OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
November 10, 2021
4:00pm

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

Viewing Access Only:
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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 10, 2021

DATE: November 3, 2021

NOTE: The DUR Board will meet at 4:00pm at the Oklahoma Health Care Authority (OHCA) at 4345 N. Lincoln Blvd. in Oklahoma City, Oklahoma.

There will be Zoom access to this meeting; however, Zoom access will be set up in view-only mode with no voting, speaking, video, or chat box privileges. Zoom access will allow for viewing of the presentation slides as well as audio of the presentations and discussion during the meeting; however, the DUR Board meeting will not be delayed or rescheduled due to any technical issues that may arise.

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

Call to Order

Public Comment Forum

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

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

Action Item – 2022 DUR Board Meeting Dates – Appendix C

Action Item – Vote to Prior Authorize Jakafi® (Ruxolitinib) and Rezurock™ (Belumosudil) – Appendix D

Action Item – Vote to Prior Authorize Bylvay™ (Odevixibat) – Appendix E

Action Item – Vote to Prior Authorize Lupkynis™ (Voclosporin) and Saphnelo™ (Anifrolumab-fnia) and Update the Approval Criteria for the Targeted Immunomodulator Agents – Appendix F

Action Item – Annual Review of Botulinum Toxins – Appendix G

Action Item – Annual Review of Asthma and Chronic Obstructive Pulmonary Disease (COPD) Maintenance Medications – Appendix H

Action Item – Annual Review of Carbaglu® (Carglumic Acid) – Appendix I

Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) – Appendix J

Annual Review of Lenvima® (Lenvatinib) and 30-Day Notice to Prior Authorize Jemperli® (Dostarlimab-gxly) – Appendix K

Annual Review of Atopic Dermatitis Medications and 30-Day Notice to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream) – Appendix L

Annual Review of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide) – Appendix M

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – November 10, 2021 @ 4:00pm
at the
Oklahoma Health Care Authority (OHCA)
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

NOTE: ***The DUR Board will meet at 4:00pm at OHCA (see address above). There will be Zoom access to this meeting; however, Zoom access will be set up in view-only mode with no voting, speaking, video, or chat box privileges. Zoom access will allow for viewing of the presentation slides as well as audio of the presentations and discussion during the meeting; however, the DUR Board meeting will not be delayed or rescheduled due to any technical issues that may arise.***

AGENDA

Discussion and action on the following items:

Items to be presented by Dr. Muchmore, Chairman:

1. **Call to Order**

A. Roll Call - Dr. Wilcox

DUR Board Members:

Dr. Stephen Anderson –	participating in person
Dr. Jennifer de los Angeles –	participating in person
Ms. Jennifer Boyett –	participating in person
Dr. Markita Broyles –	participating in person
Dr. Megan Hanner –	participating in person
Dr. Lynn Mitchell –	participating in person
Dr. John Muchmore –	participating in person
Dr. Lee Muñoz –	participating in person
Dr. James Osborne –	participating in person

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After registering, you will receive a confirmation email containing information about joining the webinar.

Or join by phone:
Dial: +1-602-753-0140 or +1-669-219-2599
Webinar ID: 995 8131 2722
Passcode: 71209450

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 the DUR Board page on the OHCA website at www.oklahoma.gov/ohca/about/boards-and-committees/drug-utilization-review/dur-board 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.
- Any speakers who sign up for public comment must attend the DUR Board meeting in person at OHCA (see above address). Public comment through Zoom will not be allowed for the DUR Board meeting.

Items to be presented by Dr. Muchmore, Chairman:

2. **Public Comment Forum**
   A. Acknowledgement of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

3. **Action Item – Approval of DUR Board Meeting Minutes – See Appendix A**
   A. October 13, 2021 DUR Board Meeting Minutes
   B. October 13, 2021 DUR Board Recommendations Memorandum
   C. Correspondence

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

4. **Update on Medication Coverage Authorization Unit/U.S. Food and Drug Administration (FDA) Safety Alerts – See Appendix B**
   A. Pharmacy Helpdesk Activity for October 2021
   B. Medication Coverage Activity for October 2021
   C. FDA Safety Alerts

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

5. **Action Item – 2022 DUR Board Meeting Dates – See Appendix C**

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

6. **Action Item – Vote to Prior Authorize Jakafi® (Ruxolitinib) and Rezurock™ (Belumosudil) – See Appendix D**
   A. Market News and Updates
   B. Jakafi® (Ruxolitinib) Product Summary
   C. Rezurock™ (Belumosudil) Product Summary
   D. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Bylvay™ (Odevixibat) – See Appendix E**
   A. Market News and Updates
   B. Bylvay™ (Odevixibat) Product Summary
   C. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Lupkynis™ (Voclosporin) and Saphnelo™ (Anifrolumab-fnia) and Update the Approval Criteria for the Targeted Immunomodulator Agents – See Appendix F**
   A. Market News and Updates
   B. Lupkynis™ (Voclosporin) Product Summary
   C. Saphnelo™ (Anifrolumab-fnia) Product Summary
   D. College of Pharmacy Recommendations

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

9. **Action Item – Annual Review of Botulinum Toxins – See Appendix G**
   A. Current Prior Authorization Criteria
   B. Utilization of Botulinum Toxins
   C. Prior Authorization of Botulinum Toxins
   D. Market News and Updates
   E. College of Pharmacy Recommendations
   F. Utilization Details of Botulinum Toxins

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

10. **Action Item – Annual Review of Asthma and Chronic Obstructive Pulmonary Disease (COPD) Maintenance Medications – See Appendix H**
    A. Current Prior Authorization Criteria
    B. Utilization of Asthma and COPD Maintenance Medications
    C. Prior Authorizations of Asthma and COPD Maintenance Medications
    D. Market News Updates
    E. Nucala (Mepolizumab) Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) Product Summary
    F. Xolair® (Omalizumab) Nasal Polyps Product Summary
    G. College of Pharmacy Recommendations
    H. Utilization Details of Asthma and COPD Maintenance Medications

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

11. **Action Item – Annual Review of Carbaglu® (Carglumic Acid) – See Appendix I**
    A. Current Prior Authorization Criteria
    B. Utilization of Carbaglu® (Carglumic Acid)
    C. Prior Authorization of Carbaglu® (Carglumic Acid)
    D. Market News and Updates

E. College of Pharmacy 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 Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) – See Appendix J

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Multiple Myeloma Medications
D. Prior Authorization of Multiple Myeloma Medications
E. Market News and Updates
F. Abecma® (Idecabtagene Vicleucel) Product Summary
G. Farydak® (Panobinostat) Product Summary
H. Pepaxto® (Melphalan Flufenamide) Product Summary
I. College of Pharmacy Recommendations
J. Utilization Details of Multiple Myeloma Medications

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

13. Annual Review of Lenvima® (Lenvatinib) and 30-Day Notice to Prior Authorize Jemperli® (Dostarlimab-gxly) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Lenvima® (Lenvatinib)
D. Prior Authorization of Lenvima® (Lenvatinib)
E. Market News and Updates
F. Jemperli® (Dostarlimab-gxly) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Lenvima® (Lenvatinib)

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

14. Annual Review of Atopic Dermatitis (AD) Medications and 30-Day Notice to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of AD Medications
C. Prior Authorization of AD Medications
D. Market News and Updates
E. Opzelura™ (Ruxolitinib 1.5% Cream) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of AD Medications

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

15. Annual Review of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide)

C. Prior Authorization of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide)
D. Market News and Updates
E. College of Pharmacy Recommendations

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

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

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

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

A. Anticoagulants and Platelet Aggregation Inhibitors
B. Antidepressants
C. Crohn's Disease and Ulcerative Colitis (UC) Medications
D. Skin Cancer Medications

*Future product and class reviews subject to change.

18. Adjournment

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

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING OCTOBER 13, 2021

DUR 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	
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	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	X	
Erin Ford, Pharm.D.; Clinical Pharmacist	X	
Beth Galloway; Business Analyst	X	
Thomas Ha, Pharm.D.; Clinical Pharmacist	X	
Katrina Harris, Pharm.D.; Clinical Pharmacist		X
Robert Klatt, Pharm.D.; Clinical Pharmacist		X
Morgan Masterson, Pharm.D; Clinical Pharmacist		X
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	X	
Alicia O'Halloran, Pharm.D.; Clinical Pharmacist		X
Wynn Phung, Pharm.D.; Clinical Pharmacist		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): Sarah El-Koubysi	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		X
Mark Brandenburg, M.D., MSC; Medical Director	X	
Ellen Buettner; Chief of Staff		X
Kevin Corbett, C.P.A.; Chief Executive Officer		X
Terry Cothran, D.Ph.; Pharmacy Director	X	

Michael Herndon, D.O.; Chief Medical Officer		X
Josh Holloway, J.D.; Deputy General Counsel	X	
Jill Ratterman, D.Ph.; Clinical Pharmacist	X	
Paula Root, M.D.; Senior Medical Director		X
Kara Smith, J.D.; General Counsel		X
Michelle Tahah, Pharm.D.; Clinical Pharmacist	X	
Toney Welborn, M.D., MPH, MS; Medical Director	X	

OTHERS PRESENT:	
Joe Garcia, AbbVie	Stacy Sandate, Albireo Pharma
Karen Evenson, Albireo Pharma	Nima Nabavi, Amgen
Cindi Pearson, Arkansas DHS	Lori Howarth, Bayer
Robert Greely, Biogen	Bob Atkins, Biogen
Maynard Friesz, CureSMA	Michael Dunn, Genentech
Meghan Moore, Genentech	Jimmy Dick, Genentech
Eardie Curry, Genentech	Doug Pierce, Genentech
Jennifer Davis, Gilead	Porsha Showers, Gilead
Frank Alvarado, Janssen	Kevin Hinthorne, Leo Pharma
Brent Parker, Merck	Evie Knisely, Novartis
Janelle Hardisty, Novartis	Lindsey Walter, Novartis
Ashok Vegesna, Novartis	David Prather, Novo Nordisk
Gina Heinen, Novo Nordisk	Mark Kaiser, Otsuka
Brian Maves, Pfizer	Jomy Joseph, Sanofi
Eric Berthelot, Sobi	Marc Parker, Sunovion
Melanie Curlett, Takeda	Raquel Jordan, Takeda
Dave Miley, Teva Pharm	Doug Wood, ViiV Healthcare
Burl Beasley, OMES	

PRESENT FOR PUBLIC COMMENT:	
Eardie Curry, Genentech	Robert Greely, Biogen
Stacy Sandate, Albireo Pharma	Evie Knisely, Novartis

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. 7 EARDIE CURRY
2B: AGENDA ITEM NO. 7 ROBERT GREELY
2C: AGENDA ITEM NO. 11 EVIE KNISELY
2D: AGENDA ITEM NO. 12 STACY SANDATE

ACTION: NONE REQUIRED

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

3A: SEPTEMBER 8, 2021 DUR MINUTES

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/FALL 2021 PIPELINE UPDATE**

4A: PHARMACY HELPDESK ACTIVITY FOR SEPTEMBER 2021
4B: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2021
4C: FALL 2021 PIPELINE UPDATE

Materials included in agenda packet; presented by Dr. Nawaz, Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE HERCEPTIN® (TRASTUZUMAB) AND MARGENZA® (MARGETUXIMAB-CMKB) AND UPDATE THE APPROVAL CRITERIA FOR THE BREAST CANCER MEDICATIONS**

5A: MARKET NEWS AND UPDATES
5B: MARGENZA® (MARGETUXIMAB-CMKB) PRODUCT SUMMARY
5C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders
Dr. Mitchell moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ORGOVYX™ (RELUGOLIX)**

6A: MARKET NEWS AND UPDATES
6B: ORGOVYX™ (RELUGOLIX) PRODUCT SUMMARY
6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders
Dr. Broyles moved to approve; seconded by Dr. Mitchell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF SPINAL MUSCULAR ATROPHY (SMA) MEDICATIONS**

7A: CURRENT PRIOR AUTHORIZATION CRITERIA
7B: UTILIZATION OF SMA MEDICATIONS
7C: PRIOR AUTHORIZATION OF SMA MEDICATIONS
7D: MARKET NEWS AND UPDATES
7E: COLLEGE OF PHARMACY RECOMMENDATIONS
7F: UTILIZATION DETAILS OF SMA MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Mitchell moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF HEPATITIS C MEDICATIONS**

8A: INTRODUCTION
8B: CURRENT PRIOR AUTHORIZATION CRITERIA
8C: UTILIZATION OF HEPATITIS C MEDICATIONS
8D: PRIOR AUTHORIZATION OF HEPATITIS C MEDICATIONS
8E: MARKET NEWS AND UPDATES
8F: COLLEGE OF PHARMACY RECOMMENDATIONS
8G: UTILIZATION DETAILS OF HEPATITIS C MEDICATIONS

Materials included in agenda packet; presented by Dr. Ford
Dr. Broyles moved to approve; seconded by Dr. Mitchell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF OVARIAN CANCER MEDICATIONS**

9A: INTRODUCTION

9B: CURRENT PRIOR AUTHORIZATION CRITERIA
9C: UTILIZATION OF OVARIAN CANCER MEDICATIONS
9D: PRIOR AUTHORIZATION OF OVARIAN CANCER MEDICATIONS
9E: COLLEGE OF PHARMACY RECOMMENDATIONS
9F: UTILIZATION DETAILS OF OVARIAN CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE JAKAFI® (RUXOLITINIB) AND REZUROCK™ (BELUMOSUDIL)
10A: INTRODUCTION
10B: MARKET NEWS AND UPDATES
10C: JAKAFI® (RUXOLITINIB) PRODUCT SUMMARY
10D: REZUROCK™ (BELUMOSUDIL) PRODUCT SUMMARY
10E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER

AGENDA ITEM NO. 11: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE LUPKYNIS™ (VOCLOSPORIN) AND SAPHNELO™ (ANIFROLUMAB-FNIA)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS
11C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS
11D: MARKET NEWS AND UPDATES
11E: LUPKYNIS™ (VOCLOSPORIN) PRODUCT SUMMARY
11F: SAPHNELO™ (ANIFROLUMAB-FNIA) PRODUCT SUMMARY
11G: COLLEGE OF PHARMACY RECOMMENDATIONS
11H: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS
Materials included in agenda packet; presented by Dr. Ha
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER

AGENDA ITEM NO. 12: 30-DAY NOTICE TO PRIOR AUTHORIZE BYLVAY™ (ODEVIXIBAT)
12A: INTRODUCTION
12B: BYLVAY™ (ODEVIXIBAT) PRODUCT SUMMARY
12C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER

AGENDA ITEM NO. 13: ANNUAL REVIEW OF BETA THALASSEMIA AND SICKLE CELL DISEASE (SCD) MEDICATIONS
13A: INTRODUCTION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA
13C: UTILIZATION OF BETA THALASSEMIA AND SCD MEDICATIONS
13D: PRIOR AUTHORIZATION OF BETA THALASSEMIA AND SCD MEDICATIONS
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF BETA THALASSEMIA AND SCD MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTATION (DEA) UPDATES

Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 15:</u> FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
15A: ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MAINTENANCE MEDICATIONS
15B: ATOPIC DERMATITIS MEDICATIONS
15C: BOTULINUM TOXINS
15D: MULTIPLE MYELOMA MEDICATIONS
*Future product and class reviews subject to change.
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 16:</u> ADJOURNMENT
The meeting was adjourned at 5:16pm.

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

Memorandum

Date: October 15, 2021

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

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

Subject: DUR Board Recommendations from Meeting on October 13, 2021

Recommendation 1: Fall 2021 Pipeline Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Herceptin® (Trastuzumab) and Margenza® (Margetuximab-cmkb) and Update the Approval Criteria for the Breast Cancer Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Margenza® (margetuximab-cmkb) with the following criteria:

Margenza® (Margetuximab-cmkb) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-positive; and
3. Member has received 2 or more prior anti-HER2 regimens, at least 1 of which was for metastatic disease; and
4. Used in combination with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine).

Additionally, the College of Pharmacy recommends the prior authorization of Herceptin® (trastuzumab) and updating the prior authorization criteria for

Herzuma® (trastuzumab-pkrb), Kanjinti® (trastuzumab-anns), Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), and Trazimera™ (trastuzumab-qyyp) based on net costs (changes noted in red):

Herceptin® (Trastuzumab), Herzuma® (Trastuzumab-pkrb), Kanjinti® (Trastuzumab-anns), Ogivri® (Trastuzumab-dkst), Ontruzant® (Trastuzumab-dttb), and Trazimera™ (Trastuzumab-qyyp) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
2. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), or Kanjinti® (trastuzumab-anns) will also require a patient-specific, clinically significant reason why the member cannot use ~~Herceptin® (trastuzumab)~~ Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), or Trazimera™ (trastuzumab-qyyp). Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

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

1. Diagnosis of human epidermal growth factor receptor 2 (HER2)-positive metastatic gastric or GEJ adenocarcinoma; and
2. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), or Kanjinti® (trastuzumab-anns) will also require a patient-specific, clinically significant reason why the member cannot use ~~Herceptin® (trastuzumab)~~ Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), or Trazimera™ (trastuzumab-qyyp). Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

The College of Pharmacy also recommends updating the approval criteria for Enhertu® (fam-trastuzumab deruxtecan-nxki), Keytruda® (pembrolizumab), and Trodelvy® (sacituzumab govitecan-hziy) based on recent FDA approvals (changes and new criteria noted in red; only criteria with updates are listed):

Enhertu® (Fam-Trastuzumab Deruxtecan-nxki) Approval Criteria [Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma Diagnosis]:

1. Diagnosis of locally advanced or metastatic gastric or GEJ adenocarcinoma; and

2. Human epidermal growth factor receptor 2 (HER2)-positive disease; and
3. Member has received at least 1 prior trastuzumab-based regimen.

Keytruda® (Pembrolizumab) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of locally recurrent, unresectable or metastatic triple-negative breast cancer; and
   a. Tumors express programmed death ligand 1 (PD-L1) with a combined positive score (CPS) ≥10; and
   b. Used in combination with chemotherapy; or
2. Diagnosis of early stage triple-negative breast cancer; and
   a. Disease is considered high-risk; and
   b. Used in combination with chemotherapy as neoadjuvant therapy.

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

1. Diagnosis of triple-negative breast cancer; and
2. Unresectable locally advanced or metastatic disease; and
3. Member must have received ≥2 prior therapies, at least 1 of which was for metastatic disease.

Trodelvy® (Sacituzumab Govitecan-hziy) Approval Criteria [Urothelial Cancer Diagnosis]:

1. Diagnosis of unresectable locally advanced or metastatic disease; and
2. Member must have previously received a platinum-containing chemotherapy; and
3. Member must have previously received either a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor.

Further, the College of Pharmacy recommends updating the prior authorization criteria for Ibrance® (palbociclib) based on NCCN Compendium approval (changes noted in red):

Ibrance® (Palbociclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced, metastatic, hormone receptor positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer; and
2. In combination with:
   a. ~~Letrozole as initial endocrine-based therapy~~ An aromatase inhibitor in postmenopausal women; or
   b. Fulvestrant in women with disease progression following endocrine therapy; or
   c. An aromatase inhibitor or fulvestrant in male patients.

Finally, the College of Pharmacy recommends the removal of the Tecentriq® (atezolizumab) approval criteria for the indication of unresectable locally advanced or metastatic triple negative breast cancer (mTNBC) based on FDA-guided voluntary withdrawal of this indication by the manufacturer (changes noted in red):

~~**Tecentriq® (Atezolizumab) Approval Criteria [Breast Cancer Diagnosis]:**~~

~~1. Unresectable locally advanced or metastatic triple-negative breast cancer; and~~
~~2. Used in combination with nab-paclitaxel (Abraxane®); and~~
~~3. Positive expression of programmed death ligand-1 (PD-L1); and~~
~~4. Member has not failed other immunotherapy(ies).~~

Recommendation 3: Vote to Prior Authorize Orgovyx™ (Relugolix)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Orgovyx™ (relugolix) with the following criteria listed in red:

Orgovyx™ (Relugolix) Approval Criteria [Prostate Cancer Diagnosis]:

1. Diagnosis of advanced prostate cancer; and
2. A patient-specific, clinically significant reason why the member cannot use Eligard® (leuprolide acetate), Firmagon® (degarelix), and Lupron Depot® (leuprolide acetate) must be provided [reason(s) must address each medication]; and
3. A quantity limit of 30 tablets per 30 days will apply. Upon meeting approval criteria, a quantity limit override will be approved for the day 1 loading dose of 360mg.

Recommendation 4: Annual Review of Spinal Muscular Atrophy (SMA) Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the approval criteria for Evrysdi® (risdiplam) based on the recent FDA update to the *Prescribing Information* (changes noted in red):

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~~ to evaluate member's liver function prior to initiating Evrysdi® and must verify the member does not have severe hepatic impairment (Child-Pugh C); 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.

Recommendation 5: Annual Review of Hepatitis C Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Epclusa® (sofosbuvir/velpatasvir) pellets with criteria similar to Epclusa® tablets and the prior authorization of Mavyret® (glecaprevir/pibrentasvir) pellets with criteria

similar to Mavyret® tablets. Additionally, the College of Pharmacy recommends updating the Epclusa® (sofosbuvir/velpatasvir) and Mavyret® (glecaprevir/pibrentasvir) prior authorization criteria based on new FDA label updates. The following criteria will apply (changes and additions noted in red):

Epclusa® (Sofosbuvir/Velpatasvir Tablets and Pellets) Approval Criteria:

1. Member must be ~~6~~ 3 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. 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
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. Two 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. **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
7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. Prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and

10. Prescriber must agree to counsel members on 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. Documentation of initiation of immunization with the hepatitis A and B vaccines must be provided; and
12. 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
13. Member must not be taking the following medications: H_2-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
14. If member is using antacids they must agree to separate antacid and Epclusa® administration by 4 hours; and
15. 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
16. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
17. Prescriber must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
19. Approvals for treatment regimen initiation for 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.

Mavyret® (Glecaprevir/Pibrentasvir Tablets and Pellets) Approval Criteria:

1. Member must be ~~12~~ 3 years of age or older ~~or weigh at least 45kg~~; 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. Mavyret® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and

4. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on the prior authorization request; and
5. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 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. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
6. The following regimens and requirements based on cirrhosis status, viral genotype, and treatment history will apply (new regimens will apply as approved by the FDA):

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

PRS = pegylated interferon, ribavirin, and/or sofosbuvir; w/o = without; PI = protease inhibitor
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
Examples of NS3/4A PIs include: boceprevir, glecaprevir, grazoprevir, paritaprevir, simeprevir, telaprevir, voxilaprevir
HCV/HIV-1 co-infection and patients with any degree of renal impairment follow the same dosage recommendations in the table above. For liver or kidney transplant recipients, Mavyret® is recommended for 12 weeks in adult and pediatric patients 12 years and older or weighing at least 45kg. A 16-week treatment duration is recommended in genotype (GT) 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A PI or in GT 3-infected patients who are PRS treatment-experienced.

7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. Prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
10. Prescriber must agree to counsel members on the potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
11. Documentation of initiation of immunization with the hepatitis A and B vaccines must be provided; 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. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy; and
15. Member must not be taking the following medications: carbamazepine, rifampin, ethinyl estradiol-containing medications, St. John's wort, atazanavir, darunavir, lopinavir, ritonavir, efavirenz, atorvastatin, lovastatin, simvastatin, rosuvastatin doses greater than 10mg per day, or cyclosporine doses greater than 100mg per day; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
17. Prescriber must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Approval of the 8-week carton (in place of the 4-week carton) requires a patient-specific, clinically significant reason why the member requires the 8-week carton in place of the 4-week carton; and
19. 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
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 16 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 6: Annual Review of Ovarian Cancer Medications

NO ACTION REQUIRED.

Recommendation 7: 30-Day Notice to Prior Authorize Jakafi® (Ruxolitinib) and Rezurock™ (Belumosudil)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER 2021.

Recommendation 8: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior

Authorize Lupkynis™ (Voclosporin) and Saphnelo™ (Anifrolumab-fnia)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER 2021.

Recommendation 9: 30-Day Notice to Prior Authorize Bylvay™ (Odevixibat)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN NOVEMBER 2021.

Recommendation 10: Annual Review of Beta Thalassemia and Sickle Cell Disease (SCD) Medications

NO ACTION REQUIRED.

Recommendation 11: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 12: Future Business

NO ACTION REQUIRED.

Make today a breakthrough.

October 11, 2021

Oklahoma Drug Utilization (DUR) Board
c/o Oklahoma Health Care Authority
4345 N. Lincoln Blvd
Oklahoma City, OK 73105

Re: Annual Review of Spinal Muscular Atrophy (SMA) Medications

Dear Oklahoma DUR Board Members,

As the leading national organization that represents individuals with spinal muscular atrophy (SMA)—including those enrolled in the Oklahoma Medicaid Program**, Cure SMA asks that you remove all coverage restrictions that are inconsistent with the U.S. Food and Drug Administration (FDA) labels for the three existing FDA-approved SMA treatments.** We are especially concerned with the prior authorization criteria that restricts access to SMA treatments based on ventilation status.

SMA, which is a neurodegenerative disease that affects the motor nerve cells in the spinal cord, results in progressive loss of physical strength and function, such as walking and eating. Losses due to the natural history of SMA do not stop without one of the three FDA-approved treatments, which include Spinraza (2016), Zolgensma (2019), and Evrysdi (2020).[i] Clinical studies and real-world data show these treatments are effective in halting or slowing disease progression and helping individuals, regardless of disease type or status, to retain or achieve key motor skills that impact function and quality of life.

Cure SMA strongly believes that all individuals with SMA should be able to access the SMA treatment of their choice in consultation with their physician and that is consistent with the FDA label and based on their clinical needs and individual circumstance. Unfortunately, the Oklahoma Medicaid Program policies restrict access to all three SMA treatments based on ventilation status. The following restriction is included as a Prior Authorization Criteria in all SMA treatments:

> *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)*[ii]

Cure SMA respectfully asks that you remove this restriction from the Prior Authorization Criteria for all SMA treatments. This harmful restriction, which limits based on ventilation status, will mean missed opportunities for motor function improvements and/or stabilization and quality of life gains for SMA patients who meet the FDA's labels, leading to continued costly healthcare interventions and medical services, such as emergency care and frequent hospitalizations. *No one impacted by SMA, including those with advanced disease, should be denied access to a potentially life-saving therapy.*

All individuals with SMA who meet the FDA labels for SMA treatments, including those with advanced disease who also can benefit from these treatments, should be able to access the treatment of their choice, based on their clinical needs and individual circumstance.

Thank you for considering the views of Cure SMA. Please do not hesitate to contact Cure SMA if you have questions or need additional information. Cure SMA can be reached through Maynard Friesz, Vice President for Policy and Advocacy at Cure SMA, at maynard.friesz@curesma.org or 202-871-8004.

Sincerely,

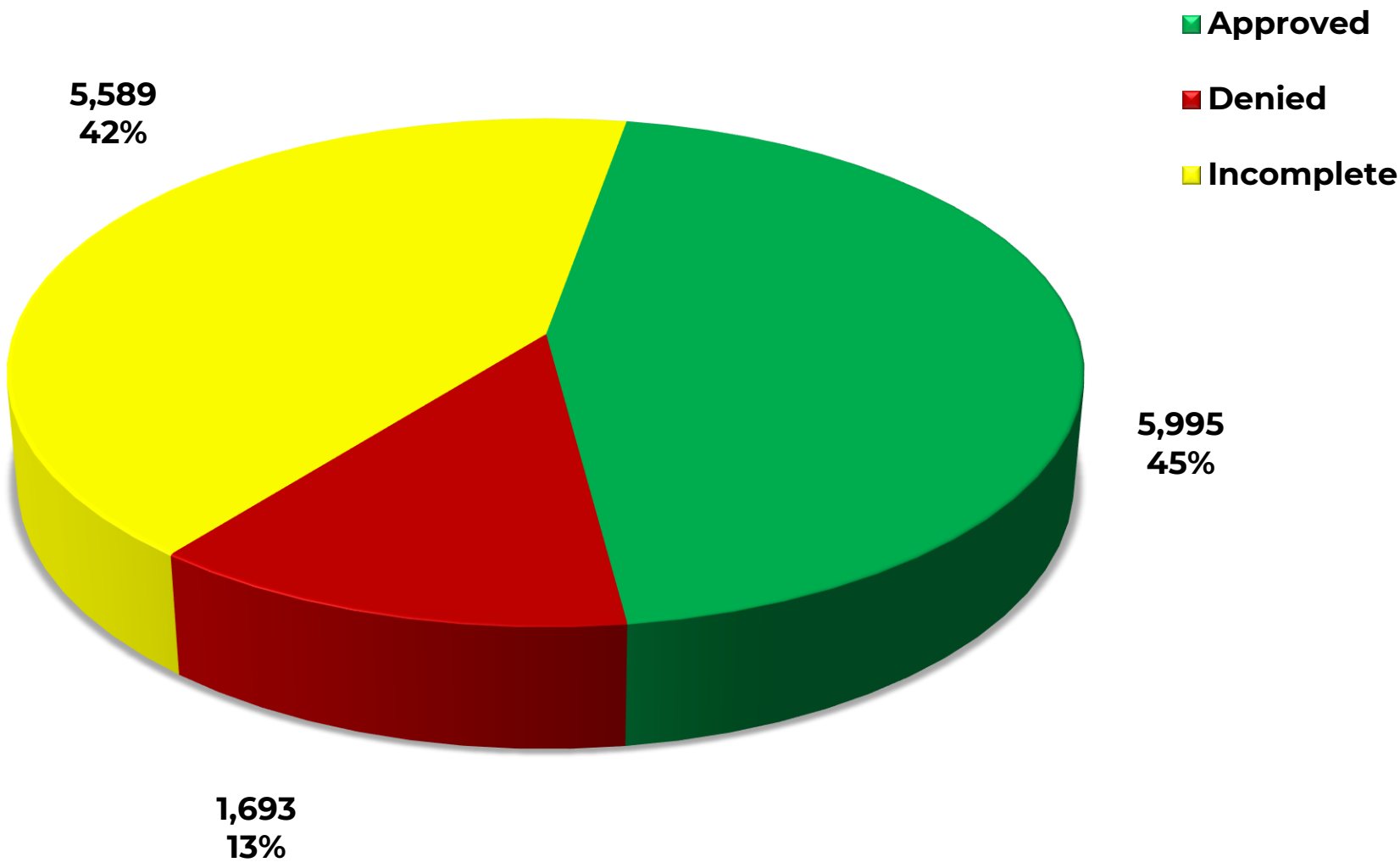
Kenneth Hobby
President

Mary Schroth, M.D
Chief Medical Officer

[i] Cure SMA, About Spinal Muscular Atrophy, 2021, https://www.curesma.org/about-sma/
[ii] Oklahoma Health Care Authority Board Packet, October, 2021, https://oklahoma.gov/content/dam/ok/en/okhca/docs/about/boards-and-committees/dur/2021/october/DUR%20Packet%2010132021.pdf

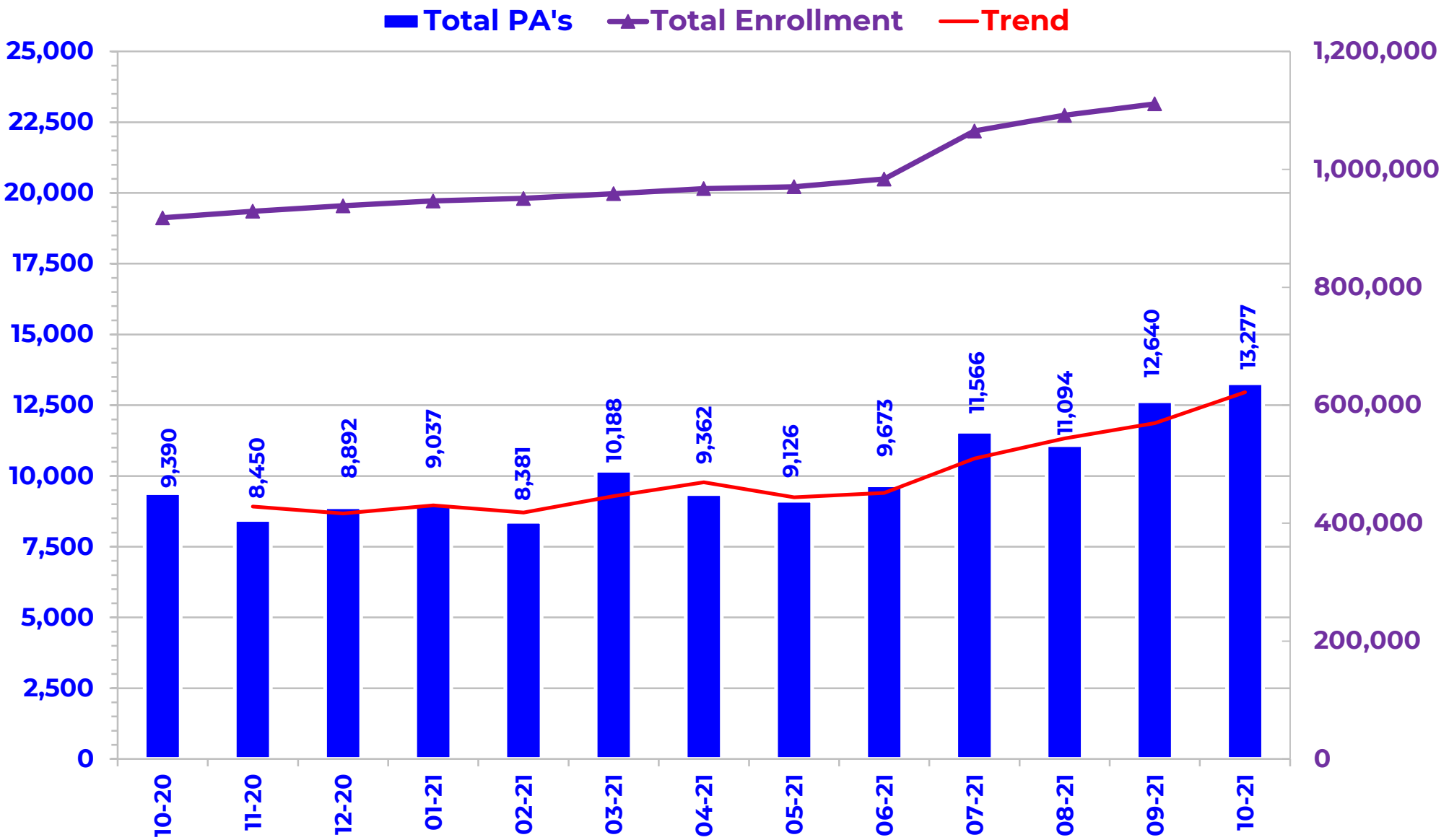
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER 2021



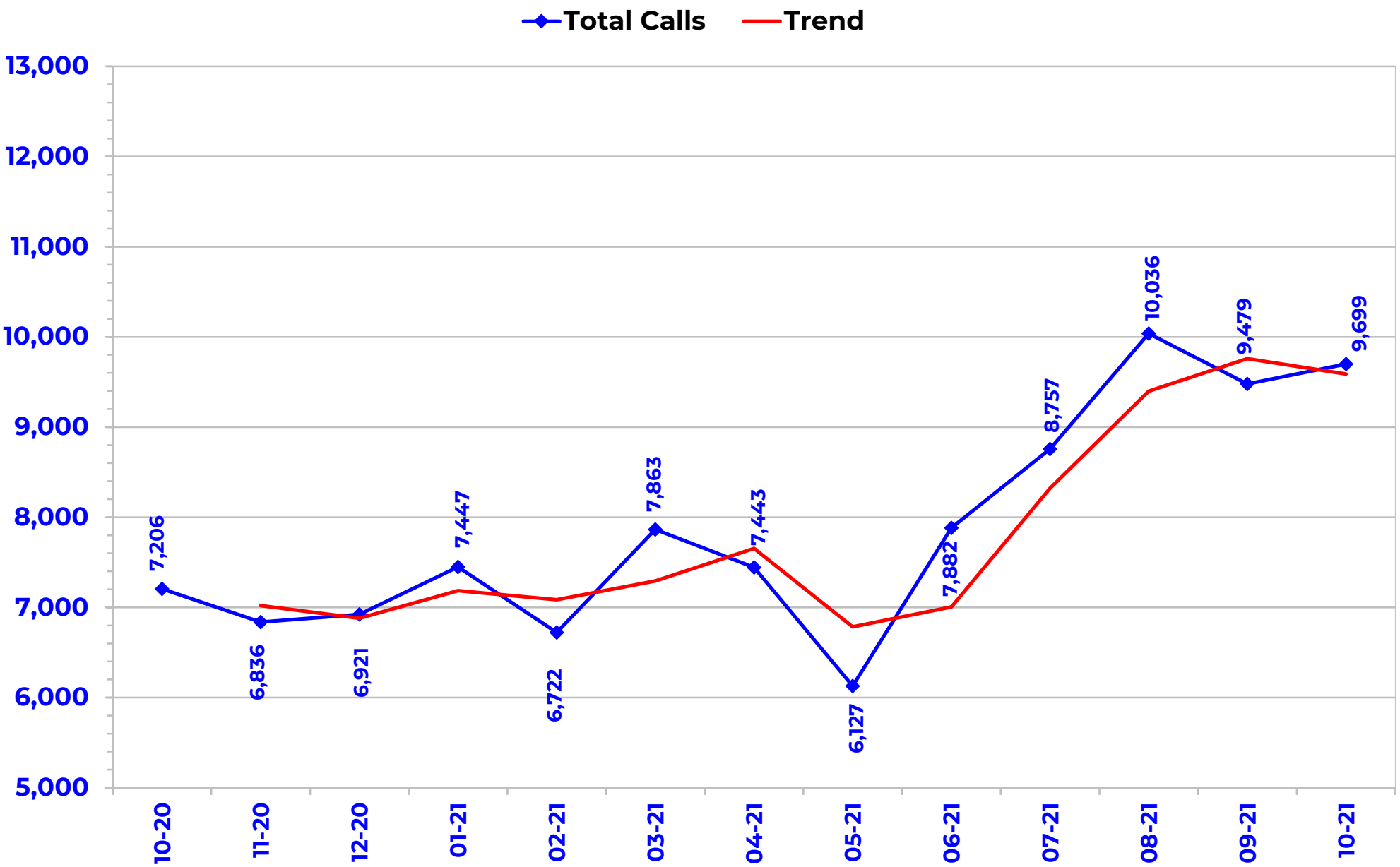
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: OCTOBER 2020 – OCTOBER 2021



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: OCTOBER 2020 – OCTOBER 2021



Prior Authorization Activity

10/1/2021 Through 10/31/2021

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	83	29	7	47	336
Analgesic - NonNarcotic	17	0	5	12	0
Analgesic, Narcotic	313	119	28	166	146
Antiasthma	65	22	9	34	239
Antibiotic	49	29	1	19	268
Anticonvulsant	200	92	12	96	291
Antidepressant	335	86	41	208	333
Antidiabetic	1,026	392	130	504	357
Antihemophilic Factor	22	13	0	9	297
Antihistamine	39	8	12	19	359
Antimigraine	392	59	144	189	264
Antineoplastic	164	105	13	46	174
Antiobesity	15	0	15	0	0
Antiparasitic	28	8	11	9	12
Antiulcers	47	10	5	32	162
Anxiolytic	19	3	1	15	258
Atypical Antipsychotics	432	218	30	184	350
Benign Prostatic Hypertrophy	16	0	6	10	0
Biologics	297	163	27	107	291
Bladder Control	65	9	18	38	329
Blood Thinners	690	396	38	256	337
Botox	57	42	9	6	254
Buprenorphine Medications	93	46	8	39	81
Calcium Channel Blockers	16	4	1	11	359
Cardiovascular	82	35	13	34	288
Chronic Obstructive Pulmonary Disease	275	60	59	156	326
Constipation/Diarrhea Medications	178	35	51	92	195
Contraceptive	31	13	5	13	317
Corticosteroid	19	1	6	12	360
Dermatological	383	112	109	162	203
Diabetic Supplies	1,118	497	115	506	261
Endocrine & Metabolic Drugs	92	51	5	36	162
Erythropoietin Stimulating Agents	22	7	7	8	114
Fibromyalgia	2	0	0	2	0
Fish Oils	32	7	6	19	359
Gastrointestinal Agents	220	44	52	124	248
Genitourinary Agents	20	5	8	7	293

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Glaucoma	23	4	8	11	116
Growth Hormones	123	72	19	32	148
Hematopoietic Agents	22	12	1	9	211
Hepatitis C	205	119	21	65	10
HFA Rescue Inhalers	26	1	2	23	40
Insomnia	74	9	15	50	189
Insulin	245	89	16	140	352
Miscellaneous Antibiotics	21	7	4	10	22
Multiple Sclerosis	114	44	18	52	198
Muscle Relaxant	60	6	19	35	101
Nasal Allergy	86	11	22	53	234
Neurological Agents	175	67	28	80	227
NSAIDs	48	1	13	34	360
Ocular Allergy	20	1	3	16	85
Ophthalmic	14	2	2	10	190
Ophthalmic Anti-infectives	17	6	1	10	11
Ophthalmic Corticosteroid	16	5	1	10	171
Osteoporosis	32	10	8	14	334
Other*	421	103	61	257	298
Otic Antibiotic	31	5	6	20	9
Pediculicide	19	3	0	16	21
Respiratory Agents	76	45	1	30	190
Smoking Cess.	53	9	41	3	108
Statins	29	6	7	16	192
Stimulant	1,403	852	91	460	347
Synagis	83	31	21	31	26
Testosterone	111	28	19	64	309
Thyroid	21	10	2	9	357
Topical Antifungal	38	4	10	24	20
Topical Corticosteroids	76	2	34	40	47
Vitamin	161	25	71	65	201
Pharmacotherapy	49	45	1	3	251
Emergency PAs	0	0	0	0	
Total	**10,846**	**4,354**	**1,573**	**4,919**	

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Overrides					
Brand	31	12	0	19	328
Compound	13	13	0	0	12
Cumulative Early Refill	8	1	0	7	180
Diabetic Supplies	9	8	1	0	155
Dosage Change	403	376	0	27	14
High Dose	5	3	0	2	166
IHS-Brand	1	1	0	0	360
Ingredient Duplication	6	5	0	1	7
Lost/Broken Rx	130	121	1	8	19
MAT Override	291	217	5	69	81
NDC vs. Age	349	207	40	102	252
NDC vs. Sex	13	5	0	8	84
Nursing Home Issue	65	61	0	4	11
Opioid MME Limit	148	48	7	93	111
Opioid Quantity	48	31	6	11	141
Other	41	36	0	5	16
Quantity vs. Days Supply	805	451	57	297	231
STBS/STBSM	12	8	2	2	76
Step Therapy Exception	1	1	0	0	360
Stolen	13	12	0	1	13
Third Brand Request	39	24	1	14	43
Overrides Total	**2,431**	**1,641**	**120**	**670**	
Total Regular PAs + Overrides	**13,277**	**5,995**	**1,693**	**5,589**	

Denial Reasons	
Unable to verify required trials.	4,748
Does not meet established criteria.	1,746
Lack required information to process request.	768
Other PA Activity	
Duplicate Requests	1,349
Letters	24,775
No Process	5
Changes to Existing PAs	1,097
Helpdesk Initiated Prior Authorizations	974
PAs Missing Information	0

* 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 2021

Introduction[1,2,3,4,5,6]

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
10/16/2020	**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**	**Low amniotic fluid in pregnancy at 20 weeks or later**
Issue Details: The FDA issued a Drug Safety Communication warning against the use of NSAIDs around 20 weeks or later in pregnancy due to the risk of rare, but serious kidney problems in the unborn baby. After around 20 weeks of pregnancy, the unborn baby's kidneys begin to produce most of the amniotic fluid, so these kidney problems can lead to lower levels of this fluid. The FDA reviewed 35 cases of low amniotic fluid levels or kidney problems in unborn babies associated with NSAID use during pregnancy that were reported through 2017. Two newborns who died in these reports had kidney failure and low amniotic fluid when mothers took NSAIDs while pregnant, and in 11 cases where there was low amniotic fluid levels, the fluid volume returned to normal after the NSAIDs were stopped. **FDA Recommendation(s):** The FDA is requiring changes to the *Prescribing Information* of prescription NSAIDs to describe the risk of kidney problems in unborn babies that can result in low amniotic fluid. The FDA is also lowering the recommendation of avoiding NSAID use in pregnant women from 30 weeks to 20 weeks of gestation and recommends ultrasound monitoring of amniotic fluid if NSAID treatment extends beyond 48 hours. Over-the-counter (OTC) NSAIDs already have a warning to avoid use in the last 3 months of pregnancy due to problems in the unborn baby or complications during delivery. **Pharmacy Claims Evaluation:** During fiscal year (FY) 2021 (07/01/2020 to 06/30/2021), a total of 41,973 SoonerCare members of childbearing age had paid claims for an NSAID, accounting for 68,742 paid claims and an average of 1.64 claims per member. **SoonerCare Action:** The College of Pharmacy will continue to monitor the FDA recommendations.		

Date	Drug	Issue
03/31/2021	**Lamotrigine**	**Increased risk of arrhythmias in patients with heart disease**

Issue Details: The FDA issued a Drug Safety Communication warning on the use of lamotrigine in patients with structural and functional heart disorders such as heart failure, valvular heart disease, and congenital heart disease due to serious and life-threating arrhythmias. *In vitro* studies have shown that lamotrigine and other sodium-channel blockers can increase the risks of arrhythmias and this risk increases with combination use of other sodium channel blockers such as carbamazepine, phenytoin, and topiramate.
FDA Recommendation(s): The FDA recommends the prescriber assess whether the potential benefits of lamotrigine outweigh the potential risk of arrhythmias for each patient and be aware of the increased risks when multiple sodium channel blockers are used concurrently.
Pharmacy Claims Evaluation: During FY 2021, a total of 5,641 SoonerCare members had paid claims for lamotrigine, accounting for 30,965 paid claims and an average of 5.49 claims per member.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations.

Date	Drug	Issue
07/20/2021	**Statins**	**Removal of contraindication warning against statin use during pregnancy**

Issue Details: The FDA issued a Drug Safety communication about the use of statins in women who are pregnant and recommends removing the contraindication against the use of these medications in pregnant women. A contraindication is the FDA's strongest warning and is only added when a medication should not be used at all due to the risk clearly outweighing any possible benefits. Although most women should stop statins once pregnant, there is a small subset of very high-risk pregnant women who could possibly benefit from statin therapy, such as those with homozygous familial hypercholesterolemia (HoFH) or established cardiovascular (CV) disease. Statins should not be used in women who are breastfeeding since statins can pass into human milk and may cause harm to the breastfed infant. The FDA reviewed data from case series and prospective and retrospective observational cohort studies over decades of statin use in pregnant women. Multiple larger, well-designed, and controlled observational studies did not find an increase in major birth defects associated with statin use during pregnancy. Also, published data from prospective and retrospective observational cohort studies with statin use in pregnant women were insufficient in determining if there is a drug-associated risk of miscarriage.

FDA Recommendation(s): The FDA recommends removing the contraindication in the *Prescribing Information* for all statins. The FDA hopes the revised language will enable prescribers and patients to make individual decisions about the benefits and risks of statins in pregnant women, especially those with a very high risk of heart attack or stroke.
Pharmacy Claims Evaluation: During FY 2021, a total of 2,570 SoonerCare members of childbearing age had paid claims for a statin, accounting for 7,312 paid claims and an average of 2.85 claims per member.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations.

Date	Drug	Issue
09/01/2021	**Janus kinase (JAK) inhibitors**	**Increased risk of major adverse CV events, malignancy, and blood clots**

Issue Details: The FDA issued a Drug Safety Communication on the JAK inhibitors due to their increased risk of myocardial infarction, stroke, cancer, blood clots, and death in patients with rheumatoid arthritis (RA) and on concomitant methotrexate (MTX). The JAK inhibitors in this warning include Xeljanz® (tofacitinib), Xeljanz® XR [tofacitinib extended-release(ER)], Olumiant® (baricitinib), and Rinvoq™ (upadacitinib). Two other JAK inhibitors, Jakafi® (ruxolitinib) and Inrebic® (fedratinib), were not included in this warning since they are not used for RA or other inflammatory conditions. When the FDA first approved Xeljanz®, they required the manufacturer to conduct a randomized safety clinical study in patients with RA who were taking MTX to evaluate the risk of CV events, malignancy, and infections. The data from this study showed a dose-dependent increased risk of major adverse CV events, all-cause mortality, and thrombosis at both doses of Xeljanz® when compared to treatment with tumor necrosis factor (TNF) blockers.
FDA Recommendation(s): The FDA is requiring revisions to the *Boxed Warning* for the JAK inhibitors listed above to include the risk of serious CV-related events, cancer, blood clots, and death. In addition, the FDA is also limiting all approved use to certain patients who have not responded or cannot tolerate 1 or more TNF blockers.
Pharmacy Claims Evaluation: During FY 2021, a total of 80 SoonerCare members had paid claims for a JAK inhibitor, accounting for 373 paid claims and an average of 4.66 claims per member. Jakafi® and Inrebic® were not included in this analysis.
SoonerCare Action: The College of Pharmacy will continue to monitor the FDA recommendations. Currently, all JAK inhibitors included in the Drug Safety Communication require prior authorization.

[1] U.S. Food and Drug Administration (FDA). 2020 Drug Safety Communications. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/2020-drug-safety-communications. Last revised 10/15/2020. Last accessed 10/04/2021.
[2] U.S. FDA. 2021 Drug Safety Communications. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/2021-drug-safety-communications. Last revised 09/01/2021. Last accessed 10/04/2021.
[3] U.S. FDA. FDA Recommends Avoiding Use of NSAIDs in Pregnancy at 20 Weeks or Later Because They Can Result in Low Amniotic Fluid. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-avoiding-use-nsaids-pregnancy-20-weeks-or-later-because-they-can-result-low-amniotic. Issued 10/16/2020. Last accessed 10/04/2021.
[4] U.S. FDA. Studies Show Increased Risk of Heart Rhythm Problems with Seizure and Mental Health Medicine Lamotrigine (Lamictal®) in Patients with Heart Disease. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/studies-show-increased-risk-heart-rhythm-problems-seizure-and-mental-health-medicine-lamotrigine. Issued 03/31/2021. Last accessed 10/04/2021.
[5] U.S. FDA. FDA Requests Removal of Strongest Warning Against Using Cholesterol-Lowering Statins During Pregnancy; Still Advises Most Pregnant Patients Should Stop Taking Statins. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-removal-strongest-warning-against-using-cholesterol-lowering-statins-during-pregnancy. Issued 07/20/2021. Last accessed 10/04/2021.
[6] U.S. FDA. FDA Requires Warnings about Increased Risk of Serious Heart-Related Events, Cancer, Blood Clots, and Death for JAK Inhibitors That Treat Certain Chronic Inflammatory Conditions. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death. Issued 09/01/2021. Last accessed 10/04/2021.

Appendix C

2022 Drug Utilization Review (DUR) Board Meeting Dates

Oklahoma Health Care Authority
November 2021

DUR Board meetings are held the second Wednesday of every month at 4:00pm at the Oklahoma Health Care Authority

January 12, 2022

February 9, 2022

March 9, 2022

April 13, 2022

May 11, 2022

June 8, 2022

July 13, 2022

August 10, 2022

September 14, 2022

October 12, 2022

November 9, 2022

December 14, 2022

Appendix D

Vote to Prior Authorize Jakafi® (Ruxolitinib) and Rezurock™ (Belumosudil)

Oklahoma Health Care Authority
November 2021

Market News and Updates[1,2]

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

- **July 2021:** The FDA approved Rezurock™ (belumosudil), a kinase inhibitor, for adult and pediatric patients 12 years of age and older with chronic graft-versus-host disease (cGVHD) after failure of at least 2 prior lines of systemic therapy.
- **September 2021:** The FDA approved Jakafi® (ruxolitinib) for cGVHD after failure of 1 or 2 lines of systemic therapy in adult and pediatric patients 12 years of age and older. Jakafi® was originally FDA approved in 2011 for intermediate or high-risk myelofibrosis. Since that time, Jakafi® also received FDA approval for polycythemia vera in 2014 and acute GVHD (aGVHD) in 2019.

Jakafi® (Ruxolitinib) Product Summary[3]

Therapeutic Class: Kinase inhibitor

Indication(s):

- Intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis in adults
- Polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea
- Steroid-refractory aGVHD in adult and pediatric patients 12 years of age and older
- cGVHD after failure of 1 or 2 lines of systemic therapy in adult and pediatric patients 12 years of age and older

How Supplied: 5mg, 10mg, 15mg, 20mg, and 25mg oral tablets

Dosing and Administration:

- Myelofibrosis: Starting dose is based on the patient's baseline platelet count:

Baseline Platelet Count	Recommended Starting Dose
>200 × 10^9/L	20mg twice daily
100 to 200 × 10^9/L	15mg twice daily
50 to <100 × 10^9/L	5mg twice daily

- Polycythemia Vera: Starting dose is 10mg twice daily; dose may be titrated based on safety and efficacy
- aGVHD: Starting dose is 5mg twice daily; dose may be increased to 10mg twice daily after 3 days of treatment if the absolute neutrophil count (ANC) and platelet counts are not decreased by 50% or more
- cGVHD: Starting dose is 10mg twice daily; dose may be adjusted based on safety and efficacy

Cost: The Wholesale Acquisition Cost (WAC) is $252.05 per tablet for all available strengths. This results in a cost of $15,123 per 30 days based on the recommended starting dose for cGVHD of 10mg twice daily. Cost will vary based on diagnosis and treatment regimen.

Rezurock™ (Belumosudil) Product Summary[4]

Therapeutic Class: Kinase inhibitor

Indication(s): Treatment of adult and pediatric patients 12 years of age and older with cGVHD after failure of at least 2 prior lines of systemic therapy

How Supplied: 200mg oral tablets

Dosing and Administration: 200mg once daily with food

Cost: The WAC is $516.67 per 200mg tablet, resulting in a cost of $15,500.10 per 30 days based on the recommended dose of 200mg daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Jakafi® (ruxolitinib) and Rezurock™ (belumosudil) with the following criteria listed in red:

Jakafi® (Ruxolitinib) Approval Criteria [Graft-Versus-Host Disease (GVHD) Diagnosis]:

1. Diagnosis of acute or chronic GVHD; and
2. Failure of at least 1 prior line of systemic therapy; and
3. Member must be 12 years of age or older.

Jakafi® (Ruxolitinib) Approval Criteria [Myelofibrosis (MF) Diagnosis]:

1. Diagnosis of MF; and
2. Used in 1 of the following settings:
    a. Symptomatic lower-risk MF with no response or loss of response to peginterferon alfa-2a or hydroxyurea; or
    b. Intermediate to high-risk MF; and
3. Member must be 18 years of age or older.

Jakafi® (Ruxolitinib) Approval Criteria [Polycythemia Vera Diagnosis]:

1. Diagnosis of polycythemia vera; and
2. Inadequate response or loss of response to hydroxyurea or peginterferon alfa-2a therapy; and
3. Member must be 18 years of age or older.

Rezurock™ (Belumosudil) Approval Criteria [Graft-Versus-Host Disease (GVHD) Diagnosis]:

1. Diagnosis of chronic GVHD; and
2. Failure of at least 2 prior lines of systemic therapy; and
3. Member must be 12 years of age or older.

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[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 10/07/2021. Last accessed 10/12/2021.

[2] U.S. FDA. Drugs@FDA: FDA-Approved Drugs. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process. Last revised 10/2021. Last accessed 10/12/2021.

[3] Jakafi® (Ruxolitinib) Prescribing Information. Incyte Corporation. Available online at: https://www.jakafi.com/pdf/prescribing-information.pdf. Last revised 09/2021. Last accessed 10/12/2021.

[4] Rezurock™ (Belumosudil) Prescribing Information. Kadmon Pharmaceuticals, LLC. Available online at: https://www.rezurock.com/full-prescribing-information.pdf. Last revised 07/2021. Last accessed 10/12/2021.

Appendix E

Vote to Prior Authorize Bylvay™ (Odevixibat)

Oklahoma Health Care Authority
November 2021

Market News and Updates[1]

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

- **July 2021:** The FDA approved Bylvay™ (odevixibat) for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC). Odevixibat is a reversible inhibitor of the ileal bile acid transporter (IBAT) and is the first medication to be FDA approved for this indication. Pruritus is one of the most common and distressing symptoms of PFIC and is often severe, particularly in PFIC-1 and PFIC-2 patients. The severe, intractable pruritus experienced by some PFIC patients can have a major impact on quality of life and may lead to scarring, sleep deprivation, fatigue, and depression. In some refractory cases, severe persistent pruritus can be an indication for liver transplantation even in the absence of liver failure.

Bylvay™ (Odevixibat) Product Summary[2,3,4]

Indication(s): Bylvay™ (odevixibat) is an IBAT inhibitor indicated for the treatment of pruritus in patients 3 months of age and older with PFIC.

Limitation(s) of Use:

- Bylvay™ may not be effective in PFIC-2 patients with *ABCB11* gene variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3).

How Supplied: 200mcg and 600mcg oral pellets; 400mcg and 1,200mcg oral capsules

Dosing and Administration:

- 40mcg/kg by mouth once daily in the morning with a meal
- If no improvement in pruritus after 3 months, dose may be increased in 40mcg/kg increments up to 120mcg/kg once daily, not to exceed 6mg per day
- The oral pellets are intended for use by patients weighing <19.5kg:
  - The capsule containing the oral pellets should be opened and the contents mixed into soft food (e.g., apple sauce, oatmeal, banana or carrot puree, chocolate or rice pudding)
  - After mixing, the entire dose should be administered immediately and followed with water

    - The capsule contents should not be mixed in liquids
    - The capsule containing the pellets should not be swallowed, chewed, or crushed
- The oral capsules are intended for use by patients weighing ≥19.5kg:
    - Capsules should be swallowed whole with a glass of water
    - For patients unable to swallow the capsule whole, the capsules may be opened, sprinkled, and mixed with a small amount of soft food

Mechanism of Action: Odevixibat is a reversible inhibitor of the IBAT. Inhibition of IBAT results in reduced reabsorption of bile acids from the terminal ileum. The complete mechanism by which odevixibat improves pruritus in patients with PFIC is unknown; however, it may involve inhibition of IBAT leading to reduced reuptake of bile salts and decreased serum bile acids.

Contraindication(s): None

Safety:

- Liver Test Abnormalities: Patients with PFIC may have impaired hepatic function and abnormal liver tests at baseline. During the Phase 3 study of odevixibat, treatment-emergent elevations or worsening of liver tests relative to baseline values were observed, including elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, and direct bilirubin. Baseline liver tests should be obtained before initiating treatment with odevixibat and should be monitored during treatment. Dose reductions or treatment interruptions should be considered if liver test abnormalities occur, and treatment discontinuation should be considered for persistent or recurrent liver test abnormalities. The efficacy and safety of odevixibat in patients with clinically significant portal hypertension and in patients with decompensated cirrhosis have not been established. Liver tests should be closely monitored, and odevixibat should be permanently discontinued if the patient progresses to portal hypertension or experiences a hepatic decompensation event during treatment.
- Diarrhea: In the Phase 3 study of odevixibat, diarrhea was reported in 39% of patients treated with odevixibat 40mcg/kg/day, 21% of patients treated with odevixibat 120mcg/kg/day, and 10% of patients who received placebo. Treatment interruptions, lasting from 3 to 7 days, due to diarrhea occurred in 2 patients with 3 events in the odevixibat 120mcg/kg/day treatment group. One patient in the 120mcg/kg/day group withdrew from the study due to persistent diarrhea. Patients who experience diarrhea during treatment with odevixibat should be monitored for dehydration, and dehydration should be promptly treated if it occurs. If a patient experiences persistent diarrhea,

treatment with odevixibat should be interrupted and may be restarted at the initial 40mcg/kg/day dose when diarrhea resolves. Treatment with odevixibat should be discontinued if diarrhea persists and no alternate etiology is identified.

- Fat-soluble vitamin (FSV) Deficiency: Patients with PFIC may have FSV (vitamins A, D, E, and K) deficiency at baseline. Treatment with odevixibat may affect absorption of FSVs. In the Phase 3 study of odevixibat, new onset or worsening of FSV deficiency was observed in 5% of placebo patients, 16% of patients in the 120mcg/kg/day treatment group, and none of the patients in the 40mcg/kg/day treatment group. Baseline FSV levels should be obtained before initiating treatment with odevixibat and during treatment. If FSV deficiency is diagnosed during treatment, FSV supplementation should be given. Odevixibat should be discontinued if FSV deficiency persists or worsens despite adequate FSV supplementation.
- Pregnancy: There are no human data available on the use of odevixibat in pregnant women to evaluate the drug-associated risk of major birth defects, miscarriage, or adverse developmental outcomes. Studies in animals suggest odevixibat may cause cardiac malformations when a fetus is exposed during pregnancy.
- Lactation: There are no data available on the presence of odevixibat in human milk, the effects on the breastfed child, or the effects of the drug on milk production. Following oral administration, absorption of odevixibat is low and breastfeeding is not expected to result in exposure of the infant to odevixibat at the recommended doses. Odevixibat may reduce absorption of FSVs. Levels of FSVs should be monitored and intake should be increased if FSV deficiency is observed during lactation.
- Pediatric Use: The safety and efficacy of odevixibat have been established in pediatric patients 3 months to 17 years of age for the treatment of pruritus in PFIC. Use of odevixibat in this age range is supported by evidence from 2 studies: a randomized, double-blind, placebo-controlled, 24-week study in 62 patients with confirmed PFIC-1 or PFIC-2 and a single-arm, open-label, 72-week extension study in 79 patients with PFIC (regardless of subtype). The safety and efficacy of odevixibat have not been established in patients younger than 3 months of age.
- Geriatric Use: The safety and efficacy of odevixibat for the treatment of pruritus in PFIC in adult patients, including those 65 years of age and older, have not been established.

Adverse Reactions: The most common adverse reactions in the Phase 3 study of odevixibat were diarrhea, liver test abnormalities, vomiting, abdominal pain, and FSV deficiency.

Efficacy: The efficacy of odevixibat for the treatment of pruritus in PFIC was assessed in the Phase 3 PEDFIC 1 study, a 24-week, randomized, double-blind, placebo-controlled study in 62 pediatric patients, 6 months to 17 years of age. The median age in the study was 3.2 years (range: 0.5 to 15.9 years of age). Patients were randomized to receive placebo (N=20), odevixibat 40mcg/kg/day (N=23), or odevixibat 120mcg/kg/day (N=19) once daily in the morning with a meal.

- Inclusion Criteria: All patients had genetically confirmed PFIC-1 or PFIC-2 and presence of significant pruritus (average caregiver-reported observed scratching score ≥2 at baseline on a scale of 0 to 4, with higher scores indicating worse symptoms). Additionally, all patients had elevated serum bile acid levels ≥100micromol/L prior to randomization. Patients were allowed to continue use of ursodeoxycholic acid (UDCA) and/or rifampin during the study. Of the 62 patients enrolled in the study, 89% were receiving UDCA and/or rifampin. Of those patients on UDCA and/or rifampin, 81% were receiving UDCA and 66% were receiving rifampin, as some patients were receiving both medications.
- Exclusion Criteria: Patients were excluded if they had *ABCB11* gene variants predicting a nonfunctional or absent BSEP protein, had experienced prior hepatic decompensation events, had other concomitant liver disease, had an international normalized ratio (INR) >1.4, had an ALT or total bilirubin >10x the upper limit of normal (ULN), or had received a liver transplant.
- Primary Endpoint: The primary efficacy endpoint was the mean percentage of itch assessments over the treatment period scored as 0 (no scratching) or 1 (a little scratching) on a scale of 0 to 4, with higher scores indicating worse symptoms.
- Results: In the placebo group, an average of 13.2% of assessments were scored as 0 or 1 over the 24-week treatment period, compared with 35.4% in the 40mcg/kg/day group and 30.1% in the 120mcg/kg/day group. For the 40mcg/kg/day treatment group, the mean difference from placebo was 22.2% [95% confidence interval (CI): 4.7, 39.6], which was statistically significant in favor of odevixibat. For the 120mcg/kg/day treatment group, the mean difference from placebo of 16.9% (95% CI: -2.0, 35.7) was not statistically significant for the primary efficacy endpoint. Additionally, a secondary endpoint assessed the mean of the worst weekly average scratching scores in each treatment group for each month of treatment. Both doses of odevixibat resulted in lower scratching scores over the 6 months of treatment relative to placebo; however, there was no significant difference between the 40mcg/kg/day and 120mcg/kg/day odevixibat treatment groups.

Cost: The Wholesale Acquisition Cost (WAC) of Bylvay™ is $220 per unit for the 200mcg oral pellets, $440 per unit for the 400mcg oral capsule, $660 per

unit for the 600mcg oral pellets, and $1,320 per unit for the 1,200mcg oral capsule. For a member weighing 18kg using the initial dose of 40mcg/kg/day, the estimated cost of Bylvay™ is $26,400 per 30 days and $316,800 per year. For a member weighing 18kg using the maximum dose of 120mcg/kg/day, the estimated cost of Bylvay™ is $72,600 per 30 days and $871,200 per year.

Recommendations

The College of Pharmacy recommends the prior authorization of Bylvay™ (odevixibat) with the following criteria:

Bylvay™ (Odevixibat) Approval Criteria:

1. An FDA approved indication for the treatment of pruritus in members with progressive familial intrahepatic cholestasis (PFIC); and
    a. Diagnosis must be confirmed by genetic testing identifying mutations in the *ATP8B1, ABCB11, or ABCB4* genes; and
2. Member must be 3 months of age or older; and
3. Bylvay™ must be prescribed by a gastroenterologist, hepatologist, geneticist, or other specialist with expertise in the treatment of PFIC (or an advanced care practitioner with a supervising physician who is a gastroenterologist, hepatologist, geneticist, or other specialist with expertise in the treatment of PFIC); and
4. Prescriber must verify member has a history of significant pruritus that is unresponsive to treatment with at least 3 of the following medications, unless contraindicated:
    a. Ursodeoxycholic acid (UDCA); or
    b. Cholestyramine; or
    c. Rifampin; or
    d. Sertraline; or
    e. Naltrexone; and
5. Member must have elevated serum bile acid concentration ≥100micromol/L at baseline; and
6. Prescriber must verify member does not have known pathologic variants of the *ABCB11* gene predicting a non-functional or absent bile salt export pump protein (BSEP-3); and
7. Members with a history of liver transplantation will generally not be approved for Bylvay™; and
8. Prescriber must verify ~~the member is not currently a candidate for~~ surgical intervention (e.g., biliary diversion, liver transplantation) is not currently clinically appropriate for the member; and
9. Prescriber must agree to monitor alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, and international normalized ratio (INR) at baseline and during treatment with Bylvay™; and

10. Member's current weight (taken within the past 3 weeks) must be provided on initial and subsequent prior authorization requests in order to authorize the appropriate amount of drug required according to package labeling; and
11. Initial approvals will be for 40mcg/kg/day for a duration of 3 months. After 3 months of treatment, further approval may be granted at the 40mcg/kg/day dose if the prescriber documents the member is responding well to treatment and ~~is still not a candidate for~~ surgical intervention is still not clinically appropriate; or
12. Dose increases to 80mcg/kg/day (for 3 months) and 120mcg/kg/day (for 3 months) may be approved if there is no improvement in pruritus after 3 months of treatment with the lower dose(s). Further approval may be granted if the prescriber documents the member is responding well to treatment at the current dose and is still not a candidate for surgical intervention; and
13. If there is no improvement in pruritus after 3 months of treatment with the maximum 120mcg/kg/day dose, further approval of Bylvay™ will not be granted.

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[1] Albireo Pharma, Inc. Albireo Announces FDA Approval of Bylvay™ (Odevixibat), the First Drug Treatment for Patients with Progressive Familial Intrahepatic Cholestasis (PFIC). Available online at: https://ir.albireopharma.com/news-releases/news-release-details/albireo-announces-fda-approval-bylvaytm-odevixibat-first-drug. Issued 07/20/2021. Last accessed 10/18/2021.

[2] Bylvay™ (Odevixibat) Prescribing Information. Albireo Pharma, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215498s000lbl.pdf. Last revised 07/2021. Last accessed 10/18/2021.

[3] This Study Will Investigate the Efficacy and Safety of A4250 in Children with PFIC Types 1 or 2 (PEDFIC 1). *ClinicalTrials.gov*. Available online at: https://www.clinicaltrials.gov/ct2/show/NCT03566238. Last revised 09/05/2021. Last accessed 10/18/2021.

[4] U.S. Food and Drug Administration (FDA). Drugs@FDA. Drug Approval Package: Bylvay™: Integrated Review. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/215498Orig1s000IntegratedR.pdf. Issued 07/19/2021. Last accessed 10/18/2021.

Appendix F

Vote to Prior Authorize Lupkynis™ (Voclosporin) and Saphnelo™ (Anifrolumab-fnia) and Update the Approval Criteria for the Targeted Immunomodulator Agents

Oklahoma Health Care Authority
November 2021

Market News and Updates[1,2]

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

- **January 2021:** The FDA approved Lupkynis™ (voclosporin) as the first oral therapy in combination with mycophenolate mofetil (MMF) and low dose oral corticosteroids (OCS) for the treatment of lupus nephritis (LN), a condition that can cause irreversible kidney damage. In the pivotal Phase 3 study, AURORA, patients who were on Lupkynis™ plus MMF and low dose OCS were more than 2 times as likely to achieve a complete renal response than those taking placebo plus MMF and low dose OCS. Also, patients in the Lupkynis™ group achieved a 50% reduction in urine protein-to-creatinine ratio (UPCR) twice as fast as those in the placebo arm. UPCR is a standard measurement used to monitor protein levels in the kidney. The most common side effects reported were decreased glomerular filtration rate (GFR), hypertension, and diarrhea.
- **August 2021:** The FDA approved Saphnelo™ (anifrolumab-fnia) as the first-in-class type I interferon (IFN) receptor antibody for the treatment of moderate-to-severe systemic lupus erythematosus (SLE) in patients receiving standard therapy. The approval of Saphnelo™ was based on 2 Phase 3 studies (TULIP-1 and TULIP-2) and 1 Phase 2 study (MUSE) that compared the safety and efficacy of Saphnelo™ versus placebo in which both groups received standard therapy which included OCS, antimalarials, and immunosuppressants. In these studies, more patients treated with Saphnelo™ experienced a reduction in overall disease activity across organ systems, including skin and joints, and achieved a sustained reduction in OCS use when compared to placebo. The most common side effects reported were nasopharyngitis, upper respiratory tract infection, and bronchitis.

Lupkynis™ (Voclosporin) Product Summary[3]

Indication(s): Voclosporin is a calcineurin-inhibitor immunosuppressant indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with LN.

How Supplied: 7.9mg oral capsule

Dosing and Administration:

- Prior to initiating voclosporin, baseline estimated GFR (eGFR) and blood pressure (BP) need to be established
- Voclosporin is not recommended in patients with a baseline eGFR ≤45mL/min/1.73m^2 unless the benefit exceeds the risk
- Voclosporin should not be initiated in patients with a baseline BP of >165/105mmHg or in patients experiencing a hypertensive emergency
- The recommended starting dose is 23.7mg [(3) 7.9mg capsules] twice daily
- Voclosporin should be swallowed whole on an empty stomach and administered consistently as close to a 12-hour schedule as possible and with at least 8 hours between doses
- Discontinuation of voclosporin should be considered in patients who do not experience a therapeutic benefit by 24 weeks
- For patients with severe renal impairment or mild-to-moderate hepatic impairment, the recommended dose is 15.8mg [(2) 7.9mg capsules] twice daily

Cost: The Wholesale Acquisition Cost (WAC) of Lupkynis™ is $65.83 per 7.9mg capsule. The estimated annual cost based on the recommended dose of 23.7mg twice daily is $142,192.80.

Saphnelo™ (Anifrolumab-fnia) Product Summary[4]

Indication(s): Anifrolumab is a type I IFN receptor antagonist indicated for the treatment of adult patients with moderate-to-severe SLE, who are receiving standard therapy. The efficacy of anifrolumab has not been evaluated in patients with severe active LN or severe active central nervous system (CNS) lupus.

How Supplied: 300mg/2mL (150mg/mL) in a single-dose vial (SDV)

Dosing and Administration: The recommended dose is 300mg via intravenous (IV) infusion over 30 minutes every 4 weeks

Cost: The WAC of Saphnelo™ is $4,600.54 per 300mg/2mL SDV. The estimated annual cost based on the recommended dose of 300mg every 4 weeks is $59,807.02.

Recommendations

The College of Pharmacy recommends the prior authorization of Lupkynis™ (voclosporin) and Saphnelo™ (anifrolumab-fnia) with the following criteria:

Lupkynis™ (Voclosporin) Approval Criteria:

1. An FDA approved indication for the treatment of adults with active lupus nephritis (LN) in combination with a background immunosuppressive therapy regimen; and
    a. Lupkynis™ must be used in combination with mycophenolate mofetil and low dose oral corticosteroids; and
2. Member must be 18 years of age or older; and
3. Lupkynis™ must be prescribed by a nephrologist, rheumatologist, or other specialist with expertise in the treatment of LN; and
4. Member's current urine protein-to-creatinine ratio (UPCR) must be provided and must be ≥1.5mg/mg; and
5. Member's current estimated glomerular filtration rate (eGFR) must be provided and must be >45mL/min/1.73m^2 prior to initiating treatment with Lupkynis™; and
    a. Prescriber must agree to monitor renal function regularly during treatment with Lupkynis™ and modify the dose as needed in accordance with the Lupkynis™ *Prescribing Information*; and
6. Member's current blood pressure (BP) must be ≤165/105mmHg prior to initiating treatment with Lupkynis™; and
    a. Prescriber must agree to monitor BP regularly during treatment with Lupkynis™ and agree to discontinue treatment if BP is >165/105mmHg or member experiences a hypertensive emergency; and
7. Member must not be taking strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin) concomitantly with Lupkynis™; and
8. Prescriber must verify member has been counseled on proper administration of Lupkynis™ including taking it on an empty stomach every 12 hours; and
9. Lupkynis™ will not be approved in combination with biologic therapies or cyclophosphamide; and
10. A quantity limit of 180 capsules per 30 days will apply; and
11. Initial approvals will be for the duration of 6 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by a reduction in the member's UPCR. If the member does not experience therapeutic benefit by 6 months, discontinuation of Lupkynis™ should be considered; and
12. The safety and efficacy of Lupkynis™ have not been established beyond 1 year of treatment. For continued authorization consideration after 1 year of treatment, a patient-specific, clinically significant reason why a longer treatment duration is appropriate for the member must be provided.

Saphnelo™ (Anifrolumab-fnia) Approval Criteria:

1. An FDA approved indication for the treatment of adult patients with moderate-to-severe systemic lupus erythematosus (SLE), who are receiving standard therapy; and
2. Member must be 18 years of age or older; and
3. Documented inadequate response to at least 1 of the following medications appropriate to member's specific disease state:
   a. High-dose oral corticosteroids; or
   b. Methotrexate; or
   c. Azathioprine; or
   d. Mycophenolate; or
   e. Cyclophosphamide; or
   f. Hydroxychloroquine/chloroquine; and
4. Member must not have severe active lupus nephritis (LN) or severe active central nervous system lupus; and
5. Saphnelo™ will not be approved for combination use with biologic therapies or cyclophosphamide; and
6. Initial approvals will be for the duration of 6 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment.

Additionally, the College of Pharmacy recommends the following changes to the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) Tier chart based on net costs (changes and new criteria noted in red; only criteria with updates are listed):

1. Updating the prior authorization criteria for Tier-3 Targeted Immunomodulator Agents; and
2. Moving Kineret® (anakinra), Otezla® (apremilast), Rituxan® (rituximab), Xeljanz® (tofacitinib), Xeljanz® XR [tofacitinib extended-release (ER)], and Xeljanz® oral solution (tofacitinib) from Tier-3 to Tier-2 of the Targeted Immunomodulator Agents PBPA Tier chart

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®, Orencia® ClickJect™)≠
azathioprine	**anakinra (Kineret®)**	adalimumab-afzb (Abrilada™)±
hydroxychloroquine	**apremilast (Otezla®)ß**	adalimumab-atto (Amjevita™)±
leflunomide	etanercept (Enbrel®)	adalimumab-adbm (Cyltezo™)±
mesalamine	**rituximab (Rituxan®)~**	adalimumab-bwwd (Hadlima™)±
methotrexate	**tofacitinib (Xeljanz®, Xeljanz® XR, Xeljanz® oral solution)**	adalimumab-fkjp (Hulio®)±
minocycline		adalimumab-adaz (Hyrimoz™)±

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
NSAIDs		~~anakinra (Kineret®)~~
oral corticosteroids		~~apremilast (Otezla®)ß~~
sulfasalazine		baricitinib (Olumiant®)
		brodalumab (Siliq™)**
		canakinumab (Ilaris®)¥
		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi®)±
		etanercept-ykro (Eticovo™)±
		golimumab (Simponi®, Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)±
		infliximab-axxq (Avsola™)±
		infliximab-dyyb (Inflectra™)±
		infliximab-abda (Renflexis™)±
		ixekizumab (Taltz®)
		risankizumab-rzza (Skyrizi™)
		~~rituximab (Rituxan®)~~~
		rituximab-abbs (Truxima®)±
		rituximab-arrx (Riabni™)±
		rituximab-pvvr (Ruxience®)±
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®) Ω
		tildrakizumab-asmn (Ilumya™)
		tocilizumab (Actemra®)π
		~~tofacitinib (Xeljanz®, Xeljanz® XR)**~~
		upadacitinib (Rinvoq™)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio®)**

DMARDs = disease modifying anti-rheumatic drugs; NSAIDs = non-steroidal anti-inflammatory drugs
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC). Products may be moved to a higher tier based on net cost if the manufacturer chooses not to participate in supplemental rebates. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.
±Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.
+Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) and noninfectious intermediate and posterior uveitis and panuveitis.
ß Unique criteria applies for a diagnosis of Behçet's disease (BD).
¥Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), Familial Mediterranean Fever (FMF), Systemic Juvenile Idiopathic Arthritis (SJIA), or Adult-Onset Still's Disease (AOSD).
~Unique criteria applies for a diagnosis of pemphigus vulgaris (PV). Unique criteria applies for a diagnosis of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).
ΩFor Cosentyx® (secukinumab), only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).
πUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome (CRS).
≠Orencia® ClickJect™ requires a patient-specific, clinically significant reason why the member cannot use the typical pre-filled syringe formulation.
** Unique criteria applies to this medication for approval.

Targeted Immunomodulator Agents Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least 1 Tier-1 medication (appropriate to the member's disease state) in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Targeted Immunomodulator Agents Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials (within the last 360 days) of 1 Tier-1 medication (appropriate to the member's disease state) and ~~all available~~ at least 2 Tier-2 medications (appropriate to the member's disease state) that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 medications.

Xeljanz® (Tofacitinib Oral Solution) Approval Criteria:

1. Member must meet Tier-2 approval criteria; and
2. An age restriction of 2 years of age to 10 years of age will apply. Members older than 10 years of age require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

~~**Xeljanz® (Tofacitinib) Approval Criteria:**~~

~~1. Member must meet Tier-3 approval criteria; and~~
~~2. Member must have a negative tuberculosis test, successful treatment of active tuberculosis, or close evaluation and appropriate treatment of latent tuberculosis; and~~
~~3. Severe hepatic impairment has been ruled out; and~~
~~4. Approval will be for 12 weeks, after which time, prescriber must confirm performance of the following tests (and verification that the results are acceptable to prescriber) for further approval:~~
   ~~a. Lymphocytes; and~~
   ~~b. Neutrophils; and~~
   ~~c. Hemoglobin; and~~
   ~~d. Liver enzymes; and~~
   ~~e. Lipid panel; and~~
~~5. Subsequent approvals will be for the duration of 1 year. Yearly approvals require performance of repeat tuberculosis test.~~

~~**Xeljanz® XR [Tofacitinib Extended-Release (ER)] Approval Criteria:**~~

~~1. Member must meet Tier-3 approval criteria and all Xeljanz® approval criteria; and~~

~~2. A patient-specific, clinically significant reason why the member cannot take the twice daily formulation of Xeljanz® must be provided.~~

Lastly, the College of Pharmacy recommends the following changes to the criteria for the Targeted Immunomodulator Agents that have biosimilar product(s) (changes noted in red):

Abrilada™ (Adalimumab-afzb), Amjevita™ (Adalimumab-atto), Cyltezo™ (Adalimumab-adbm), Hadlima™ (Adalimumab-bwwd), Hulio® (Adalimumab-fkjp), and Hyrimoz™ (Adalimumab-adaz) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Humira® (adalimumab) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Erelzi® (Etanercept-szza) and Eticovo™ (Etanercept-ykro) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Enbrel® (etanercept) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

~~Avsola® (Infliximab-axxq),~~ Inflectra® (Infliximab-dyyb) and Remicade® (Infliximab), ~~and Renflexis® (Infliximab-abda)~~ Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use ~~Remicade® (infliximab)~~ Avsola® (infliximab-axxq) and Renflexis® (infliximab-abda) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Riabni™ (Rituximab-arrx), Ruxience® (Rituximab-pvvr), and Truxima® (Rituximab-abbs) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Rituxan® (rituximab) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and

may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

[1] Aurinia Pharmaceuticals. FDA Approves Aurinia Pharmaceuticals' Lupkynis™ (Voclosporin) for Adult Patients with Active Lupus Nephritis. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20210122005501/en/FDA-Approves-Aurinia-Pharmaceuticals%E2%80%99-LUPKYNIS%E2%84%A2-voclosporin-for-Adult-Patients-with-Active-Lupus-Nephritis. Issued 01/22/2021. Last accessed 10/26/2021.

[2] AstraZeneca. Saphnelo™ (Anifrolumab) Approved in the U.S. for Moderate to Severe Systemic Lupus Erythematosus. Available online at: https://www.astrazeneca.com/media-centre/press-releases/2021/saphnelo-approved-in-the-us-for-sle.html. Issued 08/02/2021. Last accessed 10/26/2021.

[3] Lupkynis™ (Voclosporin) Prescribing Information. Aurinia Pharmaceuticals, Inc. Available online at: https://www.auriniapharma.com/lupkynis-prescribing-information. Last revised 01/2021. Last accessed 10/26/2021.

[4] Saphnelo™ (Anifrolumab-fnia) Prescribing Information. AstraZeneca Pharmaceuticals. Available online at: http://www.azpicentral.com/pi.html?product=saphnelo. Last revised 07/2021. Last accessed 10/26/2021.

Appendix G

Fiscal Year 2021 Annual Review of Botulinum Toxins

Oklahoma Health Care Authority
November 2021

Current Prior Authorization Criteria

Botulinum Toxins Approval Criteria:

1. For approval of Xeomin® or Myobloc®, a patient-specific, clinically significant reason the member cannot use Botox® or Dysport® must be provided; and
2. Cosmetic indications will not be covered; and
3. A diagnosis of chronic migraine (tension headaches are not a covered diagnosis), neurogenic overactive bladder, and non-neurogenic overactive bladder will require manual review (see specific criteria below); and
4. The following indications have been determined to be appropriate and are covered:
    a. Spasticity associated with:
        i. Cerebral palsy; or
        ii. Paralysis; or
        iii. Generalized weakness/incomplete paralysis; or
        iv. Larynx; or
        v. Anal fissure; or
        vi. Esophagus (achalasia and cardiospasms); or
        vii. Eye and eye movement disorders; or
    b. Cervical dystonia.

Botox® (OnabotulinumtoxinA) Approval Criteria [Chronic Migraine Diagnosis*]:

1. FDA indications are met:
    a. Member is 18 years of age or older; and
    b. Member has documented chronic migraine headaches:
        i. Frequency of ≥15 headache days per month with ≥8 migraine days per month and occurring for >3 months; and
        ii. Headache duration of ≥4 hours per day; and
2. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); and
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and

3. Migraine headache exacerbation secondary to other medical conditions or medication therapies have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
4. Member has no contraindications to Botox® injections; and
5. The member has failed medical migraine preventative therapy, including ≥2 agents with different mechanisms of action. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta blockers); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
6. Member is not frequently taking medications which are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and
7. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last 6 months by a neurologist for chronic migraine headaches and Botox® recommended as treatment (not necessarily prescribed or administered by a neurologist); and
9. Prescriber must verify that other aggravating factors that are contributing to the development of chronic migraine headaches are being treated when applicable (e.g., smoking); and
10. Member will not use the requested medication concurrently with a calcitonin gene-related peptide (CGRP) inhibitor for the prevention of migraine headaches.

Botox® (OnabotulinumtoxinA) Approval Criteria [Neurogenic Overactive Bladder Diagnosis*]:

1. Diagnosis of neurogenic bladder including underlying pathological dysfunction subtype confirmed by:
    a. Urodynamic studies to determine pathology and serve to provide objective evidence of bladder and external sphincter function; and
    b. A diary of fluid intake, incontinence, voiding, and catheterization times and amounts to provide a record of actual occurrences; and
2. Member must have a patient-specific, clinically significant reason why anticholinergic medications are no longer an option for the member; and
3. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
4. Botox® must be administered by a urologist.

Botox® (OnabotulinumtoxinA) Approval Criteria [Non-Neurogenic Overactive Bladder Diagnosis*]:

1. Member must have severe disease (≥5 urinary incontinence episodes per day on medication) and specific pathology determined via urodynamic studies; and
2. Member must have participated in behavioral therapy for ≥12 weeks that did not yield adequate clinical results; and
3. Member must have had compliant use of ≥3 anti-muscarinic or beta-3 adrenoceptor agonist medications for ≥12 weeks each, alone or in combination with behavioral therapy, that did not yield adequate clinical results. One of those trials must have been an extended-release formulation; and
4. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
5. Botox® must be administered by a urologist.

***Other botulinum toxins will not be approved for this diagnosis**

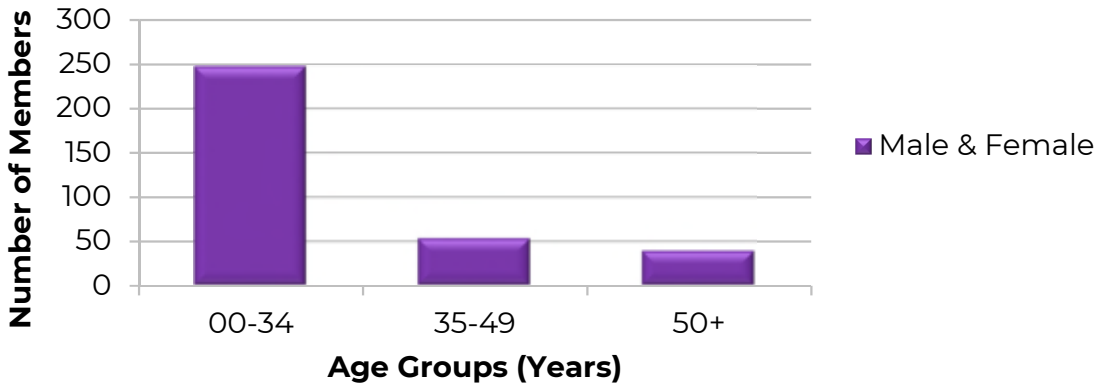
Utilization of Botulinum Toxins: Fiscal Year 2021

Comparison of Fiscal Years: Medical Claims

Fiscal Year	Total Members*	Total Claims†	Total Cost	Cost/ Claim	Total Units
2020	281	479	$678,650.25	$1,416.81	112,400
2021	339	589	$851,759.50	$1,446.11	139,631
% Change	**20.64%**	**23.17%**	**25.51%**	**1.90%**	**24.23%**
Change	**58**	**111**	**$173,109.25**	**$26.85**	**27,231**

*Total number of unduplicated utilizing 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, Fiscal Year 2021 = 07/01/2020 to 06/30/2021

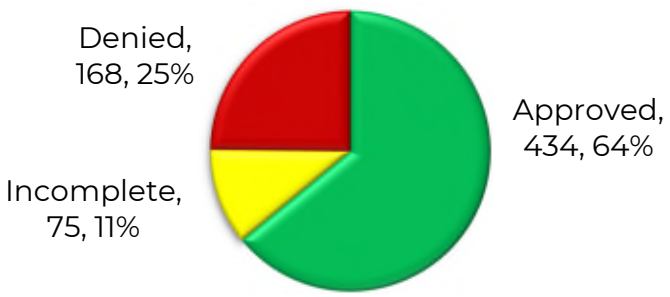
Demographics of Members Utilizing Botulinum Toxins: Medical Claims



Prior Authorization of Botulinum Toxins

There were 677 prior authorization requests submitted for botulinum toxins during fiscal year 2021. Botulinum toxins require a manual prior authorization for any covered diagnosis to ensure appropriate reimbursement for the billing provider. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



Market News and Updates[1,2]

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

- **February 2021:** The FDA approved an expanded indication for Botox® to include the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older who have an inadequate response to or are intolerant to anticholinergic medications. NDO occurs when the spinal cord and bladder are not able to communicate effectively, leading to involuntary bladder muscle contractions and urine leakage. Over time, this can lead to bladder and kidney damage. The approval was based on data from a randomized, double-blind Phase 3 study evaluating the safety and efficacy of Botox® in >100 pediatric patients with NDO. The results of the study showed a clinically significant reduction in daytime urinary incontinence episodes and also showed a decreased maximum bladder pressure and increased bladder capacity at week 6. The most common adverse reactions reported in the study were bacteriuria, urinary tract infection, leukocyturia, and hematuria.
- **July 2021:** The FDA expanded the label for Botox® to include administration in 8 additional muscles to treat adult patients with upper limb spasticity. The additional muscles include muscles of the elbow and forearm (brachialis, brachioradialis, pronator teres, and pronator quadratus), intrinsic hand muscles (lumbricals and interossei), and thumb muscles (flexor pollicis brevis and opponens pollicis). The label also has updated information on the use of ultrasound as a muscle localization technique in adult spasticity.

Recommendations

The College of Pharmacy recommends the following changes to the botulinum toxins prior authorization criteria to be consistent with the migraine prevention criteria for the calcitonin gene-related peptide (CGRP) inhibitors and based on the new FDA approved indication of pediatric NDO for Botox® (changes noted in red):

Botulinum Toxins Approval Criteria:

1. For approval of Xeomin® or Myobloc®, a patient-specific, clinically significant reason the member cannot use Botox® or Dysport® must be provided; and
2. Cosmetic indications will not be covered; and
3. A diagnosis of chronic migraine (tension headaches are not a covered diagnosis), neurogenic ~~overactive bladder~~ detrusor overactivity, and non-neurogenic overactive bladder will require manual review (see specific criteria below); and

4. The following indications have been determined to be appropriate and are covered:
    a. Spasticity associated with:
        i. Cerebral palsy; or
        ii. Paralysis; or
        iii. Generalized weakness/incomplete paralysis; or
        iv. Larynx; or
        v. Anal fissure; or
        vi. Esophagus (achalasia and cardiospasms); or
        vii. Eye and eye movement disorders; or
    b. Cervical dystonia.

Botox® (OnabotulinumtoxinA) Approval Criteria [Chronic Migraine Diagnosis*]:

1. FDA indications are met:
    a. Member is 18 years of age or older; and
    b. Member has documented chronic migraine headaches:
        i. Frequency of ≥15 headache days per month with ≥8 migraine days per month and occurring for >3 months; and
        ii. Duration of 4 hours of headache per day or longer; and
2. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); and
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
3. Migraine headache exacerbation secondary to other medical conditions or medication therapies have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
4. Member has no contraindications to Botox® injections; and
5. The member has failed medical migraine preventative therapy, including ≥2 agents with different mechanisms of action. Trials must be at least 8 weeks in duration (or documented adverse effects) within the last 365 days. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta blockers); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
6. Member is not frequently taking medications which are known to cause medication overuse headaches (MOH or rebound headaches) in

the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:

a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
c. Opioids (≥10 days/month for >3 months); and
d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
e. Ergotamine-containing medications (≥10 days/month for >3 months); and
f. Triptans (≥10 days/month for >3 months); and

7. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last 6 months by a neurologist for chronic migraine headaches and Botox® recommended as treatment (not necessarily prescribed or administered by a neurologist); and
9. Prescriber must verify that other aggravating factors that are contributing to the development of chronic migraine headaches are being treated when applicable (e.g., smoking); and
10. Member will not use the requested medication concurrently with a calcitonin gene-related peptide (CGRP) inhibitor for the prevention of migraine headaches.

Botox® (OnabotulinumtoxinA) Approval Criteria [Neurogenic ~~Overactive Bladder~~ Detrusor Overactivity (NDO) Diagnosis*]:

1. Diagnosis of ~~neurogenic bladder~~ 1 of the following:
   a. Urinary incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury, multiple sclerosis] in adult members; or
   b. NDO in pediatric members; and
2. Underlying pathological dysfunction subtype confirmed by:
   a. Urodynamic studies to determine pathology and serve to provide objective evidence of bladder and external sphincter function; and
   b. A diary of fluid intake, incontinence, voiding, and catheterization times and amounts to provide a record of actual occurrences; and
3. Member must have a clinically significant reason why anticholinergic medications are no longer an option for the member; and
4. Member must be 5 ~~18~~ years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder

needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and

5. Botox® must be administered by a urologist.

***Other botulinum toxins will not be approved for this diagnosis**

Utilization Details of Botulinum Toxins: Fiscal Year 2021

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
BOTOX (J0585)	564	325	$826,183.30	$1,464.86	1.74
DYSPORT (J0586)	16	10	$14,170.20	$885.64	1.60
MYOBLOC (J0587)	5	4	$7,382.00	$1,476.40	1.25
XEOMIN (J0588)	4	2	$4,024.00	$1,006.00	2
TOTAL	**589⁺**	**339***	**$851,759.50**	**$1,446.11**	**1.74**

*Total number of unduplicated utilizing members.
⁺Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

[1] AbbVie. FDA Approves Expanded Botox® (OnabotulinumtoxinA) Label to Include Eight New Muscles to Treat Adults with Upper Limb Spasticity. Available online at: https://www.prnewswire.com/news-releases/fda-approves-expanded-botox-onabotulinumtoxina-label-to-include-eight-new-muscles-to-treat-adults-with-upper-limb-spasticity-301343906.html. Issued 07/29/2021. Last accessed 10/05/2021.
[2] AbbVie. Botox® (OnabotulinumtoxinA) Receives FDA Approval for Pediatric Detrusor Overactivity Associated With a Neurologic Condition. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/botox-onabotulinumtoxina-receives-fda-approval-for-pediatric-detrusor-overactivity-associated-with-a-neurologic-condition-301225563.html. Issued 02/10/2021. Last accessed 10/05/2021.

Appendix H

Fiscal Year 2021 Annual Review of Asthma and Chronic Obstructive Pulmonary Disease (COPD) Maintenance Medications

Oklahoma Health Care Authority
November 2021

Current Prior Authorization Criteria

Inhaled Corticosteroids (ICS) and Combination Products	
Tier-1	**Tier-2***
budesonide (Pulmicort Flexhaler®)	beclomethasone dipropionate (QVAR® RediHaler®)
budesonide/formoterol (Symbicort®) – **Brand Preferred**	fluticasone furoate (Arnuity® Ellipta®)
ciclesonide (Alvesco®)	fluticasone furoate/vilanterol (Breo® Ellipta®)
fluticasone propionate (Flovent®)	fluticasone propionate/salmeterol (AirDuo® Digihaler®)
fluticasone propionate/salmeterol (Advair®)	fluticasone propionate/salmeterol (AirDuo RespiClick®)
mometasone furoate (Asmanex®)¥	fluticasone propionate (ArmonAir® Digihaler®)
mometasone furoate/formoterol (Dulera®)◊	mometasone furoate 50mcg (Asmanex® HFA)
	mometasone furoate/formoterol 50mcg/5mcg (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), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
¥Includes all strengths and formulations other than Asmanex® HFA 50mcg.
◊ Includes all strengths other than Dulera® 50mcg/5mcg.
*Unique criteria applies to each Tier-2 product.

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 (ICS) 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.

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.

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.

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 corticosteroids (ICS) are 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.

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 appropriate for the member must be provided.

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

1. An FDA approved diagnosis of asthma; and
2. Member must be at the age indicated for the requested product:
    a. Asmanex® HFA 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.

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.

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

1. An FDA approved diagnosis; 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.

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 (ICS) 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.

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA)	
Tier-1	**Tier-2**
Long-Acting Beta$_2$ Agonists* (LABA)	
salmeterol inhalation powder (Serevent®)	arformoterol nebulizer solution (Brovana®)
	formoterol nebulizer solution (Perforomist®)
	indacaterol inhalation powder (Arcapta® Neohaler®)
	olodaterol inhalation spray (Striverdi® Respimat®)
Long-Acting Muscarinic Antagonists (LAMA)	
tiotropium inhalation powder (Spiriva® HandiHaler®)	aclidinium inhalation powder (Tudorza® PressAir®)
tiotropium soft mist inhaler (Spiriva® Respimat®)	glycopyrrolate inhalation solution (Lonhala® Magnair®)
	revefenacin inhalation solution (Yupelri®)
	umeclidinium inhalation powder (Incruse® Ellipta®)

*Tier-1 combination products that contain a long-acting beta$_2$ agonist (LABA) qualify for the LABA trial requirement.
Tier-1 medications do not require prior authorization.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).

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.

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 members with severe asthma with an eosinophilic phenotype; and
2. Member must be 18 years of age or older; and
3. Member must have a blood eosinophil count ≥400cells/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⁺ [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.

⁺The current prior authorization criteria for Dupixent® for the indication of atopic dermatitis will be provided in the Fiscal Year 2021 Annual Review of Atopic Dermatitis Medications report, which is also being presented at the November 2021 Drug Utilization Review (DUR) Board meeting.

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

1. An FDA approved indication for add-on maintenance treatment of members with 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 ≥150cells/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 for Dupixent® for the indication of atopic dermatitis will be provided in the Fiscal Year 2021 Annual Review of Atopic Dermatitis (AD) Medications report, which is also being presented at the November 2021 Drug Utilization Review (DUR) Board meeting.

Fasenra® (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of members with 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 ≥150cells/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 [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.

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

1. An FDA approved indication for add-on maintenance treatment of members with 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 [Hypereosinophilic Syndrome (HES) Diagnosis]:

1. An FDA approved diagnosis of 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 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 from glucocorticoid therapy; 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.

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 aeroallergens 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 medium-to-high dose inhaled corticosteroids (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 be 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 Asthma and COPD Maintenance Medications: Fiscal Year 2021

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	11,219	47,622	$17,605,378.68	$369.69	$11.28	1,458,126	1,561,142
2021	12,459	51,049	$20,581,246.25	$403.17	$11.58	1,567,244	1,776,732
% Change	**11.10%**	**7.20%**	**16.90%**	**9.10%**	**2.70%**	**7.50%**	**13.80%**
Change	**1,240**	**3,427**	**$2,975,867.57**	**$33.48**	**$0.30**	**109,118**	**215,590**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021
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.

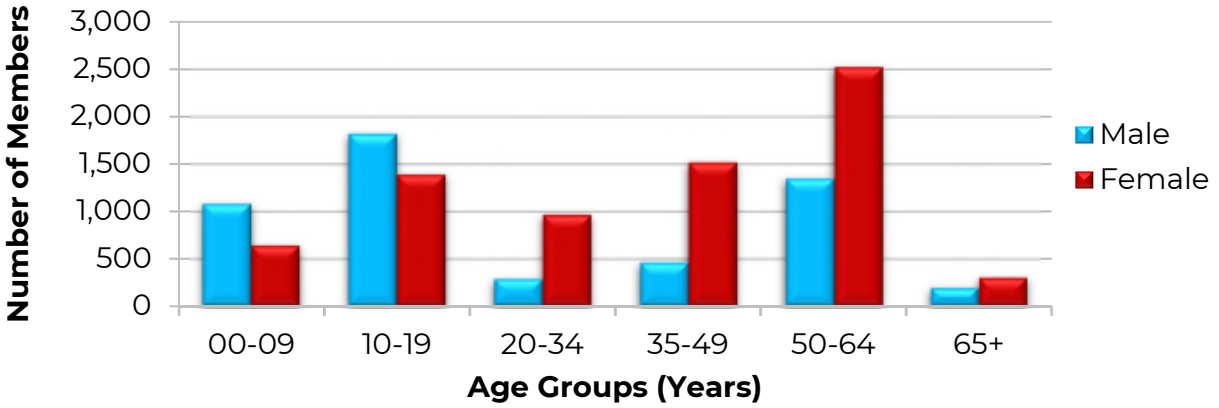
Comparison of Fiscal Years: Asthma-Indicated Monoclonal Antibodies¥

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	153	1,094	$3,218,523.73	$2,941.98	$106.73	3,455	30,157
2021	282	2,032	$6,177,109.05	$3,039.92	$106.04	6,371	58,251
% Change	**84.30%**	**85.70%**	**91.90%**	**3.30%**	**-0.60%**	**84.40%**	**93.20%**
Change	**129**	**938**	**$2,958,585.32**	**$97.94**	**-$0.69**	**2,916**	**28,094**

Costs do not reflect rebated prices or net costs.
¥Pharmacy claims data only.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021
Please note, the above utilization data includes Xolair®, Nucala, Dupixent® used for all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.

- Please note, Cinqair® (reslizumab) is billed by medical claims only and is not reflected in the above pharmacy claims data; however, there were no SoonerCare medical claims for Cinqair® (reslizumab) during fiscal year 2021. Fasenra® (benralizumab), Xolair® (omalizumab), and Nucala (mepolizumab) medical claims utilization details for fiscal year 2021 can be found at the end of this report.

Demographics of Members Utilizing Asthma and COPD Maintenance Medications: Pharmacy Claims

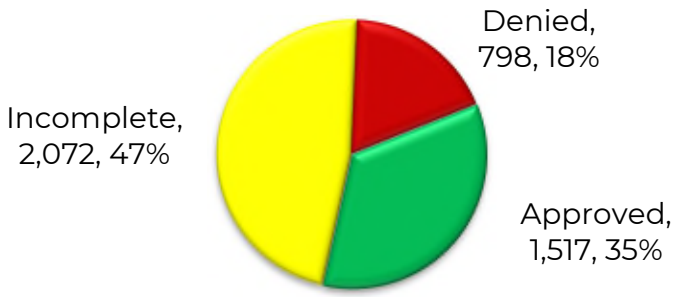


Top Prescriber Specialties of Asthma and COPD Maintenance Medications by Number of Claims: Pharmacy Claims

Prior Authorization of Asthma and COPD Maintenance Medications

There were 4,387 prior authorization requests submitted for asthma and COPD maintenance medications during fiscal year 2021. Of those prior authorization requests, 789 were submitted for monoclonal antibody medications. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Brovana® (arformoterol nebulizer solution): November 2021
- Dulera® (mometasone/formoterol inhalation aerosol): February 2023; exclusivity expiration
- 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): April 2035
- AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder): June 2039
- ArmonAir® Digihaler® (fluticasone propionate inhalation powder): June 2039

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

- **December 2020:** The FDA approved a supplemental Biologics License Application (sBLA) for Xolair® (omalizumab) for the add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids. The FDA's approval is based on results from the Phase 3 POLYP 1 and POLYP 2 trials. Both trials showed adult patients with nasal polyps who had an inadequate response to nasal corticosteroids and received Xolair® had a statistically significantly greater improvement from baseline at week 24 in Nasal Polyp Score (NPS) and weekly average Nasal Congestion Score (NCS) than patients who received placebo. The greater improvements in NPS and NCS in the Xolair® group compared to the placebo group were observed as early as the first assessment at week 4 in both trials. All patients received background nasal mometasone therapy during both the treatment period and a 5-week run-in period. The safety profile in POLYP 1 and POLYP 2 was consistent with the established safety profile for Xolair®. Xolair® is an injectable biologic that is also FDA approved for the treatment of moderate-to-severe persistent allergic asthma in patients 6 years of age or older whose asthma symptoms are not controlled by inhaled corticosteroids (ICS), and for the treatment of chronic idiopathic urticaria (CIU) in patients 12 years of age and older who continue to have hives that are not controlled by H_1 antihistamines. Approximately 460,000 patients have been treated in the United States with Xolair® since its initial approval for allergic asthma in 2003.
- **June 2021:** The FDA approved a new 200mg single-dose pre-filled pen formulation of Dupixent® (dupilumab) for use in patients 12 years of age and older for all FDA-approved indications. Previously, Dupixent® was available in a single-dose 300mg pre-filled pen as well as 200mg and 300mg single-dose pre-filled syringe formulations. The pre-filled pen features a hidden needle with single-press auto-injection and incorporates visual and audio feedback to assist with administration. After training by a health care professional, patients may self-inject

Dupixent® by subcutaneous (sub-Q) administration using either the pre-filled syringe or pre-filled pen formulations.

- **July 2021:** The FDA approved Nucala (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5), as a treatment for patients with chronic rhinosinusitis with nasal polyps (CRSwNP). This new indication for mepolizumab is for the add-on maintenance treatment of CRSwNP in adult patients 18 years of age and older with inadequate response to nasal corticosteroids. CRSwNP accounts for 2 to 4% of the United States population, affecting more than 5 million people. CRSwNP is one of a variety of diseases arising from inflammation in different tissues associated with elevated levels of eosinophils. It is often characterized by raised eosinophil levels, in which soft tissue growth, known as nasal polyps, develop in the sinuses and nasal cavity. CRSwNP can cause chronic symptoms such as nasal obstruction, loss of smell, facial pressure, and nasal discharge. Mepolizumab is the first anti-IL-5 biologic to be approved for adult patients with CRSwNP in the United States. The approval of mepolizumab as a treatment for CRSwNP is based on data from the SYNAPSE study which explored the effect of mepolizumab vs. placebo in more than 400 patients with CRSwNP. Mepolizumab achieved significant improvement in reducing the size of nasal polyps and nasal obstruction. All patients in the study received standard care, had a history of previous surgery (approximately 1 in 3 had ≥3 surgeries), and were in need of further surgery due to severe symptoms and increased size of their polyps. The SYNAPSE study showed there was a 57% reduction in the proportion of patients who had surgery in the group treated with mepolizumab vs. placebo [hazard ratio (HR): 0.43; 95% confidence interval (CI): 0.25, 0.76]. In addition, the proportion of patients requiring systemic corticosteroid use during the 52-week treatment period was lower in patients who received mepolizumab. Mepolizumab is also FDA approved for use in 3 other eosinophilic driven diseases: severe eosinophilic asthma in patients 6 years of age and older, eosinophilic granulomatosis with polyangiitis (EGPA) in adult patients, and hypereosinophilic syndrome (HES) in patients 12 years of age and older.
- **October 2021:** The FDA approved an age expansion for Dupixent® (dupilumab) as an add-on maintenance treatment for pediatric patients 6 to 11 years of age with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid (OCS) dependent asthma. Dupixent® was previously approved as an add-on treatment for patients 12 years of age and older with uncontrolled moderate-to-severe asthma (elevated eosinophils or OCS dependent asthma). The FDA approval is based on data from a Phase 3 randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of Dupixent® combined with standard-of-care

asthma therapy in children 6 to 11 years of age with uncontrolled moderate-to-severe asthma. The primary endpoint was the annualized rate of severe asthma exacerbations over 1 year defined as deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or hospitalization or emergency room visit due to asthma that required systemic corticosteroid treatment. The key secondary endpoint was the change from baseline in percent predicted pre-bronchodilator forced expiratory volume per second (FEV_1pp) at week 12. Two pre-specified population subsets were analyzed: patients with baseline blood eosinophils ≥300 cells/mcl and patients with markers of type 2 inflammation defined as elevated fractional exhaled nitric oxide (FeNO) ≥20 ppb or eosinophils ≥150 cells/mcl. Patients in the trial with eosinophils ≥300cells/mcL treated with Dupixent® (100mg or 200mg every 2 weeks, based on weight) in addition to standard-of-care asthma therapy had reduced rate of severe asthma attacks, with a 65% average reduction over 1 year compared to placebo (0.24 events per year for Dupixent® vs. 0.67 for placebo). Additionally, improved lung function measured by FEV_1pp was observed as early as 2 weeks of treatment and sustained for up to 52 weeks; at 12 weeks, patients receiving Dupixent® improved their lung function by 5.32 percentage points compared to placebo. Patients with elevated FeNO ≥20 ppb, an airway biomarker of inflammation, or eosinophils ≥150cell/mcL who added Dupixent® to standard-of-care asthma therapy experienced a reduction in the rate of severe asthma attacks. The safety results from the trial were generally consistent with the known safety profile of Dupixent® in patients 12 years of age and older with uncontrolled moderate-to-severe asthma, with the addition of helminth infections which were reported in 2.2% of Dupixent® patients and 0.7% of placebo patients. The overall rates of adverse events were 83% for Dupixent® and 80% for placebo. Adverse events that were more commonly observed with Dupixent® compared to placebo included injection site reactions, viral upper respiratory tract infections, and eosinophilia.

Pipeline:

- **June 2021:** The FDA accepted a Biologics License Application (BLA) and granted Priority Review for tezepelumab for the treatment of asthma. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA for tezepelumab is during the first quarter of 2022. The BLA submission is based on results from the PATHFINDER clinical trial program, including results from the pivotal NAVIGATOR Phase 3 trial in which tezepelumab demonstrated superiority across every primary and key secondary endpoint compared to placebo in a broad population of patients with uncontrolled asthma while receiving treatment with medium- or high-dose ICS plus at least 1 additional controller

medication with or without OCS. There were no clinically meaningful differences in safety results between the tezepelumab and placebo groups in the NAVIGATOR trial. The most frequently reported adverse events with tezepelumab were nasopharyngitis, upper respiratory tract infection, and headache. Results from the NAVIGATOR Phase 3 trial were published in the *New England Journal of Medicine* in May 2021. Tezepelumab was granted Breakthrough Therapy designation by the FDA for patients with severe asthma without an eosinophilic phenotype in September 2018.

Nucala (Mepolizumab) CRSwNP Product Summary[9,10]

Indication(s): Nucala (mepolizumab) is an interleukin-5 (IL-5) antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of adult patients 18 years of age and older with CRSwNP.

Limitations of Use:

- Not indicated for relief of acute bronchospasm or status asthmaticus

How Supplied: 100mg/mL single-dose, prefilled auto-injector, 100mg/mL prefilled syringe, and 100mg lyophilized powder in a single-dose vial (SDV) for reconstitution

CRSwNP Dosing and Administration:

- 100mg administered every 4 weeks by sub-Q injection into the upper arm, thigh, or abdomen

Mechanism of Action: Mepolizumab is an IL-5 antagonist (IgG1 kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Mepolizumab binds to IL-5 with a dissociation constant of 100pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. Inflammation is an important component in the pathogenesis of asthma, CRSwNP, EGPA, and HES. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation. Mepolizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma, CRSwNP, EGPA, and HES has not been definitively established.

Contraindication(s): History of hypersensitivity to mepolizumab or excipients in the formulation

Safety:

- Hypersensitivity Reactions: Hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred after administration of Nucala. Nucala should be discontinued in the event of a hypersensitivity reaction.
- Acute Asthma Symptoms or Deteriorating Disease: Nucala should not be used to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with Nucala.
- Opportunistic Infections (Herpes Zoster): Herpes zoster infections have occurred in patients receiving Nucala in clinical trials. Vaccination should be considered if medically appropriate.
- Reduction of Corticosteroid Dosage: Inhaled or systemic corticosteroids should not be discontinued abruptly upon initiation of therapy with Nucala. Corticosteroid dosage should be decreased gradually, if appropriate, under the direct supervision of a physician. Reduction in corticosteroid dosage may also be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.
- Parasitic (Helminth) Infection: Eosinophils may be involved in the immunological response to some helminth infections. Patients with pre-existing helminth infections should be treated before therapy with Nucala. If patients become infected while receiving treatment with Nucala and do not respond to anti-helminth treatment, Nucala should be discontinued until the parasitic infection resolves.

Adverse Reactions: The most common adverse reactions (≥5%) observed with Nucala used for the treatment of CRSwNP were oropharyngeal pain and arthralgia.

Efficacy: The approval of Nucala for CRSwNP was based on a randomized, double-blind, placebo-controlled clinical trial in 407 adult patients with CRSwNP. Patients received Nucala or placebo while continuing nasal corticosteroid therapy. The co-primary endpoints were change from baseline to week 52 in total endoscopic NPS (0 to 8 scale) and change from baseline in nasal obstruction visual analog scale (VAS) score (0 to 10 scale) during weeks 49 to 52. The key secondary endpoint was the time to first nasal surgery (nasal polypectomy) up to week 52.

- The mean change from baseline in total endoscopic NPS was 0.06 and -0.87 for placebo and Nucala, respectively (treatment difference: -0.93; 95% CI: -1.31, -0.55).
- The mean change from baseline in nasal obstruction VAS score was -2.54 and -4.40 for placebo and Nucala, respectively (treatment difference: -1.86; 95% CI: -2.53, -1.19).

- The proportion of patients who had nasal surgery was significantly reduced by 57% (HR: 0.43; 95% CI: 0.25, 0.76) in the group treated with Nucala vs. placebo. By week 52, 9% of patients who received Nucala had surgery vs. 23% who received placebo.

Xolair® (Omalizumab) Nasal Polyps Product Summary[11,12]

Indication(s): Xolair® (omalizumab) is an anti-IgE antibody indicated for nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.

Limitations of Use:
- Not indicated for acute bronchospasm or status asthmaticus
- Not indicated for other allergic conditions or other forms of urticaria

Boxed Warning: Anaphylaxis
- Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair®. Anaphylaxis has occurred after the first dose of Xolair® but also has occurred beyond 1 year after beginning treatment. Initiate Xolair® therapy in a healthcare setting, closely observe patients for an appropriate period of time after Xolair® administration and be prepared to manage anaphylaxis which can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur. Selection of patients for self-administration of Xolair® should be based on criteria to mitigate risk from anaphylaxis.

How Supplied: 75mg/0.5mL and 150mg/mL solution in a single-dose prefilled syringe; 150mg lyophilized powder in a SDV for reconstitution

Nasal Polyps Dosing and Administration:
- Xolair® 75mg to 600mg by sub-Q injection every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment and by body weight (kg); refer to the *Prescribing Information* for specific dosage information

Mechanism of Action: Omalizumab inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells, basophils, and dendritic cells, resulting in FcεRI down-regulation on these cells. In allergic asthmatics, treatment with omalizumab inhibits IgE-mediated inflammation, as evidenced by reduced blood and tissue eosinophils and reduced inflammatory mediators, including IL-4, IL-5, and IL-13.

Contraindication(s): Severe hypersensitivity reaction to Xolair® or any ingredient of Xolair®

Safety:

- Anaphylaxis: Anaphylaxis has been reported to occur after administration of Xolair®. Xolair® therapy should be initiated in a health care setting prepared to manage anaphylaxis which can be life-threatening, and patients should be observed closely for an appropriate period of time after administration of Xolair®. Patients should be informed of the signs and symptoms of anaphylaxis and instructed to seek medical care should signs or symptoms occur. Xolair® should be discontinued in patients who experience a severe hypersensitivity reaction.
- Malignancy: Malignant neoplasms have been observed in patients receiving Xolair® in clinical trials. The observed malignancies in Xolair®-treated patients were a variety of types, with breast, non-melanoma skin, prostate, melanoma, and parotid occurring more than once. The impact of longer exposure to Xolair® or use in patients at higher risk for malignancy is not known.
- Acute Asthma Symptoms and Deteriorating Disease: Xolair® should not be used for the treatment of acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with Xolair®.
- Corticosteroid Reduction: Inhaled or systemic corticosteroids should not be discontinued abruptly upon initiation of Xolair® therapy for asthma or nasal polyps. Corticosteroid dosage should be decreased gradually under the direct supervision of a physician. Use of Xolair® in combination with corticosteroids has not been evaluated in patients with chronic spontaneous urticaria.
- Eosinophilic Conditions: In rare cases, patients with asthma on Xolair® therapy may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition often treated with systemic corticosteroid therapy. These events usually have been associated with the reduction of OCS therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association with Xolair® and these underlying conditions has not been established.
- Fever, Arthralgia, and Rash: Some patients treated with Xolair® have experienced a constellation of signs and symptoms including arthritis/arthralgia, rash, fever, and lymphadenopathy with an onset of 1 to 5 days after the first or subsequent injections of Xolair®. These signs and symptoms have recurred after additional doses in some patients. Although circulating immune complexes or a skin biopsy consistent with a Type III reaction were not seen with these cases, these signs and symptoms are similar to those seen in patients with serum sickness.

Physicians should stop Xolair® if a patient develops this constellation of signs and symptoms.

- Parasitic (Helminth) Infection: Patients at high risk of geohelminth (i.e., roundworm, hookworm, whipworm, threadworm) infection should be monitored while on Xolair® therapy. In a 1-year clinical trial conducted in Brazil in adult and adolescent patients at high risk for geohelminth infections, 53% of Xolair®-treated patients experienced an infection compared to 42% of placebo controls. Response to appropriate anti-geohelminth treatment of infection was not different among treatment groups.
- Laboratory Tests: Serum total IgE levels increase following administration of Xolair® due to formation of Xolair®:IgE complexes. Elevated serum total IgE levels may persist for up to 1 year following discontinuation of Xolair®. Serum total IgE levels obtained less than 1 year following discontinuation of Xolair® should not be used to reassess the dosing regimen for patients with asthma or nasal polyps, as these levels may not reflect steady-state free IgE levels.

Adverse Reactions: The most common adverse reactions (≥3% of patients) in clinical studies of Xolair® in adult patients included the following: headache, injection site reaction, arthralgia, upper abdominal pain, and dizziness.

Efficacy: The approval of Xolair® for the treatment of nasal polyps was based on 2 randomized, double blind, placebo-controlled clinical trials in 265 patients with nasal polyps with inadequate response to nasal corticosteroids. The co-primary endpoints in the studies were NPS and average daily NCS at week 24. NPS was measured via endoscopy and scored (range 0 to 4 per nostril, with 0 indicating no polyps and 4 indicating large polyps causing complete obstruction of the inferior nasal cavity) for a total NPS (range 0 to 8). Nasal congestion was measured by a daily assessment on a 0 to 3 point severity scale (0 indicates no nasal congestion; higher scores indicate increased severity of nasal congestion).

- In the 2 trials, the mean change from baseline in NPS at week 24 for Xolair® compared to placebo was -1.1 vs. 0.1 (treatment difference: -1.1; 95% CI: -1.6, -0.7; P<0.0001) and -0.9 vs. -0.3 (treatment difference: -0.6; 95% CI: -1.1, -0.1; P=0.0140), respectively.
- In the 2 trials, the mean change from baseline in NCS at week 24 for Xolair® compared to placebo was -0.9 vs. -0.4 (treatment difference: -0.6; 95% CI: -0.8, -0.3; P=0.0004) and -0.7 vs. -0.2 (treatment difference: -0.5; 95% CI: -0.8, -0.2; P=0.0017), respectively.

Cost Comparison: Nasal Polyps

Product	Cost Per Month	Cost Per Year
Nucala (mepolizumab) 100mg/mL syringe*	$3,166.99	$41,170.87
Dupixent® (dupilumab) 300mg/2mL syringe+	$3,087.27	$40,134.57
Xolair® (omalizumab) 150mg/mL◊	$565.02-$9,040.32	$6,780.24-$108,483.84
fluticasone 50mcg nasal spray (generic)¥	$4.58	$54.91

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Nucala (mepolizumab) cost based on 100mg once every 4 weeks.
+Dupixent® (dupilumab) cost based on 300mg every other week.
◊Xolair® (omalizumab) cost based on the minimum dose of 75mg every 4 weeks to the maximum dose of 600mg every 2 weeks.
¥Fluticasone (generic Flonase®) cost based on a maximum of 2 sprays per nostril per day [(1) 16 gram bottle containing 120 sprays].

Recommendations

The College of Pharmacy recommends updating the approval criteria for Dupixent® (dupilumab), Nucala (mepolizumab), and Xolair® (omalizumab) based on the new FDA approved indications (changes and new criteria shown in red):

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

1. An FDA approved indication for add-on maintenance treatment of members with moderate-to-severe eosinophilic phenotype asthma or oral corticosteroid-dependent asthma; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have a blood eosinophil count of ≥150cells/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.

Nucala (Mepolizumab 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. Nucala 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 be 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. 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
10. 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
11. Requests for concurrent use of Nucala 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
12. 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
13. A quantity limit of 1 vial, prefilled autoinjector, or prefilled syringe per 28 days will apply.

Xolair® (Omalizumab) Approval Criteria [Nasal Polyps Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of nasal polyps in adult members with inadequate response to nasal corticosteroids; and
2. Member must be 18 years of age or older; and
3. Member must have a trial of intranasal corticosteroids for at minimum the past 4 weeks; and
4. Prescriber must verify member will continue to receive intranasal corticosteroid therapy, unless contraindicated; and
5. 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
6. Member has evidence of nasal polyposis by direct examination, sinus CT scan, or endoscopy; and
7. Member must have a pretreatment serum IgE level between 30 and 1,500 IU/mL; and
8. Member's weight must be between 31kg and 150kg; and
9. Prescribed Xolair® dose must be an FDA approved regimen per Xolair® *Prescribing Information*; and
10. Xolair® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
11. Xolair® 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
12. 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.

Utilization Details of Asthma and COPD Maintenance Medications: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
ICS/LABA COMBINATION PRODUCTS					
TIER-1 UTILIZATION					
SYMBICORT AER 160-4.5MCG	9,178	2,827	$3,708,641.94	$404.08	18.02%
ADVAIR HFA AER 115/21MCG	6,830	1,973	$2,609,038.72	$382.00	12.68%
ADVAIR DISKUS AER 250/50MCG	3,987	1,315	$1,688,354.37	$423.46	8.20%
SYMBICORT AER 80-4.5MCG	3,126	1,220	$1,041,266.31	$333.10	5.06%
FLUTIC/SALME AER 250/50MCG	3,124	1,149	$487,482.58	$156.04	2.37%
DULERA AER 200-5MCGMCG	2,858	740	$916,454.09	$320.66	4.45%
ADVAIR HFA AER 230/21MCG	2,009	566	$1,040,969.45	$518.15	5.06%
DULERA AER 100-5MCGMCG	1,703	564	$538,618.63	$316.28	2.62%
ADVAIR HFA AER 45/21MCG	1,629	528	$506,252.01	$310.77	2.46%
ADVAIR DISKUS AER 500/50MCG	1,482	457	$862,127.03	$581.73	4.19%
ADVAIR DISKUS AER 100/50MCG	1,309	519	$426,882.90	$326.11	2.07%
FLUTIC/SALME AER 500/50MCG	1,213	367	$255,830.26	$210.91	1.24%
FLUTIC/SALME AER 100/50MCG	1,008	389	$122,964.47	$121.99	0.60%
BUDES/FORMOT AER 160-4.5MCG	53	21	$12,931.78	$244.00	0.06%
BUDES/FORMOT AER 80-4.5MCG	3	2	$522.87	$174.29	0.00%
FLUTIC/SALME INH 113/14MCG	2	1	$182.58	$91.29	0.00%
SUBTOTAL	**39,514**	**12,638**	**$14,218,519.99**	**$359.83**	**69.08%**
TIER-2 UTILIZATION					
BREO ELLIPTA INH 100-25MCG	90	24	$34,360.13	$381.78	0.17%
DULERA AER 50-5MCG	42	19	$13,223.00	$314.83	0.06%
WIXELA INHUB AER 100/50MCG	1	1	$101.12	$101.12	0.00%
WIXELA INHUB AER 250/50MCG	1	1	$127.85	$127.85	0.00%
SUBTOTAL	**134**	**45**	**$47,812.10**	**$356.81**	**0.23%**
INDIVIDUAL COMPONENT LABA PRODUCTS					
TIER-1 UTILIZATION					
SEREVENT DISKUS AER 50MCG	615	226	$273,148.77	$444.14	1.33%
SUBTOTAL	**615**	**226**	**$273,148.77**	**$444.14**	**1.33%**
TIER-2 UTILIZATION					
BROVANA NEB 15MCG	76	21	$95,075.90	$1,251.00	0.46%
PERFOROMIST NEB 20MCG	34	9	$49,719.61	$1,462.34	0.24%
SUBTOTAL	**110**	**30**	**$144,795.51**	**$1,316.32**	**0.70%**
INDIVIDUAL COMPONENT LAMA PRODUCTS					
TIER-1 UTILIZATION					
SPIRIVA CAP HANDIHALER 18MCG	5,434	1,531	$3,345,953.43	$615.74	16.26%
SPIRIVA SPR 2.5MCG	2,287	674	$1,036,321.87	$453.14	5.04%
SPIRIVA AER 1.25MCG	1,430	426	$624,460.18	$436.69	3.03%
SUBTOTAL	**9,151**	**2,631**	**$5,006,735.48**	**$547.12**	**24.33%**
TIER-2 UTILIZATION					
INCRUSE ELLIPTA INH 62.5MCG	71	15	$24,288.59	$342.09	0.12%
LONHALA MAGNAIR SOL 25MCG	47	10	$53,518.98	$1,138.70	0.26%
TUDORZA PRES AER 400/ACT	34	7	$18,285.56	$537.81	0.09%
YUPELRI SOL 175MCG/3ML	15	10	$25,889.34	$1,725.96	0.13%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
SUBTOTAL	**167**	**42**	**$121,982.47**	**$730.43**	**0.60%**
LABA/LAMA COMBINATION PRODUCTS					
ANORO ELLIPTA AER 62.5-25MCG	330	61	$154,979.07	$469.63	0.75%
STIOLTO AER 2.5-2.5	109	17	$49,467.55	$453.83	0.24%
BEVESPI AER 9-4.8MCG	61	11	$26,988.84	$442.44	0.13%
UTIBRON CAP NEOHALER 27.5-15.6	6	2	$2,231.66	$371.94	0.01%
SUBTOTAL	**506**	**91**	**$233,667.12**	**$461.79**	**1.13%**
ICS/LABA/LAMA COMBINATION PRODUCTS					
TRELEGY AER ELLIPTA 100-62.5-25	638	128	$443,380.98	$694.95	2.15%
BREZTRI AERO AEROSPHERE 160-9-4.8	22	13	$14,937.90	$679.00	0.07%
SUBTOTAL	**660**	**141**	**$458,318.88**	**$694.42**	**2.22%**
PDE4 ENZYME INHIBITOR PRODUCTS					
DALIRESP TAB 500MCG	159	28	$59,761.75	$375.86	0.29%
DALIRESP TAB 250MCG	33	7	$16,504.18	$500.13	0.08%
SUBTOTAL	**192**	**35**	**$76,265.93**	**$397.22**	**0.37%**
TOTAL	**51,049**	**12,459***	**$20,581,246.25**	**$403.17**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
ACT = actuation; AER = aerosol; BUDES = budesonide; CAP = capsule; FLUTIC = fluticasone; FORMOT = formoterol; HFA = hydrofluoroalkane; ICS = inhaled corticosteroid; INH = inhaler; LABA = long-acting beta$_2$ agonist; LAMA = long-acting muscarinic antagonist; NEB = nebulizer; PDE4 = phosphodiesterase-4; PRES = Pressair; SALME = salmeterol; SOL = solution; SPR = spray
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: PHARMACY CLAIMS					
DUPIXENT INJ 300MG/2ML	942	125	$2,911,031.58	$3,090.27	47.13%
DUPIXENT INJ 200MG/1.14ML	465	69	$1,447,626.11	$3,113.17	23.44%
DUPIXENT INJ 300/2ML PEN	189	52	$594,235.82	$3,144.10	9.62%
XOLAIR INJ 150MG/ML	160	21	$477,044.71	$2,981.53	7.72%
XOLAIR INJ 75MG/0.5ML	86	11	$95,319.64	$1,108.37	1.54%
NUCALA INJ 100MG	74	11	$230,039.68	$3,108.64	3.72%
XOLAIR SOL 150MG	39	6	$79,207.29	$2,030.96	1.28%
FASENRA INJ 30MG/ML	38	10	$184,760.06	$4,862.11	2.99%
NUCALA INJ 100MG PEN	21	3	$65,394.72	$3,114.03	1.06%
FASENRA PEN 30MG/ML	18	4	$92,449.44	$5,136.08	1.50%
TOTAL	**2,032**	**282***	**$6,177,109.05**	**$3,039.92**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
INJ = injection; SOL = solution
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: MEDICAL CLAIMS					
OMALIZUMAB INJ (J2357)	177	17	$415,143.91	$2,345.45	79.09%
MEPOLIZUMAB INJ (J2182)	19	5	$40,995.50	$2,157.66	7.81%
BENRALIZUMAB (J0517)	15	6	$68,780.00	$4,585.33	13.10%
TOTAL	**211†**	**21***	**$524,919.41**	**$2,487.77**	**100.00%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
INJ = injection
Fiscal Year 2021 = 07/01/2020 to 06/30/2021
Please note: The above medical utilization data for omalizumab (J2357) and mepolizumab (J2182) includes all FDA-approved diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.

Utilization Details of Inhaled Corticosteroids (ICS): Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
INHALED CORTICOSTEROID (ICS) PRODUCTS					
TIER-1 UTILIZATION					
FLOVENT HFA AER 110MCG	17,257	6,760	$4,560,386.63	$264.26	45.07%
FLOVENT HFA AER 44MCG	16,073	6,497	$3,216,744.82	$200.13	31.79%
BUDESONIDE SUS 0.5MG/2ML	2,588	1,119	$210,075.51	$81.17	2.08%
BUDESONIDE SUS 0.25MG/2ML	2,073	1,299	$155,345.47	$74.94	1.54%
FLOVENT HFA AER 220MCG	2,018	862	$859,098.72	$425.72	8.49%
PULMICORT INH 90MCG	750	327	$158,389.61	$211.19	1.57%
PULMICORT INH 180MCG	646	360	$172,192.53	$266.55	1.70%
ASMANEX HFA AER 100 MCG	641	254	$124,521.08	$194.26	1.23%
FLOVENT DISKUS AER 100MCG	461	230	$99,686.30	$216.24	0.99%
ASMANEX HFA AER 200 MCG	350	132	$81,154.96	$231.87	0.80%
FLOVENT DISKUS AER 50MCG	347	124	$69,824.95	$201.22	0.69%
ALVESCO AER 80MCG	308	120	$87,598.28	$284.41	0.87%
FLOVENT DISKUS AER 250MCG	297	95	$85,643.57	$288.36	0.85%
ASMANEX 60 AER 220MCG	225	77	$50,938.73	$226.39	0.50%
ALVESCO AER 160MCG	200	75	$54,557.50	$272.79	0.54%
BUDESONIDE SUS 1MG/2ML	166	64	$64,399.33	$387.95	0.64%
ASMANEX 30 AER 220MCG	149	50	$29,853.62	$200.36	0.30%
ASMANEX 120 AER 220MCG	63	29	$18,882.23	$299.72	0.19%
ASMANEX 30 AER 110MCG	49	19	$9,744.60	$198.87	0.10%
TIER-1 SUBTOTAL	**44,661**	**18,493**	**$10,109,038.44**	**$226.35**	**99.94%**
TIER-2 UTILIZATION					
QVAR REDIHALER AER 40MCG	18	6	$3,541.56	$196.75	0.04%
ARNUITY ELLIPTA INH 100MCG	14	4	$2,438.02	$174.14	0.02%
QVAR REDIHALER AER 80MCG	11	3	$2,854.22	$259.47	0.03%
TIER-2 SUBTOTAL	**43**	**13**	**$8,833.80**	**$205.44**	**0.09%**
TOTAL	**44,704**	**17,249***	**$10,117,872.24**	**$226.33**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
AER = aerosol; HFA = hydrofluoroalkane; INH= inhaler; SUS = suspension
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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[2] Roche. FDA Approves Xolair® (Omalizumab) for Adults with Nasal Polyps. Available online at: https://www.roche.com/media/releases/med-cor-2020-12-01.htm. Issued 12/01/2020. Last accessed 10/19/2021.
[3] GSK Announces FDA Approval for Nucala (Mepolizumab) for Use in Adults with Chronic Rhinosinusitis with Nasal Polyps. *Business Wire*. Available online at: https://www.yahoo.com/now/gsk-announces-fda-approval-nucala-220300078.html. Issued 07/29/2021. Last accessed 10/19/2021.
[4] FDA Accepts Dupixent® (Dupilumab) for Review in Children with Moderate-to-Severe Asthma. *PR Newswire*. Available online at: https://investor.regeneron.com/news-releases/news-release-details/fda-accepts-dupixentr-dupilumab-review-children-moderate-severe. Issued 03/04/2021. Last accessed 10/19/2021.
[5] Tezepelumab Granted Priority Review by United States FDA. *PR Newswire*. Available online at: https://www.amgen.com/newsroom/press-releases/2021/07/tezepelumab-granted-priority-review-by-u-s--fda. Issued 07/07/2021. Last accessed 10/19/2021.
[6] Park B. FDA Approves Dupixent® 200mg Single-Dose Prefilled Pen. *MPR*. Available online at: https://www.empr.com/home/news/dupixent-dupilumab-new-single-dose-200mg-prefilled-pen-fda-approved/. Issued 06/16/2021. Last accessed 10/26/2021.
[7] Dupixent® Prescribing Information. Regeneron Pharmaceuticals, Inc. Available online at: https://www.regeneron.com/downloads/dupixent_fpi.pdf. Last revised 10/2021. Last accessed 10/27/2021.
[8] FDA Expands Approval of Dupixent® (Dupilumab) to Include Children Aged 6 to 11 Years with Moderate-to-Severe Asthma. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-expands-approval-of-dupixent-dupilumab-to-include-children-aged-6-to-11-years-with-moderate-to-severe-asthma-301405141.html. Issued 10/20/2021. Last accessed 10/27/2021.
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[11] Xolair® (Omalizumab) Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/xolair_prescribing.pdf. Last revised 07/2021. Last accessed 10/19/2021.
[12] Xolair® (Omalizumab) – New Indication. *OptumRX*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/clinical-updates/clinicalupdates_xolair_2020-1203.pdf. Issued 2020. Last accessed 10/19/2021.

Appendix I

Fiscal Year 2021 Annual Review of Carbaglu® (Carglumic Acid)

Oklahoma Health Care Authority
November 2021

Current Prior Authorization Criteria

Carbaglu® (Carglumic Acid) Approval Criteria:

1. An FDA approved indication of N-acetylglutamate synthase (NAGS) deficiency; and
2. Carbaglu® must be prescribed by a geneticist or in consultation with a geneticist; and
3. Documentation of active management with a low protein diet; and
4. Initial approvals will be for the duration of 1 year. After that time, reauthorization will require the prescriber to verify the member is responding to therapy.

Utilization of Carbaglu® (Carglumic Acid): Fiscal Year 2021

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	1	11	$1,165,778.14	$105,979.83	$3,784.99	5,820	308
2021	1	13	$1,923,817.33	$147,985.95	$4,958.29	9,180	388
% Change	**0.00%**	**18.20%**	**65.00%**	**39.60%**	**31.00%**	**57.70%**	**26.00%**
Change	**0**	**2**	**$758,039.19**	**$42,006.12**	**$1,173.30**	**3,360**	**80**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Demographics of Members Utilizing Carbaglu® (Carglumic Acid)

- Due to the limited number of members utilizing Carbaglu® during fiscal year 2021, detailed demographic information could not be provided.

Top Prescriber Specialties of Carbaglu® (Carglumic Acid) by Number of Claims

- There was 1 prescriber for Carbaglu® during fiscal year 2021, a medical geneticist.

Prior Authorization of Carbaglu® (Carglumic Acid)

There was 1 prior authorization request submitted for Carbaglu® (carglumic acid) during fiscal year 2021 which was approved.

Market News and Updates[1,2]

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

- **January 2021:** The FDA approved a new indication for Carbaglu® (carglumic acid) as adjunctive therapy to standard of care [e.g., intravenous (IV) glucose, insulin, L-carnitine, protein restriction, dialysis] for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA) in pediatric and adult patients. This approval makes Carbaglu® the first and only FDA approved medication for the treatment of acute hyperammonemia due to PA or MMA. Carbaglu® was initially approved by the FDA in 2010 for N-acetylglutamate synthase (NAGS) deficiency, another rare metabolic disorder, as adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to NAGS deficiency and as maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency.

  PA and MMA are rare inherited metabolic disorders that result in the dysfunction of a specific step of amino acid catabolism due to deficient enzyme activity. As a result, toxic metabolites accumulate, which can cause hyperammonemia, a potentially life-threatening condition. Hyperammonemia is one of the most severe and life-threatening events that can occur in patients with PA or MMA. Hyperammonemia is a medical emergency that, if left untreated, can progress to irreversible brain damage, coma, or death. Carbaglu® acts as a replacement for N-acetylglutamate (NAG) in NAGS deficiency, PA, and MMA patients by activating carbamoyl phosphate synthetase (CPS 1), which improves or restores the function of the urea cycle, thus facilitating ammonia detoxification and urea production.

  FDA approval of the new indication for Carbaglu® was supported by a randomized, double-blind, placebo-controlled, multicenter clinical study comparing the effectiveness of Carbaglu® to placebo in the treatment of hyperammonemic episodes in patients with PA or MMA. The efficacy evaluation, based on 90 hyperammonemic episodes occurring in 24 patients, showed that patients receiving Carbaglu® demonstrated a quicker reduction of plasma ammonia level compared to patients receiving placebo. The primary endpoint was the time from the first dose to the earlier of blood ammonia level <50micromol/L or hospital discharge. Throughout the first 3 days of treatment, a higher proportion of Carbaglu®-treated episodes reached the primary endpoint compared to placebo-treated episodes. In the clinical study, at least 1 adverse reaction was reported in 42.2% of the 90 hyperammonemic episodes that occurred. The most common adverse events (≥5%) in Carbaglu®-treated patients were neutropenia, anemia,

vomiting, electrolyte imbalance, decreased appetite, hypoglycemia, lethargy/stupor, encephalopathy, and pancreatitis/increased lipase.

The recommended dosing for Carbaglu® for acute hyperammonemia due to PA or MMA in pediatric and adult patients is 150mg/kg/day for patients ≤15kg and 3.3g/m^2/day for patients >15kg. The daily dose should be divided into 2 equal doses and rounded up to the next multiple of 50mg. Each dose should be administered 12 hours apart. Treatment should be continued until the ammonia level is <50micromol/L or for a maximum duration of 7 days. During acute hyperammonemic episodes, Carbaglu® should be administered with other ammonia-lowering therapies, such as IV glucose, insulin, L-carnitine, protein restriction, and dialysis.

Recommendations

The College of Pharmacy recommends updating the current Carbaglu® (carglumic acid) prior authorization criteria based on the new FDA approved indication (updates and changes shown in red):

Carbaglu® (Carglumic Acid) Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Adjunctive therapy to the standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency; or
   b. Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency; or
   c. Adjunctive therapy to the standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA); and
2. Carbaglu® must be prescribed by a geneticist or in consultation with a geneticist; and
3. For a diagnosis of hyperammonemia due to NAGS deficiency:
   a. Documentation of active management with a low protein diet; and
   b. Initial approvals will be for the duration of 1 year. After that time, reauthorization will require the prescriber to verify the member is responding to therapy; or
4. For a diagnosis of acute hyperammonemia due to PA or MMA:
   a. Documentation the member's plasma ammonia level is ≥50micromol/L; and
   b. Prescriber must confirm Carbaglu® is being used concurrently with other ammonia-lowering therapies [e.g., intravenous (IV) glucose, insulin, L-carnitine, protein restriction, dialysis]; and
   c. Number of days Carbaglu® was received while hospitalized must be provided; and

d. Approvals will be for no longer than 7 days total (including treatment days while hospitalized) as there is currently no evidence to support the use of Carbaglu® for acute hyperammonemia due to PA or MMA beyond 7 days.

[1] Recordati Rare Diseases, Inc. Recordati Rare Diseases: Carbaglu® (Carglumic Acid) Tablets 200mg Receives U.S. FDA Approval for a New Indication to Treat Acute Hyperammonemia Associated with Propionic Acidemia and Methylmalonic Acidemia. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/recordati-rare-diseases-carbaglu-carglumic-acid-tablets-200mg-receives-us-fda-approval-for-a-new-indication-to-treat-acute-hyperammonemia-associated-with-propionic-acidemia-and-methylmalonic-acidemia-301215101.html. Issued 01/26/2021. Last accessed 10/17/2021.

[2] Carbaglu® (Carglumic Acid) Prescribing Information. Recordati Rare Diseases, Inc. Available online at: https://www.recordatirarediseases.com/sites/www.recordatirarediseases.com/files/inline-files/carbaglu-prescribing-information-012021.pdf. Last revised 01/2021. Last accessed 10/17/2021.

Appendix J

Fiscal Year 2021 Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide)

Oklahoma Health Care Authority
November 2021

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. Multiple myeloma overall is a rare cancer (1.8% of all cancers) and is diagnosed at a median age of 69 years. 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 standard of care for multiple myeloma. 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.

Current Prior Authorization Criteria

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) and Darzalex Faspro® (Daratumumab/ Hyaluronidase-fihj) Approval Criteria [Light Chain Amyloidosis Diagnosis]:

1. Relapsed/refractory light chain amyloidosis as a single agent; or
2. Newly diagnosed light chain amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone.

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

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
    a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
    b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
    c. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or
    d. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or
    e. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or
    f. In combination with cyclophosphamide, bortezomib, and dexamethasone in members who have received at least 1 prior therapy; or
    g. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or
    h. 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.

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 in 1 of the following settings:
   a. As primary therapy; or
   b. Following disease relapse after 6 months following primary induction therapy with the same regimen, used in combination with 1 of the following regimens:
      i. Lenalidomide and dexamethasone; or
      ii. Cyclophosphamide and dexamethasone for transplant candidates only; or
      iii. Pomalidomide and dexamethasone if member has failed ≥2 prior therapies and demonstrated disease progression within 60 days; or
   c. 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 [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

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

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

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Used in 1 of the following settings:
   a. In combination with dexamethasone in members who have received ≥4 prior therapies including refractory disease to ≥2

proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody; or

b. Used in combination with bortezomib and dexamethasone in members who have failed at least 1 prior therapy.

Utilization of Multiple Myeloma Medications: Fiscal Year 2021

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	1	13	$132,983.61	$10,229.51	$365.34	39	364
2021	3	14	$148,100.74	$10,578.62	$377.81	42	392
% Change	**200.00%**	**7.70%**	**11.40%**	**3.40%**	**3.40%**	**7.70%**	**7.70%**
Change	**2**	**1**	**$15,117.13**	**$349.11**	**$12.47**	**3**	**28**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Comparison of Fiscal Years: Medical Claims

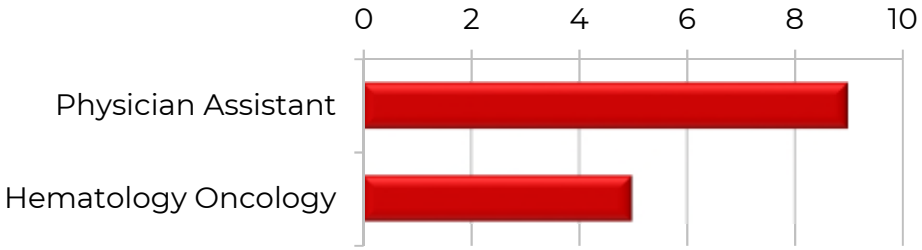
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2020	4	28	$177,398.94	$6,335.68	7
2021	5	11	$64,398.66	$5,854.42	2.2
% Change	**25.00%**	**-60.71%**	**-63.70%**	**-7.60%**	**-4.8**
Change	**1**	**-17**	**-$113,000.28**	**-$481.26**	**-68.57**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Demographics of Members Utilizing Multiple Myeloma Medications

- Due to the limited number of members utilizing multiple myeloma medications during fiscal year 2021, detailed demographic information could not be provided.

Top Prescriber Specialties of Multiple Myeloma Medications by Number of Claims



Prior Authorization of Multiple Myeloma Medications

There was 1 prior authorization request submitted for the multiple myeloma medications during fiscal year 2021, which was approved.

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

Anticipated Patent Expiration(s):

- Ninlaro® (ixazomib): November 2029
- Xpovio® (selinexor): August 2035
- Hemady® (dexamethasone): December 2037

News:

- **February 2015:** The U.S. Food and Drug Administration (FDA) approved Farydak® (panobinostat) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.
- **February 2021:** The FDA granted accelerated approval to Pepaxto® (melphalan flufenamide) in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior lines of therapy and whose disease is refractory to at least 1 PI, 1 immunomodulatory agent, and 1 CD-38 directed monoclonal antibody.
- **March 2021:** The FDA approved Abecma® (idecabtagene vicleucel) for the treatment of adult patients with RRMM after 4 or more prior lines of therapy, including an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody. This is the first FDA-approved cell-based gene therapy for multiple myeloma.
- **March 2021:** The FDA approved Sarclisa® (isatuximab-irfc) in combination with carfilzomib and dexamethasone, for the treatment of adult patients with RRMM who have received 1 to 3 prior lines of therapy.
- **July 2021:** The FDA approved Darzalex Faspro® (daratumumab/ hyaluronidase-fihj) in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least 1 prior line of therapy including lenalidomide and a PI.
- **October 2021:** Oncopeptides announced the decision to voluntarily withdraw Pepaxto® (melphalan flufenamide) from the United States' market. The decision followed an FDA hold on clinical trials of Pepaxto® after data from a confirmatory trial showed an increased mortality risk in patients treated with the drug. The Phase 3 OCEAN study compared Pepaxto® plus dexamethasone and Pomalyst® (pomalidomide) plus dexamethasone in patients with triple-refractory multiple myeloma.

The trial met the primary endpoint of progression-free survival (PFS), but an analysis of overall survival (a secondary endpoint) showed the intent to treat population with a hazard ratio of 1.104. Oncopeptides issued a letter to health care providers indicating at this time, no new patients should begin taking Pepaxto®. Oncopeptides also advised, for patients currently taking Pepaxto® and receiving a benefit, Oncopeptides is committed to keeping Pepaxto® available to these patients free of charge and is working with the FDA to ensure appropriate patients have access to treatment.

Guideline Update(s):

- According to the NCCN Panel, Darzalex® [daratumumab intravenous (IV) infusion] or Darzalex Faspro® [daratumumab/hyaluronidase-fihj subcutaneous (sub-Q) injection] may be used in all daratumumab-containing regimens following results of a randomized study comparing the 2 formulations of daratumumab as monotherapy. The sub-Q formulation resulted in a similar overall response rate (ORR), PFS, and safety profile and had fewer infusion-related reactions compared with the IV formulation.

Abecma® (Idecabtagene Vicleucel) Product Summary[9]

Therapeutic Class: B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy

Indication(s): Treatment of adult patients with RRMM after 4 or more prior lines of therapy, including an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody

How Supplied: Cell suspension with a patient-specific concentration [each dose contains 300×10^6 to 460×10^6 chimeric antigen receptor (CAR)-positive viable T-cells]

Dosing and Administration: The recommended dose range is 300×10^6 to 460×10^6 CAR-positive T-cells via single IV infusion

Cost: The Wholesale Acquisition Cost (WAC) is $419,500 per one-time treatment

Farydak® (Panobinostat) Product Summary[10]

Therapeutic Class: Histone deacetylase inhibitor

Indication(s): Treatment of adult patients with multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

How Supplied: 10mg, 15mg, and 20mg oral capsules

Dosing and Administration:

- 20mg once every other day for 3 doses per week (on days 1, 3, 5, 8, 10, and 12) of weeks 1 and 2 of each 21-day cycle for 8 cycles
- An additional 8 cycles should be considered for patients with clinical benefit who have no unresolved severe or medically significant toxicity
- The total duration of treatment may be up to 16 cycles (48 weeks)
- Dose adjustment maybe needed for toxicity, hepatic impairment, or drug interactions

Cost: The WAC is $2,347.09 per capsule for all available strengths, resulting in a cost of $14,082.54 for 1 cycle at the recommended dose and a cost of $225,320.64 for the maximum recommended duration of 16 cycles.

Pepaxto® (Melphalan Flufenamide) Product Summary[11]

Therapeutic Class: Alkylating drug

Indication(s): Treatment of adult patients with RRMM in combination with dexamethasone, in those who have received at least 4 prior lines of therapy and whose disease is refractory to at least 1 PI, 1 immunomodulatory agent, and 1 CD38-directed monoclonal antibody

How Supplied: 20mg melphalan flufenamide as a lyophilized powder in single-dose vial (SDV)

Dosing and Administration: 40mg via IV infusion over 30 minutes on day 1 of each 28-day treatment cycle

Cost: The WAC is $9,500 per SDV, resulting in a cost per 28 days of $19,000 at the recommended dose.

Recommendations

The College of Pharmacy recommends the prior authorization of Abecma® (idecabtagene vicleucel), Farydak® (panobinostat), and Pepaxto® (melphalan flufenamide) with the following criteria (shown in red):

Abecma® (Idecabtagene Vicleucel) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM):
    a. Member has received ≥4 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody; and
        i. Induction with or without autologous hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen; and

ii. Must have undergone ≥2 consecutive cycles of treatment for each regimen unless progressive disease was seen after 1 cycle; and

b. Member must have measurable disease, including at least 1 of the following:
   i. Serum M-protein ≥0.5g/dL; or
   ii. Urine M-protein ≥200mg/24hr; or
   iii. Serum free light chain (FLC) assay: involved FLC ≥10mg/dL (100mg/L); or
   iv. Bone marrow plasma cells >30% of total bone marrow cells; and

c. Member must not have any central nervous system involvement with multiple myeloma.

Farydak® (Panobinostat) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Used in combination with bortezomib and dexamethasone after 1 or more lines of therapy; or
3. Used in combination with carfilzomib or dexamethasone and lenalidomide after 2 or more lines of therapy (including bortezomib and an immunomodulatory agent).

Pepaxto® (Melphalan Flufenamide) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Member has received at least 4 prior lines of therapy (including being refractory to at least 1 proteasome inhibitor, 1 immunomodulatory agent, and 1 CD-38 directed monoclonal antibody); and
3. Members who are new to treatment with Pepaxto® will generally not be approved.

The College of Pharmacy also recommends updating the approval criteria for Sarclisa® (isatuximab-irfc) based on the recent FDA approval (changes and new criteria noted in red):

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

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Used in 1 of the following settings:
   a. Used in combination with pomalidomide and dexamethasone after ≥2 prior therapies [previous treatment must have included lenalidomide and a proteasome inhibitor (PI)]; or
   b. Used in combination with carfilzomib and dexamethasone after 1 to 3 prior therapies.

Finally, the College of Pharmacy recommends updating the prior authorization criteria for Darzalex® (daratumumab) and Darzalex Faspro® (daratumumab/hyaluronidase-fihj) based on NCCN Compendium approval (changes noted in red):

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

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
    a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
    b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
    c. In combination with bortezomib, thalidomide, and dexamethasone or bortezomib, lenalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or
    ~~d. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or~~
    ~~e. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or~~
    ~~f. In combination with cyclophosphamide, bortezomib, and dexamethasone in members who have received at least 1 prior therapy; or~~
    ~~g. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or~~
    h. After at least 1 prior therapy in combination with 1 of the following:
        i. Dexamethasone and bortezomib; or
        ii. Carfilzomib and dexamethasone; or
        iii. Dexamethasone and lenalidomide; or
        iv. Cyclophosphamide, bortezomib, and dexamethasone; or
        v. Pomalidomide and dexamethasone* [*previous therapy for this combination must include lenalidomide and a protease inhibitor (PI)]; or
        vi. Selinexor and dexamethasone; or
    i. In combination with lenalidomide and dexamethasone for members who are ineligible for ASCT or with cyclophosphamide, bortezomib, and dexamethasone as primary therapy or for disease relapse after 6 months following primary induction therapy with the same regimen; or

j. 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.

Utilization Details of Multiple Myeloma Medications: Fiscal Year 2021

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
IXAZOMIB PRODUCTS						
NINLARO CAP 3MG	12	1	$127,647.92	12	$10,637.33	86.19%
NINLARO CAP 4MG	2	2	$20,452.82	1	$10,226.41	13.81%
TOTAL	**14**	**3***	**$148,100.74**	**4.67**	**$10,578.62**	**100.00%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
CAP = capsule
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
J9145 DARATUMUMAB INJ	9	4	$48,612.66	$5,401.41	2.25
J9144 DARATUMUMAB/ HYALURONIDASE INJ	2	1	$15,786.00	$7,893.00	2
TOTAL	**11**	**5**	**$64,398.66**	**$5,854.42**	**2.2**

Costs do not reflect rebated prices or net costs.
+Total number of unduplicated claims.
*Total number of unduplicated members.
INJ = injection
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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[4] U.S. FDA. Drugs@FDA: FDA-Approved Drugs. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process. Last revised 10/2021. Last accessed 10/14/2021.
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[7] Bankhead, C. Myeloma Drug Pulled From Market Just Months after Approval. *MedPage Today*. Available online at: https://www.medpagetoday.com/hematologyoncology/myeloma/95223?xid=nl_mpt_DHE_2021-10-23&eun=g1080562d0r&utm_source=Sailthru&utm_medium=email&utm_campaign=Daily%20Headlines%20Top%20Cat%20HeC%20%202021-10-23&utm_term=NL_Daily_DHE_dual-gmail-definition. Issued 10/22/2021. Last accessed 10/26/2021.
[8] Oncopeptides. Important Information Regarding Pepaxto® in the United States. Available online at: https://www.oncopeptides-us.com/en/media-center/important-information-regarding-pepaxto-in-the-united-states. Issued 10/22/2021. Last accessed 10/26/2021.
[9] Abecma® (Idecabtagene Vicleucel) Prescribing Information. Bristol-Myers Squibb. Available online at: https://packageinserts.bms.com/pi/pi_abecma.pdf. Last revised 03/2021. Last accessed 10/14/2021.
[10] Farydak® (Panobinostat) Prescribing Information. Secura Bio, Inc. Available online at: https://us.farydak.com/assets/pdf/Farydak-SBI-USPI-201909.pdf. Last revised 09/2019. Last accessed 10/14/2021.
[11] Pepaxto® (Melphalan Flufenamide) Prescribing Information. Oncopeptides AB. Available online at: https://pepaxto.com/docs/pepaxto_pi.pdf. Last revised 02/2021. Last accessed 10/14/2021.

Appendix K

Fiscal Year 2021 Annual Review of Lenvima® (Lenvatinib) and 30-Day Notice to Prior Authorize Jemperli® (Dostarlimab-gxly)

Oklahoma Health Care Authority
November 2021

Introduction[1,2]

Thyroid carcinomas are uncommon cancers in the United States with approximately 44,280 new cases estimated for 2021. 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. Treatment plans typically involve surgery, radioactive iodine ablation, and thyroxine therapy. Treatment options are limited in the rare cases of metastatic and relapsed diseases. Newer targeted agents and immune therapies are emerging for these unique clinical cases.

Current Prior Authorization Criteria

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 [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.

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

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

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.

Utilization of Lenvima® (Lenvatinib): Fiscal Year 2021

Comparison of Fiscal Years

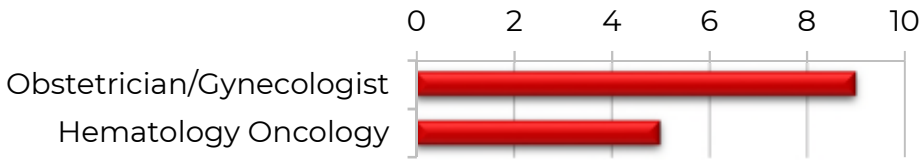
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	4	10	$185,110.98	$18,511.10	$617.04	750	300
2021	2	14	$269,735.74	$19,266.84	$642.23	810	420
% Change	**-50.00%**	**40.00%**	**45.70%**	**4.10%**	**4.10%**	**8.00%**	**40.00%**
Change	**-2**	**4**	**$84,624.76**	**$755.74**	**$25.19**	**60**	**120**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/0/12019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Demographics of Members Utilizing Lenvima® (Lenvatinib)

- Due to the limited number of members utilizing Lenvima® (lenvatinib) during fiscal year 2021, detailed demographic information could not be provided.

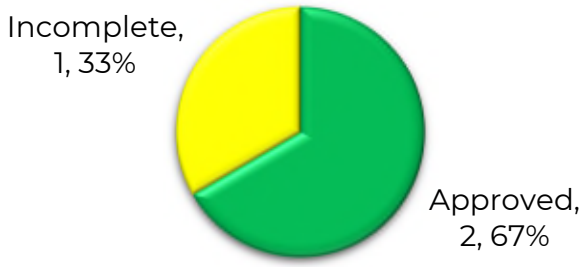
Top Prescriber Specialties of Lenvima® (Lenvatinib) by Number of Claims



Prior Authorization of Lenvima® (Lenvatinib)

There were 3 prior authorization requests submitted for Lenvima® (lenvatinib) during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



Market News and Updates[3,4]

Anticipated Patent Expiration(s):

- Lenvima® (lenvatinib): August 2035

News:

- **April 2021:** The FDA granted accelerated approval to Jemperli® (dostarlimab-gxly) for the treatment of adults with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer that has progressed on or following a prior platinum-containing regimen.
- **July 2021:** The FDA granted regular approval to Keytruda® (pembrolizumab) in combination with Lenvima® (lenvatinib) for the treatment of adults with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation. The FDA previously granted accelerated approval for this indication in September 2019.
- **August 2021:** The FDA approved the combination of Lenvima® (lenvatinib) plus Keytruda® (pembrolizumab) for first-line treatment of adults with advanced renal cell carcinoma (RCC).
- **August 2021:** The FDA granted accelerated approval to Jemperli® (dostarlimab-gxly) for the treatment of adults with dMMR recurrent or advanced solid tumors that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

Jemperli® (Dostarlimab-gxly) Product Summary[5]

Therapeutic Class: Programmed death receptor-1 (PD-1)–blocking antibody

Indication(s):

- The treatment of adults with dMMR recurrent or advanced cancer including:
  - Endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen
  - Solid tumors that have progressed on or following prior treatment and have no satisfactory alternative treatment options

How Supplied: 500mg/10mL (50mg/mL) solution in a single-dose vial (SDV)

Dosing and Administration:

- Administered as an intravenous (IV) infusion over 30 minutes
- Doses 1 through 4: 500mg every 3 weeks
- Subsequent dosing beginning 3 weeks after dose 4 (dose 5 and thereafter): 1,000mg every 6 weeks

Cost: The Wholesale Acquisition Cost (WAC) is $1,036.94 per mL, resulting in a cost of $10,369.40 per 10mL SDV. The total cost of the first 4 doses of 500mg is

$41,477.60 followed by a cost per dose of $20,738.80 for 1,000mg, resulting in an annual cost of $186,649.20.

Recommendations

The College of Pharmacy recommends the prior authorization of Jemperli® (dostarlimab-gxly) with the following criteria (noted in red):

Jemperli® (Dostarlimab-gxly) Approval Criteria [Endometrial Cancer Diagnosis]:

1. Diagnosis of advanced, recurrent, or metastatic endometrial cancer; and
2. Mismatch repair deficient (dMMR) disease; and
3. Disease has progressed on or following prior treatment with a platinum-containing regimen.

Jemperli® (Dostarlimab-gxly) Approval Criteria [Mismatch Repair Deficient (dMMR) Solid Tumor Diagnosis]:

1. Diagnosis of recurrent or advanced solid tumors that are mismatch repair deficient (dMMR); and
2. Disease has progressed on or following prior treatment; and
3. There are no satisfactory treatment alternatives for the member.

Additionally, the College of Pharmacy recommends updating the approval criteria for Keytruda® (pembrolizumab) and Lenvima® (lenvatinib) based on recent FDA approvals (changes and new criteria noted in red; only criteria with updates are listed):

Keytruda® (Pembrolizumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of new or recurrent stage 4 clear-cell RCC; and
2. Member has not received previous systemic therapy for advanced disease; and
3. Must be used in combination with axitinib or lenvatinib; and
4. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of advanced RCC; and
    a. Used in combination with pembrolizumab; or
    b. Following 1 prior anti-angiogenic therapy; and
        i. Used in combination with everolimus.

Utilization Details of Lenvima® (Lenvatinib): Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
LENVATINIB PRODUCTS					
LENVIMA CAP 14MG	9	1	$174,589.69	$19,398.85	9
LENVIMA CAP 20MG	4	1	$76,117.64	$19,029.41	4
LENVIMA CAP 10MG	1	1	$19,028.41	$19,028.41	1
TOTAL	**14**	**2***	**$269,735.74**	**$19,266.84**	**4.67**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
CAP = capsule
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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Appendix L

Fiscal Year 2021 Annual Review of Atopic Dermatitis (AD) Medications and 30-Day Notice to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream)

Oklahoma Health Care Authority
November 2021

Current Prior Authorization Criteria

Approval criteria for Dupixent® (dupilumab injection) for indications other than AD can be found in the Fiscal Year 2021 Annual Review of Asthma and Chronic Obstructive Pulmonary Disease (COPD) Maintenance Medications report, which is also being presented at the November 2021 Drug Utilization Review (DUR) Board meeting.

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 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.

Elidel® (Pimecrolimus Cream) and Protopic® (Tacrolimus Ointment) 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 with a Tier-1 topical corticosteroid at least 6 weeks in duration within the past 90 days; 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® or Protopic® include the following:
    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® or Protopic® include the following:
    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 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® include the following:
    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.

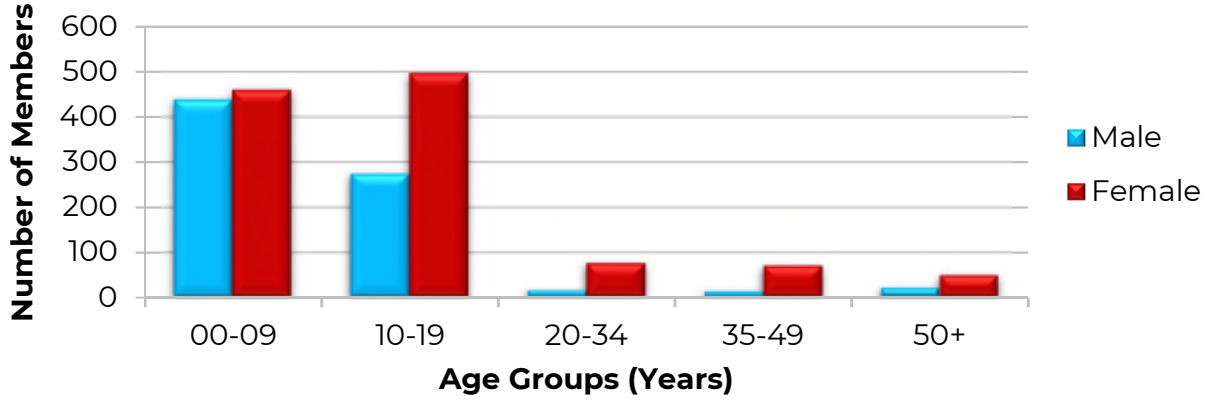
Utilization of AD Medications: Fiscal Year 2021

Comparison of Fiscal Years

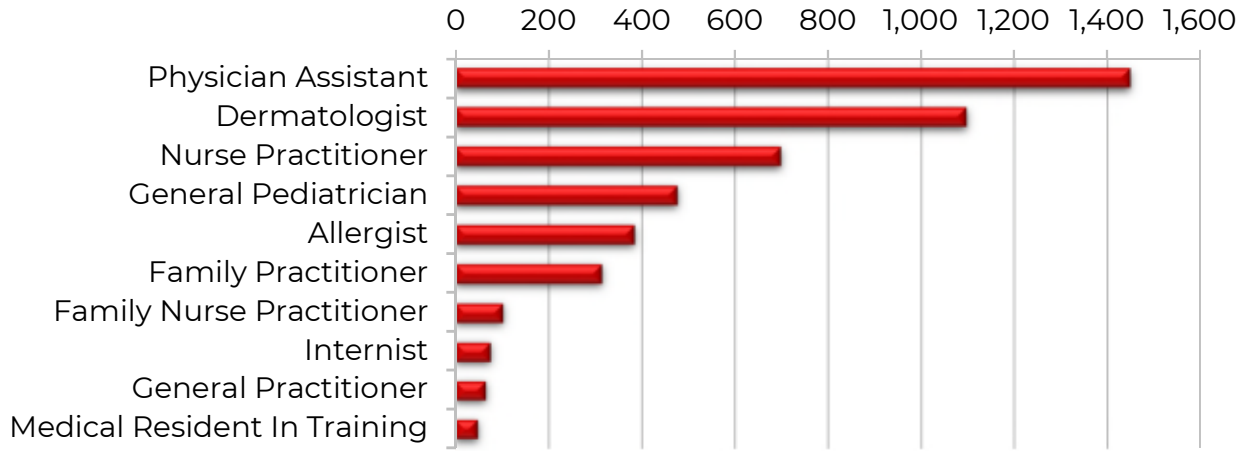
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	1,972	4,244	$4,202,201.62	$990.15	$33.10	190,990	126,955
2021	1,904	4,788	$6,255,685.45	$1,306.53	$43.50	181,748	143,802
% Change	**-3.40%**	**12.80%**	**48.90%**	**32.00%**	**31.40%**	**-4.80%**	**13.30%**
Change	**-68**	**544**	**$2,053,483.83**	**$316.38**	**$10.40**	**-9,242**	**16,847**

*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Utilization data includes Dupixent® used for all diagnoses and does not differentiate between AD diagnoses and other diagnoses, for which use may be appropriate.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Demographics of Members Utilizing AD Medications



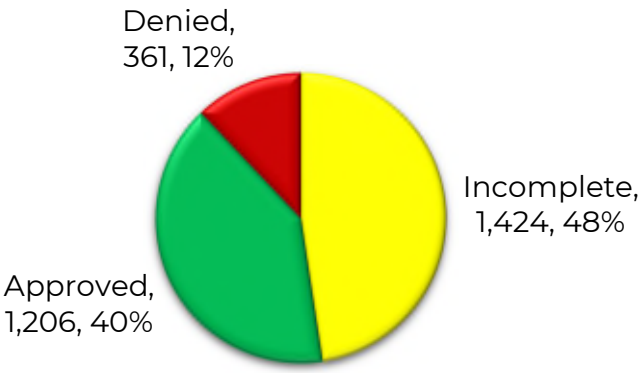
Top Prescriber Specialties of AD Medications by Number of Claims



Prior Authorization of AD Medications

There were 2,991 prior authorization requests submitted for 1,261 unique members for AD medications during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.

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):

- Eucrisa® (crisaborole): July 2030
- Opzelura™ (ruxolitinib): May 2031

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

- **June 2021:** The FDA approved a new 200mg single-dose pre-filled pen formulation of Dupixent® (dupilumab) for use in patients 12 years of age and older for all FDA-approved indications. Previously, Dupixent® was available in a single-dose 300mg pre-filled pen as well as 200mg and 300mg single-dose pre-filled syringe formulations. The pre-filled pen

features a hidden needle with single-press auto-injection and incorporates visual and audio feedback to assist with administration. After training by a health care professional, patients may self-inject Dupixent® by subcutaneous (sub-Q) administration using either the pre-filled syringe or pre-filled pen formulations.

- **September 2021:** The FDA approved Opzelura™ (ruxolitinib 1.5% cream) for the short-term and non-continuous chronic treatment of mild-to-moderate AD in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Opzelura™ is the first topical Janus kinase (JAK) inhibitor to be approved by the FDA. Incyte, the manufacturer of Opzelura™, is currently conducting additional Phase 3 studies to assess the efficacy of ruxolitinib cream for the treatment of patients with vitiligo.

News:

- **September 2021:** The FDA recently completed a review of safety data from a safety study comparing Xeljanz® (tofacitinib) and Xeljanz® XR [tofacitinib extended-release (ER)] to tumor necrosis factor (TNF) blockers in patients with rheumatoid arthritis (RA) also on methotrexate (MTX). The FDA concluded there is an increased risk of serious events including myocardial infarction (MI), stroke, cancer, blood clots, and death with tofacitinib. Based on this data, the FDA issued a Drug Safety Communication and is now requiring a warning in the labeling for tofacitinib and 2 other JAK inhibitors, Olumiant® (baricitinib) and Rinvoq™ (upadacitinib). Two other oral JAK inhibitors, Jakafi® (ruxolitinib) and Inrebic® (fedratinib), are not indicated for the treatment of RA or other inflammatory conditions and are not a part of the warning at this time. Opzelura™ (ruxolitinib), a topical JAK inhibitor which was approved by the FDA shortly after the Drug Safety Communication was issued, did receive a *Boxed Warning* regarding the increased risk of adverse events seen with other JAK inhibitors.

Pipeline:

- **Abrocitinib:** Pfizer has completed multiple Phase 3 studies of abrocitinib, an investigational, small molecule 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 August 2021, Pfizer announced positive top-line results from the JADE DARE Phase 3 study, which was a 26-week, randomized, double-blind, double-dummy, active-controlled study in adults with moderate-to-severe AD. The study assessed the efficacy and safety of oral abrocitinib 200mg once daily vs. dupilumab 300mg sub-Q every other week following a 600mg induction dose. The co-primary

endpoints were the proportion of patients achieving at least a 4-point improvement in the severity of Peak Pruritus Numerical Rating Scale (PP-NRS4) from baseline at week 2 and the proportion of patients achieving at least a 90% improvement from baseline at week 4 in the Eczema Area and Severity Index (EASI-90). The results of the study demonstrated that abrocitinib was statistically superior to dupilumab for the co-primary endpoints, as well as the secondary endpoint (EASI-90) at week 16. Adverse events were more common with abrocitinib than with dupilumab, although the incidence of serious adverse events and adverse events leading to study discontinuation were similar between the 2 drugs. Pfizer's New Drug Application (NDA) for abrocitinib was previously accepted for review by the FDA in October 2020. The FDA's review of abrocitinib has been delayed twice, most recently in July 2021, when it was announced the FDA would not meet its third quarter 2021 deadline due to the agency's ongoing review of Pfizer's post-marketing safety study of tofacitinib, another JAK inhibitor, for the treatment of RA.

- **Baricitinib:** Eli Lilly has completed multiple Phase 3 studies of baricitinib for the treatment of moderate-to-severe AD. Baricitinib is an oral JAK1 and JAK2 inhibitor currently FDA approved for the treatment of RA under the brand name Olumiant®. A supplemental NDA (sNDA) for baricitinib has been submitted for the treatment of moderate-to-severe AD but has been delayed by the FDA's ongoing review of the safety of the JAK inhibitor class of medications.
- **Delgocitinib:** In May 2021, LEO Pharma announced the initiation of the first Phase 3 study of delgocitinib cream for the treatment of adults with moderate-to-severe chronic hand eczema (CHE). Delgocitinib is a topical pan-JAK inhibitor which was previously granted Fast Track designation by the FDA for this indication. Currently, no treatment options have been specifically approved for CHE, which is a potentially disabling skin disease that can impair the ability to work and be self-sufficient. The Phase 3 DELTA 1 and DELTA 2 studies will evaluate the efficacy of twice daily delgocitinib cream vs. vehicle in adult patients with CHE.
- **Dupilumab:** In August 2021, Regeneron announced positive results from a Phase 3 study of dupilumab in 162 patients 6 months of age to 5 years of age with uncontrolled moderate-to-severe AD. The LIBERTY AD PRESCHOOL study evaluated the efficacy and safety of dupilumab added to standard-of-care low-potency topical corticosteroid (TCS) compared to low-potency TCS alone. The study met all primary and secondary endpoints, demonstrating dupilumab added to TCS reduced disease severity and improved skin clearance, itch, and health-related quality of life at week 16 relative to TCS alone. The safety results in this age range were similar to the known safety profile of dupilumab in AD.

Dupilumab is currently FDA approved for the treatment of moderate-to-severe AD in patients 6 years of age or older whose AD is not well controlled with prescription therapies or when topical therapies cannot be used.

- **Lebrikizumab:** Eli Lilly is conducting Phase 3 studies of 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 August 2021, Lilly announced positive results from 2 Phase 3 studies of lebrikizumab in patients with moderate-to-severe AD. In the ongoing ADvocate 1 and ADvocate 2 studies, patients 12 years of age and older with moderate-to-severe AD were randomly assigned to receive lebrikizumab sub-Q or placebo, with the primary efficacy endpoints assessed at week 16. The primary efficacy endpoints were an Investigator Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with a reduction of ≥2 points from baseline at week 16 and ≥75% change from baseline in the EASI score (EASI-75). Both primary endpoints and additional secondary endpoints were met in the study, demonstrating skin clearance and itch improvement with lebrikizumab monotherapy relative to placebo. Additional Phase 3 studies are ongoing to assess lebrikizumab as both monotherapy and in addition to TCS in patients with AD.
- **Roflumilast:** Arcutis is conducting Phase 3 studies of topical roflumilast for the treatment of mild-to-moderate AD involving ≥3% body surface area (BSA). Roflumilast is a potent small molecule inhibitor of phosphodiesterase-4 (PDE4). PDE4 is an enzyme responsible for increasing the production of pro-inflammatory mediators and decreasing the production of anti-inflammatory mediators. Roflumilast for the treatment of AD is being formulated as a topical cream in 2 strengths (0.05% and 0.15%) for once daily administration. Arcutis previously initiated 2 Phase 3 studies in patients 6 years of age and older (INTEGUMENT-1 and INTEGUMENT-2) to assess the efficacy and safety of the 0.15% cream used for 4 weeks relative to vehicle. In April 2021, it was announced a third Phase 3 study has been initiated in patients 2 to 5 years of age (INTEGUMENT-PED) to assess the efficacy and safety of the 0.05% cream used for 4 weeks relative to vehicle. Arcutis plans to release topline data in the second half of 2022.
- **Tapinarof:** In September 2021, Dermavant announced the first patient has been dosed in the Phase 3 ADORING clinical program evaluating tapinarof for the topical treatment of AD. Tapinarof is a novel, investigational aryl hydrocarbon receptor modulating agent being developed as a once-daily steroid-free topical cream for the treatment

of both plaque psoriasis and AD. The Phase 3 ADORING clinical program will consist of 2 identical studies (ADORING 1 and ADORING 2), which will be multi-center, randomized, double-blind, parallel group studies conducted in North America. Dermavant plans to enroll up to 800 patients 2 years of age and older with moderate-to-severe AD across the 2 studies. Patients will be randomized to treatment with tapinarof 1% cream or vehicle cream once daily for 8 weeks. Additionally, ADORING 3, a long-term, open-label extension study will evaluate the use of tapinarof for up to 48 weeks of treatment.

- **Upadacitinib:** AbbVie has conducted multiple Phase 3 studies evaluating upadacitinib for the treatment of moderate-to-severe AD. Upadacitinib is a once-daily, oral, selective JAK1 inhibitor. In May 2021, AbbVie announced the publication in *The Lancet* of results from the Phase 3 Measure Up 1, Measure Up 2, and AD Up studies. In Measure Up 1 and Measure Up 2, patients were treated with upadacitinib monotherapy or placebo for 16 weeks. In AD Up, patients were treated with upadacitinib plus TCS or placebo plus TCS for 16 weeks. In all 3 studies, all primary and secondary endpoints were met. Upadacitinib was previously FDA approved for the treatment of moderately-to-severely active RA in patients with inadequate response or intolerance to MTX and is marketed under the brand name Rinvoq™. AbbVie submitted a sNDA for upadacitinib for the treatment of moderate-to-severe AD, but the review has been delayed by the FDA's ongoing review of the safety of the JAK inhibitor class of medications.

Opzelura™ (Ruxolitinib 1.5% Cream) Product Summary[17,18,19,20]

Indication(s): Opzelura™ (ruxolitinib) is a JAK inhibitor indicated for the topical short-term and non-continuous chronic treatment of mild-to-moderate AD in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Limitations of Use:

- Use of Opzelura™ in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

Boxed Warning: Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events (MACE), and Thrombosis (see the Safety section for additional details)

- **Serious Infections:** Patients treated with oral JAK inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Use of ruxolitinib should be avoided in patients with active, serious infection, including localized infections.
- **Mortality:** Higher rate of all-cause mortality, including sudden cardiovascular (CV) death, have been observed in patients treated with oral JAK inhibitors for inflammatory conditions.
- **Malignancies:** Lymphoma and other malignancies have been observed in patients treated with JAK inhibitors for inflammatory conditions.
- **MACE:** Higher rate of MACE (including CV death, MI, and stroke) has been observed in patients treated with JAK inhibitors for inflammatory conditions.
- **Thrombosis:** Thrombosis, including deep vein thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis has been observed at an increased incidence in patients treated with oral JAK inhibitors for inflammatory conditions compared to placebo. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.

How Supplied: 1.5% cream containing 15mg of ruxolitinib per gram in a 60-gram tube

Dosing and Administration:

- A thin layer of cream should be applied twice daily to affected areas of up to 20% BSA
- Patients should not use more than 60 grams per week
- Opzelura™ should be discontinued when signs and symptoms of AD (e.g., itch, rash, redness) resolve
- If signs and symptoms of AD do not improve within 8 weeks, patients should be re-examined by their health care provider

Mechanism of Action: Ruxolitinib is a JAK inhibitor that inhibits JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of signal transducers and activators of transcription (STATs) to cytokine receptors, activation, and subsequent localization of STATs to the nucleus leading to modulation of gene expression. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.

Contraindication(s): None

Safety:

- Serious Infections: In patients receiving oral JAK inhibitors, serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported. Additionally, serious lower respiratory tract infections were reported in the clinical development program with topical ruxolitinib. Use of topical ruxolitinib should be avoided in patients with active, serious infection, including localized infections. The risks and benefits of topical ruxolitinib should be considered in patients with chronic or recurrent infection, with history of a serious or an opportunistic infection, with previous exposure to tuberculosis, who previously resided or traveled in areas of endemic tuberculosis or endemic mycoses, or with underlying conditions that may predispose them to infection. Patients should be closely monitored for signs and symptoms of infection during and after treatment with topical ruxolitinib. If a serious infection, opportunistic infection, or sepsis develops, treatment with topical ruxolitinib should be interrupted and should not be resumed until the infection is controlled.
- Mortality: In clinical studies of oral JAK inhibitors used for inflammatory conditions, a higher rate of all-cause mortality, including sudden CV death, was observed. The benefits and risks should be considered for the individual patient before initiating treatment with topical ruxolitinib.
- Malignancy and Lymphoproliferative Disorders: In clinical studies of oral JAK inhibitors for inflammatory conditions, malignancies, including lymphomas, were observed. Current or past smokers are at an additional increased risk. The benefits and risks should be considered for the individual patient before initiating or continuing treatment with topical ruxolitinib, particularly in patients with a known malignancy, who develop a malignancy, and who are current or past smokers. Additionally, non-melanoma skin cancers have occurred in patients treated with topical ruxolitinib. Periodic skin examinations should be performed during treatment with topical ruxolitinib and following treatment as appropriate.
- MACE: In clinical studies of JAK inhibitors used for inflammatory conditions, MACE (defined as CV death, non-fatal MI, and non-fatal stroke) were observed. The benefits and risks should be considered for the individual patient before initiating or continuing treatment with topical ruxolitinib, particularly in patients who are current or past smokers and in patients with other CV risk factors. Patients should be informed about the symptoms of serious CV events and the steps to take if these symptoms occur.

- Thrombosis: In patients treated with oral JAK inhibitors for inflammatory conditions, thrombosis, including DVT, PE, and arterial thrombosis has been observed at an increased incidence compared to patients treated with placebo. Many of these were serious and some resulted in death. In the clinical studies of topical ruxolitinib, thromboembolic events were observed; however, there was no clear relationship between platelet count elevations and thrombotic events. Topical ruxolitinib should be used with caution in patients at increased risk of thrombosis.
- Thrombocytopenia, Anemia, and Neutropenia: Thrombocytopenia, anemia, and neutropenia were reported in the clinical studies of topical ruxolitinib. For patients with a known history of these events, the benefits and risks of treatment with topical ruxolitinib should be considered, and complete blood count (CBC) should be monitored as clinically indicated. Patients should discontinue topical ruxolitinib if signs or symptoms of clinically significant thrombocytopenia, anemia, or neutropenia occur.
- Lipid Elevations: The use of oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.
- Drug Interactions: No drug interaction studies have been conducted with topical ruxolitinib, which is a known substrate for CYP3A4. Ruxolitinib systemic concentrations may be increased or decreased by inhibitors or inducers of CYP3A4, respectively. Patients should avoid concomitant use of strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, ketoconazole) with topical ruxolitinib due to the potential for increased systemic exposure of ruxolitinib and increased risk of adverse reactions.
- Pregnancy: Available data from pregnancies reported during clinical studies of topical ruxolitinib are not sufficient to evaluate the drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal studies, oral administration of ruxolitinib during organogenesis resulted in adverse developmental outcomes in pregnant rats and rabbits at doses associated with maternal toxicity. There will be a pregnancy registry that monitors pregnancy outcomes in pregnant patients exposed to topical ruxolitinib during pregnancy. Pregnant patients exposed to topical ruxolitinib and their health care providers should report the exposure to the pregnancy registry.
- Lactation: There are no data available on the presence of ruxolitinib in human milk, the effects on the breastfed child, or the effects of the drug on milk production. Ruxolitinib was present in the milk of lactating rats and would likely be present in human milk as well. Because of the serious adverse event findings in adults, including the

risk of serious infections, thrombocytopenia, anemia, and neutropenia, women should not breastfeed during treatment with topical ruxolitinib and for approximately 4 weeks after the last dose.

- Pediatric Use: The safety and efficacy of topical ruxolitinib have been established in pediatric patients 12 to 17 years of age for the treatment of mild-to-moderate AD. Use of topical ruxolitinib 1.5% cream in this age range is supported by evidence from 2 Phase 3 studies which included 92 patients 12 to 17 years of age. No clinically meaningful differences in safety or efficacy were observed between adult and pediatric patients. The safety and efficacy of topical ruxolitinib have not been established in patients younger than 12 years of age.
- Geriatric Use: In the Phase 3 studies of topical ruxolitinib in patients with AD, 115 of the 1,249 patients were 65 years of age or older. No clinically meaningful differences in safety or efficacy were observed between younger patients and those 65 years of age and older.

Adverse Reactions: The most common adverse reactions in Phase 3 studies (occurring in ≥1% of patients treated with ruxolitinib and at a greater incidence than with vehicle) were nasopharyngitis, bronchitis, ear infection, increased eosinophil count, urticaria, diarrhea, folliculitis, tonsillitis, and rhinorrhea.

Efficacy: The efficacy of topical ruxolitinib for the treatment of AD was assessed in 2 Phase 3 studies (TRuE AD1 and TRuE AD2) which were randomized, double-blind, vehicle-controlled studies in 1,249 non-immunocompromised patients 12 years of age and older with mild-to-moderate AD. Patients were randomized 2:2:1 to treatment with ruxolitinib 1.5% cream, ruxolitinib 0.75% cream, or vehicle twice daily for 8 weeks. In the 2 studies, 20% of patients were 12 to 17 years of age and 9% of patients were 65 years of age or older.

- Inclusion Criteria: All patients were required to have a history of AD for at least 2 years and an IGA score of 2 to 3 (corresponding to mild-to-moderate AD) at baseline. Additionally, patients had a BSA involvement of 3% to 20% (excluding the scalp) at baseline and were required to discontinue all agents used to treat AD from the time of screening and throughout the duration of the study.
- Exclusion Criteria: Patients were excluded from the study if they were immunocompromised, had recent acute infections, or had use of other agents for the treatment of AD within the specified washout period.
- Primary Endpoint: The primary efficacy endpoint in both studies was the proportion of patients achieving IGA treatment success (IGA-TS), defined as an IGA score of 0 (clear) or 1 (almost clear) at week 8 with a ≥2 point improvement from baseline.

- Results: In both studies, the primary efficacy endpoint was met in patients receiving ruxolitinib 1.5% cream twice daily relative to patients receiving vehicle. In TRuE AD1, 53.8% of patients achieved IGA-TS compared to 15.1% of patients who received vehicle [treatment difference: 38.9%; 95% confidence interval (CI): 30.3%, 47.4%; P<0.0001]. In TRuE AD2, 51.3% of patients achieved IGA-TS compared to 7.6% of patients who received vehicle (treatment difference: 44.1%; 95% CI: 36.2%, 52.0%; P<0.0001). Additionally, both studies met a secondary endpoint assessing the proportion of patients achieving a ≥4 point improvement in the Itch Numerical Rating Scale (Itch NRS) relative to baseline. A statistically greater proportion of patients treated with ruxolitinib 1.5% achieved a ≥4 point improvement in Itch NRS relative to patients who received vehicle.

Cost Comparison:

Product	Cost Per Gram	Cost Per 60 Grams
Opzelura™ (ruxolitinib) 1.5% cream	**$32.50**	**$1,950.00**
Eucrisa® (crisaborole) 2% ointment	$10.73	$643.80
pimecrolimus 1% cream (generic)	$5.37	$322.20
tacrolimus 0.03% ointment (generic)	$2.65	$159.00
triamcinolone acetonide 0.1% cream (generic)	$0.12	$7.20

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

Recommendations

The College of Pharmacy recommends the prior authorization of Opzelura™ (ruxolitinib 1.5% cream) with the following criteria:

Opzelura™ (Ruxolitinib 1.5% Cream) Approval Criteria:

1. An FDA approved indication for short-term and non-continuous treatment of mild-to-moderate atopic dermatitis; and
2. Member must be 12 years of age or older; and
3. Member must not be immunocompromised; and
4. Member must have a body surface area (BSA) involvement ≤20%; and
5. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with all 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
    c. Eucrisa® (crisaborole); and

6. Concurrent use with therapeutic biologics, other Janus kinase (JAK) inhibitors, or potent immunosuppressants (e.g., azathioprine, cyclosporine) will not generally be approved; and
7. Prescriber must verify female members are not breastfeeding; and
8. If the member is pregnant or becomes pregnant, prescriber must verify member has been counseled on potential risks of this medication and will report the exposure to the Opzelura™ pregnancy registry; and
9. Approvals will be for a maximum duration of 8 weeks of treatment; and
10. Reauthorization may be considered if member has a recent TCS, TCI, or Eucrisa® trial (or a contraindication or documented intolerance); and
    a. Additionally, the prescriber must document the member had a positive response to and tolerated previous treatment with Opzelura™; and
11. Subsequent approvals will only be considered once each 90-day period to ensure appropriate short-term and non-continuous utilization.

Utilization Details of AD Medications: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
EUCRISA OIN 2%	1,563	772	$994,450.89	$636.24	2.02	15.90%
DUPIXENT SYR INJ 300MG/2ML	942	125	$2,911,031.58	$3,090.27	7.54	46.53%
PIMECROLIMUS CREAM 1%	676	490	$154,295.71	$228.25	1.38	2.47%
TACROLIMUS OIN 0.03%	652	415	$108,682.27	$166.69	1.57	1.74%
DUPIXENT SYR INJ 200MG/1.14ML	465	69	$1,447,626.11	$3,113.17	6.74	23.14%
TACROLIMUS OIN 0.1%	301	224	$45,363.07	$150.71	1.34	0.73%
DUPIXENT PEN INJ 300MG/2ML	189	52	$594,235.82	$3,144.10	3.63	9.50%
TOTAL	**4,788**	**1,904***	**$6,255,685.45**	**$1,306.53**	**2.51**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
INJ = injection; OIN = ointment; SYR = syringe
Utilization data includes Dupixent® used for all diagnoses and does not differentiate between AD diagnoses and other diagnoses, for which use may be appropriate.
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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Appendix M

Fiscal Year 2021 Annual Review of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide)

Oklahoma Health Care Authority
November 2021

Current Prior Authorization 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. 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.

Signifor® LAR (Pasireotide) Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Members with acromegaly who have had an inadequate response to surgery or for whom surgery is not an option; or
    b. Members with Cushing's disease from a pituitary tumor for whom pituitary surgery is not an option or has not been curative; and
2. For a diagnosis of acromegaly, the member must have a documented trial with long-acting octreotide or lanreotide depot with an inadequate response or have a patient-specific, clinically significant reason why the other long-acting release (LAR) somatostatin analogs (SSAs) are not appropriate for the member; and
3. Must be prescribed by, or in consultation with, an endocrinologist; and
4. Must be administered by a health care professional; and
5. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and

6. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored when starting treatment and periodically thereafter; and
7. Authorizations will be for the duration of 12 months; and
8. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Utilization of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide): Fiscal Year 2021

There was no SoonerCare utilization of Mycapssa® (octreotide) and Signifor® LAR (pasireotide) during fiscal year 2021 (fiscal year 2021 = 07/01/2020 to 06/30/2021).

Prior Authorization of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide)

There were no prior authorization requests submitted for Mycapssa® (octreotide) and Signifor® LAR (pasireotide) during fiscal year 2021.

Market News and Updates[1]

Anticipated Patent Expiration(s):

- Signifor® LAR (pasireotide): May 2028
- Mycapssa® (octreotide): February 2036

Recommendations

The College of Pharmacy does not recommend any changes to the current prior authorization criteria for Mycapssa® (octreotide) and Signifor® LAR (pasireotide) at this time.

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 10/2021. Last accessed 10/15/2021.

Appendix N

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 14, 2021

FDA to Hold Advisory Committee Meeting to Discuss Merck and Ridgeback's EUA Application for COVID-19 Oral Treatment

The FDA announced an upcoming meeting of its Antimicrobial Drugs Advisory Committee (AMDAC) to discuss Merck and Ridgeback's request for an emergency use authorization (EUA) for molnupiravir, an investigational antiviral drug to treat COVID-19. The committee will meet to discuss the available data supporting the use of molnupiravir to treat mild-to-moderate COVID-19 in adults who have tested positive for COVID-19, and who are at high risk for progression to severe COVID-19, including hospitalization or death. The meeting was scheduled as soon as possible following the submission of the EUA request by the company. This timeline allows for the FDA to thoroughly evaluate the data and information submitted in the EUA request before the meeting and to be prepared for a robust public discussion with the advisory committee members. During the meeting, the committee will hear presentations from the company regarding the data for the antiviral drug. The FDA will also present its perspective regarding the sponsor's data. There will be an open public hearing during which the public will be given an opportunity to provide comments.

FDA NEWS RELEASE

For Immediate Release: October 14, 2021

FDA Awards 11 Grants to Clinical Trials to Develop New Medical Products for Rare Disease Treatments

The FDA announced it has awarded 11 new clinical trial research grants, equaling more than $25 million of funding over the next 4 years. The FDA's Congressionally-funded Orphan Products Grants Program awards these grants to clinical investigators to support the development of medical products for patients with rare diseases. The grant awards support clinical studies of products that address unmet needs in rare diseases or conditions or provide highly significant improvements in treatment or diagnosis. Many of these studies involve children, as young as newborns, including 1 study evaluating the treatment of a rare inherited skin disease known as recessive dystrophic epidermolysis bullosa (RDEB) which can lead to painful blisters and wounds that are often disfiguring and fatal. Another study seeks to evaluate early treatment before the onset of seizures in infants with tuberous sclerosis complex, which is an inherited disease that can affect a variety of organs and can result in long term brain development issues.

This grant also includes an innovative demonstration project that will utilize a collaborative approach to evaluate a tool with the potential to improve data accuracy for clinical studies taking place at more than 1 location. Some of the new awards fund clinical studies of products for use in brain cancers. Specifically, 1 will evaluate a novel peptide vaccine to treat pediatric brain cancers. The vaccine is designed to be directed specifically to areas of tumor in the brain and has the potential to significantly impact the way these rare and deadly tumors are treated.

FDA NEWS RELEASE

For Immediate Release: October 6, 2021

FDA Revises Hospital and Health System Compounding Guidance to Help Preserve Patient Access to Compounded Drugs

Compounded drugs can serve an important role for patients in hospitals and other health care settings whose medical needs cannot be met by an FDA-approved product, and hospital care raises unique considerations and needs for compounded drugs. Recognizing this, in 2016 the FDA proposed a policy in draft guidance, which described certain flexibilities for hospital and health system pharmacies that distribute compounded drugs within their health system before receiving patient-specific prescriptions. Since that time, the FDA has received many comments on this proposed policy, including regarding a provision about the FDA's intent not to take action if a hospital or health system pharmacy distributes compounded drugs to health care facilities within a 1-mile radius that are owned and controlled by the same entity that owns and controls the pharmacy. Stakeholders commented that the proposed 1-mile policy was not reflective of the structure of health systems, many of which operate under a centralized compounding model and may service facilities at other sites located outside a 1-mile radius without similar compounding capabilities.

After considering these comments, to help preserve access to compounded drugs, the FDA is revising their draft guidance to, among other things, remove the 1-mile radius provision. The FDA is proposing a 2-part compliance policy. The policy describes circumstances under which the agency generally does not intend to take action against a hospital or health system pharmacy that is not an outsourcing facility that compounds and distributes a drug without first receiving a valid prescription or order for an individual patient. These circumstances include that compounded drugs be administered only to patients within the hospital or health system and the drugs are used or discarded within 24 hours of leaving the pharmacy.

With respect to hospital and health system pharmacies that deviate from these circumstances, the revised draft guidance outlines the FDA's intention to take a risk-based approach to enforcement. Hospital and health system pharmacies can measure their operations against certain factors to assess whether their practices are likely to be an enforcement priority. The FDA generally intends to consider the following factors for prioritizing risk-based regulatory action:

- Poor compounding practices or a lack of sterility assurance
- Non-patient-specific compounded drugs that are not for emergency uses
- Routine, large amounts of non-patient-specific compounded drugs
- Interstate distribution of large amounts of non-patient-specific compounded drugs
- Lack of a procedure to obtain non-patient-specific compounded drugs from an outsourcing facility.

While the revised draft guidance provides additional flexibility, the agency encourages hospitals and health systems to have procedures in place to obtain non-patient-specific compounded drugs from outsourcing facilities and to consider registering their pharmacies as outsourcing facilities.

FDA NEWS RELEASE

For Immediate Release: October 4, 2021

Coronavirus (COVID-19) Update: FDA Authorizes Additional OTC Home Test to Increase Access to Rapid Testing for Consumers

The FDA issued an EUA for the ACON Laboratories Flow*flex* COVID-19 Home Test, an over-the-counter (OTC) COVID-19 antigen test, which adds to the growing list of tests that can be used at home without a prescription. This action highlights the continued commitment to increasing the availability of appropriately accurate and reliable OTC tests to meet public health needs and increase access to testing for consumers.

The authorization for the ACON Laboratories Flow*flex* COVID-19 Home Test should significantly increase the availability of rapid, at-home tests and is expected to double rapid at-home testing capacity in the United States over the next several weeks. By year's end, the manufacturer plans to produce >100 million tests per month, and this number will rise to 200 million per month by February 2022.

Since March 2020, the FDA has authorized >400 COVID-19 tests and sample collection devices, including authorizations for rapid, OTC at-home tests. The FDA considers at-home COVID-19 diagnostic tests to be a high priority and has continued to prioritize their review given their public health importance.

Most antigen tests for at-home use are authorized for serial testing, or testing the same individual more than once within a few days. These authorizations followed the announcement of a streamlined approach to help facilitate the authorization of rapid tests for use with serial testing programs, which has increased consumer access to testing. Notably, based on the data provided for asymptomatic individuals, the ACON Laboratories Flow*flex* COVID-19 Home Test does not require serial testing. The authorization of Flow*flex* COVID-19 Home Test will facilitate even greater access and testing capacity.

The FDA advises that all tests can provide false negative and false positive results. Individuals with positive results should self-isolate and seek additional care from their health care provider. Individuals who test negative and experience COVID-like symptoms should follow up with their health care provider as negative results do not rule out a COVID-19 infection.

FDA NEWS RELEASE

For Immediate Release: October 1, 2021

FDA to Hold Advisory Committee Meetings to Discuss Emergency Use Authorization for Booster Doses and COVID-19 Vaccines for Younger Children

The FDA announced 2 meetings of its Vaccines and Related Biological Products Advisory Committee (VRBPAC) to discuss newly available data for the currently available COVID-19 vaccines. First is the VRBPAC meeting on Janssen and Moderna COVID-19 vaccine boosters. The advisory committee will meet to discuss the use of booster doses of the Moderna COVID-19 vaccine and the Janssen COVID-19 vaccine. Both vaccines are currently authorized for emergency use to prevent COVID-19 in individuals 18 years of age and older. The committee will also hear presentations and discuss the available data on the use of a booster of a different vaccine than the one used for the primary series of an authorized or approved COVID-19 vaccine (heterologous or "mix and match" booster). The committee will also discuss an amendment to the EUA of the Moderna COVID-19 vaccine for the administration of a booster dose, in individuals 18 years of age and older. Additionally, the VRBPAC will discuss amending the EUA of Johnson and Johnson's Janssen COVID-19 vaccine for the administration of a booster dose, in

individuals 18 years of age and older. The committee will hear a presentation from the National Institute of Health's National Institute of Allergy and Infectious Diseases on the heterologous use of booster doses following the primary series of the 3 currently authorized or approved COVID-19 vaccines. During the meeting, the committee will hear presentations from the companies on the data for their respective vaccines. The FDA will also present its own analyses of each of the manufacturers' data. There will be an open public hearing each day during which the public will be given an opportunity to provide comments.

Second is the VRBPAC meeting on Pfizer data on its COVID-19 vaccine for children 5 to 11 years of age. The FDA anticipates receiving a request from Pfizer to amend its EUA to allow the use of its COVID-19 vaccine in children 5 to 11 years of age. In anticipation of the request, the FDA is moving forward with scheduling an advisory committee meeting to inform the agency's decision-making.

FDA NEWS RELEASE

For Immediate Release: September 22, 2021

FDA Authorizes Booster Dose of Pfizer-BioNTech COVID-19 Vaccine for Certain Populations

The FDA amended the EUA for the Pfizer-BioNTech COVID-19 vaccine to allow for use of a single booster dose, to be administered at least 6 months after completion of the primary series in the following (this authorization applies only to the Pfizer-BioNTech COVID-19 vaccine):

- Individuals 65 years of age and older
- Individuals 18 through 64 years of age at high risk of severe COVID-19
- Individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19

To support the authorization for emergency use of a single booster dose, the FDA analyzed safety and immune response data from a subset of participants from the original clinical trial of the Pfizer-BioNTech COVID-19 vaccine. In addition, consideration was given to real-world data on the vaccine's efficacy over a sustained period of time provided by both United States and international sources, including the Centers for Disease Control and Prevention (CDC), the United Kingdom, and Israel. The immune responses of approximately 200 participants 18 through 55 years of age who received a single booster dose approximately 6 months after their second dose were assessed. The antibody response against SARS-CoV-2 virus 1 month after a booster dose of the vaccine compared to the response 1 month after the 2-dose primary series in the same individuals demonstrated a booster response.

Additional analysis conducted by the manufacturer, as requested by the FDA, compared the rates of COVID-19 accrued during the current Delta variant surge among original clinical trial participants who completed the primary 2-dose vaccination series early in the clinical trial to those who completed a 2-dose series later in the study. The analysis submitted by the company showed that during the study period of July and August 2021, the incidence of COVID-19 was higher among the participants who completed their primary vaccine series earlier, compared to participants who completed it later. The FDA determined that the rate of breakthrough COVID-19 reported during this time period translates to a modest decrease in the efficacy of the vaccine among those vaccinated earlier.

Safety was evaluated in 306 participants 18 through 55 years of age, and 12 participants 65 years of age and older who were followed for an average of over 2 months. The most commonly reported side effects by the clinical trial participants who received the booster dose of the vaccine were pain, redness and swelling at the injection site, as well as fatigue, headache, muscle or joint pain, and chills. Of note, swollen lymph nodes in the underarm were observed more frequently following the booster dose than after the primary 2-dose series.

FDA NEWS RELEASE

For Immediate Release: September 17, 2021

FDA Approves First Biosimilar to Treat Macular Degeneration Disease and Other Eye Conditions

The FDA approved Byooviz™ (ranibizumab-nuna) as the first biosimilar to Lucentis® (ranibizumab injection) for the treatment of several eye diseases and conditions, including neovascular (wet) age-related macular degeneration (nAMD), a leading cause of vision loss and blindness for Americans 65 years of age and older. Byooviz™ is also approved to treat macular edema (fluid build-up) following retinal vein occlusion and myopic choroidal neovascularization, a vision-threatening complication of myopia. The FDA's approval of Byooviz™ was based on a review of evidence that included extensive structural and functional characterization, comparative clinical efficacy and safety evaluations, including potential immunogenicity that demonstrated Byooviz™ is biosimilar to Lucentis®.

Byooviz™ is administered by intravitreal injection once a month. Administration of Byooviz™ may cause serious side effects, including: endophthalmitis and retinal detachments; increases in intraocular pressure; and thromboembolic events. The most common side effects of Byooviz™ include conjunctival hemorrhage, eye pain, vitreous floaters, and increased intraocular fluid pressure.

FDA NEWS RELEASE

For Immediate Release: September 17, 2021

Federal Court Enters Consent Decree Against Florida Compounder, Prohibiting Manufacture and Distribution of Drugs Due to Insanitary Conditions

The U.S. District Court for the Middle District of Florida has entered a consent decree of permanent injunction that prohibits a Florida-based company from producing or distributing any drugs until the company complies with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and other requirements. Under the consent decree, Premier Pharmacy may not resume compounding operations until it establishes and implements, among other things, a comprehensive quality control system and receives authorization from the FDA.

According to the complaint, filed by the U.S. Department of Justice on behalf of the FDA, Premier Pharmacy Labs, Inc. and the company's owner, Vern A. Allen, manufactured and distributed drugs made under insanitary conditions at Premier Pharmacy's facility, despite multiple warnings from the FDA. Premier stopped manufacturing drugs following an FDA inspection in June 2019. The complaint alleged that Premier Pharmacy manufactured and distributed drugs, including drugs that were intended to be sterile, that were adulterated because the drugs were made under insanitary conditions and in violation of good manufacturing practice requirements under the FD&C Act. Insanitary conditions can cause a compounded drug to become contaminated or otherwise cause patient harm. According to the complaint, Premier Pharmacy also manufactured and

distributed drugs that were neither approved nor exempt from approval because the products did not meet all statutory requirements for outsourcing facilities.

In the spring of 2014, the FDA conducted an inspection of Premier Pharmacy that resulted in a warning letter for insanitary conditions and other violations of the FD&C Act. The FDA conducted a follow-up inspection in June 2016, leading to a regulatory meeting with the company in January 2018. In April 2018, Premier Pharmacy recalled affected sterile injectable products due to potential lack of sterility assurance. The FDA conducted another follow-up inspection which started in April 2019. In June 2019, following the April inspection and the FDA's recommendation to recall, Premier Pharmacy recalled all unexpired drugs intended to be sterile. Premier Pharmacy had been registered as an outsourcing facility for compounded drugs; however, the company deregistered in 2019 and has since stopped compounding drugs.

FDA NEWS RELEASE

For Immediate Release: September 17, 2021

FDA In Brief: FDA Hosts Third Summit Focused on Reducing the Availability of Opioids Online

According to the acting FDA commissioner Janet Woodcock, M.D, "The opioid crisis continues to be a national public health emergency with devastating and far-reaching consequences extending into nearly every community. A key component of the FDA's multipronged response is reducing the volume of opioids entering the country outside of the legitimate supply chain, including through illegal online sales. The most recent Online Opioid Summit was part of the agency's continued efforts to find and implement innovative solutions to prevent the illegal sale of opioids through internet platforms and services. Given the complexity of the issue, it is imperative that we include stakeholders from a variety of sectors in the conversation. These summits provide stakeholders a unique opportunity to collaborate, leverage expertise, and explore meaningful ways to help reduce the availability of opioids online. Responding to this crisis remains a top priority for the FDA and we will maintain our focus on examining and responding to all facets of opioid abuse, misuse, addiction, overdose, and death in the U.S."

- The FDA hosted its third Online Opioid Summit, "Reducing the Availability of Opioids Online," on September 9, 2021, as part of the agency's efforts to address the illegal availability of opioids online.
- The Summit attendees included internet stakeholders, government entities, academia, and other important partners within the internet ecosystem.
- Discussions during the virtual meeting addressed topics including the evolving landscape of online opioid purchasing, such as younger and more vulnerable populations being exposed to these dangerous opioids through social media and other online platforms; ways to enhance cross-industry and global collaboration; successes and novel solutions implemented since prior summits; and new ways to continue to prevent the illegal sale of opioids through internet platforms and services.
- Despite the tremendous health risks associated with opioids illegally being sold online and the successes with limiting online opioid distribution, there continues to be websites and other online platforms that make it far too easy for United States consumers to purchase these dangerous products. This includes substances with abuse potential other than opioids such as benzodiazepines and stimulants that are sold illegally online.

- The FDA is committed to addressing the national crisis of opioid abuse, misuse, addiction, and overdose on all fronts, with a significant focus on decreasing exposure to opioids and preventing new addiction; supporting the treatment of those with opioid use disorder; fostering the development of novel pain treatment therapies; and taking action against those involved in the illegal importation and sale of unapproved and misbranded opioids.

Current Drug Shortages Index (as of October 18, 2021):

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

Acetazolamide Injection	***Currently in Shortage***
Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azacitidine for Injection	***Currently in Shortage***
Bumetanide Injection	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection	***Currently in Shortage***
Bupivacaine Hydrochloride Injection	***Currently in Shortage***
Calcium Disodium Versenate Injection	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection	***Currently in Shortage***
Ceftazidime and Avibactam (AVYCAZ) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Ceftolozane and Tazobactam (Zerbaxa) Injection	***Currently in Shortage***
Chlordiazepoxide Hydrochloride Capsules	***Currently in Shortage***
Chloroprocaine Hydrochloride Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cortisone Acetate Tablets	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***
Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Cytarabine Injection	***Currently in Shortage***
Desmopressin Acetate Nasal Spray	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Digoxin Injection	***Currently in Shortage***
Diltiazem Hydrochloride Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection	***Currently in Shortage***
Epinephrine Injection, 0.1mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***

Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Floxuridine for Injection	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Gentamicin Sulfate Injection	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydrocortisone Tablets	***Currently in Shortage***
Hydromorphone Hydrochloride Injection	***Currently in Shortage***
Hydroxocobalamin Injection	***Currently in Shortage***
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert	***Currently in Shortage***
Imipenem and Cilastatin for Injection	***Currently in Shortage***
Isoniazid Injection	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Kit for the Preparation of Technetium Tc 99m Sulfur Colloid Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Mannitol Injection	***Currently in Shortage***
Mepivacaine Hydrochloride Injection	***Currently in Shortage***
Methohexital Sodium (Brevital) Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Midazolam Injection	***Currently in Shortage***
Misoprostol Tablets	***Currently in Shortage***
Morphine Sulfate Injection	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Paclitaxel Injection (Protein-Bound Particles)	***Currently in Shortage***

Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Protamine Sulfate Injection	***Currently in Shortage***
Rifampin Injection	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection	***Currently in Shortage***
Sodium Bicarbonate Injection	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sodium Phosphates Injection	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Teprotumumab-trbw	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Tocilizumab Injection	***Currently in Shortage***
Triamcinolone Acetonide Injectable Suspension	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension	***Currently in Shortage***
Trimethobenzamide Hydrochloride Capsules	***Currently in Shortage***
Valproate Sodium Injection	***Currently in Shortage***
Varenicline Tartrate (Chantix) Tablets	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***