TSHR) and anti-insulin-like growth factor-1 (anti-IGF-1)]. Teprotumumab is a targeted inhibitor of the IGF-1 receptor (IGF-1R) that interrupts this autoimmune activity and decreases the inflammatory response.

Current Prior Authorization Criteria

Tepezza® (Teprotumumab-trbw) Approval Criteria:

1. An FDA approved indication for the treatment of thyroid eye disease in adult members 18 years of age and older; and
    a. Member must be experiencing eye symptoms related to thyroid eye disease; and
    b. Member must have thyroid blood levels in the normal range or must be undergoing active treatment working toward normal range; and
2. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
3. Female members of reproductive potential must be willing to use effective contraception prior to initiation, during treatment with Tepezza®, and for at least 6 months after the last dose of Tepezza®; and
4. Member must not have had prior surgical treatment for thyroid eye disease; and
    a. A prior authorization request with patient-specific information may be submitted for consideration of Tepezza® for members who have had prior surgical treatment for thyroid eye disease, including but not limited to patient-specific, clinically significant information

regarding the member's prior surgery and the need for Tepezza®; and

5. Medical supervision by an ophthalmologist in conjunction with an endocrinologist for the treatment of thyroid eye disease; and
   a. The name of the ophthalmologist and endocrinologist recommending treatment with Tepezza® must be provided on the prior authorization request; and
6. Tepezza® must be administered as an intravenous (IV) infusion at the recommended infusion rate per package labeling, with appropriate pre-medication(s) based on the member's risk of infusion reactions; and
7. Tepezza® must be administered by a health care professional. Prior authorization requests must indicate how Tepezza® will be administered; and
   a. Tepezza® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
   b. Tepezza® must be shipped via cold chain supply to the member's home and administered by a home health care provider and the member (or the member's caregiver) must be trained on the proper storage of Tepezza®; and
8. The member's current weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
9. Approvals will be for a maximum of 8 total infusions.

Utilization of Tepezza® (Teprotumumab-trbw): Fiscal Year 2020

Fiscal Year 2020 Utilization: Pharmacy Claims

Fiscal Year	Total Members*	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	1	3	$193,734.23	$64,578.08	$3,075.15	13	63

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
Please note: There was no SoonerCare utilization of Tepezza® (teprotumumab-trbw) during fiscal year 2019, as it was FDA approved during fiscal year 2020.

Demographics of Members Utilizing Tepezza® (Teprotumuab-trbw)

- There was 1 unique member utilizing Tepezza® (teprotumumab-trbw) during fiscal year 2020. However, due to the limited number of members utilizing Tepezza® (teprotumumab-trbw) during fiscal year 2020, detailed demographic information could not be provided.

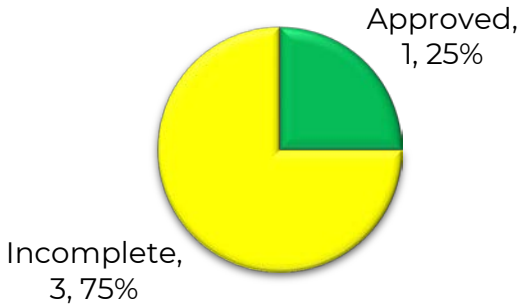
Top Prescriber Specialties of Tepezza® (Teprotumumab-trbw) by Number of Claims

- The only prescriber specialty listed on paid claims for Tepezza® (teprotumumab-trbw) during fiscal year 2020 was an ophthalmologist.

Prior Authorization of Tepezza® (Teprotumumab-trbw)

There were 4 prior authorization requests for 1 unique member submitted for Tepezza® (teprotumumab-trbw) during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[5,6]

Pipeline:

- **Tepezza® (Teprotumumab-trbw):** In July 2020, Horizon began recruiting patients for Phase 1 clinical trials to explore the use of Tepezza® (teprotumumab-trbw) for diffuse cutaneous systemic sclerosis (dcSSc). The Phase 1 trial was estimated to start in September 2020. Horizon also plans to initiate a Phase 1 clinical trial exploring the pharmacokinetic properties of Tepezza® (teprotumumab-trbw) via subcutaneous injection. Currently the medication is only available as an intravenous infusion.
- **IMVT-1401:** Immunovant's investigational product, IMVT-1401, is a fully monoclonal antibody targeting neonatal Fc receptor (FcRn). FcRn is responsible for preventing the degradation of IgG antibodies. TED is mediated by pathogenic IgG antibodies that target the TSH receptor (TSHR) and activate adipogenesis and hyaluronic acid production in orbital fibroblasts, leading to inflammation and tissue expansion in the extraocular space. IMVT-1401 enhances the degradation of IgG by preventing the binding of IgG to FcRn, thus decreasing the amount of pathogenic IgG antibodies targeting the TSHR.

Recommendations

The College of Pharmacy does not recommend any changes to the current Tepezza® (teprotumumab-trbw) prior authorization criteria at this time.

Utilization Details of Tepezza® (Teprotumumab-trbw): Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TEPEZZA INJ 500MG	3	1	$193,734.23	$64,578.08	3
TOTAL	**3**	**1***	**$193,734.23**	**$64,578.08**	**3**

INJ = injection
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

[1] McAlinden C. An Overview of Thyroid Eye Disease. *Eye Vis* 2014; 1:9. doi: 10.1186/s40662-014-0009-8.
[2] U.S. Food and Drug Administration (FDA). FDA Approves First Treatment for Thyroid Eye Disease. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease. Issued 01/21/2020. Last accessed 09/28/2020.
[3] Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. *N Engl J Med* 2020; 382:341-352. doi: 10.1056/NEJMoa1910434.
[4] Tepezza® (Teprotumumab-trbw) Prescribing Information. Horizon Therapeutics. Available online at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Last revised 01/2020. Last accessed 09/28/2020.
[5] Horizon Therapeutics. Our Pipeline. Available online at: https://www.horizontherapeutics.com/our-pipeline/. Last revised 08/10/2020. Last accessed 09/28/2020.
[6] Immunovant. Pipeline. Available online at: https://immunovant.com/pipeline/. Last revised 11/09/2019. Last accessed 09/28/2020.

Appendix P

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: October 22, 2020

FDA Approves First Treatment for COVID-19

The FDA approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40kg for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a health care setting capable of providing acute care comparable to inpatient hospital care. Veklury is the first treatment for COVID-19 to receive FDA approval. The FDA granted this application Fast Track and Priority Review designations as well as a Material Threat Medical Countermeasure Priority Review Voucher.

This approval does not include the entire population that had been authorized to use Veklury under an Emergency Use Authorization (EUA) originally issued on May 1, 2020. In order to ensure continued access to the pediatric population previously covered under the EUA, the FDA revised the EUA for Veklury to authorize the drug's use for treatment of suspected or laboratory confirmed COVID-19 in hospitalized pediatric patients weighing 3.5kg to <40kg or hospitalized pediatric patients younger than 12 years of age weighing at least 3.5kg. Clinical trials assessing the safety and efficacy of Veklury in this pediatric patient population are ongoing.

The approval of Veklury was supported by the agency's analysis of data from 3 randomized, controlled clinical trials that included patients hospitalized with mild-to-severe COVID-19. There was 1 randomized, double-blind, placebo-controlled clinical trial (ACTT-1), conducted by the National Institute of Allergy and Infectious Diseases, that evaluated how long it took for patients to recover from COVID-19 within 29 days of being treated. The trial looked at 1,062 hospitalized patients with mild, moderate, and severe COVID-19 who received Veklury (N=541) or placebo (N=521), plus standard of care. The median time to recovery from COVID-19 was 10 days for the Veklury group compared to 15 days for the placebo group, a statistically significant difference. A second randomized, open-label multi-center clinical trial of hospitalized adult patients with moderate COVID-19 compared treatment with Veklury for 5 days (N=191) and treatment with Veklury for 10 days (N=193) with standard of care (N=200). Researchers evaluated the clinical status of patients on day 11. Overall, the odds of a patient's COVID-19 symptoms improving were statistically significantly higher in the 5-day Veklury group at day 11 when compared to those receiving only standard of care. A third separate, randomized, open-label multi-center clinical trial of hospitalized adult patients with severe COVID-19 compared treatment with Veklury for 5 days (N=200) and treatment with Veklury for 10 days (N=197). Researchers evaluated the clinical status of patients on day 14. Overall, the odds of a patient's COVID-19 symptoms improving were similar for those in the 5-day Veklury group as those in the 10-day Veklury group, and there were no statistically significant differences in recovery rates or mortality rates between the 2 groups.

Side effects that may occur with the use of Veklury include increased levels of liver enzymes and allergic reactions, which may include changes in blood pressure and heart

rate, low blood oxygen level, fever, shortness of breath, wheezing, swelling, rash, nausea, sweating, or shivering.

FDA NEWS RELEASE

For Immediate Release: October 15, 2020

FDA Warns that Using a Type of Pain and Fever Medication in Second Half of Pregnancy Could Lead to Complications

The FDA announced in a Drug Safety Communication that it is requiring labeling changes for nonsteroidal anti-inflammatory drugs (NSAIDs). These changes include new labeling explaining that taking NSAIDs around 20 weeks or later in pregnancy, can cause rare but serious kidney problems in the unborn baby, which can lead to low levels of amniotic fluid and the potential for pregnancy-related complications.

As noted in the Drug Safety Communication, the warning follows the FDA's review of the medical literature and cases reported to the agency about low amniotic fluid levels or kidney problems in unborn babies associated with NSAID use during pregnancy. After about 20 weeks of pregnancy, the unborn baby's kidneys begin producing most of the amniotic fluid, so fetal kidney problems can cause low levels of this fluid. Low levels of amniotic fluid may be detected after taking the medication for days or weeks, but it may be detected as soon as 2 days after initiation of regular NSAID use. This condition usually goes away if the pregnant woman stops taking the NSAID.

For prescription NSAIDs, the FDA is requiring changes to the *Prescribing Information* to describe the risk of kidney problems in unborn babies that result in low amniotic fluid and to recommend that NSAID use be limited between about 20 weeks to 30 weeks of pregnancy because of this risk. Warnings to avoid taking NSAIDs after about 30 weeks of pregnancy are already included in the *Prescribing Information* because taking these medications during this time may lead to heart issues in the unborn baby. If a health care provider believes NSAID use is necessary between about 20 and 30 weeks of pregnancy, use should be limited to the lowest effective dose and shortest duration possible. The manufacturers of over-the-counter (OTC) NSAIDs intended for adult use will also make similar updates to the *Drug Facts* labels. These recommendations do not apply to the use of low-dose aspirin (81 mg). Low-dose aspirin may be an important treatment for some women during pregnancy and should be taken under the direction of a health care professional.

Although certain health care providers treating pregnant women generally know about the risk of low levels of amniotic fluid, the FDA is communicating this information more broadly to educate other health care professionals and pregnant women.

FDA NEWS RELEASE

For Immediate Release: October 14, 2020

FDA Approves First Treatment for Ebola Virus

The FDA approved Inmazeb (atoltivimab/maftivimab/odesivimab-ebgn), a mixture of 3 monoclonal antibodies, as the first FDA-approved treatment for *Zaire ebolavirus* (Ebola virus) infection in adult and pediatric patients. The FDA granted Inmazeb Orphan Drug and Breakthrough Therapy designations for the treatment of *Zaire ebolavirus* infection.

Zaire ebolavirus, commonly known as Ebola virus, is 1 of 4 *Ebolavirus* species that can cause a potentially fatal human disease. Ebola virus is transmitted through direct contact with blood, body fluids, and tissues of infected people or wild animals, as well as with surfaces and materials, such as bedding and clothing, contaminated with these

fluids. Individuals who provide care for people with Ebola virus, including health care workers who do not use correct infection control precautions, are at the highest risk for infection. Inmazeb targets the glycoprotein that is on the surface of Ebola virus. Glycoprotein attaches to the cell receptor and fuses the viral and host cell membranes allowing the virus to enter the cell. The 3 antibodies that make up Inmazeb can bind to this glycoprotein simultaneously and block attachment and entry of the virus.

Inmazeb was evaluated in 382 adult and pediatric patients with confirmed *Zaire ebolavirus* infection in 1 clinical trial (the PALM trial) and as part of an expanded access program conducted in the Democratic Republic of the Congo (DRC) during an Ebola virus outbreak in 2018-2019. The PALM trial was led by the U.S. National Institutes of Health (NIH) and the DRC's Institut National de Recherche Biomédicale with contributions from several other international organizations and agencies. In the PALM trial, the safety and efficacy of Inmazeb was evaluated in a multi-center, open-label, randomized controlled trial, in which 154 patients received Inmazeb (50mg of each monoclonal antibody) intravenously (IV) as a single infusion, and 168 patients received an investigational control. The primary efficacy endpoint was 28-day mortality. The primary analysis population was all patients who were randomized and concurrently eligible to receive either Inmazeb or the investigational control during the same time period of the trial. Of the 154 patients who received Inmazeb, 33.8% died after 28 days, compared to 51% of the 153 patients who received a control. In the expanded access program, an additional 228 patients received Inmazeb.

The most common symptoms experienced while receiving Inmazeb included: fever, chills, tachycardia, tachypnea, and vomiting; however, these are also common symptoms of Ebola virus infection. Patients who receive Inmazeb should avoid the concurrent administration of a live vaccine due to the treatment's potential to inhibit replication of a live vaccine virus indicated for prevention of Ebola virus infection and possibly reduce the vaccine's efficacy.

FDA NEWS RELEASE

For Immediate Release: October 8, 2020

FDA Awards 6 Grants to Fund New Clinical Trials to Advance the Development of Medical Products for the Treatment of Rare Diseases

The FDA announced that it has awarded 6 new clinical trial research grants to principal investigators from academia and industry totaling over $16 million over the next 4 years. These trial research grants, awarded through the Congressionally-funded Orphan Products Grants Program, enhance the development of medical products for patients with rare diseases.

The FDA received 47 clinical trial grant applications that were reviewed and evaluated for scientific and technical merit by more than 90 rare disease and clinical trial experts, including members of academia. The grants awarded support clinical studies of products that address unmet needs in rare diseases or conditions, or provide highly significant improvements in treatment or diagnosis. Grant recipients include the following:

- Acucela, Inc. (Seattle, Washington), Phase 3 study of emixustat hydrochloride for the treatment of Stargardt disease ($1.6 million over 3 years).
- Fred Hutchinson Cancer Research Center (Seattle, Washington), Phase 2 study of ustekinumab for the prevention of graft versus host disease ($3.5 million over 4 years).

- Seattle Children's Hospital (Seattle, Washington), Phase 1b study of IV gallium nitrate for the treatment of cystic fibrosis patients colonized with nontuberculosis mycobacterium ($3 million over 4 years).
- State University of New York Stony Brook (Stony Brook, New York), Phase 1 study of CD4 redirected chimeric antigen receptor T cell therapy for the treatment of CD4 positive T-cell neoplasms ($3.1 million over 4 years).
- University of Cincinnati (Cincinnati, Ohio), Phase 1/2 study of ABTL0812 (a small molecule with anti-cancer activity) for the treatment of pancreatic cancer ($1.9 million over 4 years).
- University of Virginia (Charlottesville, Virginia), Phase 2 study of oral azacytidine plus romidepsin for the treatment of peripheral T-cell lymphoma ($3.2 million over 4 years).

FDA NEWS RELEASE

For Immediate Release: October 2, 2020

FDA Approves Drug Combination for Treating Mesothelioma

The FDA approved Opdivo (nivolumab) in combination with Yervoy (ipilimumab) for the first-line treatment of adults with malignant pleural mesothelioma (MPM) that cannot be removed by surgery. This is the first drug regimen approved for mesothelioma in 16 years and the second FDA-approved systemic therapy for mesothelioma.

About 20,000 Americans are diagnosed with MPM each year. MPM is a life-threatening cancer of the lungs' lining caused by inhaling asbestos fibers, and it accounts for most mesothelioma diagnoses. Most patients have an unresectable tumor at the time of diagnosis. With currently available therapy, overall survival is generally poor. Opdivo and Yervoy are both monoclonal antibodies that, when combined, decrease tumor growth by enhancing T-cell function.

This combination therapy was evaluated during a randomized, open-label trial in 605 patients with previously untreated, unresectable MPM. Patients received IV infusions of Opdivo every 2 weeks with IV infusions of Yervoy every 6 weeks for up to 2 years, or platinum-doublet chemotherapy for up to 6 cycles. Treatment continued until disease progression, unacceptable toxicity, or completion of 2 years. The objective was to determine if Opdivo in combination with Yervoy improved overall survival compared to chemotherapy. At the time of the analysis, patients who received Opdivo in combination with Yervoy survived a median of 18.1 months while patients who underwent chemotherapy survived a median of 14.1 months.

The most common side effects of Opdivo in combination with Yervoy in patients with MPM include: fatigue, musculoskeletal pain, rash, diarrhea, dyspnea, nausea, decreased appetite, cough, and pruritis. Yervoy can cause serious conditions known as immune-mediated side effects, including inflammation of healthy organs, such as pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis.

This review 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 (TGA), the Brazilian Health Regulatory Agency (ANVISA), Health Canada, and Switzerland's Swissmedic. The application reviews are ongoing at the other regulatory agencies. The FDA approval occurred approximately 5 months ahead of the goal date.

Current Drug Shortages Index (as of October 20, 2020):

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

Amifostine Injection	***Currently in Shortage***
Aminophylline Injection, USP	***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***
Avycaz® (ceftazidime and avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Azithromycin Tablets	***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 Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Chlorothiazide (Diuril®) Oral Suspension	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Diphenhydramine Injection	***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***

Doxycycline Hyclate Injection	***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 Lactobionate for Injection, USP	***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 Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***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***
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***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride 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***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***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***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***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***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan®) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sertraline Hydrochloride Oral Solution, USP	***Currently in Shortage***
Sertraline Hydrochloride Tablets	***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***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Timolol Maleate Ophthalmic Solution	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Tobramycin Lyophilized Powder for Injection	***Currently in Shortage***
Triamcinolone Acetonide (Triesence®) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***