OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
December 8, 2021
4:00pm

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

Viewing Access Only:
Please register for the webinar at:
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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 – December 8, 2021

DATE: December 1, 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 December 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/Academic Detailing (AD) Program Update – Appendix B

Action Item – Maintenance Drug List – Appendix C

Action Item – Vote to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream) – Appendix D

Action Item – Vote to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) and Update the Approval Criteria for the Multiple Myeloma Medications – Appendix E

Action Item – Vote to Prior Authorize Jemperli® (Dostarlimab-gxly) and Update the Renal Cell Carcinoma (RCC) Approval Criteria for Keytruda® (Pembrolizumab) and Lenvima® (Lenvatinib) – Appendix F

Action Item – Annual Review of Skin Cancer Medications – Appendix G

Action Item – Annual Review of Crohn's Disease and Ulcerative Colitis (UC) Medications – Appendix H

Action Item – Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – Appendix I

Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Sertraline Capsules – Appendix J

30-Day Notice to Prior Authorize Livmarli™ (Maralixibat) – Appendix K

30-Day Notice to Prior Authorize Byooviz™ (Ranibizumab-nuna Injection) and Susvimo™ (Ranibizumab Intravitreal Implant) – Appendix L

Annual Review of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon) and 30-Day Notice to Prior Authorize Empaveli™ (Pegcetacoplan) – 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 – December 8, 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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https://zoom.us/webinar/register/WN_6JzMh8UaS_CJkFpBJSlgHg
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: 931 5637 1121
Passcode: 12421766

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. November 10, 2021 DUR Board Meeting Minutes
   B. November 10, 2021 DUR Board Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Academic Detailing (AD) Program Update – See Appendix B**
   A. Pharmacy Helpdesk Activity for November 2021
   B. Medication Coverage Activity for November 2021
   C. AD Program Update

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

5. **Action Item – Maintenance Drug List – See Appendix C**
   A. Introduction
   B. SoonerCare Maintenance Drug List
   C. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream) – See Appendix D**
   A. Market News and Updates
   B. Opzelura™ (Ruxolitinib 1.5% Cream) Product Summary

C. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) and Update the Approval Criteria for the Multiple Myeloma Medications – See Appendix E**
   A. Market News and Updates
   B. Abecma® (Idecabtagene Vicleucel) Product Summary
   C. Farydak® (Panobinostat) Product Summary
   D. Pepaxto® (Melphalan Flufenamide) Product Summary
   E. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Jemperli® (Dostarlimab-gxly) and Update the Renal Cell Carcinoma (RCC) Approval Criteria for Keytruda® (Pembrolizumab) and Lenvima® (Lenvatinib) – See Appendix F**
   A. Market News and Updates
   B. Jemperli® (Dostarlimab-gxly) Product Summary
   C. College of Pharmacy Recommendations

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

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

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

10. **Action Item – Annual Review of Crohn's Disease and Ulcerative Colitis (UC) Medications – See Appendix H**
    A. Current Prior Authorization Criteria
    B. Utilization of Crohn's Disease and UC Medications
    C. Prior Authorization of Crohn's Disease and UC Medications
    D. Market News and Updates
    E. College of Pharmacy Recommendations
    F. Utilization Details of Crohn's Disease and UC Medications

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

11. **Action Item – Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – See Appendix I**
    A. Current Prior Authorization Criteria

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

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

12. Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Sertraline Capsules – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Antidepressants
C. Prior Authorization of Antidepressants
D. Market News and Updates
E. Sertraline Capsule Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Antidepressants

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

13. 30-Day Notice to Prior Authorize Livmarli™ (Maralixibat) – See Appendix K

A. Introduction
B. Livmarli™ (Maralixibat) Product Summary
C. College of Pharmacy Recommendations

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

14. 30-Day Notice to Prior Authorize Byooviz™ (Ranibizumab-nuna Injection) and Susvimo™ (Ranibizumab Intravitreal Implant) – See Appendix L

A. Introduction
B. Market News and Updates
C. Byooviz™ (Ranibizumab-nuna Injection) Product Summary
D. Susvimo™ (Ranibizumab Intravitreal Implant) Product Summary
E. College of Pharmacy Recommendations
F. Utilization Details of Ophthalmic Vascular Endothelial Growth Factor (VEGF) Inhibitor Medications

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

15. Annual Review of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon) and 30-Day Notice to Prior Authorize Empaveli™ (Pegcetacoplan) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon)
C. Prior Authorization of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon)

D. Market News and Updates
E. Empaveli™ (Pegcetacoplan) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon)

Items to be presented by Dr. Ha, 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)
No live DUR Board meeting scheduled for January 2022. January 2022 will be a packet-only meeting.

A. Antihyperlipidemics
B. Dry Eye Disease (DED) Medications
C. Glaucoma Medications
D. Gonadotropin-Releasing Hormone (GnRH) 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 NOVEMBER 10, 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	
Melissa White; IT Manager	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): N/A		

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	
Debra Montgomery, D.O.; Medical Director	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	Kristi Kemp, AbbVie
Karen Evenson, Albireo Pharma	Lisa Dunn, Amgen
Nima Nabavi, Amgen	Jarrett Smith, Artia Solutions
Matthew Wright, Artia Solutions	Dwight Fierle, Aurinia Pharma
Robert Greely, Biogen	Jennifer Davis, Gilead
Robert Firnberg, Gilead	Porscha Showers, Gilead
Jim Musick, GSK	Shellie Keast, Mercer
Jody Legg, Mirum Pharma	Gina Heinen, Novo Nordisk
Dave Prather, Novo Nordisk	Mark Kaiser, Otsuka
Ronald Cain, Pfizer	Brian Maves, Pfizer
Charlie Collins, Sanofi	Chrystal Mayes, Sanofi
Eric Berthelot, Sobi	Marc Parker, Sunovion
Raquel Jordan, Takeda	Victoria Jones, OUHSC

PRESENT FOR PUBLIC COMMENT: N/A

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

ACTION: NONE REQUIRED

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

3A: OCTOBER 13, 2021 DUR MINUTES – VOTE

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS

4A: PHARMACY HELPDESK ACTIVITY FOR OCTOBER 2021

4B: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2021

4C: FDA SAFETY ALERTS

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **2022 DUR BOARD MEETING DATES**
Materials included in agenda packet; presented by Dr. Adams
Dr. Broyles moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE JAKAFI® (RUXOLITINIB) AND REZUROCK™ (BELUMOSUDIL)**
6A: MARKET NEWS AND UPDATES
6B: JAKAFI® (RUXOLITINIB) PRODUCT SUMMARY
6C: REZUROCK™ (BELUMOSUDIL) PRODUCT SUMMARY
6D: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Muñoz moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE BYLVAY™ (ODEVIXIBAT)**
7A: MARKET NEWS AND UPDATES
7B: BYLVAY™ (ODEVIXIBAT) PRODUCT SUMMARY
7C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Wilson
Dr. Broyles moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE LUPKYNIS™ (VOCLOSPORIN) AND SAPHNELO™ (ANIFROLUMAB-FNIA) AND UPDATE THE APPROVAL CRITERIA FOR THE TARGETED IMMUNOMODULATOR AGENTS**
8A: MARKET NEWS AND UPDATES
8B: LUPKYNIS™ (VOCLOSPORIN) PRODUCT SUMMARY
8C: SAPHNELO™ (ANIFROLUMAB-FNIA) PRODUCT SUMMARY
8D: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Ha
Dr. Muñoz moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF BOTULINUM TOXINS**
9A: CURRENT PRIOR AUTHORIZATION CRITERIA
9B: UTILIZATION OF BOTULINUM TOXINS
9C: PRIOR AUTHORIZATION OF BOTULINUM TOXINS
9D: MARKET NEWS AND UPDATES
9E: COLLEGE OF PHARMACY RECOMMENDATIONS
9F: UTILIZATION DETAILS OF BOTULINUM TOXINS
Materials included in agenda packet; presented by Dr. Ha
Dr. Broyles moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MAINTENANCE MEDICATIONS**
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF ASTHMA AND COPD MAINTENANCE MEDICATIONS
10C: PRIOR AUTHORIZATION OF ASTHMA AND COPD MAINTENANCE MEDICATIONS
10D: MARKET NEWS AND UPDATES

10E: NUCALA (MEPOLIZUMAB) CHRONIC RHINOSINUSITIS WITH NASAL POLYPS (CRSWNP)
10F: XOLAIR® (OMALIZUMAB) NASAL POLYPS PRODUCT SUMMARY
10G: COLLEGE OF PHARMACY RECOMMENDATIONS
10H: UTILIZATION DETAILS OF ASTHMA AND COPD MAINTENANCE MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Muñoz moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF CARBAGLU® (CARGLUMIC ACID)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF CARBAGLU® (CARGLUMIC ACID)
11C: PRIOR AUTHORIZATION OF CARBAGLU® (CARGLUMIC ACID)
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Broyles moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF MULTIPLE MYELOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ABECMA® (IDECABTAGENE VICLEUCEL), FARYDAK® (PANOBINOSTAT), AND PEPAXTO® (MELPHALAN FLUFENAMIDE)
12A: INTRODUCTION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF MULTIPLE MYELOMA MEDICATIONS
12D: PRIOR AUTHORIZATION OF MULTIPLE MYELOMA MEDICATIONS
12E: MARKET NEWS AND UPDATES
12F: ABECMA® (IDECABTAGENE VICLEUCEL) PRODUCT SUMMARY
12G: FARYDAK® (PANOBINOSTAT) PRODUCT SUMMARY
12H: PEPAXTO® (MELPHALAN FLUFENAMIDE) PRODUCT SUMMARY
12I: COLLEGE OF PHARMACY RECOMMENDATIONS
12J: UTILIZATION DETAILS OF MULTIPLE MYELOMA MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN DECEMBER

AGENDA ITEM NO. 13: ANNUAL REVIEW OF LENVIMA® (LENVATINIB) AND 30-DAY NOTICE TO PRIOR AUTHORIZE JEMPERLI® (DOSTARLIMAB-GXLY)
13A: INTRODUCTION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA
13C: UTILIZATION OF LENVIMA® (LENVATINIB)
13D: PRIOR AUTHORIZATION OF LENVIMA® (LENVATINIB)
13E: MARKET NEWS AND UPDATES
13F: JEMPERLI® (DOSTARLIMAB-GXLY) PRODUCT SUMMARY
13G: COLLEGE OF PHARMACY RECOMMENDATIONS
13H: UTILIZATION DETAILS OF LENVIMA® (LENVATINIB)
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN DECEMBER

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ATOPIC DERMATITIS (AD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OPZELURA™ (RUXOLITINIB 1.5% CREAM)

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF AD MEDICATIONS
14C: PRIOR AUTHORIZATION OF AD MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: OPZELURA™ (RUXOLITINIB 1.5% CREAM) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF AD MEDICATIONS
Materials included in agenda packet; presented by Dr. Wilson
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN DECEMBER

<u>AGENDA ITEM NO. 15:</u> ANNUAL REVIEW OF MYCAPSSA® (OCTREOTIDE) AND SIGNIFOR® LAR (PASIREOTIDE)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF MYCAPSSA® (OCTREOTIDE) AND SIGNIFOR® LAR (PASIREOTIDE)
15C: PRIOR AUTHORIZATION OF MYCAPSSA® (OCTREOTIDE) AND SIGNIFOR® LAR (PASIREOTIDE)
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 16:</u> U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 17:</u> FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
17A: ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
17B: ANTIDEPRESSANTS
17C: CROHN'S DISEASE AND ULCERATIVE COLITITS (UC) MEDICATIONS
17D: SKIN CANCER 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. 18:</u> ADJOURNMENT
The meeting was adjourned at 5:15pm.

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

Memorandum

Date: November 12, 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 November 10, 2021

Recommendation 1: U.S. Food and Drug Administration (FDA) Safety Alerts

NO ACTION REQUIRED.

Recommendation 2: 2022 Drug Utilization Review (DUR) Board Meeting Dates

MOTION CARRIED by unanimous approval.

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

Recommendation 3: Vote to Prior Authorize Jakafi® (Ruxolitinib) and Rezurock™ (Belumosudil)

MOTION CARRIED by unanimous approval.

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.

Recommendation 4: Vote to Prior Authorize Bylvay™ (Odevixibat)

MOTION CARRIED by unanimous approval.

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 is still not clinically appropriate; 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.

Recommendation 5: Vote to Prior Authorize Lupkynis™ (Voclosporin) and Saphnelo™ (Anifrolumab-fnia) and Update the Approval Criteria for the Targeted Immunomodulator Agents

MOTION CARRIED by unanimous approval.

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™)±

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
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™)±
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.

Recommendation 6: Annual Review of Botulinum Toxins

MOTION CARRIED by unanimous approval.

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 neurogenic detrusor overactivity 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**

Recommendation 7: Annual Review of Asthma and Chronic Obstructive Pulmonary Disease (COPD) Maintenance Medications

MOTION CARRIED by unanimous approval.

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.

Recommendation 8: Annual Review of Carbaglu® (Carglumic Acid)

MOTION CARRIED by unanimous approval.

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 is not due to liver failure; 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.

Recommendation 9: Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide)

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

Recommendation 10: Annual Review of Lenvima® (Lenvatinib) and 30-Day Notice to Prior Authorize Jemperli® (Dostarlimab-gxly)

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

Recommendation 11: Annual Review of Atopic Dermatitis (AD) Medications and 30-Day Notice to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream)

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

Recommendation 12: Annual Review of Mycapssa® (Octreotide) and Signifor® LAR (Pasireotide)

NO ACTION REQUIRED.

Recommendation 13: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

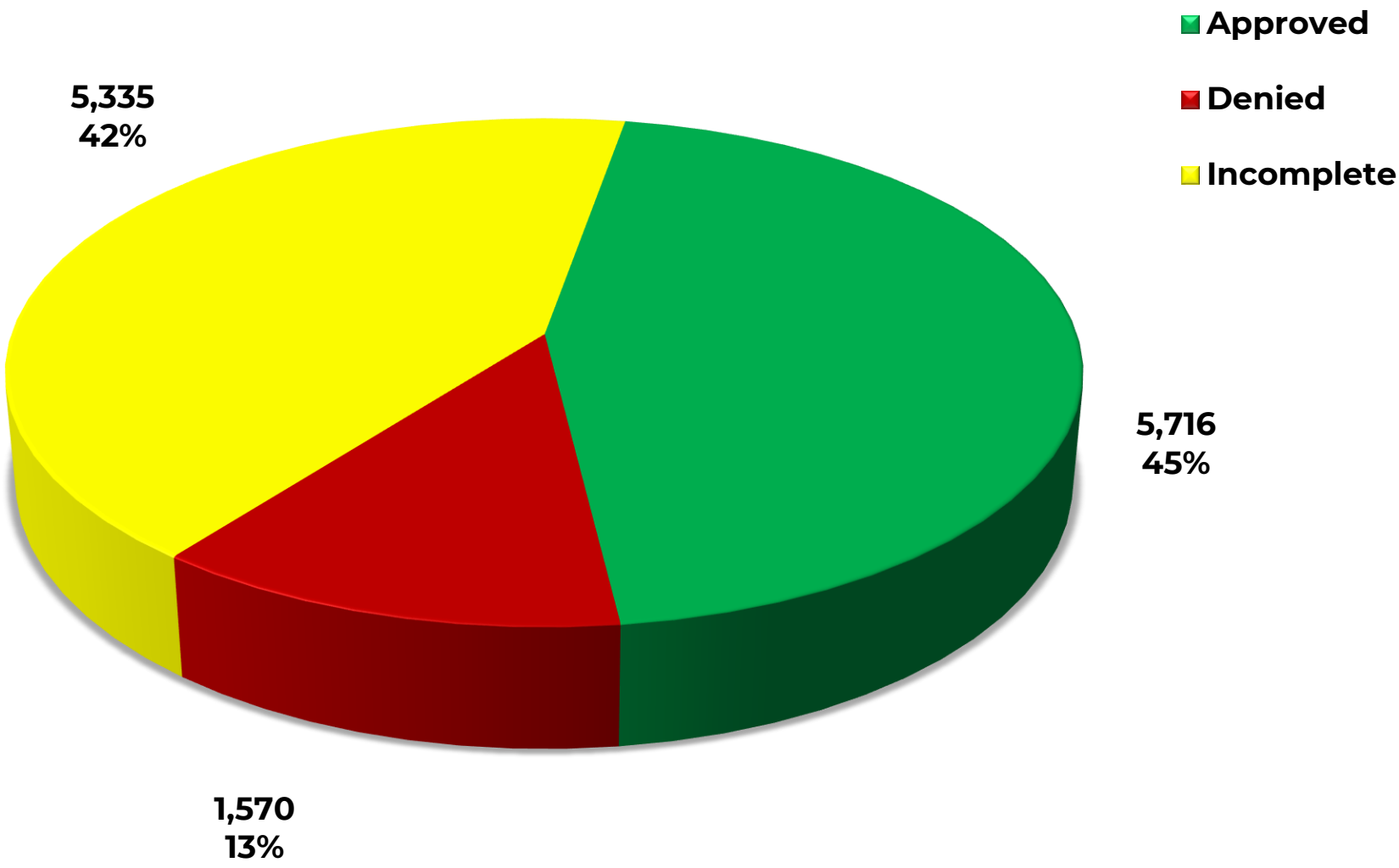
NO ACTION REQUIRED.

Recommendation 14: Future Business

NO ACTION REQUIRED.

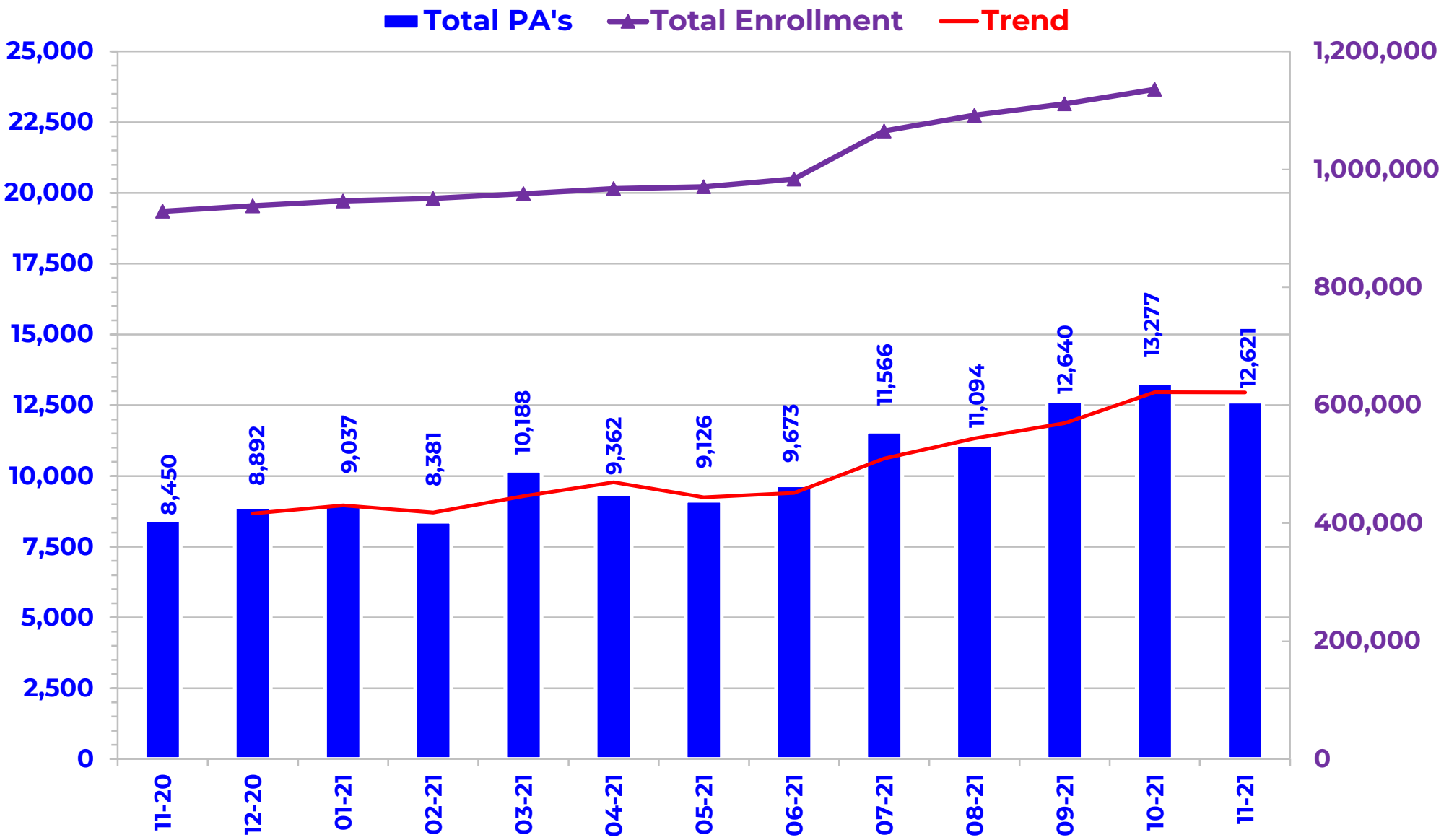
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER 2021



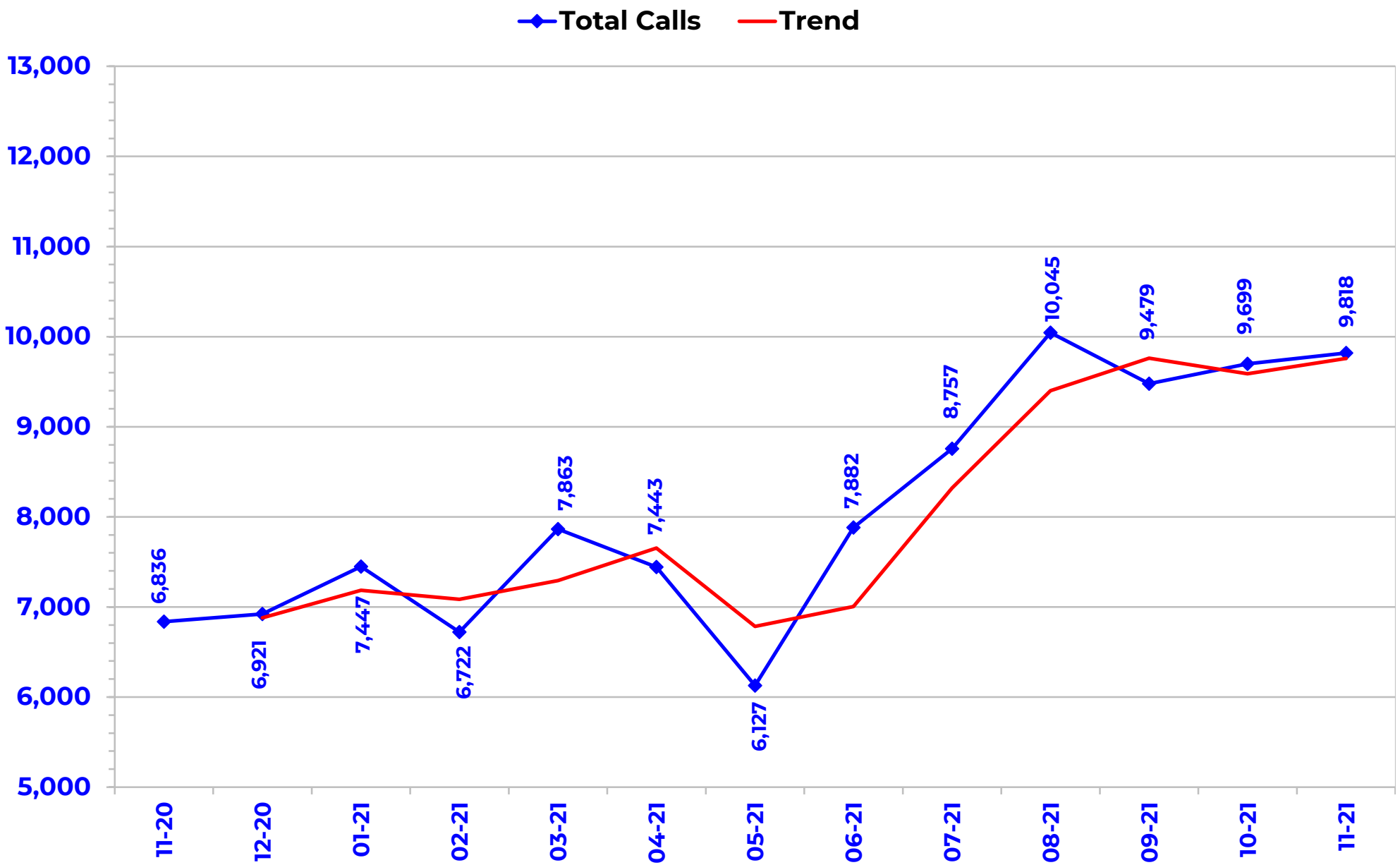
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2020 – NOVEMBER 2021



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
NOVEMBER 2020 – NOVEMBER 2021



Prior Authorization Activity

11/1/2021 Through 11/30/2021

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	87	26	6	55	358
Analgesic - NonNarcotic	19	0	4	15	0
Analgesic, Narcotic	253	98	32	123	145
Angiotensin Receptor Antagonist	10	2	1	7	359
Antiasthma	74	22	14	38	215
Antibiotic	58	30	1	27	243
Anticonvulsant	189	79	14	96	278
Antidepressant	311	63	46	202	323
Antidiabetic	1,024	400	140	484	359
Antifungal	15	4	1	10	50
Antigout	13	5	0	8	356
Antihemophilic Factor	22	13	0	9	146
Antihistamine	34	6	9	19	347
Antimigraine	381	57	133	191	226
Antineoplastic	188	116	10	62	168
Antiparasitic	41	10	12	19	11
Antiulcers	51	6	7	38	60
Anxiolytic	19	5	0	14	201
Atypical Antipsychotics	422	184	36	202	349
Biologics	328	201	25	102	284
Bladder Control	55	9	14	32	328
Blood Thinners	619	359	29	231	334
Botox	57	41	11	5	282
Buprenorphine Medications	98	40	7	51	81
Calcium Channel Blockers	34	8	6	20	248
Cardiovascular	83	43	7	33	340
Chronic Obstructive Pulmonary Disease	257	55	44	158	343
Constipation/Diarrhea Medications	216	51	47	118	219
Contraceptive	28	8	4	16	284
Corticosteroid	11	0	4	7	0
Dermatological	343	96	106	141	179
Diabetic Supplies	970	434	106	430	248
Endocrine & Metabolic Drugs	89	36	18	35	152
Erythropoietin Stimulating Agents	36	18	1	17	95
Fibric Acid Derivatives	10	2	1	7	359
Fibromyalgia	18	1	6	11	349
Fish Oils	34	8	5	21	354
Gastrointestinal Agents	169	51	38	80	211
Glaucoma	22	3	6	13	155
Growth Hormones	110	68	11	31	159

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Hepatitis C	220	135	20	65	9
HFA Rescue Inhalers	19	1	2	16	11
Insomnia	93	9	21	63	196
Insulin	258	87	17	154	346
Miscellaneous Antibiotics	21	7	1	13	10
Multiple Sclerosis	105	47	9	49	161
Muscle Relaxant	79	13	18	48	112
Nasal Allergy	97	12	25	60	214
Neurological Agents	103	36	18	49	226
Neuromuscular Agents	10	4	2	4	267
NSAIDs	41	2	12	27	358
Ocular Allergy	22	4	6	12	154
Ophthalmic	17	2	7	8	359
Ophthalmic Anti-infectives	18	10	0	8	36
Ophthalmic Corticosteroid	15	3	5	7	358
Osteoporosis	21	8	3	10	334
Other*	353	90	51	212	295
Otic Antibiotic	26	2	5	19	9
Pediculicide	20	5	0	15	19
Respiratory Agents	66	34	0	32	243
Smoking Cess.	28	0	23	5	0
Statins	37	4	12	21	109
Stimulant	1,275	808	78	389	352
Synagis	138	37	56	45	81
Testosterone	120	22	34	64	338
Thyroid	16	8	0	8	329
Topical Antifungal	29	5	6	18	94
Topical Corticosteroids	71	2	40	29	115
Vitamin	141	18	48	75	284
Pharmacotherapy	49	33	0	16	253
Emergency PAs	0	0	0	0	
Total	**10,306**	**4,106**	**1,481**	**4,719**	

* 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	37	24	2	11	330
Compound	19	16	0	3	18
Cumulative Early Refill	6	6	0	0	9
Diabetic Supplies	7	5	0	2	82
Dosage Change	381	350	1	30	16
High Dose	2	2	0	0	358
Ingredient Duplication	7	6	0	1	15
Lost/Broken Rx	118	111	2	5	18
MAT Override	270	197	5	68	89
NDC vs. Age	375	235	29	111	270
NDC vs. Sex	12	7	1	4	115
Nursing Home Issue	51	41	1	9	12
Opioid MME Limit	138	39	8	91	111
Opioid Quantity	54	38	1	15	153
Other	72	60	3	9	13
Quantity vs. Days Supply	688	414	33	241	248
STBS/STBSM	20	13	2	5	101
Step Therapy Exception	6	2	1	3	360
Stolen	24	23	0	1	15
Third Brand Request	28	21	0	7	15
Overrides Total	**2,315**	**1,610**	**89**	**616**	
Total Regular PAs + Overrides	**12,621**	**5,716**	**1,570**	**5,335**	

Denial Reasons	
Unable to verify required trials.	4,422
Does not meet established criteria.	1,596
Lack required information to process request.	880
Other PA Activity	
Duplicate Requests	1,363
Letters	25,797
No Process	3
Changes to existing PAs	952
Helpdesk Initiated Prior Authorizations	915
PAs Missing Information	1

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

Academic Detailing Program Update

Oklahoma Health Care Authority
December 2021

Background[1,2]

The Academic Detailing (AD) program is an educational initiative combining standards of care with the most current peer-reviewed studies and presenting them in an unbiased, independent, evidence-based manner. AD programs link prescribers with an educator, resulting in improved patient health and cost outcomes. Historically, AD programs that focus specifically on prescribing patterns are shown to reduce inappropriate prescribing to a modest, but significant degree, with a median difference of up to 7%. While not specifically designed to be a tool of cost containment, traditionally AD programs save $2 for every dollar spent.

Since July 2015, under the direction of the Oklahoma Health Care Authority (OHCA), Pharmacy Management Consultants (PMC) has operated an AD program to improve implementation of published guidelines and standards of care. PMC clinical pharmacists, data analysts, and pharmacy graduate students analyze prescription claims data to determine AD topics, identify providers who may benefit from individualized support from an AD pharmacist, and assess outcomes. Continued funding for the PMC-AD program comes from a Health Service Initiative (HSI) grant under the Children's Health Insurance Program (CHIP). As such, special care is taken to identify topics with particular relevance to the care of pediatric members. Current and previous areas of focus include treatment of acute and chronic conditions, preventive care, and specialized technical training related to the delivery of pharmacy services.

For each topic, the PMC-AD pharmacist prepares educational materials in consultation with the National Resource Center for Academic Detailing (NaRCAD) and offers the program to providers. Educational materials include the following:

- Clinical treatment guidelines
- Provider resources
- Patient and parent resources
- Diagnostic and treatment tools
- Topic-specific continuing medical education (CME) course listings
- Drug alerts and statements from the U.S. Food and Drug Administration (FDA)
- National quality measures [e.g., Healthcare Effectiveness Data and Information Set (HEDIS)]

- OHCA Product Based Prior Authorization (PBPA) coverage criteria

To date, AD services have been provided to 1,010 health care providers and/or their administrative staff. As previously reported, changes in prescribing patterns and associated improvements in health care utilization have led to cost savings to OHCA in the amount of $1,045,872. This amount is inclusive of all federal and supplemental rebates for the analysis periods following AD on the treatment of attention-deficit/hyperactivity disorder (ADHD), use of second generation/atypical antipsychotic medications (SGAs), and treatment of upper respiratory infections (URIs) for pediatric SoonerCare members.

Current Topic: Treatment of Persistent Asthma[3,4,5]

The Global Initiative for Asthma (GINA) report, Global Strategy for Asthma Management and Prevention, has been updated annually since 2002 and describes best practices for a worldwide audience based on comprehensive literature reviews. The National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines are updated much less frequently, but no less rigorously. The most recent NHLBI comprehensive guideline was published in 2007. However, in December of 2020, the NHLBI completed a focused update addressing 6 prioritized topics including:

- Intermittent inhaled steroids
- Long-acting muscarinic antagonists
- Indoor allergy relief
- Immunotherapy in the treatment of allergic asthma
- Fractional exhaled nitrous oxide (FeNO) testing
- Bronchial thermoplasty

Considering the most recent GINA and NHLBI updates, there is agreement across multiple areas impacting the treatment of pediatric asthma. Both guidelines recommend against the use of short-acting beta-agonists (SABAs) as monotherapy for persistent asthma across all levels of severity. The emergence of single maintenance and reliever therapy (SMART) represents both a point of guideline agreement and a significant change in approach to treatment for many providers. Both groups continue to emphasize the importance of appropriate inhaler technique, providing support for smoking cessation, managing environmental triggers, developing an asthma action plan as part of a shared decision-making process, and adjusting asthma treatment in a stepwise manner.

Changes and reinforced messaging from both GINA and NHLBI served as the source material for the fourth AD topic: Persistent Asthma – Using the Best Evidence to Improve Pediatric Outcomes.

Data from SoonerCare paid pharmacy claims and member diagnoses were used to identify providers who stood to benefit from receiving AD services.

Prescribing and diagnosis data for pediatric members was compared across the following criteria, with Asthma-AD offered to SoonerCare providers meeting 3 or more of the following criteria:

1. Having ≥50% increase in the number of rescue inhaler claims from 2019 to 2020
2. Having ≥50% increase in the number of claims for any asthma medication from 2019 to 2020
3. Having claims for any member with a diagnosis of status asthmaticus or ≥12 asthma-focused office visits per year during 2020
4. Submitting >10 petitions for prior authorization (PA) requests for asthma medications during 2020
5. Having ≥3 members each using ≥3 rescue inhalers during 2020
6. Having >100 members in their practice with claims for any asthma medication (excluding specialty providers)
7. Having ≥50% more rescue inhaler claims than their same specialty peers (e.g., general practitioner, physician assistant)
8. Having ≥50% more claims for any asthma medication than their same specialty peers (e.g., general practitioner, physician assistant)

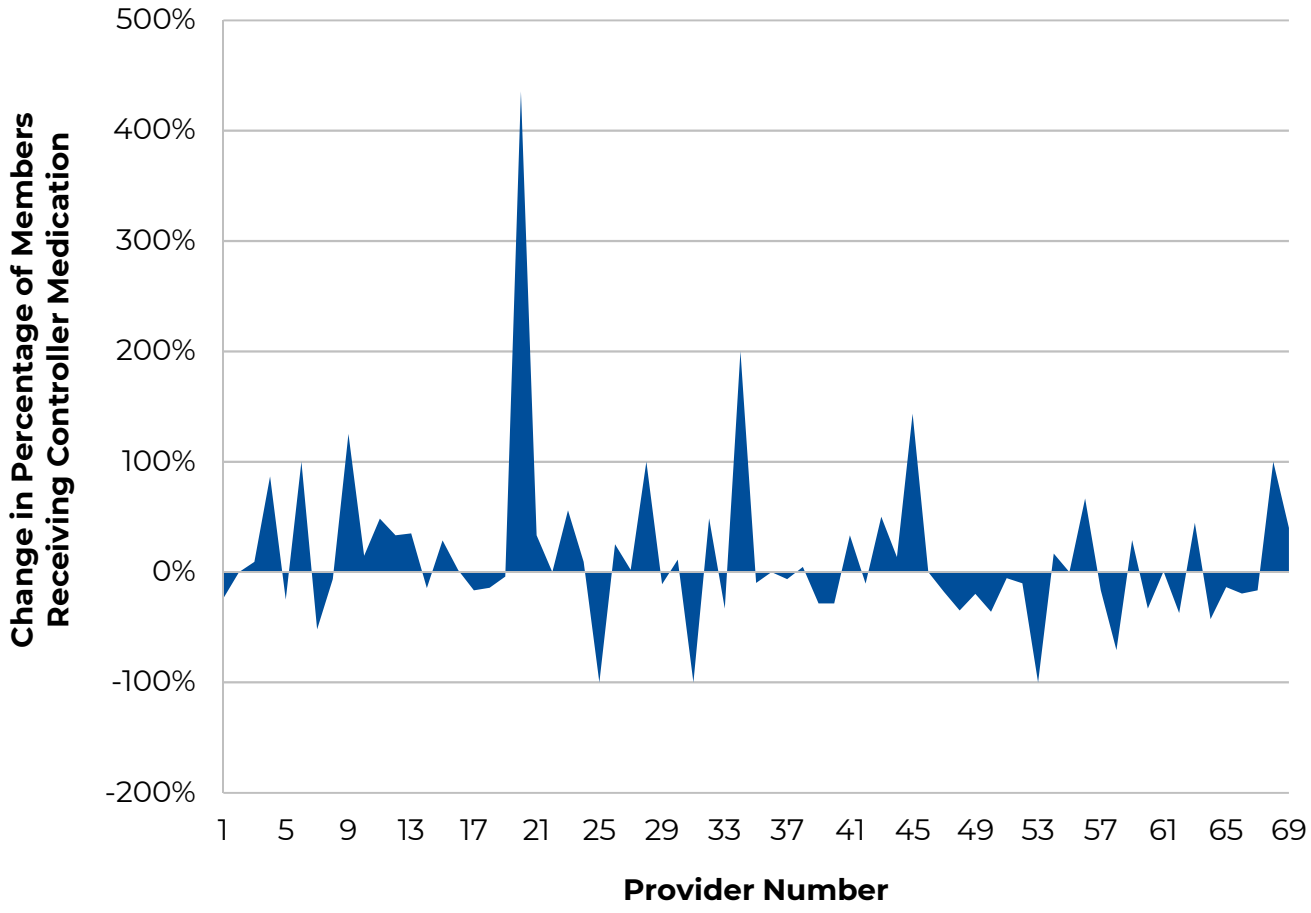
Asthma-AD services were delivered by the PMC-AD pharmacist. Providers in co-practice with identified providers and those who had previously received detailing for other topics were also eligible to receive AD services. In total, 195 providers received Asthma-AD services. Asthma prescribing patterns were shared with providers on request. Unlike previous AD visits, which were delivered almost exclusively in person, Asthma-AD was delivered exclusively through phone calls and Zoom meetings due to ongoing social distancing precautions associated with COVID-19.

Results: Treatment of Persistent Asthma[6]

Inappropriate Prescribing:

Potentially inappropriate asthma prescribing has been assessed by 3 separate measures for all detailed providers meeting criteria as described above. Prescribing patterns were compared for providers with members having paid claims for both office visits and asthma medications during both the pre- and post-AD periods. Outcomes are reported as a 6-month average per provider during the pre-AD period and as a 6-month average per provider during the post-AD period. The first measure assessed the use of controller medication. Changes in the percentage of members receiving a controller medication during the post-AD period are represented in Figure 1. In the pre-AD period, 45% of members with persistent asthma were receiving controller medications. Across all providers, prescribing of controller medications for members with persistent asthma increased by 14%.

Figure 1: Changes in Controller Medication Use



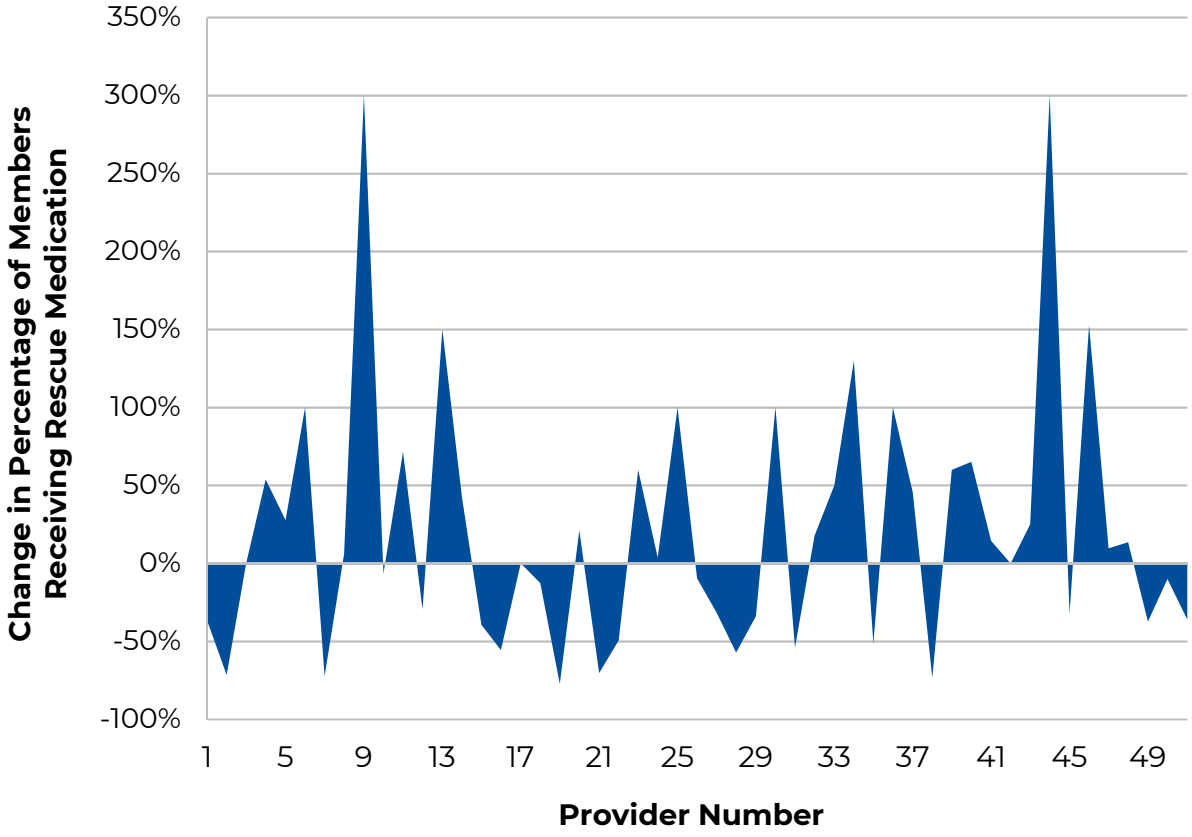
Each peak and trough represents a distinct provider and the changes in that provider's prescribing in the post-AD period. As shown in Figure 1, a peak above the 0% line represents a provider with a larger percentage of patients with persistent asthma receiving a controller medication after Asthma-AD. A trough below the 0% line represents a provider with a smaller percentage of patients with persistent asthma receiving a controller medication after Asthma-AD.

The second measure assessed the use of rescue medication. Changes in the percentage of members receiving a rescue medication during the post-AD period are represented in Figure 2. In the pre-AD period, only 21% of members with persistent asthma were receiving rescue medications. Across all providers, prescribing of rescue medications for members with persistent asthma increased by 21%.

Each peak and trough represents a distinct provider and the changes in that provider's prescribing in the post-AD period. As shown in Figure 2, a peak above the 0% line represents a provider with a larger percentage of patients

with persistent asthma receiving a rescue medication after Asthma-AD. A trough below the 0% line represents a provider with a smaller percentage of patients with persistent asthma receiving a rescue medication after Asthma-AD.

Figure 2: Changes in Rescue Medication Use



Overall, detailed providers increased their prescribing of both controller and rescue medications in treating persistent asthma. These changes bring them into closer alignment with the recommendations for treatment of persistent asthma, namely that each of their members receive both controller and rescue medication, either as SMART or as 2 agents. These changes are particularly significant in light of recent reports demonstrating children 3 to 17 years of age exhibit a persistent pattern of decreased numbers of office visits compared to those in older age groups. As of December 2020, weekly visits to pediatric specialists continued to be 24% lower than the baseline value seen in March 2020. By comparison, December 2020 adult primary care weekly visits had rebounded to 5% higher than the March 2020 baseline.

The third measure assessed the volume of asthma medication PA submissions. Since asthma treatment recommendations are the same for patients 12 years of age and older, PA submission patterns were assessed across all ages. Detailed providers submitted 5% fewer asthma medication

PAs per day after detailing. Changes in PA submissions may also be influenced by changes in the submission process or PA criteria during the analysis period. These changes could reasonably be expected to increase the number of asthma-related PAs and include:

- Dupixent® (dupilumab) became available in a 200mg/2mL and a 300mg/2mL pre-filled pen for use in adults and adolescents 12 years of age and older
- Dupixent® (dupilumab) received an expanded indication 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
- Xolair® (omalizumab) received a new indication for the add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older
- Nucala® (mepolizumab) received a new indication for the add-on maintenance treatment of chronic rhinosinusitis with nasal polyposis in adult patients 18 years of age and older
- Oklahoma Medicaid expansion increased eligibility for adults 19 to 64 years of age

Across all parameters, Asthma-AD providers increased member use of controller and rescue medications and decreased submissions of asthma-related PAs. Associated costs will be determined during an extended post-AD time analysis.

Provider Satisfaction

Provider satisfaction continues to remain very high as measured by post-visit satisfaction surveys. Providers meeting comparison criteria and those in co-practice were given satisfaction surveys in order to determine their acceptance of the program and to predict the likelihood of participation in future AD topics. Participants in the detailing sessions were given an online survey with an anonymous link and survey results are shown in Figure 3. To date, only 7 providers have been excluded due to an unwillingness to participate. Other reasons for exclusion of targeted providers included the following:

- No longer treating the targeted disease or medication class
- Retired, moved out of state, or inactive license
- No longer treating pediatric patients
- No longer treating SoonerCare members

Figure 3: Provider Satisfaction	
The information provided was:	**% choosing agree or strongly agree**
Easily understood	96%
Clearly presented	99%
Evidence-based	97%
Based on the information, I intend to:	**% choosing agree or strongly agree**
Make practice changes as a result	83%
Recommend this program to colleagues	89%
Participate in future topics	90%

Academic Meeting Presentation(s)

Since July 2016, the PMC-AD program leaders have been invited to present program outcomes and breakout sessions at the International Conference on Academic Detailing, the Academy of Managed Care Pharmacy (AMCP), and the American Drug Utilization Review Society (ADURS). Additionally, a poster presentation featuring ADHD-AD results was awarded a silver ribbon at the Nexus 2017 meeting of AMCP. The primary PMC-AD pharmacist is also currently 1 of 7 national training facilitators for NaRCAD.

Summary

As a result of AD interventions, the currently available data shows medication costs, PA submissions, inappropriate prescribing, and health care utilization costs have all been reduced substantially. Prescription data has been analyzed using rebated and non-rebated data, pre-and post-detailing patterns for individual providers, and federal fiscal year and calendar year comparisons. Each analysis shows improvements following delivery of AD services.

Providers report satisfaction with the program and intend to participate in future topics. The AD program is well received by providers. Targeted providers have fulfilled their stated intentions to make practice changes as prompted by the AD sessions. Continued implementation and expansion of the PMC-AD program is expected to increase delivery of evidence-based health care and reduce health care costs to OHCA.

[1] Soumerai SB, Avorn J. Economic and Policy Analysis of University-Based Drug "Detailing." *Med Care* 1986; 24(4):313-331.
[2] Yeh JS, Van Hoof TJ, Fischer MA. Key Features of Academic Detailing: Development of an Expert Consensus Using the Delphi Method. *Am Health Drug Benefits* 2016; 9(1):42-50.
[3] Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021. Available online at: https://ginasthma.org/. Last accessed 11/12/2021.
[4] National Asthma Education and Prevention Program. Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda, Maryland: National Heart, Lung, and Blood Institute, National Institutes of Health. Aug. 2007. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK7232/. Last accessed 11/12/2021.
[5] National Asthma Education and Prevention Program. Coordinating Committee Expert Panel Working Group: 2020 Focused Updates to the Asthma Guidelines. Bethesda, Maryland: National Heart, Lung, and Blood Institute, National Institutes of Health. Available online at: https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines. Issued 12/2020. Last accessed 11/15/2021.
[6] Mehrotra A, Chernew ME, Linetsky D, et al., The Impact of COVID-19 on Outpatient Visits in 2020: Visits Remained Stable, Despite a Late Surge in Cases. *Commonwealth Fund*. Available online at: https://doi.org/10.26099/bvhf-e411. Issued 02/22/2021. Last accessed 11/16/2021.

Appendix C

Maintenance Drug List

Oklahoma Health Care Authority
December 2021

Introduction[1]

Most adult SoonerCare members have a 6 prescription limit each month; therefore, prescribing for and dispensing 90-day supplies of chronic maintenance medications will help members who are on multiple medications obtain the maintenance medications necessary. Dispensing of 90-day supplies of chronic maintenance medications has been shown to increase medication adherence and persistence, compared to dispensing of 30-day supplies. Additionally, a 90-day supply will reduce the SoonerCare member's financial burden as they will pay the same copay for a 90-day or 30-day supply.

In November 2019, the Oklahoma Health Care Authority (OHCA) Board voted to update the current policy and rules regarding dispensing limitations. Previously, medications could only be dispensed and reimbursed by SoonerCare up to a 34-day supply or if the quantity did not exceed 100 units. The newly voted OHCA policy and rules state the following regarding dispensing limitations and a maintenance drug list (317:30-5-77.1):

> "Prescription quantities shall be limited to a 34-day supply, except in the following situations:
> 1. The Drug Utilization Review (DUR) Board has recommended a different day supply or quantity limit based on published medical data, including the manufacturer's package insert;
> 2. The product is included on the Maintenance List of medications which are exempted from this limit and may be dispensed up to a 90-day supply;
> 3. The manufacturer of the drug recommends a dispensing quantity less than a 34-day supply…."
>
> "The DUR Board shall develop a Maintenance List of medications which are used in general practice on a continuing basis. These drugs shall be made available through the Vendor Drug Program in quantities up to a 90-day supply when approved by the prescriber. The DUR Board shall review the Maintenance List at least annually."

The DUR Board recommended and voted on categories of medications for inclusion on the maintenance drug list in December 2019, and the SoonerCare Maintenance Drug List was implemented in January 2020. The

purpose of this report is to provide the DUR Board with the current maintenance drug list for review, which is to be maintained by the DUR Board. Medications included in the maintenance drug list are set up to allow a 90-day supply of medications in the claims processing system without the need for an override. Action by the DUR Board is not required unless the DUR Board recommends changes to the current maintenance drug list.

SoonerCare Maintenance Drug List

The current SoonerCare Maintenance Drug List is available on the OHCA website (https://oklahoma.gov/ohca/providers/types/pharmacy) and includes the following categories of medications:

- Alzheimer's Medications
- Anticonvulsants
- Antidepressants
- Antihypertensive Medications
- Antipsychotic Medications
- Anti-Ulcer Medications
- Bladder Control Medications
- Benign Prostatic Hyperplasia (BPH) Medications
- Cardiovascular Medications
- Chronic Obstructive Pulmonary Disease (COPD) Medications
- Diabetes Medications
- Glaucoma Medications
- Hyperlipidemia Medications
- Parkinson's Medications

Please note that not all medications in each category can be processed for a 90-day supply.

Recommendations

The College of Pharmacy recommends adding a new medication category, Thyroid Medications, to the SoonerCare Maintenance Drug List.

[1] Taitel M, Fensterheim L, Kirkham H, et al. Medication Days' Supply, Adherence, Wastage, and Cost Among Chronic Patients in Medicaid. *MMRR* 2012; 2(3):E1-E13. doi: dx.doi.org/10.5600/mmrr.002.03.a04.

Appendix D

Vote to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream)

Oklahoma Health Care Authority
December 2021

Market News and Updates[1,2]

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

- **September 2021:** The FDA approved Opzelura™ (ruxolitinib 1.5% cream) as the first topical Janus kinase (JAK) inhibitor to be FDA approved for the treatment of atopic dermatitis (AD).

Opzelura™ (Ruxolitinib 1.5% Cream) Product Summary[3,4,5,6]

Indication(s): 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

Limitation(s) 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

- **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, myocardial infarction (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% body surface area (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

Contraindication(s): None

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.

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. One medium potency to very-high potency Tier-1 topical corticosteroid (TCS); and
    b. One topical calcineurin inhibitor (TCI) [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.

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Appendix E

Vote to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) and Update the Approval Criteria for the Multiple Myeloma Medications

Oklahoma Health Care Authority
December 2021

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

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 proteasome inhibitor (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, they are committed to keeping Pepaxto® available to these patients free of charge and are working with the FDA to ensure appropriate patients have access to treatment.

Guideline Update(s):

- According to the National Comprehensive Cancer Network (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[6]

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 a single IV infusion

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

Farydak® (Panobinostat) Product Summary[7]

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 may be 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[8]

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 a 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.

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Appendix F

Vote to Prior Authorize Jemperli® (Dostarlimab-gxly) and Update the Renal Cell Carcinoma (RCC) Approval Criteria for Keytruda® (Pembrolizumab) and Lenvima® (Lenvatinib)

Oklahoma Health Care Authority
December 2021

Market News and Updates[1]

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

- **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.
- **November 2021:** The FDA approved Keytruda® (pembrolizumab) for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Jemperli® (Dostarlimab-gxly) Product Summary[2]

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
   a. Member has not received previous systemic therapy for advanced disease; and
   b. Must be used in combination with axitinib or lenvatinib; and

c. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; or

2. Diagnosis of RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

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.

[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 11/17/2021. Last accessed 11/23/2021.

[2] Jemperli® (Dostarlimab-gxly) Prescribing Information. GlaxoSmithKline. Available online at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Jemperli/pdf/JEMPERLI-PI-MG.PDF. Last revised 08/2021. Last accessed 11/11/2021.

Appendix G

Fiscal Year 2021 Annual Review of Skin Cancer Medications

Oklahoma Health Care Authority
December 2021

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

Skin cancers are commonly divided into 2 different types: non-melanoma skin cancer (NMSC) and melanoma skin cancer. In general, NMSC are far more common than melanomas but result in lower mortality. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common forms of NMSC. BCC is the most common cancer diagnosed in the United States, occurring in over 2 million people annually, and the incidence of BCC continues to increase. More people are diagnosed with BCC than all other cancers combined. The incidence of SCC is approximately half that of BCC. Because NMSC rarely metastasizes, treatment is largely focused on localized therapies including different surgical approaches and topical agents. Systemic therapy is reserved for the select number of advanced and metastatic cases.

According to the National Cancer Institute, in 2021, an estimated 106,110 new cases of melanoma skin cancer will be diagnosed in the United States, and an estimated 7,180 deaths will occur from the disease. The average lifetime risk of developing melanoma in the United States is 1 in 40 for women and 1 in 27 for men. While the incidence of melanoma is far lower than NMSC, melanomas behave much more aggressively and have high rates of metastases leading to poor survival outcomes in advanced cases. Survival rates vary based on the clinical stage of the disease at diagnosis, with 5-year survival ranging from 15 to 60% in patients with distant and local metastases, respectively. Traditional cytotoxic chemotherapy has failed to provide successful treatment outcomes in this patient population and has a very small role in treating patients with melanoma. Surgery, immunotherapy, molecularly targeted agents, and radiation are the cornerstones to the treatment of melanoma.

Over the past 10 years, drug developers have focused on agents that target various immune checkpoints, specifically cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and the programmed death 1/programmed death ligand 1 (PD-1/PD-L1) pathway, which result in a tumor-specific immune response in a subset of patients. Additionally, the development of molecularly targeted therapy began after it was found that activating *BRAF* mutations occur in half

of all melanomas. *BRAF* mutations lead to activation of the mitogen-activated protein kinase (MAPK) pathway and promote tumor development. Research in these areas has led to U.S. Food and Drug Administration (FDA) approval of the following agents in the last 5 years: encorafenib, binimetinib, ipilimumab, vemurafenib, pembrolizumab, dabrafenib, trametinib, cobimetinib, and nivolumab. The National Comprehensive Cancer Network (NCCN) guidelines for melanoma treatment recommend all of these agents as first-line therapy, some as monotherapy and others in combination. Use of these agents has also expanded into the adjuvant setting. Development of these new drugs has produced an increase in response rates and modest improvements in survival in some melanoma cases. The cost associated with treating skin cancer, approximately $8.1 billion, increased 5 times faster than treatments for any other cancer between 2002 and 2011.

Current Prior Authorization Criteria

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

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

Bavencio® (Avelumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of advanced RCC; and
2. Used as first-line treatment; and
3. Used in combination with axitinib.

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

1. Diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Disease has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy; or
3. Used as maintenance therapy for members not progressing on first-line platinum-containing regimen.

Braftovi® (Encorafenib) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]:

1. Diagnosis of advanced or metastatic CRC; and
2. *BRAF* V600E mutation positive; and
3. Used in combination with cetuximab or panitumumab; and
4. Disease must have progressed following adjuvant therapy within 12 months; or
5. Used following progression of any line of metastatic therapy.

Braftovi® (Encorafenib) Approval Criteria [Melanoma Diagnosis]:

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

Cotellic® (Cobimetinib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600E or V600K mutation; and
    a. Cobimetinib is not indicated for wild-type *BRAF* melanoma; and
3. Member meets 1 of the following:
    a. Used as first-line therapy in combination with vemurafenib; or
    b. Used as second-line therapy or subsequent therapy with vemurafenib.

Erivedge® (Vismodegib) Approval Criteria [Basal Cell Carcinoma (BCC) Diagnosis]:

1. Diagnosis of locally advanced BCC that has either:
    a. Recurred following surgery or radiation therapy; or
    b. Surgery or radiation is contraindicated; or
2. Diagnosis of metastatic BCC.

Imlygic® (Talimogene Laherparepvec) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable cutaneous, subcutaneous, or nodal lesions that are recurrent after initial surgery; and
    a. Not indicated in members with visceral metastases; and
2. Member is not immunocompromised or pregnant.

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.

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

1. Diagnosis of recurrent or metastatic cervical cancer; and
2. Member has had disease progression on or after chemotherapy; and
3. Tumors must express programmed death ligand 1 (PD-L1) [combined positive score (CPS) ≥1]; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. First-line treatment; and
2. Metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); or
3. Unresectable disease.

Keytruda® (Pembrolizumab) Approval Criteria [Cutaneous Squamous Cell Carcinoma (cSCC) Diagnosis]:

1. Diagnosis of recurrent or metastatic disease; and
2. Not curable by radiation or surgery.

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

1. Diagnosis of advanced endometrial cancer that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
2. Progressive disease following prior systemic therapy; and
3. Member is not a candidate for curative surgery or radiation; and
4. Used in combination with lenvatinib; and
5. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

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

Keytruda® (Pembrolizumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. First-line or recurrent setting; and
2. Squamous cell histology; and
3. If used in the recurrent setting, member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of relapsed or progressive HCC; and
2. Member must have been previously treated with sorafenib; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Classical Hodgkin Lymphoma (cHL) Diagnosis]:

1. As a single-agent; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e. Opdivo® (nivolumab)]; and
3. For adult members:
    a. Diagnosis of relapsed or refractory cHL; and
        i. Exception: Lymphocyte-predominant Hodgkin lymphoma; or
4. For pediatric members:
    a. Diagnosis of refractory cHL; or
    b. Relapsed disease after ≥2 therapies.

Keytruda® (Pembrolizumab) Approval Criteria [Melanoma Diagnosis]:

1. Member meets 1 of the following:
    a. Adjuvant treatment of members with melanoma with involvement of lymph node(s) following complete resection; or
    b. Diagnosis of unresectable or metastatic melanoma; and
2. Used as a single-agent; and
3. Member meets 1 of the following:
    a. Used as first-line therapy; or
    b. Used as second-line therapy or subsequent therapy for disease progression if not previously used; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
5. For adjuvant treatment of melanoma, approvals will be for a maximum duration of 1 year.

Keytruda® (Pembrolizumab) Approval Criteria [Merkel Cell Carcinoma (MCC) Diagnosis]:

1. Diagnosis of recurrent, locally advanced, or metastatic MCC; and
2. No history of prior systemic chemotherapy; and
3. Used as a single-agent; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of metastatic NSCLC; and

2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for programmed death ligand 1 (PD-L1) expression as follows:
    a. As a single-agent, first-line: ≥1%; or
    b. First-line in combination: No expression required; or
    c. As a single-agent, second-line: ≥1%; and
4. Member meets 1 of the following:
    a. Previously untreated, metastatic squamous NSCLC in combination with carboplatin and either paclitaxel or nab-paclitaxel; or
    b. Previously untreated, metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    c. New diagnosis as first-line therapy (member has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translocations; or
    d. Used as a single-agent for disease progression on or after platinum-containing chemotherapy (i.e., cisplatin, carboplatin):
        i. Members with EGFR-mutation-positive tumors should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations* (*examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib);* and
        ii. Members with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations (examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib).*

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

1. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e., Opdivo® (nivolumab)]; and
2. MSI-H or dMMR solid tumors that have progressed following prior treatment with no satisfactory alternative treatment options.

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

1. Diagnosis of stage III NSCLC; and
2. Ineligible for surgery or definitive chemoradiation; and

3. Tumor proportion scores for programmed death ligand 1 (PD-L1) expression ≥1%; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Non-Muscle Invasive Bladder Cancer (NMIBC) Diagnosis]:

1. Diagnosis of high-risk, NMIBC; and
2. Member must have failed therapy with Bacillus Calmette-Guerin (BCG)-therapy; and
3. Member must be ineligible for or has elected not to undergo cystectomy.

Keytruda® (Pembrolizumab) Approval Criteria [Primary Mediastinal Large B-cell Lymphoma (PMBCL) Diagnosis]:

1. Diagnosis of PMBCL; and
2. Member must have refractory disease or relapsed after 2 or more prior lines of therapy; and
3. Authorizations will not be granted for members who require urgent cytoreduction; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of new or recurrent stage 4 clear-cell RCC; and
    a. Member has not received previous systemic therapy for advanced disease; and
    b. Must be used in combination with axitinib or lenvatinib; and
    c. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; or
2. Diagnosis of RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

*The above updated prior authorization criteria for Keytruda® (pembrolizumab) for RCC is currently pending a vote by the Drug Utilization Review (DUR) Board at the December 2021 DUR Board meeting; please refer to the vote report [Vote to Prior Authorize Jemperli® (Dostarlimab-gxly) and Update the Renal Cell Carcinoma (RCC) Approval Criteria for Keytruda® (Pembrolizumab) and Lenvima® (Lenvatinib)] in the December 2021 DUR packet for additional information.

Keytruda® (Pembrolizumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of metastatic SCLC; and

2. Progressed on or following a platinum-based regimen and at least 1 other regimen; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Tumor Mutational Burden-High (TMB-H) Solid Tumors Diagnosis]:

1. Diagnosis of unresectable or metastatic TMB-H [≥10 mutations/megabase (mut/Mb)] solid tumors; and
2. Used following disease progression after prior treatment; and
3. No satisfactory alternative treatment options.

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

1. Member must have 1 of the following:
    a. Locally advanced or metastatic urothelial carcinoma with disease progression during or following platinum-containing chemotherapy; or
    b. Within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; or
    c. Frontline for members with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy; and
        i. Cisplatin ineligibility is defined as:
            1. Baseline creatinine clearance of <60mL/min; or
            2. ECOG performance status of 2; or
            3. Class III heart failure; or
            4. Grade 2 or greater peripheral neuropathy; or
            5. Grade 2 or greater hearing loss; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e., Opdivo® (nivolumab)].

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

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

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

1. Diagnosis of metastatic or locally advanced cSCC; and
2. Member is ineligible for curative surgery or radiation; and

3. Member has not received prior immunotherapy agent(s) [e.g., Keytruda® (pembrolizumab), Opdivo® (nivolumab), Yervoy® (ipilimumab)].

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

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

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

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

Mekinist® (Trametinib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type *BRAF* melanoma; and
3. Must meet 1 of the following:
    a. Used as first-line therapy in combination with dabrafenib; or
    b. Used as second-line or subsequent therapy with dabrafenib; or
    c. Used as second-line therapy or subsequent therapy as a single-agent if:
        i. Member was intolerant to prior BRAF inhibitor therapy (i.e., dabrafenib, vemurafenib); and
        ii. No evidence of disease progression on prior BRAF inhibitor therapy (i.e., dabrafenib, vemurafenib).

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

1. Diagnosis of refractory or metastatic NSCLC; and
2. *BRAF* V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type *BRAF* NSCLC; and
3. Used in combination with dabrafenib.

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

1. Diagnosis of persistent disease or recurrent low-grade serous carcinoma; and
2. Meets 1 of the following:

a. Immediate treatment for serially rising CA-125 in members who previously received chemotherapy; or
b. Progression on primary, maintenance, or recurrence therapy; or
c. Stable or persistent disease (if not on maintenance therapy); or
d. Complete remission and relapse after completing chemotherapy.

Mektovi® (Binimetinib) Approval Criteria [Melanoma Diagnosis]:
1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600E or V600K mutation; and
3. Used in combination with encorafenib.

Odomzo® (Sonidegib) Approval Criteria [Basal Cell Carcinoma (BCC) Diagnosis]:
1. Diagnosis of locally advanced BCC that has either:
   a. Recurred following surgery or radiation therapy; or
   b. Surgery or radiation is contraindicated; or
2. Diagnosis of metastatic BCC.

Opdivo® (Nivolumab) Approval Criteria [Adjuvant Treatment of Melanoma Diagnosis]:
1. Member has had complete resection of melanoma; and
2. Diagnosis of stage III B/C melanoma following complete resection; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Used as a single-agent; and
5. Dose as follows:
   a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; and
   b. Maximum duration of 1 year.

Opdivo® (Nivolumab) Approval Criteria [Esophageal Squamous Cell Carcinoma (ESCC) Diagnosis]:
1. Diagnosis of unresectable, advanced, recurrent, or metastatic ESCC; and
2. Used following prior fluoropyrimidine- and platinum-based chemotherapy.

Opdivo® (Nivolumab) Approval Criteria [Head and Neck Cancer Diagnosis]:
1. Diagnosis of recurrent or metastatic head and neck cancer; and
2. Squamous cell histology; and
3. Member has received prior platinum-containing regimen (i.e., cisplatin, carboplatin); and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Member must have unresectable disease and is not a transplant candidate; or
2. Metastatic disease or extensive liver tumor burden; and
3. Must meet 1 of the following:
    a. If used as first-line therapy, must be used as single-agent; and
        i. Ineligible for tyrosine kinase inhibitors or anti-angiogenic agents; or
    b. If used as second-line or greater therapy, may be used as single-agent or in combination with ipilimumab; and
        i. Must not have failed other checkpoint inhibitors.

Opdivo® (Nivolumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
    a. Exception: Lymphocyte-predominant Hodgkin lymphoma; and
2. Used as a single-agent; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Mesothelioma Diagnosis]:

1. Diagnosis of malignant pleural mesothelioma that cannot be surgically removed; and
2. Used as first-line therapy; and
3. Used in combination with ipilimumab.

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

1. Diagnosis of MSI-H or dMMR mCRC; and
2. Progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

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

1. First-line therapy for recurrent, advanced, or metastatic disease, meets the following:
    a. No epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations; and
    b. Used in combination with ipilimumab; and
    c. Expresses programmed death ligand 1 (PD-L1) ≥1%; or
    d. Given in combination with 2 cycles of platinum-doublet chemotherapy.

2. Second-line therapy for metastatic disease, meets the following:
    a. Tumor histology is 1 of the following:
        i. Adenocarcinoma; or
        ii. Squamous cell; or
        iii. Large cell; and
    b. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
    c. The patient has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
    d. As a single-agent; and
    e. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
2. Used in 1 of the following settings:
    a. For nivolumab monotherapy:
        i. Diagnosis of relapsed or surgically unresectable stage IV disease; and
        ii. Failed prior therapy with 1 of the following medications:
            1. Sunitinib; or
            2. Sorafenib; or
            3. Pazopanib; or
            4. Axitinib; or
    b. For nivolumab use in combination with ipilimumab:
        i. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; or
    c. For nivolumab use in combination with cabozantinib:
        i. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with advanced RCC; and
        ii. Nivolumab, when used in combination with cabozantinib for RCC, will be approved for a maximum duration of 2 years; and
3. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
    b. In combination with ipilimumab: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks thereafter; or
    c. In combination with cabozantinib: cabozantinib 40mg once daily with nivolumab 240mg every 2 weeks or 480mg every 4 weeks;

nivolumab, when used in combination with cabozantinib for RCC, will be approved for a maximum duration of 2 years.

Opdivo® (Nivolumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Must meet 1 of the following criteria:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
2. Used as a single-agent or in combination with ipilimumab; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. Used as a single-agent or in combination with ipilimumab:
    a. As first-line therapy for untreated melanoma; or
    b. As second-line or subsequent therapy for documented disease progression while receiving or since completing most recent therapy:
        i. If the member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
3. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
    b. In combination with ipilimumab: nivolumab 1mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Diagnosis of metastatic or unresectable locally advanced cancer; and
2. Used as second-line or greater therapy; and
3. Member has failed a platinum-containing regimen; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

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

4. Diagnosis of ATC; and
5. Locally advanced or metastatic disease; and
6. *BRAF* V600E mutation; and
7. No satisfactory locoregional treatment options.

Tafinlar® (Dabrafenib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600E or V600K mutation; and
    a. Dabrafenib is not indicated for wild-type *BRAF* melanoma; and
3. Used as a single-agent or in combination with trametinib; and
4. Must meet 1 of the following:
    a. Used as first-line therapy; or
    b. Used as second-line or subsequent therapy.

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

1. Diagnosis of refractory or metastatic NSCLC; and
2. *BRAF* V600E or V600K mutation; and
    a. Dabrafenib is not indicated for wild-type *BRAF* NSCLC; and
3. Used as a single-agent or in combination with trametinib.

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

1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600 mutation-positive; and
3. In combination with cobimetinib and vemurafenib.

Yervoy® (Ipilimumab) Approval Criteria [Adjuvant Treatment of Melanoma Diagnosis]:

1. Member has had complete resection of melanoma with lymphadenectomy; and
2. Member has stage III disease with regional nodes of >1mm and no in-transit metastasis; and
3. Used as a single-agent; and
4. Maximum dose of 10mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Member must have unresectable disease and is not a transplant candidate; or
2. Metastatic disease or extensive liver tumor burden; and
3. Used as second-line or greater therapy; and
4. Used in combination with nivolumab; and
5. Must not have failed other checkpoint inhibitors.

Yervoy® (Ipilimumab) Approval Criteria [Mesothelioma Diagnosis]:

1. Diagnosis of malignant pleural mesothelioma that cannot be surgically removed; and
2. Used as first-line therapy; and
3. Used in combination with nivolumab.

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC; and
    a. First-line therapy for metastatic disease; and
    b. No epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations; and
    c. Given in combination with nivolumab; and
    d. Expresses programmed death ligand 1 (PD-L1) ≥1%; or
    e. Given in combination with 2 cycles of platinum-doublet chemotherapy.

Yervoy® (Ipilimumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; and
2. Used in combination with nivolumab; and
3. Member has not failed previous programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Dose as follows: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks.

Yervoy® (Ipilimumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of SCLC; and
2. Must meet 1 of the following criteria:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
3. Used in combination with nivolumab.

Yervoy® (Ipilimumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. Used in combination with nivolumab as:
    a. First-line therapy; or
    b. Second-line or subsequent therapy for disease progression if nivolumab was not previously used; or
3. Used as a single-agent for 1 of the following:
    a. First-line therapy as a single course of 4 treatments; or
    b. Second-line or subsequent lines of therapy as a single course of 4 treatments; or
    c. Retreatment, consisting of a 4-dose limit, for a member who had:
        i. No significant systemic toxicity during prior ipilimumab therapy; and

ii. Whose disease progressed after being stable >6 months following completion of a prior course of ipilimumab; and
iii. For whom no intervening therapy has been administered; and
4. Maximum dose of 3mg/kg will apply.

Zelboraf® (Vemurafenib) Approval Criteria [Erdheim-Chester Disease (ECD) Diagnosis]:
1. Diagnosis of ECD; and
2. *BRAF* V600E or V600K mutation; and
3. Used as a single-agent.

Zelboraf® (Vemurafenib) Approval Criteria [Hairy-Cell Leukemia Diagnosis]:
1. Diagnosis of hairy-cell leukemia; and
2. Used as a single-agent; and
3. Disease progression following failure of purine analog therapy (i.e., pentostatin, cladribine).

Zelboraf® (Vemurafenib) Approval Criteria [Melanoma Diagnosis]:
1. Diagnosis of unresectable or metastatic melanoma; and
2. *BRAF* V600E or V600K mutation; and
   a. Vemurafenib is not indicated for wild-type *BRAF* melanoma; and
3. Must meet 1 of the following:
   a. Used as first-line therapy; or
   b. Used as second-line or subsequent therapy; and
4. Used as a single-agent or in combination with cobimetinib.

Zelboraf® (Vemurafenib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. Diagnosis of refractory or metastatic NSCLC; and
2. *BRAF* V600E or V600K mutation; and
   a. Vemurafenib is not indicated for wild-type *BRAF* NSCLC; and
3. Used as a single-agent.

Approval criteria for Tecentriq® (atezolizumab) for indications other than skin cancer diagnoses can be found in the April 2021 DUR Board packet. Atezolizumab approval criteria are reviewed annually with the lung cancer medications.

Utilization of Skin Cancer Medications: Fiscal Year 2021

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

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	11	60	$536,080.53	$8,934.68	$303.56	5,076	1,766
2021	13	58	$416,088.90	$7,173.95	$245.77	3,990	1,693
% Change	**18.20%**	**-3.30%**	**-22.40%**	**-19.70%**	**-19.00%**	**-21.40%**	**-4.10%**
Change	**2**	**-2**	**-$119,991.63**	**-$1,760.73**	**-$57.79**	**-1,086**	**-73**

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

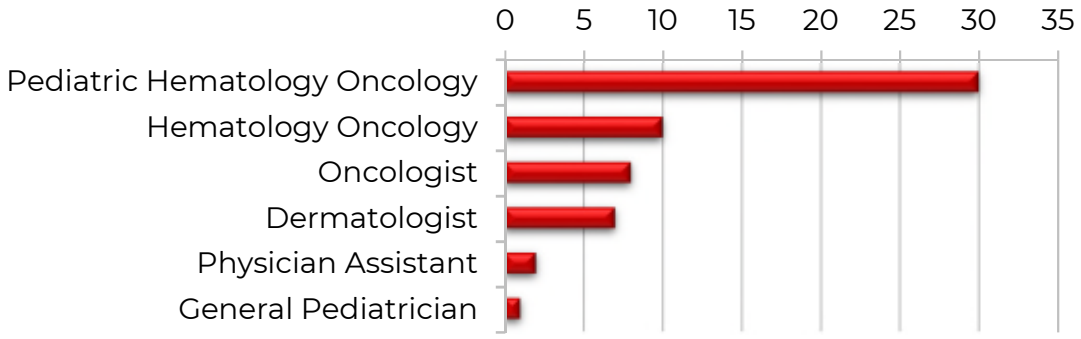
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2020	173	829	$9,258,902.82	$11,168.76	4.79
2021	187	845	$9,985,447.24	$11,817.10	4.52
% Change	**8.09%**	**1.93%**	**7.85%**	**5.80%**	**-5.64%**
Change	**14**	**16**	**$726,544.42**	**$648.34**	**-0.27**

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 Skin Cancer Medications: Pharmacy Claims

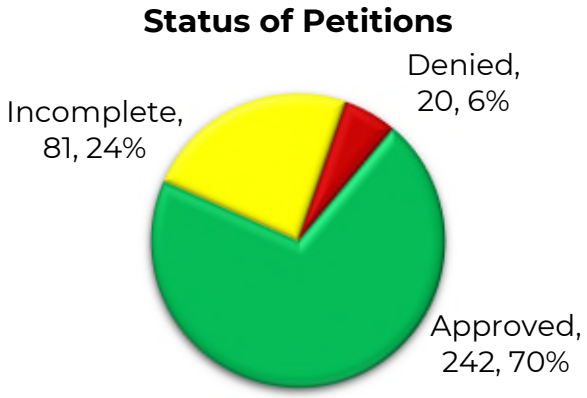
- Due to the limited number of members utilizing skin cancer medications during fiscal year 2021, detailed demographic information could not be provided.

Top Prescriber Specialties of Skin Cancer Medications by Number of Claims: Pharmacy Claims



Prior Authorization of Skin Cancer Medications

There were 343 prior authorization requests submitted for skin cancer medications during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.



Market News and Updates[17,18]

Anticipated Patent Expiration(s):

- Erivedge® (vismodegib): December 2028
- Odomzo® (sonidegib phosphate): September 2029
- Zelboraf® (vemurafenib): June 2032
- Braftovi® (encorafenib): August 2033
- Mekinist® (trametinib dimethyl sulfoxide): August 2033
- Tafinlar® (dabrafenib mesylate): August 2033
- Mektovi® (binimetinib): October 2033
- Cotellic® (cobimetinib fumarate): June 2036

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

- **April 2021:** The FDA approved Opdivo® (nivolumab) in combination with fluoropyrimidine- and platinum-containing chemotherapy for the treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction (GEJ) cancer, and esophageal adenocarcinoma.
- **May 2021:** The FDA granted accelerated approval for Keytruda® (pembrolizumab) in combination with trastuzumab, fluoropyrimidine-, and platinum-containing chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic human epidermal receptor 2 (HER2)-positive gastric or GEJ cancer.
- **May 2021:** The FDA approved Opdivo® (nivolumab) for the treatment of patients with completely resected esophageal or GEJ cancer with residual pathologic disease who have received neoadjuvant chemoradiotherapy.
- **August 2021:** The FDA approved Opdivo® (nivolumab) for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection. This is the first FDA approval for adjuvant treatment of patients with high-risk UC. The results supporting this approval also supported the conversion of

nivolumab's accelerated approval for advanced/metastatic UC to a regular approval.

- **October 2021:** The FDA approved Keytruda® (pembrolizumab) in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent or metastatic cervical cancer whose tumors express PD-L1 [combined positive score (CPS ≥1)].
- **October 2021:** The FDA approved Tecentriq® (atezolizumab) for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥1% of tumor cells.

Guideline Update(s): NCCN guidelines were updated to include the use of Opdivo® (nivolumab) as palliative therapy for patients with esophageal adenocarcinoma who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease in combination with oxaliplatin and fluorouracil or capecitabine.

Recommendations

The College of Pharmacy recommends updating the approval criteria for Keytruda® (pembrolizumab), Opdivo® (nivolumab), and Tecentriq® (atezolizumab) based on the recent FDA approvals (changes and new criteria noted in red):

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

1. Diagnosis of recurrent or metastatic cervical cancer; and
2. Tumor must express programmed death ligand 1 (PD-L1) [combined positive score (CPS) ≥1)]; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
   a. Disease progression on or after chemotherapy; or
   b. As first-line therapy in combination with chemotherapy, with or without bevacizumab.

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

1. Diagnosis of locally advanced, recurrent, or metastatic esophageal~~, gastric,~~ or GEJ carcinoma; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
~~3. Tumor must have positive programmed death ligand 1 (PD-L1) expression [combined positive score (CPS) ≥10]; and~~
4. For first-line therapy:

a. In combination with ~~either oxaliplatin or cisplatin plus a~~ platinum- and fluoropyrimidine-based chemotherapy; or

5. For second-line or greater therapy:
   a. Following disease progression after 1 or more prior lines of systemic therapy; and
   b. Tumor must be squamous cell histology; and
   c. As a single agent~~.~~; and
   d. Tumor expresses programmed death ligand 1 (PD-L1) [combined positive score (CPS ≥10).

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

1. Diagnosis of locally advanced, unresectable, or metastatic gastric or GEJ adenocarcinoma; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
3. For first-line therapy:
   a. Human epidermal receptor 2 (HER2)-positive disease; and
   b. In combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy; or
4. For second-line or greater therapy:
   a. As a single agent; and
   b. Tumor expresses programmed death ligand 1 (PD-L1) [combined positive score (CPS) ≥1]; and
   c. Following disease progression on or after 2 or more lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2-targeted therapy.

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

1. Diagnosis of urothelial carcinoma; and
   a. Member has undergone radical resection; and
   b. Disease is at high risk of recurrence; or
2. Diagnosis of metastatic or unresectable locally advanced disease; and
   a. Used as second-line or greater therapy; and
   b. Previous failure of a platinum-containing regimen; and
   c. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Esophageal ~~Squamous Cell Carcinoma (ESCC)~~ and Gastroesophageal Junction (GEJ) Cancer Diagnosis]:

~~1. Diagnosis of unresectable, advanced, recurrent or metastatic esophageal squamous cell carcinoma disease; and~~

~~a. Following prior fluoropyrimidine- and platinum-based chemotherapy; or~~

2. Diagnosis of esophageal or GEJ cancer; and
    a. Member has received preoperative chemoradiation; and
    b. Member underwent R0 (complete) resection and has residual disease; and
    c. As a single agent; or
3. Palliative therapy for members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease; and
    a. Human epidermal receptor 2 (HER2)-negative disease; and
        i. In first-line therapy; and
            1. In combination with oxaliplatin and fluorouracil or capecitabine; and
            2. Adenocarcinoma pathology; or
        ii. In second-line or greater therapy; and
            1. As a single agent; and
            2. Squamous cell pathology.

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

1. Diagnosis of advanced or metastatic disease; and
2. Used in combination with fluoropyrimidine- and platinum-containing chemotherapy.

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

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

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

b. For subsequent therapy for metastatic disease:
   i. As a single-agent; or

3. Diagnosis of stage 2 or 3A NSCLC; and
   a. Member has undergone resection and completed platinum-based chemotherapy; and
   b. PD-L1 expression of ≥1% of TC.

Utilization Details of Skin Cancer Medications: Fiscal Year 2021

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
DABRAFENIB PRODUCTS						
TAFINLAR CAP 75MG	19	3	$108,052.41	6.33	$5,686.97	25.97%
TAFINLAR CAP 50MG	8	2	$35,643.90	4	$4,455.49	8.57%
SUBTOTAL	**27**	**5**	**$143,696.31**	**5.4**	**$5,322.09**	**34.54%**
VISMODEGIB PRODUCTS						
ERIVEDGE CAP 150MG	12	4	$139,936.16	3	$11,661.35	33.63%
SUBTOTAL	**12**	**4**	**$139,936.16**	**3**	**$11,661.35**	**33.63%**
VEMURAFENIB PRODUCTS						
ZELBORAF TAB 240MG	10	3	$64,117.86	3.33	$6,411.79	15.41%
SUBTOTAL	**10**	**3**	**$64,117.86**	**3.33**	**$6,411.79**	**15.41%**
COBIMETINIB PRODUCTS						
COTELLIC TAB 20MG	6	2	$42,082.28	3	$7,013.71	10.11%
SUBTOTAL	**6**	**2**	**$42,082.28**	**3**	**$7,013.71**	**10.11%**
TRAMETINIB PRODUCTS						
MEKINIST TAB 0.5MG	2	2	$14,059.94	1	$7,029.97	3.38%
SUBTOTAL	**2**	**2**	**$14,059.94**	**1**	**$7,029.97**	**3.38%**
ENCORAFENIB PRODUCTS						
BRAFTOVI CAP 75MG	1	1	$12,196.35	1	$12,196.35	2.93%
SUBTOTAL	**1**	**1**	**$12,196.35**	**1**	**$12,196.35**	**2.93%**
TOTAL	**58**	**13***	**$416,088.90**	**4.46**	**$7,173.95**	**100.00 %**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
J9271 PEMBROLIZUMAB INJ	439	91	$5,279,444.12	$12,026.07	4.82
J9299 NIVOLUMAB INJ	256	47	$2,840,263.96	$11,094.78	5.45
J9022 ATEZOLIZUMAB INJ	108	35	$1,082,672.24	$10,024.74	3.09
J9228 IPILIMUMAB INJ	31	12	$676,335.72	$21,817.28	2.58
J9119 CEMIPLIMAB-RWLC INJ	9	1	$86,324.00	$9,591.56	9
J9023 AVELUMAB INJ	2	1	$20,407.20	$10,203.60	2
TOTAL	**845†**	**187***	**$9,985,447.24**	**$11,817.10**	**4.52**

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

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Appendix H

Fiscal Year 2021 Annual Review of Crohn's Disease (CD) and Ulcerative Colitis (UC) Medications

Oklahoma Health Care Authority
December 2021

Current Prior Authorization Criteria

Apriso® (Mesalamine Extended-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Asacol® HD (Mesalamine Delayed-Release Tablets) Approval Criteria:

1. An FDA approved indication for the treatment of moderately active ulcerative colitis (UC); and
2. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that do not require prior authorization must be provided; and
3. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 180 tablets per 30 days will apply.

Canasa® (Mesalamine Suppositories) Quantity Limit Approval Criteria:

1. A quantity limit of 30 suppositories per 30 days will apply.
2. The first 6 weeks of treatment do not require prior authorization.
3. After 6 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs a longer duration of treatment.

Colazal® (Balsalazide Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 270 capsules per 30 days will apply.
2. The first 12 weeks of treatment do not require prior authorization.
3. After 12 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs a longer duration of treatment.
4. An age restriction of 5 years and older will apply.

Delzicol® (Mesalamine Delayed-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 180 capsules per 30 days will apply.

Dipentum® (Olsalazine Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Giazo® (Balsalazide Tablets) Approval Criteria:

1. An FDA approved indication of mildly-to-moderately active ulcerative colitis (UC); and
2. Member must be 18 years of age or older; and
3. Member must be male (effectiveness of Giazo® was not demonstrated in female patients in clinical trials); and
4. A patient-specific, clinically significant reason why the member cannot use generic balsalazide 750mg capsules or other products available without prior authorization must be provided; and
5. Approvals will be for the duration of 8 weeks. After 8 weeks of treatment, the prescriber must document a patient-specific, clinically significant reason the member needs a longer duration of treatment.

Lialda® (Mesalamine Delayed-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 60 capsules per 30 days will apply.
2. For quantity limit requests for >2 capsules per day:
    a. An FDA approved indication for the induction of remission in members with active, mild-to-moderate ulcerative colitis (UC); and
    b. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that are indicated to induce remission that do not require prior authorization must be provided; and
    c. Approvals will be for the duration of 8 weeks in accordance with manufacturer recommended duration of therapy; and
    d. A maximum approval of 120 capsules per 30 days will apply.

Ortikos™ [Budesonide Extended-Release (ER) Capsule] Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. For the treatment of mild-to-moderate active Crohn's disease (CD) involving the ileum and/or the ascending colon, in members 8 years of age or older; or
    b. For the maintenance of clinical remission of mild-to-moderate CD involving the ileum and/or the ascending colon for up to 3 months duration in adult members; and
2. Member must have previous failure of Entocort® EC (budesonide controlled ileal-release enteric coated capsules) within the last 3 months at recommended dosing and a reason for trial failure with Entocort® EC must be provided; or
3. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use other oral corticosteroids, including Entocort® EC, that are available without prior authorization must be provided; and

4. Dosing regimen and duration of therapy must be in accordance with the Ortikos™ *Prescribing Information*; and
5. Approval length will be based on the manufacturer maximum recommended duration of therapy; and
6. A quantity limit of 30 capsules per 30 days will apply.

Pentasa® (Mesalamine 250mg Controlled-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 480 capsules per 30 days will apply.
2. The first 8 weeks of treatment do not require prior authorization.
3. After 8 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason the member needs a longer duration of treatment.

Pentasa® (Mesalamine 500mg Controlled-Release Capsules) Approval Criteria:

1. An FDA approved indication for the induction of remission or for the treatment of patients with mildly-to-moderately active ulcerative colitis (UC); and
2. A patient-specific, clinically significant reason the member cannot use Pentasa® 250mg controlled-release capsules or other available mesalamine products that do not require prior authorization must be provided; and
3. Approvals will be for the duration of 8 weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 240 capsules per 30 days will apply.

Rowasa® (Mesalamine Rectal Suspension Enema) Approval Criteria:

1. The first 3 weeks of treatment do not require prior authorization.
2. An FDA approved indication for the treatment of active, mild-to-moderate, distal ulcerative colitis (UC), proctosigmoiditis, or proctitis; and
3. A patient-specific, clinically significant reason the member cannot use mesalamine suppositories (Canasa®) which do not require prior authorization must be provided; and
4. Provider documentation that member is still having active symptoms after 3 weeks of treatment; and
5. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and
6. A quantity limit of 30 enemas (1,800mL) per 30 days will apply.

Uceris® (Budesonide Extended-Release Tablets) Approval Criteria:

1. An FDA approved indication of induction of remission in members with active, mild-to-moderate ulcerative colitis (UC); and

2. Previous failure of at least 2 of the following (or a contraindication to all preferred medications):
   a. Oral aminosalicylates; or
   b. Topical mesalamine; or
   c. Topical corticosteroids; and
3. A patient-specific, clinically significant reason why the member cannot use other oral corticosteroids available without prior authorization must be provided; and
4. Approvals will be for the duration of 8 weeks in accordance with manufacturer maximum recommended duration of therapy; and
5. A quantity limit of 30 tablets per 30 days will apply.

Uceris® (Budesonide Rectal Foam) Approval Criteria:

1. An FDA approved indication of induction of remission in members with active, mild-to-moderate, distal ulcerative colitis (UC) extending up to 40cm from the anal verge; and
2. A patient-specific, clinically significant reason why the member cannot use oral aminosalicylates, topical mesalamine, or other topical (rectally administered) corticosteroids available without prior authorization must be provided; and
3. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 133.6 grams per 42 days will apply.

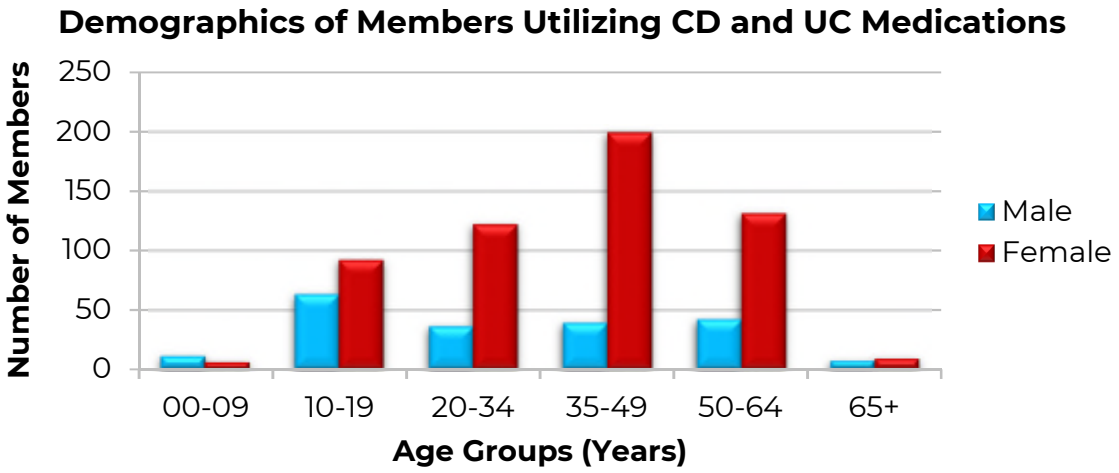
The following medications do not require prior authorization: Colazal® (balsalazide) capsules, hydrocortisone enemas, Apriso® (mesalamine) extended-release capsules, Canasa® (mesalamine) suppositories, Delzicol® (mesalamine) delayed-release (DR) capsules, Lialda® (mesalamine) DR capsules, Pentasa® (mesalamine) 250mg controlled-release capsules, Rowasa® (mesalamine) rectal suspension enemas, Dipentum® (olsalazine) capsules, sulfasalazine 500mg tablets, and sulfasalazine DR 500mg tablets.

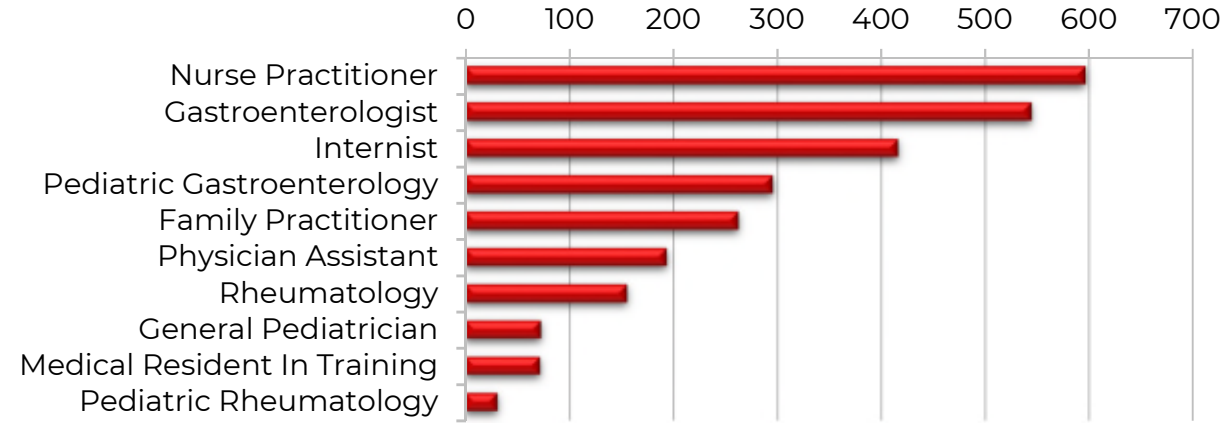
Utilization of CD and UC Medications: Fiscal Year 2021

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	605	2,215	$412,227.51	$186.11	$6.19	263,640	66,552
2021	757	2,734	$409,330.13	$149.72	$4.93	310,153	82,953
% Change	**25.10%**	**23.40%**	**-0.70%**	**-19.60%**	**-20.40%**	**17.60%**	**24.60%**
Change	**152**	**519**	**-$2,897.38**	**-$36.39**	**-$1.26**	**46,513**	**16,401**

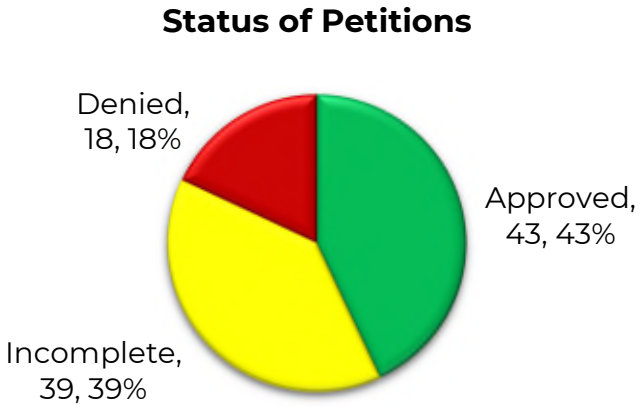
Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021





Prior Authorization of CD and UC Medications

There were 100 prior authorization requests submitted for CD and UC medications during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.



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

Anticipated Patent Expiration(s):

- Asacol® HD [mesalamine delayed-release (DR) tablets]: November 2021
- Colazal® (balsalazide capsules): February 2027
- Canasa® (mesalamine suppositories): June 2028
- Apriso® [mesalamine extended-release (ER) tablets]: May 2030
- Giazo® (balsalazide tablets): June 2031; discontinued
- Uceris® (budesonide ER tablets): September 2031
- Ortikos™ (budesonide ER capsules): September 2036

News:

- **Giazo® Product Discontinuation:** Giazo® (balsalazide 1.1g tablet) has been discontinued by the manufacturer. Giazo® was indicated for the treatment of mildly-to-moderately active UC in male patients 18 years of age and older. There are currently no generic formulations of Giazo®, but balsalazide continues to be available as Colazal® 750mg capsules, with both brand and generic capsule formulations available.

Guideline Update(s):

- **June 2021:** The American Gastroenterological Association (AGA) published updated guidelines for the management of moderate-to-severe luminal and perianal fistulizing CD. Historically, about 20% of patients with CD have been hospitalized each year for severe disease. More recent advances in treatment options and trends toward earlier diagnosis and treatment with biologic agents have resulted in a decrease in the percentage of CD patients requiring surgery each year.
  - Moderate-to-severe luminal CD is defined by the AGA as:
    - Crohn's Disease Activity Index (CDAI) score ≥220; or
    - Dependence on or refractory to corticosteroids; or
    - Severe endoscopic disease activity (large and/or deep ulcers).
  - Key recommendations from the AGA 2021 guidelines for patients with moderate-to-severe CD include:
    - The use of anti-TNFα agents and ustekinumab is recommended over no treatment (*strong recommendation*) and the use of vedolizumab is suggested over no treatment (*conditional recommendation*) for induction and maintenance of remission.
    - The use of natalizumab is suggested against for induction and maintenance of remission due to the potential for progressive multifocal leukoencephalopathy (PML) and the availability of other medications (*conditional recommendation*).
    - In biologic-naïve patients, the use of infliximab, adalimumab, or ustekinumab is recommended over certolizumab pegol

(*strong recommendation*) and the use of vedolizumab is suggested over certolizumab pegol (*conditional recommendation*) for induction of remission.
    - In biologic-naïve and immunomodulator-naïve patients, the use of infliximab or adalimumab in combination with thiopurines is suggested over infliximab or adalimumab monotherapy (*conditional recommendation*) for induction and maintenance of remission.
    - Early introduction with a biologic, with or without an immunomodulator, is suggested rather than delaying their use until after failure of 5-aminosalicylates (5-ASA) and/or corticosteroids (*conditional recommendation*).
    - The use of 5-ASA or sulfasalazine is recommended against over no treatment (*strong recommendation*) for induction or maintenance of remission.

Pipeline:

- **Filgotinib:** Gilead and Galapagos are currently conducting Phase 3 studies of filgotinib for the treatment of both UC and CD. Filgotinib is an oral selective Janus kinase 1 (JAK1) inhibitor. In June 2021, positive results of the Phase 3 SELECTION study in patients with moderately-to-severely active UC were published in *The Lancet*. Additionally, in October 2021 Galapagos announced the completion of patient enrollment in the Phase 3 DIVERSITY study in patients with moderately-to-severely active CD. Filgotinib is also being evaluated for the treatment of rheumatoid arthritis (RA).
- **Mirikizumab:** Lilly is conducting Phase 3 studies of mirikizumab for the treatment of both UC and CD. Mirikizumab is a humanized IgG4 monoclonal antibody that binds to the P19 subunit of IL-23. In March 2021, Lilly announced positive results from a Phase 3 12-week induction study in patients with moderate-to-severe UC. Additionally, in May 2021, Lilly announced positive results from a Phase 2 study in patients with moderately-to-severely active CD.

Recommendations

The College of Pharmacy recommends the following changes to the CD and UC prior authorization criteria (changes noted in red):

1. Removing the Giazo® prior authorization criteria based on product discontinuation; and
2. Removing the prior authorization on Pentasa® 500mg based on net costs; and
3. Updating the Pentasa® quantity limit approval criteria to include information for both strengths of Pentasa®.

~~**Giazo® (Balsalazide) Approval Criteria:**~~

~~1. An FDA approved indication of mildly-to-moderately active ulcerative colitis (UC); and~~
~~2. Member must be 18 years of age or older; and~~
~~3. Member must be male (effectiveness of Giazo® was not demonstrated in female patients in clinical trials); and~~
~~4. A patient-specific, clinically significant reason why the member cannot use generic balsalazide 750mg capsules or other products available without prior authorization must be provided; and~~
~~5. Approvals will be for the duration of 8 weeks. After 8 weeks of treatment the prescriber must document a patient-specific, clinically significant reason the member needs a longer duration of treatment.~~

Pentasa® (Mesalamine ~~250mg~~ Controlled-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 480 capsules per 30 days will apply for the 250mg strength and a quantity limit of 240 capsules per 30 days will apply for the 500mg strength; and
2. The first 8 weeks of treatment do not require prior authorization; and
3. After 8 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs a longer duration of treatment.

~~**Pentasa® (Mesalamine 500mg Controlled-Release Capsules) Approval Criteria:**~~

~~1. An FDA approved indication for the induction of remission or for the treatment of patients with mildly-to-moderately active ulcerative colitis (UC); and~~
~~2. A patient-specific, clinically significant reason the member cannot use Pentasa® 250mg controlled-release capsules or other available mesalamine products that do not require prior authorization must be provided; and~~
~~3. Approvals will be for the duration of 8 weeks in accordance with manufacturer recommended duration of therapy; and~~
~~4. A quantity limit of 240 capsules per 30 days will apply.~~

The following medications do not require prior authorization: Colazal® (balsalazide) capsules, hydrocortisone enemas, Apriso® (mesalamine) extended-release capsules, Canasa® (mesalamine) suppositories, Delzicol® (mesalamine) delayed-release (DR) capsules, Lialda® (mesalamine) DR capsules, Pentasa® (mesalamine) ~~250mg~~ controlled-release capsules, Rowasa® (mesalamine) rectal suspension enemas, Dipentum® (olsalazine) capsules, sulfasalazine 500mg tablets, and sulfasalazine DR 500mg tablets.

Utilization Details of CD and UC Medications: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SULFASALAZINE PRODUCTS						
SULFASALAZINE TAB 500MG	777	285	$19,672.81	$25.32	2.73	4.81%
SULFASALAZINE TAB 500MG DR	601	207	$17,466.90	$29.06	2.9	4.27%
SUBTOTAL	**1,378**	**492**	**$37,139.71**	**$26.95**	**2.8**	**9.07%**
MESALAMINE PRODUCTS						
MESALAMINE TAB 1.2GM	466	108	$143,589.79	$308.13	4.31	35.08%
MESALAMINE CAP 0.375GM	148	34	$40,611.97	$274.41	4.35	9.92%
MESALAMINE SUP 1,000MG	88	44	$12,078.02	$137.25	2	2.95%
PENTASA CAP 250MG CR	84	20	$45,282.90	$539.08	4.2	11.06%
PENTASA CAP 500MG CR	64	22	$56,308.12	$879.81	2.91	13.76%
MESALAMINE CAP 400MG DR	43	16	$11,803.48	$274.50	2.69	2.88%
MESALAMINE TAB 800MG DR	37	17	$19,234.15	$519.84	2.18	4.70%
MESALAMINE ENE 4GM	18	13	$3,486.06	$193.67	1.38	0.85%
APRISO CAP 0.375GM	12	3	$3,602.33	$300.19	4	0.88%
DELZICOL CAP 400MG	5	3	$1,501.03	$300.21	1.67	0.37%
SUBTOTAL	**965**	**280**	**$337,497.85**	**$349.74**	**3.45**	**82.45%**
BUDESONIDE PRODUCTS						
BUDESONIDE CAP 3MG DR	353	115	$29,356.32	$83.16	3.07	7.17%
BUDESONIDE CAP 3MG	6	3	$471.02	$78.50	2	0.12%
UCERIS AER 2MG/ACT	3	2	$1,348.56	$449.52	1.5	0.33%
BUDESONIDE TAB ER 9MG	1	1	$976.38	$976.38	1	0.24%
SUBTOTAL	**363**	**121**	**$32,152.28**	**$88.57**	**3**	**7.85%**
BALSALAZIDE PRODUCTS						
BALSALAZIDE CAP 750MG	21	7	$1,521.00	$72.43	3	0.37%
SUBTOTAL	**21**	**7**	**$1,521.00**	**$72.43**	**3**	**0.37%**
HYDROCORTISONE PRODUCTS						
HYDROCORTISONE ENE 100MG	7	7	$1,019.29	$145.61	1	0.25%
SUBTOTAL	**7**	**7**	**$1,019.29**	**$145.61**	**1**	**0.25%**
TOTAL	**2,734**	**757***	**$409,330.13**	**$149.72**	**3.61**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
ACT = actuation; AER = foam; CAP = capsule; CR = controlled-release; DR = delayed-release; ENE = enema; ER = extended-release; SUP = suppository; TAB = tablet
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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[2] Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology* 2021; 160(7):2496-2508.
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Appendix I

Fiscal Year 2021 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

Oklahoma Health Care Authority
December 2021

Current Prior Authorization Criteria

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

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

Bevyxxa® (Betrixaban) Approval Criteria:

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

Brilinta® (Ticagrelor) Approval Criteria:

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

Eliquis® (Apixaban) Approval Criteria:

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

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

Pradaxa® (Dabigatran) Approval Criteria:

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

Savaysa® (Edoxaban) Approval Criteria:

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

Xarelto® (Rivaroxaban) Approval Criteria:

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

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

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

Zontivity® (Vorapaxar) Approval Criteria:

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

Utilization of Anticoagulants and Platelet Aggregation Inhibitors: Fiscal Year 2021

Comparison of Fiscal Years: Anticoagulants

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	2,664	15,607	$4,866,209.62	$311.80	$9.57	761,642	508,545
2021	2,851	14,479	$5,838,797.02	$403.26	$10.56	844,881	553,006
% Change	**7.00%**	**-7.20%**	**20.00%**	**29.30%**	**10.30%**	**10.90%**	**8.70%**
Change	**187**	**-1,128**	**$972,587.40**	**$91.46**	**$0.99**	**83,239**	**44,461**

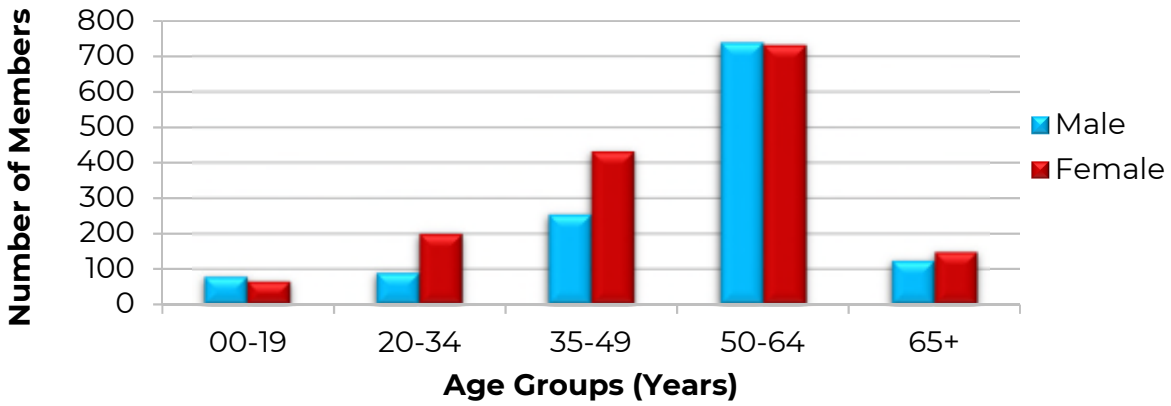
Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Comparison of Fiscal Years: Platelet Aggregation Inhibitors

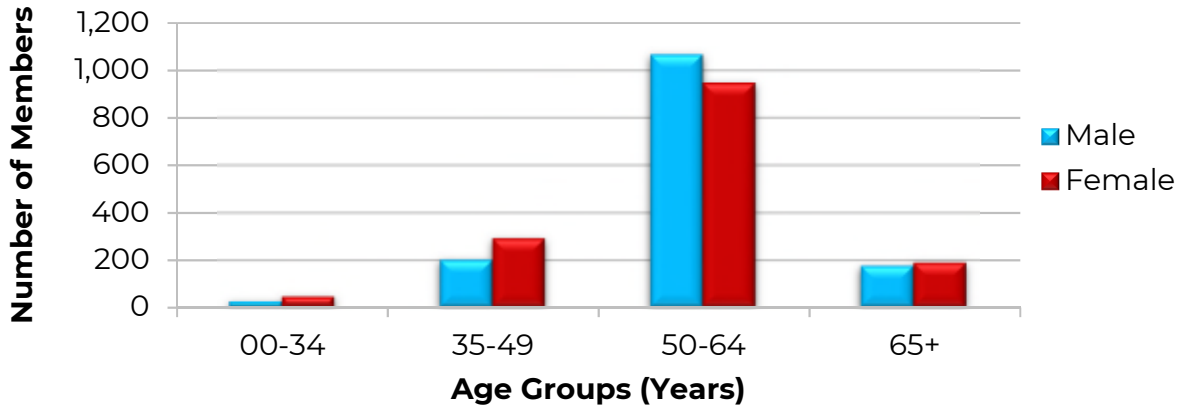
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	2,845	11,585	$724,900.39	$62.57	$1.28	615,180	567,434
2021	2,935	11,663	$791,831.66	$67.89	$1.33	643,931	594,646
% Change	**3.20%**	**0.70%**	**9.20%**	**8.50%**	**3.90%**	**4.70%**	**4.80%**
Change	**90**	**78**	**$66,931.27**	**$5.32**	**$0.05**	**28,751**	**27,212**

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

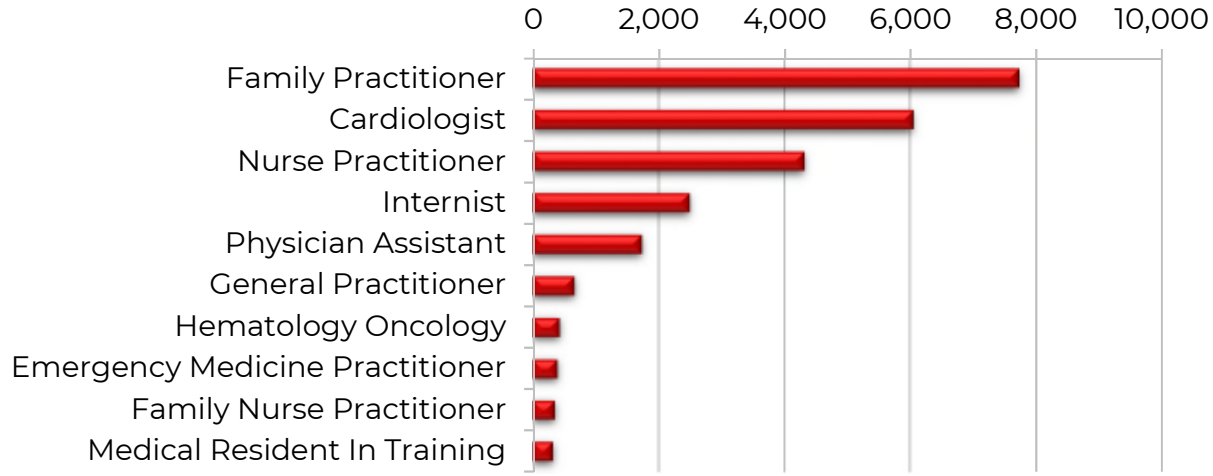
Demographics of Members Utilizing Anticoagulants



Demographics of Members Utilizing Platelet Aggregation Inhibitors



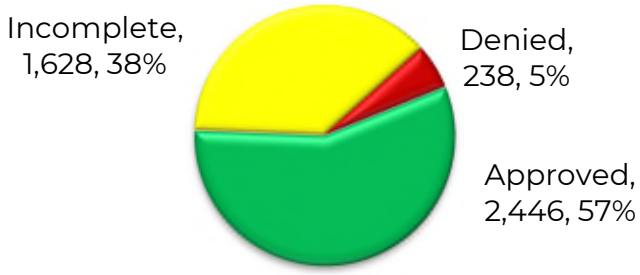
Top Prescriber Specialties of Anticoagulants and Platelet Aggregation Inhibitors by Number of Claims



Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

There were 4,312 prior authorization requests submitted for anticoagulants and platelet aggregation inhibitors 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]

Anticipated Patent Expiration(s):

- Zontivity® (vorapaxar): May 2024
- Xarelto® (rivaroxaban): November 2024
- Pradaxa® (dabigatran pellets): March 2026
- Savaysa® (edoxaban): March 2028
- Eliquis® (apixaban): February 2031
- Bevyxxa® (betrixaban): March 2031; discontinued by the manufacturer in April 2020 due to business reasons
- Pradaxa® (dabigatran capsules): July 2031
- Brilinta® (ticagrelor): January 2036

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

- **June 2021:** The FDA approved the first oral anticoagulant for pediatric patients, Pradaxa® (dabigatran) oral pellets, to treat children 3 months to 12 years of age with venous thromboembolism (VTE) following at least 5 days of treatment with a parenteral anticoagulant, and to reduce the risk of recurrence of VTE in pediatric patients 3 months to 12 years of age who have been previously treated for VTE. In addition, Pradaxa® was approved in capsule form to treat blood clots in patients 8 years of age and older with VTE following at least 5 days of treatment with a parenteral anticoagulant, and to prevent recurrent clots in patients 8 years and older who have previously been treated for VTE.

  Pradaxa® was originally FDA approved in 2010 to reduce the risk of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation. Additionally, Pradaxa® is indicated for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in adult patients following 5 to 10 days of treatment with a parenteral anticoagulant, to reduce the risk of recurrence of DVT and PE in adult patients who have been previously treated, and for the prophylaxis of DVT and PE in adult patients who have undergone hip replacement surgery.

  The approval of Pradaxa® for treatment of VTE in pediatric patients was based on DIVERSITY, an open-label, randomized, non-inferiority study in 267 pediatric patients from birth to 18 years of age. Patients were randomized according to either an age-appropriate formulation of Pradaxa® (doses adjusted for age and weight) after at least 5 days and no longer than 21 days of treatment with a parenteral anticoagulant, or to standard of care (SOC) comprised of low molecular weight heparins, vitamin K antagonists, or fondaparinux (Arixtra®). The primary composite endpoint was complete thrombus resolution, freedom from recurrent VTE, and freedom from mortality related to VTE. Of the 267 randomized patients, 81 patients (45.8%) in the Pradaxa® group and 38 patients (42.2%) in the SOC group met the criteria for the composite primary endpoint [difference in rate: -0.038; 95% confidence interval (CI): -0.161, 0.086]. Non-inferiority of Pradaxa® to SOC was met ($P<0.0001$), since the upper bound of the 95% CI was lower than the predefined non-inferiority margin of 20%.

  The approval of Pradaxa® for reduction in the risk of recurrence of VTE in pediatric patients was based on an open-label, single-arm safety study in 214 pediatric patients from birth to 18 years of age. Patients who required further anticoagulation due to the presence of a clinical risk factor after completing the initial treatment for confirmed VTE (for at least 3 months) or after completing the DIVERSITY study were

included in the study. The primary endpoints of the study included the recurrence of VTE, major and minor bleeding events, and mortality (overall and related to thrombotic or thromboembolic events) at 6 and 12 months. The overall probability of being free from recurrence of VTE during the on-treatment period was 0.990 (95% CI: 0.960, 0.997) at 3 months, 0.984 (95% CI: 0.950, 0.995) at 6 months, and 0.984 (95% CI: 0.950, 0.995) at 12 months. The probability of being free from bleeding events during the on-treatment period was 0.849 (95% CI: 0.792, 0.891) at 3 months, 0.785 (95% CI: 0.718, 0.838) at 6 months, and 0.723 (95% CI: 0.645, 0.787) at 12 months.

No on-treatment deaths occurred. Pradaxa® carries a *Boxed Warning* for an increased risk of thrombotic events due to premature discontinuation and spinal/epidural hematoma. Boehringer Ingelheim's launch plans for Pradaxa® oral pellets are pending, and the new pellet formulation will be available in the following strengths: 20mg, 30mg, 40mg, 50mg, 110mg, and 150mg per packet.

Pipeline:

- **Abelacimab:** Anthos Therapeutics announced the final results from the Phase 2 ANT-005 study with its novel investigational anticoagulant abelacimab. Abelacimab is a highly selective, fully human monoclonal antibody with novel dual activity against both Factor XI and its activated form, Factor XIa, achieving Factor XI suppression for up to 30 days following a single intravenous (IV) or subcutaneous (sub-Q) dose. Published in the August 2021 edition of the *New England Journal of Medicine* and simultaneously presented as a late breaker at the International Society of Thrombosis and Haemostasis (ISTH) 2021 Congress, the data showed that a single postoperative dose of abelacimab reduced the rate of VTE by approximately 80% compared to enoxaparin, following elective total knee arthroplasty, the gold standard setting for potential new anticoagulants to demonstrate efficacy. In this parallel group study, 412 participants were randomly assigned to 1 of 3 single postoperative IV doses of abelacimab (150mg, 75mg, or 30mg) in a blinded fashion or open-label SOC enoxaparin 40mg given sub-Q once daily for approximately 10 days after surgery. The primary composite efficacy outcome, which included DVT detected by venography of the operated leg and documented symptomatic VTE events, occurred in 4%, 5%, and 13% of patients in the 150mg, 75mg, and 30mg abelacimab groups, respectively, compared with 22% of patients in the enoxaparin group. The 75mg and 150mg abelacimab regimens were both statistically superior to enoxaparin ($P<0.001$) while the 30mg dose was non-inferior. Abelacimab was well tolerated with no safety signals and bleeding was insignificant in both study arms. A Phase 2

ANT-006 study (AZALEA-TIMI 71), investigating long-term once-monthly sub-Q administration of abelacimab for stroke prevention in patients with non-valvular atrial fibrillation, is ongoing and expected to provide insight on the bleeding risk with abelacimab compared to a commonly used direct oral anticoagulant (DOAC), rivaroxaban.

Recommendations

The College of Pharmacy recommends the following changes to the anticoagulants and platelet aggregation inhibitors prior authorization criteria (changes noted in red):

1. Removing the Bevyxxa® (betrixaban) prior authorization criteria based on product discontinuation; and
2. Updating the approval criteria for Pradaxa® (dabigatran) based on the new FDA approved indications and formulations.

~~**Bevyxxa® (Betrixaban) Approval Criteria:**~~

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

Pradaxa® (Dabigatran) Approval Criteria:

1. Pradaxa® (dabigatran) capsules require the following:
    a. An FDA approved indication of 1 of the following:
        i. Non-valvular atrial fibrillation; or
        ii. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with a parenteral anticoagulant for 5 to 10 days; or
        iii. To reduce the risk of recurrent DVT or PE in members who have been previously treated; or
        iv. For the prophylaxis of DVT and PE in members who have undergone hip replacement surgery; or
        v. For the treatment of venous thromboembolic events (VTE) in pediatric members 8 to 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days; or
        vi. To reduce the risk of recurrent VTE in pediatric members 8 to 18 years of age who have been previously treated.

2. Pradaxa® (dabigatran) oral pellets require the following:
    a. An FDA approved indication of 1 of the following:
        i. Treatment of VTE in members who have been treated with a parenteral anticoagulant for at least 5 days; or
        ii. To reduce the risk of recurrent VTE in members who have been previously treated; and
    b. Member must be 3 months of age or older; and
    c. Members older than 10 years of age require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used.

Utilization Details of Anticoagulants: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
APIXABAN PRODUCTS						
ELIQUIS TAB 5MG	6,294	1,352	$3,600,470.59	4.66	$572.05	61.66%
ELIQUIS TAB 2.5MG	668	170	$365,461.00	3.93	$547.10	6.26%
ELIQUIS ST P TAB 5MG	17	15	$9,742.94	1.13	$573.11	0.17%
SUBTOTAL	**6,979**	**1,537**	**$3,975,674.53**	**4.54**	**$569.66**	**68.09%**
WARFARIN PRODUCTS						
WARFARIN TAB 5MG	1,367	373	$16,672.34	3.66	$12.20	0.29%
WARFARIN TAB 1MG	610	156	$8,077.16	3.91	$13.24	0.14%
WARFARIN TAB 3MG	462	123	$5,966.30	3.76	$12.91	0.10%
WARFARIN TAB 4MG	452	112	$5,533.90	4.04	$12.24	0.09%
WARFARIN TAB 6MG	408	99	$5,295.65	4.12	$12.98	0.09%
WARFARIN TAB 7.5MG	333	98	$3,917.36	3.4	$11.76	0.07%
WARFARIN TAB 2MG	315	100	$4,070.70	3.15	$12.92	0.07%
WARFARIN TAB 10MG	276	92	$3,219.74	3	$11.67	0.06%
WARFARIN TAB 2.5MG	221	76	$2,952.33	2.91	$13.36	0.05%
JANTOVEN TAB 5MG	24	8	$377.27	3	$15.72	0.01%
JANTOVEN TAB 2MG	20	3	$301.27	6.67	$15.06	0.01%
JANTOVEN TAB 1MG	18	4	$288.59	4.5	$16.03	0.00%
JANTOVEN TAB 4MG	9	1	$83.85	9	$9.32	0.00%
JANTOVEN TAB 6MG	8	3	$115.14	2.67	$14.39	0.00%
JANTOVEN TAB 3MG	5	2	$66.92	2.5	$13.38	0.00%
JANTOVEN TAB 2.5MG	4	2	$61.70	2	$15.43	0.00%
JANTOVEN TAB 10MG	2	1	$30.62	2	$15.31	0.00%
JANTOVEN TAB 7.5MG	2	2	$29.62	1	$14.81	0.00%
SUBTOTAL	**4,536**	**1,255**	**$57,060.46**	**3.61**	**$12.58**	**0.98%**
RIVAROXABAN PRODUCTS						
XARELTO TAB 20MG	1,882	407	$1,213,303.03	4.62	$644.69	20.78%
XARELTO TAB 10MG	460	184	$248,165.07	2.5	$539.49	4.25%
XARELTO TAB 15MG	290	69	$151,053.83	4.2	$520.88	2.59%
XARELTO TAB 2.5MG	199	48	$114,827.89	4.15	$577.02	1.97%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
XARELTO STAR TAB	3	3	$2,397.07	1	$799.02	0.04%
SUBTOTAL	**2,834**	**711**	**$1,729,746.89**	**3.99**	**$610.36**	**29.63%**
DABIGATRAN PRODUCTS						
PRADAXA CAP 150MG	93	15	$59,277.40	6.2	$637.39	1.02%
PRADAXA CAP 75MG	19	3	$8,645.13	6.33	$455.01	0.15%
SUBTOTAL	**112**	**18**	**$67,922.53**	**6.22**	**$606.45**	**1.17%**
EDOXABAN PRODUCTS						
SAVAYSA TAB 30MG	11	1	$4,258.55	11	$387.14	0.07%
SAVAYSA TAB 60MG	7	1	$4,134.06	7	$590.58	0.07%
SUBTOTAL	**18**	**2**	**$8,392.61**	**9**	**$466.26**	**0.14%**
TOTAL	**14,479**	**2,851***	**$5,838,797.02**	**5.08**	**$403.26**	**100%**

CAP = capsule; STAR = starter; ST P = starter pack; TAB = tablet
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

Utilization Details of Platelet Aggregation Inhibitors: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	% COST
CLOPIDOGREL PRODUCTS						
CLOPIDOGREL TAB 75MG	9,214	2,545	$111,585.02	3.62	$12.11	14.09%
SUBTOTAL	**9,214**	**2,545**	**$111,585.02**	**3.62**	**$12.11**	**14.09%**
TICAGRELOR PRODUCTS						
BRILINTA TAB 90MG	1,474	313	$565,488.52	4.71	$383.64	71.42%
BRILINTA TAB 60MG	244	37	$94,904.46	6.59	$388.95	11.99%
SUBTOTAL	**1,718**	**350**	**$660,392.98**	**4.91**	**$384.40**	**83.41%**
PRASUGREL PRODUCTS						
PRASUGREL TAB 10MG	679	118	$14,424.01	5.75	$21.24	1.82%
PRASUGREL TAB 5MG	28	5	$612.43	5.6	$21.87	0.08%
SUBTOTAL	**707**	**123**	**$15,036.44**	**5.75**	**$21.27**	**1.90%**
VORAPAXAR PRODUCTS						
ZONTIVITY TAB 2.08MG	12	1	$3,906.92	12	$325.58	0.49%
SUBTOTAL	**12**	**1**	**$3,906.92**	**12**	**$325.58**	**0.49%**
ASPIRIN/DIPYRIDAMOLE PRODUCTS						
ASA/DIPYRIDA 25/200MG	12	1	$910.30	12	$75.86	0.11%
SUBTOTAL	**12**	**1**	**$910.30**	**12**	**$75.86**	**0.11%**
TOTAL	**11,663**	**2,935***	**$791,831.66**	**3.97**	**$67.89**	**100%**

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

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Appendix J

Fiscal Year 2021 Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Sertraline Capsules

Oklahoma Health Care Authority
December 2021

Current Prior Authorization Criteria

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			citalopram 20mg/10mL soln (UDC)
escitalopram (Lexapro®)			escitalopram 10mg/10mL soln (UDC)
fluoxetine caps (Prozac®)			fluoxetine 20mg/5mL soln (UDC)
fluvoxamine (Luvox®)			fluoxetine tabs
paroxetine (Paxil®)			fluoxetine DR (Prozac® Weekly™)
sertraline (Zoloft®)			fluvoxamine CR (Luvox CR®)
			paroxetine CR (Paxil CR®)
			paroxetine (Pexeva®)
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, XL®)	desvenlafaxine (Pristiq®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron SolTab®)		nefazodone (Serzone®)	duloxetine (Drizalma Sprinkle™)
trazodone 50mg, 100mg, & 150mg tabs (Desyrel®)		vilazodone (Viibryd®)	duloxetine 40mg (Irenka™)

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
venlafaxine (Effexor®, Effexor XR® caps)			trazodone 300mg tabs (Desyrel®)
			venlafaxine ER tabs (Effexor XR® tabs)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	isocarboxazid (Marplan®)
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	esketamine nasal spray (Spravato®)

*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).
caps = capsules; CR = controlled-release; DR = delayed-release; ER = extended-release; PA = prior authorization; soln = solution; tabs = tablets; UDC = unit dose cups

Antidepressants Tier-2 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial of 2 Tier-1 medications at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response. Tier-1 selection must include at least 1 medication from the SSRI category and 1 trial with duloxetine; or
2. Prior stabilization on the Tier-2 medication documented within the last 100 days. A past history of success on the Tier-2 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by Tier-1 medications or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressants Tier-3 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial with 2 Tier-1 medications (1 medication from the SSRI category and 1 trial with duloxetine) and a trial of a Tier-2 medication at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or

4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressants Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists; and
3. Tier structure rules still apply.
4. **Citalopram 20mg/10mL Solution, Escitalopram 10mg/10mL Solution, and Fluoxetine 20mg/5mL Solution Unit Dose Cup (UDC) Approval Criteria:**
    a. An FDA approved indication; and
    b. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.
5. **Desyrel® (Trazodone 300mg Tablet) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including 2 trazodone 150mg tablets or 3 trazodone 100mg tablets to achieve a 300mg dose must be provided.
6. **Drizalma Sprinkle™ (Duloxetine Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use generic duloxetine 20mg, 30mg, or 60mg capsules, which are available without prior authorization, in place of Drizalma Sprinkle™ must be provided; and
    c. A quantity limit of 30 capsules per 30 days will apply.
7. **Fluoxetine Tablet Approval Criteria:**
    a. Fluoxetine capsules are available without a prior authorization. The tablet formulation will require prior authorization and a patient-specific, clinically significant reason why the tablet formulation is required in place of the capsule formulation.
8. **Irenka™ (Duloxetine 40mg Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use 2 duloxetine 20mg capsules in place of Irenka™ 40mg capsules must be provided; and

c. A quantity limit of 30 capsules per 30 days will apply; and

9. **Marplan® (Isocarboxazid) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan® must be provided.

Approval Criteria for Atypical Antipsychotics as Adjunctive Treatment of Major Depressive Disorder (MDD):*

1. For Rexulti® (brexipiprazole) or Symbyax® (olanzapine/fluoxetine): a diagnosis of MDD requires current use of an antidepressant and requires previous trials with at least 2 other antidepressants from both categories (an SSRI and duloxetine) and a trial of aripiprazole tablets that did not yield adequate response; and
2. Tier structure rules still apply.

*Rexulti® (brexipiprazole) and Symbyax® (olanzapine/fluoxetine) are reviewed annually with the atypical antipsychotic medications. A full review of these medications can be found in the June 2021 Drug Utilization Review (DUR) Board packet.

Spravato® (Esketamine Nasal Spray) Approval Criteria [Depressive Symptoms in Adults with Major Depressive Disorder (MDD) with Acute Suicidal Ideation or Behavior Diagnosis]:

1. An FDA approved indication of depressive symptoms in adults with MDD with acute suicidal ideation or behavior; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
5. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
6. Member must not have any contraindications to therapy [i.e., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
7. Member must not have severe hepatic impairment (Child Pugh C); and
8. Prescriber must verify that female member is not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
9. Prescriber must verify female member is not breastfeeding; and
10. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and

11. Member must be enrolled in the Spravato® REMS program; and
12. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
13. For initial approval, the number of doses the member received while hospitalized, if applicable, and the dates of these doses must be provided to allow authorization of the appropriate quantity for the initial 4 weeks of treatment; and
14. For continued authorization, prescriber must verify member demonstrated an adequate response during the initial 4 weeks of treatment, verify member is using Spravato® in combination with an oral antidepressant, and provide patient-specific, clinically significant information to support continued use of Spravato®; and
15. A quantity limit of 8 kits per 28 days will apply.

Spravato® (Esketamine Nasal Spray) Approval Criteria [Treatment-Resistant Depression Diagnosis]:

1. An FDA approved indication of treatment-resistant depression in adults; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Member must have had an inadequate response to at least 2 different antidepressants from different classes at least 4 weeks in duration each and titrated to recommended dosing during the current depressive episode, unless contraindicated or clinically significant adverse effects; and
5. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
6. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
7. Member must not have any contraindications to therapy [e.g., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
8. Member must not have severe hepatic impairment (Child Pugh C); and
9. Prescriber must verify that female member is not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
10. Prescriber must verify female member is not breastfeeding; and
11. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
12. Member must be enrolled in the Spravato® REMS program; and

13. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
14. Initial approvals will be for the duration of the induction phase. For continued authorization, prescriber must verify member demonstrated an adequate response during the induction phase and verify member is using Spravato® in combination with an oral antidepressant; and
15. A quantity limit of 4 kits per 28 days will apply for maintenance dosing.

Utilization of Antidepressants: Fiscal Year 2021

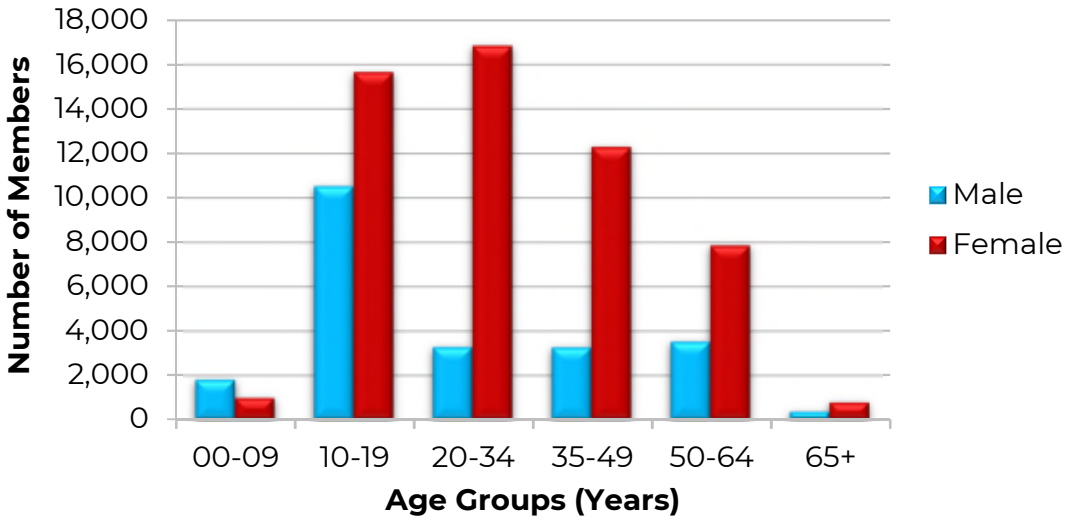
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	69,535	390,909	$6,436,379.88	$16.47	$0.46	16,275,487	14,052,524
2021	77,105	423,093	$7,188,149.44	$16.99	$0.45	18,330,769	15,852,763
% Change	**10.90%**	**8.20%**	**11.70%**	**3.20%**	**-2.20%**	**12.60%**	**12.80%**
Change	**7,570**	**32,184**	**$751,769.56**	**$0.52**	**-$0.01**	**2,055,282**	**1,800,239**

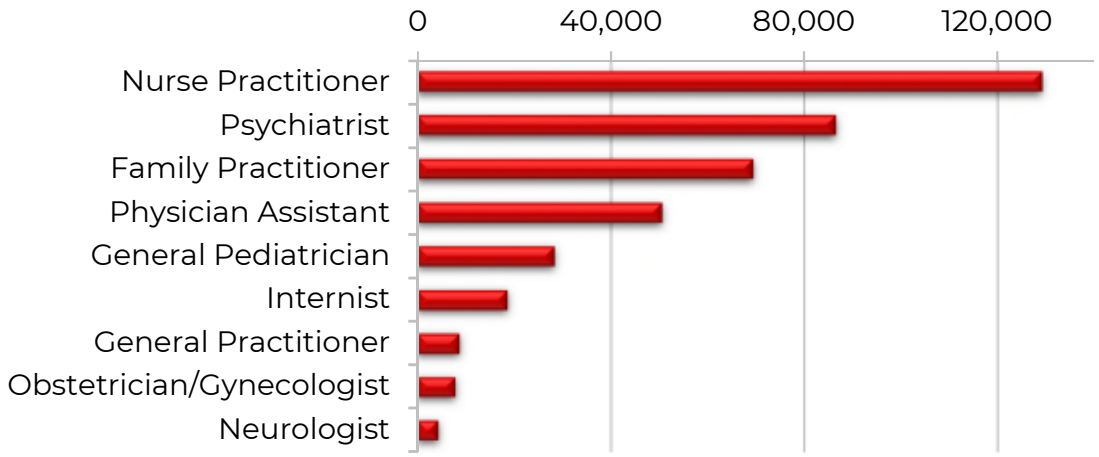
Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

- There were no SoonerCare paid medical claims for antidepressants in fiscal year 2021 (07/01/2020 to 06/30/2021).

Demographics of Members Utilizing Antidepressants



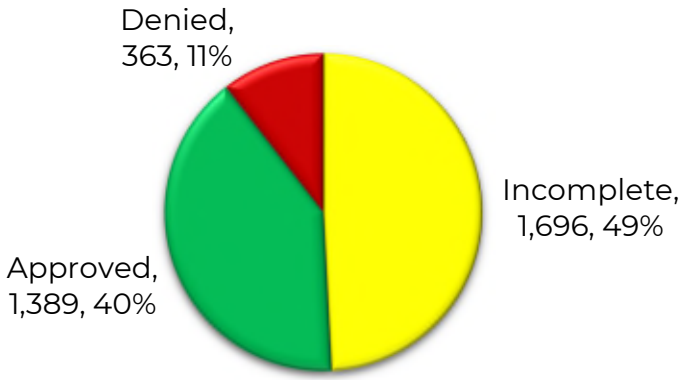
Top Prescriber Specialties of Antidepressants by Number of Claims



Prior Authorization of Antidepressants

There were 3,448 prior authorization requests submitted for antidepressants 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]

Anticipated Patent Expiration(s):

- Pexeva® (paroxetine tablets): May 2025
- Aplenzin® [bupropion extended-release (ER) tablets]: June 2026
- Forfivo XL® (bupropion ER tablets): June 2027
- Trintellix® (vortioxetine tablets): March 2032
- Fetzima® (levomilnacipran ER capsules): May 2032
- Spravato® (esketamine nasal spray): September 2035
- Drizalma Sprinkle™ [duloxetine delayed-release (DR) capsules]: April 2037

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

- **October 2021:** The FDA approved a capsule formulation of sertraline under a new drug application (NDA) for the indications of major depressive disorder (MDD) in adults and obsessive-compulsive disorder (OCD) in adults and pediatric patients 6 years of age and older. Sertraline capsules are supplied in 2 strengths, 150mg and 200mg. For comparison, Zoloft® (sertraline tablet) is indicated for MDD and OCD in adults and pediatric patients 6 years of age and older, as well as for panic disorder, post-traumatic stress disorder, social anxiety disorder, and premenstrual dysphoric disorder. Zoloft® oral tablets are available generically and are supplied in 3 strengths, 25mg, 50mg, and 100mg, as well as a 20mg/mL oral solution.

News:

- **October 2021:** *The Lancet Global Health* published results from the TOGETHER trial that indicates a potential therapeutic role of fluvoxamine for COVID-19. The efficacy of fluvoxamine versus placebo in preventing hospitalization defined as either retention in a COVID-19 emergency setting or transfer to a tertiary hospital due to COVID-19 was assessed. This placebo-controlled, randomized, adaptive platform trial done among high-risk symptomatic Brazilian adults confirmed positive for SARS-CoV-2 included eligible patients from 11 clinical sites in Brazil with a known risk factor for progression to severe disease. Patients were randomly assigned (1:1) to either fluvoxamine (100mg twice daily for 10 days) or placebo; 741 patients were allocated to fluvoxamine and 756 to placebo. The proportion of patients observed in a COVID-19 emergency setting for >6 hours or transferred to a tertiary hospital due to COVID-19 was lower for the fluvoxamine group compared with placebo [79 (11%) of 741 vs. 119 (16%) of 756]. There was 1 death in the fluvoxamine group and 12 in the placebo group for the per-protocol population. There were no significant differences in number of treatment emergent adverse events among patients in the fluvoxamine and placebo groups.
- **November 2021:** Pooled data from TRANSFORM-1 and TRANSFORM-2, both 4-week, randomized trials, demonstrated reductions on the 10-item Montgomery-Åsberg Depression Rating Scale (MADRS) total score from days 2 to 28 for patients receiving a newly initiated oral antidepressant plus esketamine versus those assigned to an oral antidepressant plus placebo. Statistically significant reductions in depression severity were seen with esketamine at days 15 and 28 both on MADRS and the 9-item Patient Health Questionnaire (PHQ-9), according to a poster presented at Psych Congress 2021. Additionally, in an analysis of SUSTAIN-1, a relapse prevention study of oral antidepressants with either esketamine or placebo in adults who

achieved stable remission following esketamine optimization, reported a numerically higher number of patients on maintenance esketamine achieved remission from treatment-resistant depression, defined as ≤4 on the PHQ-9 (57.3% vs 44.2% in the placebo group; P=0.083). A noted limitation was the trials included in these analyses were not designed to specifically address the endpoints in the current post hoc analysis. Additionally, the researchers noted TRANSFORM-1 and TRANSFORM-2 involved fixed dosing and flexible dosing, respectively, which may have contributed to some skewed data. The self-reported nature of the PHQ-9 was also cited as a limitation, due to its inherent variability and dependence on patient recall over time.

Pipeline:

- **AXS-05:** Axsome Therapeutics announced positive results from the open-label Phase 2 COMET-SI trial of AXS-05, a novel, oral, investigational N-methyl-D-aspartate (NMDA) receptor antagonist with multimodal activity, in patients with MDD who have suicidal ideation (SI). Patients treated with AXS-05 experienced rapid reduction of SI, rapid functional improvement, and rapid, substantial, and durable improvements in overall depressive symptoms. The COMET-SI trial evaluated 37 patients with SI, defined as a score ≥3 on the Suicidality Item of the MADRS (MADRS-SI), at baseline. Patients were treated with AXS-05 (45mg dextromethorphan/105mg bupropion modulated delivery tablet) twice daily for up to 12 months. A rapid reduction in SI was observed with AXS-05 treatment, as demonstrated by reductions in the MADRS-SI score of 67.6% by week 1, the earliest time point measured, 73.5% by week 2, and 82.4% by week 4. Resolution of SI with AXS-05 treatment was achieved by 60% of patients by week 1, 68.8% by week 2, and 77.8% of patients by week 4. Resolution was defined as a MADRS-SI score of 0 or 1 on a 0 to 6 scale.
- **Psilocybin:** Results of a randomized clinical trial of 24 patients with MDD who received immediate psilocybin-assisted therapy were published in *JAMA Psychiatry*. Psilocybin is a hallucinogenic chemical obtained from certain types of mushrooms and offers a novel approach of combined serotonergic and glutamatergic action for the treatment of depression. The results indicated that patients who received immediate psilocybin-assisted therapy compared with delayed treatment showed improvement in blinded clinician rated–assessed depression severity and in self-reported secondary outcomes through the 1-month follow-up. Psilocybin-assisted therapy was efficacious in producing large, rapid, and sustained antidepressant effects in patients with MDD. Two psilocybin sessions (session 1: 20mg/70kg; session 2: 30mg/70 kg) were given in the context of supportive psychotherapy (approximately 11 hours). Participants were randomized to begin

treatment immediately or after an 8 week delay. The primary outcome, depression severity, was assessed with the GRID-Hamilton Depression Rating Scale (GRID-HAMD) scores (0-7: no depression; 8-16: mild depression; 17-23: moderate depression; ≥24: severe depression) at baseline (score ≥17 required for enrollment) and at weeks 5 and 8 after enrollment for the delayed treatment group, which corresponded to weeks 1 and 4 after the intervention for the immediate treatment group. Of the randomized participants, 24 of 27 (89%) completed the intervention and the week 1 and week 4 post-session assessments. This population had a mean baseline GRID-HAMD score of 22.8. The mean GRID-HAMD scores at weeks 1 and 4 (8.0 and 8.5) in the immediate treatment group were statistically significantly lower than the scores at the comparable time points of weeks 5 and 8 (23.8 and 23.5) in the delayed treatment group.

- **Seltorexant (MIN-202):** Minerva Neurosciences, Inc. announced positive results from a Phase 2b clinical trial of seltorexant (MIN-202) as adjunctive therapy to antidepressants in adult patients with MDD who have responded inadequately to selective serotonin reuptake inhibitors (SSRIs) and/or serotonin-norepinephrine reuptake inhibitors (SNRIs). Seltorexant is a selective orexin-2 receptor antagonist. The orexin system in the brain is involved in the control of several key functions, including metabolism, stress response, and wakefulness. This system promotes wakefulness and is hypothesized to play a role in excessive wakefulness, which occurs in subsets of patients with mood disorders. In a dose finding study, the 20mg dose of seltorexant showed a statistically significant improvement in the MADRS score compared to placebo. The least squares mean (LS mean) difference from placebo of the change in MADRS total score at the end of week 6 was 3.1 for the 20mg dose of seltorexant (P=0.083). After 3 weeks of treatment, seltorexant at the 20mg dose also showed a statistically significant improvement over placebo, highlighting its ability to improve mood symptoms over a short period of time. In addition, a key secondary outcome measure, which was based on patient stratification according to baseline insomnia severity index (ISI), showed an even greater difference from placebo for the seltorexant 20mg arm in patients with clinically significant insomnia (ISI ≥15) with LS mean difference versus placebo of 4.9 on the MADRS total score. The 40mg dose, to which further enrollment was stopped following the interim analysis, showed an improvement in the MADRS total score versus placebo at the end of week 6 but did not reach statistical significance. Results for the 10mg dose were not interpretable due to the small sample size of patients assigned to this dose.

Sertraline Capsule Product Summary[3]

Therapeutic Class: SSRI

Indication(s):
- MDD in adults
- OCD in adults and pediatric patients 6 years of age and older

How Supplied: 150mg and 200mg oral capsules

Dosing and Administration:
- The recommended dosing is 150mg daily up to a maximum of 200mg daily.
- It is not recommended to use sertraline capsules for treatment initiation. Another sertraline product is recommended for initial dosage, dose titration, doses <150mg daily, and for gradual dose reduction if discontinuing sertraline.
- Sertraline capsules should be swallowed whole and should not be opened, crushed, or chewed.

Efficacy: The efficacy of sertraline capsules for the treatment of MDD in adult patients and OCD in adults and pediatric patients 6 years of age and older is based upon adequate and well-controlled studies of sertraline tablets (Zoloft®).

Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days
sertraline capsule 150mg & 200mg	**$4.90**	**$147.00***
sertraline tablet 100mg	$0.05	$3.00⁺
sertraline tablet 50mg	$0.04	$3.60ᐞ

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per month based once daily dosing of each strength.
⁺Cost per month based on (2) 100mg tablets once daily (200mg total daily dose).
ᐞCost per month based on (3) 50mg tablets once daily (150mg total daily dose).
Unit = capsule or tablet

Recommendations

The College of Pharmacy recommends the prior authorization of sertraline capsules and placement into the Special Prior Authorization (PA) Tier of the Antidepressants Product Based Prior Authorization (PBPA) category; the following additional criteria will also apply (updates and new criteria shown in red):

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			citalopram 20mg/10mL soln (UDC)
escitalopram (Lexapro®)			escitalopram 10mg/10mL soln (UDC)
fluoxetine caps (Prozac®)			fluoxetine 20mg/5mL soln (UDC)
fluvoxamine (Luvox®)			fluoxetine tabs
paroxetine (Paxil®)			fluoxetine DR (Prozac® Weekly™)
sertraline tabs (Zoloft®)			fluvoxamine CR (Luvox CR®)
			paroxetine CR (Paxil CR®)
			paroxetine (Pexeva®)
			sertraline 150mg & 200mg caps
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, XL®)	desvenlafaxine (Pristiq®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron SolTab®)		nefazodone (Serzone®)	duloxetine (Drizalma Sprinkle™)
trazodone 50mg, 100mg, & 150mg tabs (Desyrel®)		vilazodone (Viibryd®)	duloxetine 40mg (Irenka™)
venlafaxine (Effexor®, Effexor XR® caps)			trazodone 300mg tabs (Desyrel®)
			venlafaxine ER tabs (Effexor XR® tabs)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	isocarboxazid (Marplan®)
		selegiline (Emsam®)	

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	esketamine nasal spray (Spravato®)

*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).
caps = capsules; CR = controlled-release; DR = delayed-release; ER = extended-release; PA = prior authorization; soln = solution; tabs = tablets; UDC = unit dose cups

Antidepressants Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists; and
3. Tier structure rules still apply.
4. **Citalopram 20mg/10mL Solution, Escitalopram 10mg/10mL Solution, and Fluoxetine 20mg/5mL Solution Unit Dose Cup (UDC) Approval Criteria:**
    a. An FDA approved indication; and
    b. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.
5. **Desyrel® (Trazodone 300mg Tablet) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including 2 trazodone 150mg tablets or 3 trazodone 100mg tablets to achieve a 300mg dose must be provided.
6. **Drizalma Sprinkle™ (Duloxetine Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use generic duloxetine 20mg, 30mg, or 60mg capsules, which are available without prior authorization, in place of Drizalma Sprinkle™ must be provided; and
    c. A quantity limit of 30 capsules per 30 days will apply.
7. **Fluoxetine Tablet Approval Criteria:**
    a. Fluoxetine capsules are available without a prior authorization. The tablet formulation will require prior authorization and a patient-specific, clinically significant reason why the tablet formulation is required in place of the capsule formulation.

8. **Irenka™ (Duloxetine 40mg Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use 2 duloxetine 20mg capsules in place of Irenka™ 40mg capsules must be provided; and
    c. A quantity limit of 30 capsules per 30 days will apply.
9. **Marplan® (Isocarboxazid) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan® must be provided.
10. **Sertraline Capsule Approval Criteria:**
    a. An FDA approved indication of major depressive disorder (MDD) in adults or obsessive-compulsive disorder (OCD) in adults and pediatric patients 6 years of age and older; and
    b. Member must have initiated treatment with sertraline tablets for dose titration up to the 150mg or 200mg dose; and
    c. A patient-specific, clinically significant reason why the member cannot use sertraline tablets, which are available without a prior authorization, in place of the capsule formulation must be provided; and
    d. A quantity limit of 30 capsules per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the current Tier-2 and Tier-3 antidepressant approval criteria and approval criteria for atypical antipsychotics as adjunctive treatment of MDD to be consistent with the guideline recommendations (changes shown in red):

Antidepressants Tier-2 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial of 2 Tier-1 medications at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response. Tier-1 selection must include at least 1 medication from the SSRI category ~~and 1 trial with duloxetine~~; or
2. Prior stabilization on the Tier-2 medication documented within the last 100 days. A past history of success on the Tier-2 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by Tier-1 medications or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressants Tier-3 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial with 2 Tier-1 medications (Tier-1 selection must include at least 1 medication from the SSRI category ~~and 1 trial with duloxetine~~) and a trial of a Tier-2 medication at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Approval Criteria for Atypical Antipsychotics as Adjunctive Treatment of Major Depressive Disorder (MDD):

1. For Rexulti® (brexipiprazole) or Symbyax® (olanzapine/fluoxetine) a diagnosis of MDD requires current use of an antidepressant, and previous trials with at least 2 other antidepressants from both categories (an SSRI and a dual-acting medication ~~duloxetine~~) and a trial of aripiprazole tablets that did not yield adequate response; and
2. Tier structure rules still apply.

Utilization Details of Antidepressants: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-1 MEDICATIONS						
SERTRALINE PRODUCTS						
SERTRALINE TAB 50MG	33,155	11,721	$409,275.19	$12.34	2.83	5.69%
SERTRALINE TAB 100MG	31,268	7,547	$392,870.97	$12.56	4.14	5.47%
SERTRALINE TAB 25MG	18,448	6,984	$228,504.58	$12.39	2.64	3.18%
SERTRALINE 20MG/ML	800	216	$38,685.49	$48.36	3.7	0.54%
SUBTOTAL	**83,671**	**26,468**	**$1,069,336.23**	**$12.78**	**3.16**	**14.88%**
TRAZODONE PRODUCTS						
TRAZODONE TAB 50MG	32,402	9,534	$347,944.64	$10.74	3.4	4.84%
TRAZODONE TAB 100MG	23,936	6,038	$284,324.30	$11.88	3.96	3.96%
TRAZODONE TAB 150MG	13,414	3,060	$194,348.34	$14.49	4.38	2.70%
SUBTOTAL	**69,752**	**18,632**	**$826,617.28**	**$11.85**	**3.74**	**11.50%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 20MG	30,369	9,301	$328,591.56	$10.82	3.27	4.57%
FLUOXETINE CAP 10MG	15,996	5,919	$194,279.44	$12.15	2.7	2.70%
FLUOXETINE CAP 40MG	15,960	4,125	$194,876.96	$12.21	3.87	2.71%
FLUOXETINE 20MG/5ML	1,504	347	$100,616.19	$66.90	4.33	1.40%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PROZAC CAP 20MG	21	3	$31,947.69	$1,521.32	7	0.44%
PROZAC CAP 40MG	6	1	$5,854.92	$975.82	6	0.08%
SUBTOTAL	**63,856**	**19,696**	**$856,166.76**	**$13.41**	**3.24**	**11.90%**
ESCITALOPRAM PRODUCTS						
ESCITALOPRAM TAB 10MG	22,522	8,131	$284,982.87	$12.65	2.77	3.96%
ESCITALOPRAM TAB 20MG	19,649	4,908	$264,786.78	$13.48	4	3.68%
ESCITALOPRAM TAB 5MG	4,993	1,992	$63,950.36	$12.81	2.51	0.89%
ESCITALOPRAM 5MG/5ML	250	59	$33,344.68	$133.38	4.24	0.46%
LEXAPRO TAB 20MG	7	1	$2,601.56	$371.65	7	0.04%
ESCITALOPRAM 10MG/10ML	1	1	$301.21	$301.21	1	0.00%
SUBTOTAL	**47,422**	**15,092**	**$649,967.46**	**$13.71**	**3.14**	**9.03%**
BUPROPION PRODUCTS						
BUPROPION TAB 150MG XL	12,172	4,431	$213,593.53	$17.55	2.75	2.97%
BUPROPION TAB 300MG XL	9,072	2,415	$173,528.36	$19.13	3.76	2.41%
BUPROPION TAB 150MG SR	6,458	2,079	$103,589.54	$16.04	3.11	1.44%
BUPROPION TAB 100MG SR	2,872	1,014	$44,405.70	$15.46	2.83	0.62%
BUPROPION TAB 75MG	1,816	666	$30,978.22	$17.06	2.73	0.43%
BUPROPION TAB 200MG SR	1,511	378	$27,550.55	$18.23	4	0.38%
BUPROPION TAB 100MG	1,200	382	$22,820.26	$19.02	3.14	0.32%
WELLBUTRIN TAB XL 150MG	13	2	$56,402.44	$4,338.65	6.5	0.78%
SUBTOTAL	**35,114**	**11,367**	**$672,868.60**	**$19.16**	**3.09**	**9.35%**
DULOXETINE PRODUCTS						
DULOXETINE CAP 60MG	17,021	4,313	$263,665.89	$15.49	3.95	3.67%
DULOXETINE CAP 30MG	11,172	4,168	$163,388.01	$14.62	2.68	2.27%
DULOXETINE CAP 20MG	2,645	1,051	$38,996.22	$14.74	2.52	0.54%
CYMBALTA CAP 60MG	1	1	$253.37	$253.37	1	0.00%
SUBTOTAL	**30,839**	**9,533**	**$466,303.49**	**$15.12**	**3.23**	**6.48%**
CITALOPRAM PRODUCTS						
CITALOPRAM TAB 20MG	12,597	4,347	$124,570.33	$9.89	2.9	1.73%
CITALOPRAM TAB 40MG	7,747	2,102	$77,956.10	$10.06	3.69	1.08%
CITALOPRAM TAB 10MG	6,814	2,504	$69,955.18	$10.27	2.72	0.97%
CITALOPRAM 10MG/5ML	149	31	$6,079.03	$40.80	4.81	0.08%
SUBTOTAL	**27,307**	**8,984**	**$278,560.64**	**$10.20**	**3.04**	**3.86%**
MIRTAZAPINE PRODUCTS						
MIRTAZAPINE TAB 15MG	11,629	3,427	$142,063.40	$12.22	3.39	1.98%
MIRTAZAPINE TAB 30MG	6,263	1,585	$82,137.71	$13.11	3.95	1.14%
MIRTAZAPINE TAB 45MG	2,283	490	$33,471.98	$14.66	4.66	0.47%
MIRTAZAPINE TAB 7.5MG	1,751	556	$65,459.87	$37.38	3.15	0.91%
MIRTAZAPINE 15MG ODT	289	99	$8,499.62	$29.41	2.92	0.12%
MIRTAZAPINE 30MG ODT	155	53	$5,496.88	$35.46	2.92	0.08%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
MIRTAZAPINE 45MG ODT	127	36	$4,898.28	$38.57	3.53	0.07%
SUBTOTAL	**22,497**	**6,246**	**$342,027.74**	**$15.20**	**3.6**	**4.77%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE CAP 150MG ER	8,339	1,973	$143,173.96	$17.17	4.23	1.99%
VENLAFAXINE CAP 75MG ER	7,125	2,406	$104,276.32	$14.64	2.96	1.45%
VENLAFAXINE CAP 37.5MG ER	3,483	1,637	$51,153.72	$14.69	2.13	0.71%
VENLAFAXINE TAB 75MG	1,421	399	$21,100.00	$14.85	3.56	0.29%
VENLAFAXINE TAB 37.5MG	611	270	$8,029.47	$13.14	2.26	0.11%
VENLAFAXINE TAB 100MG	442	97	$6,843.09	$15.48	4.56	0.10%
VENLAFAXINE TAB 50MG	198	63	$3,375.93	$17.05	3.14	0.05%
VENLAFAXINE TAB 25MG	193	69	$2,992.60	$15.51	2.8	0.04%
EFFEXOR XR CAP 150MG	17	3	$15,480.30	$910.61	5.67	0.22%
EFFEXOR XR CAP 75MG	10	2	$21,962.11	$2,196.21	5	0.31%
SUBTOTAL	**21,839**	**6,919**	**$378,387.50**	**$17.33**	**3.16**	**5.27%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 20MG	4,304	1,547	$47,472.89	$11.03	2.78	0.66%
PAROXETINE TAB 40MG	3,126	810	$44,140.72	$14.12	3.86	0.61%
PAROXETINE TAB 10MG	2,204	903	$28,375.93	$12.87	2.44	0.39%
PAROXETINE TAB 30MG	1,363	402	$18,086.72	$13.27	3.39	0.25%
PAXIL 10MG/5ML	44	12	$10,895.72	$247.63	3.67	0.15%
SUBTOTAL	**11,041**	**3,674**	**$148,971.98**	**$13.49**	**3**	**2.06%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE TAB 100MG	1,291	231	$40,143.89	$31.10	5.59	0.56%
FLUVOXAMINE TAB 50MG	1,136	263	$27,469.42	$24.18	4.32	0.38%
FLUVOXAMINE TAB 25MG	455	137	$8,802.63	$19.35	3.32	0.12%
SUBTOTAL	**2,882**	**631**	**$76,415.94**	**$26.51**	**4.57**	**1.06%**
TIER-1 SUBTOTAL	**416,220**	**76,635***	**$5,765,623.62**	**$13.85**	**5.43**	**80.16%**
TIER-2 MEDICATIONS						
DESVENLAFAXINE PRODUCTS						
DESVENLAFAXINE TAB 50MG ER	1,484	397	$51,627.79	$34.79	3.74	0.72%
DESVENLAFAXINE TAB 100MG ER	1,271	263	$37,248.94	$29.31	4.83	0.52%
DESVENLAFAXINE TAB 25MG ER	236	110	$8,043.90	$34.08	2.15	0.11%
PRISTIQ TAB 100MG	4	1	$4,039.43	$1,009.86	4	0.06%
SUBTOTAL	**2,995**	**621***	**$100,960.06**	**$33.71**	**4.82**	**1.41%**
TIER-2 SUBTOTAL	**2,995**	**621***	**$100,960.06**	**$33.71**	**4.82**	**1.41%**
TIER-3 MEDICATIONS						
VORTIOXETINE PRODUCTS						
TRINTELLIX TAB 20MG	1,191	188	$468,150.13	$393.07	6.34	6.51%
TRINTELLIX TAB 10MG	476	143	$228,797.37	$480.67	3.33	3.18%
TRINTELLIX TAB 5MG	108	29	$41,613.66	$385.31	3.72	0.58%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SUBTOTAL	**1,775**	**360**	**$738,561.16**	**$416.09**	**4.93**	**10.27%**
VILAZODONE PRODUCTS						
VIIBRYD TAB 40MG	657	106	$186,658.23	$284.11	6.2	2.60%
VIIBRYD TAB 20MG	372	100	$109,047.33	$293.14	3.72	1.52%
VIIBRYD TAB 10MG	47	17	$13,257.66	$282.08	2.76	0.18%
SUBTOTAL	**1,076**	**223**	**$308,963.22**	**$287.14**	**4.83**	**4.30%**
LEVOMILNACIPRAN PRODUCTS						
FETZIMA CAP 120MG	33	3	$13,677.17	$414.46	11	0.19%
FETZIMA CAP 80MG	28	5	$11,616.75	$414.88	5.6	0.16%
FETZIMA CAP 40MG	2	2	$825.37	$412.69	1	0.01%
FETZIMA CAP TITRATION	1	1	$397.47	$397.47	1	0.01%
SUBTOTAL	**64**	**11**	**$26,516.76**	**$414.32**	**5.82**	**0.37%**
NEFAZODONE PRODUCTS						
NEFAZODONE TAB 100MG	13	5	$1,011.95	$77.84	2.6	0.01%
NEFAZODONE TAB 200MG	5	1	$362.78	$72.56	5	0.01%
NEFAZODONE TAB 150MG	5	2	$631.62	$126.32	2.5	0.01%
NEFAZODONE TAB 50MG	2	1	$108.12	$54.06	2	0.00%
SUBTOTAL	**25**	**9**	**$2,114.47**	**$84.58**	**2.78**	**0.03%**
DESVENLAFAXINE PRODUCTS						
DESVENLAFAXINE TAB 50MG ER	13	6	$3,289.88	$253.07	2.17	0.05%
DESVENLAFAXINE TAB 100MG ER	7	4	$1,685.60	$240.80	1.75	0.02%
SUBTOTAL	**20**	**10**	**$4,975.48**	**$248.77**	**2**	**0.07%**
SELEGILINE PRODUCTS						
EMSAM 12MG/24HOUR	1	1	$1,464.82	$1,464.82	1	0.02%
SUBTOTAL	**1**	**1**	**$1,464.82**	**$1,464.82**	**1**	**0.02%**
TIER-3 SUBTOTAL	**2,961**	**492***	**$1,082,595.91**	**$365.62**	**6.02**	**15.06%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
FLUOXETINE PRODUCTS						
FLUOXETINE TAB 10MG	330	91	$5,912.36	$17.92	3.63	0.08%
FLUOXETINE TAB 20MG	103	21	$2,726.88	$26.47	4.9	0.04%
FLUOXETINE CAP 90MG DR	32	5	$4,717.78	$147.43	6.4	0.07%
FLUOXETINE TAB 60MG	4	3	$137.53	$34.38	1.33	0.01%
SUBTOTAL	**469**	**120**	**$13,494.55**	**$28.77**	**3.91**	**0.2%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 25MG ER	101	14	$5,831.53	$57.74	7.21	0.08%
PAROXETINE TAB 37.5MG ER	93	11	$4,141.10	$44.53	8.45	0.06%
PAROXETINE TAB 12.5MG ER	23	3	$961.92	$41.82	7.67	0.01%
SUBTOTAL	**217**	**28**	**$10,934.55**	**$50.39**	**7.75**	**0.15%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE CAP 150MG ER	86	10	$20,752.20	$241.30	8.6	0.29%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FLUVOXAMINE CAP 100MG ER	33	5	$9,181.47	$278.23	6.6	0.13%
SUBTOTAL	**119**	**15**	**$29,933.67**	**$251.54**	**7.93**	**0.42%**
ESKETAMINE PRODUCTS						
SPRAVATO 84MG DOSE	51	10	$172,868.64	$3,389.58	5.1	2.40%
SPRAVATO 56MG DOSE	3	3	$1,950.43	$650.14	1	0.03%
SUBTOTAL	**54**	**13**	**$174,819.07**	**$3,237.39**	**4.15**	**2.43%**
DULOXETINE PRODUCTS						
DULOXETINE CAP 40MG	21	5	$3,019.57	$143.79	4.2	0.04%
DRIZALMA CAP 30MG DR	3	1	$560.73	$186.91	3	0.01%
DRIZALMA CAP 20MG DR	3	1	$1,136.39	$378.80	3	0.02%
DRIZALMA CAP 40MG DR	2	1	$373.82	$186.91	2	0.01%
SUBTOTAL	**29**	**8**	**$5,090.51**	**$175.53**	**3.63**	**0.08%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE TAB 225MG ER	23	4	$3,758.08	$163.39	5.75	0.05%
VENLAFAXINE TAB 150MG ER	2	1	$194.24	$97.12	2	0.01%
VENLAFAXINE TAB 75MG ER	1	1	$119.56	$119.56	1	0.01%
SUBTOTAL						**0.07%**
BUPROPION PRODUCTS						
BUPROPION TAB 450MG XL	2	1	$560.14	$280.07	2	0.01%
SUBTOTAL	**2**	**1**	**$560.14**	**$280.07**	**2**	**0.01%**
TRAZODONE PRODUCTS						
TRAZODONE TAB 300MG	1	1	$65.48	$65.48	1	0.01%
SUBTOTAL	**1**	**1**	**$65.48**	**$65.48**	**1**	**0.01%**
SPECIAL PA SUBTOTAL	**917**	**183***	**$238,969.85**	**$260.60**	**5.01**	**3.37%**
TOTAL	**423,093**	**77,105***	**$7,188,149.44**	**$16.99**	**5.49**	**100.00%**

CAP = capsule; DR = delayed-release; ER = extended-release; ODT = orally disintegrating tablet; SR = sustained-release; TAB = tablet; XL = extended-release
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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Appendix K

30-Day Notice to Prior Authorize Livmarli™ (Maralixibat)

Oklahoma Health Care Authority
December 2021

Introduction[1,2,3,4,5,6,7]

Alagille Syndrome (ALGS) is a rare, autosomal dominant genetic disorder that affects many organ systems throughout the body, including the liver, heart, skeleton, eyes, and kidneys. The severity and types of symptoms experienced in patients with ALGS can vary greatly; common symptoms of ALGS include cholestasis, jaundice, poor weight gain and growth, and severe pruritus. Additionally, in some patients, ALGS is associated with congenital heart defects; intellectual disability or developmental delay; impaired kidney function; bone defects; ocular abnormalities; pancreatic insufficiency; and distinctive facial features, including a broad, prominent forehead, deep-set eyes, and a small, pointed chin. Some patients with ALGS experience severe cholestasis leading to progressive liver damage, cirrhosis, and end-stage liver disease. The estimated incidence of ALGS is 1 in 30,000 to 1 in 45,000 births.

The diagnosis of ALGS is based on a combination of clinical manifestations, laboratory evaluation, liver ultrasonography, cholangiography, liver biopsy, histology, and genetic testing. ALGS is caused by mutations in 1 copy of the *JAG1* or *NOTCH2* genes. Mutations in *JAG1* are much more common and account for approximately 94% to 96% of patients with ALGS. Although these mutations can be inherited in an autosomal dominant manner, approximately 50% to 60% of patients with ALGS have a *de novo* mutation occurring in the individual patient which was not inherited from a parent. The *JAG1* and *NOTCH2* genes are important components of the Notch signaling pathway, which regulates gene transcription and is crucial for the proper development of multiple organ systems, including the liver, heart, kidneys, bones, and others. The *JAG1* gene encodes the Jagged-1 protein, a transmembrane ligand which can bind to 1 of 4 Notch receptors on adjacent cells. The *NOTCH2* gene encodes the Notch2 protein, which is 1 of the Notch receptors that can be bound by Jagged-1. Pathogenic mutations in these genes disrupt this important signaling pathway and lead to the heterogeneous symptoms observed in multiple organ systems in ALGS patients.

Patients with ALGS typically have a reduced number of bile ducts in the liver, known as bile duct paucity. Because of this, bile acids accumulate in the liver leading to chronic cholestasis and the potential for progressive liver damage

and cirrhosis. One of the most common and distressing symptoms of ALGS is severe pruritus. Although the specific cause of cholestatic pruritus is unknown, it may be related to the stimulation of nonmyelinated subepidermal free nerve endings due to increased serum bile acids. In ALGS patients, severe, intractable pruritus can have a major impact on quality of life, and may be an indication for liver transplantation even in the absence of liver failure.

Treatment options for patients with ALGS are limited mainly to supportive therapies. Fat-soluble vitamin (FSV; vitamins A, D, E, and K) supplementation can be given to ensure proper absorption and avoid FSV deficiency. Medications such as ursodeoxycholic acid (UDCA), cholestyramine, rifampin, sertraline, and naltrexone can be used off-label to help improve cholestasis and/or relieve pruritus. Despite the use of these medications, many patients with ALGS continue to experience intolerable pruritus, and surgical interventions such as biliary diversion procedures and liver transplantation are often necessary. It is estimated that approximately 15% to 31% of ALGS patients will require a liver transplant. However, in ALGS patients presenting with cholestasis, the need for liver transplantation may be as high as 75%. Liver transplantation can improve cholestasis and relieve the cholestatic pruritus in ALGS, but is associated with morbidity and mortality risks and the need for lifelong immunosuppression.

In September 2021, the U.S. Food and Drug Administration (FDA) approved Livmarli™ (maralixibat) as the first approved therapy for the treatment of cholestatic pruritus in patients with ALGS.

Livmarli™ (Maralixibat) Product Summary[8,9,10]

Indication(s): Livmarli™ (maralixibat) is an ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients with ALGS 1 year of age and older.

How Supplied: Grape-flavored oral solution containing 9.5mg/mL of maralixibat in a 30mL bottle

Dosing and Administration:

- The initiation dose is 190mcg/kg by mouth once daily for 7 days
- After 1 week, the dose should be increased to 380mcg/kg once daily, as tolerated
- Livmarli™ should be taken 30 minutes before the first meal of the day
- The maximum daily dose is 28.5mg (3mL)
- A calibrated measuring device (0.5mL, 1mL, or 3mL oral dosing dispenser) should be provided by the pharmacy to measure and deliver the prescribed dose accurately

- Livmarli™ should be stored between 20°C and 25°C (68°F and 77°F) and any remaining medication should be discarded 45 days after first opening the bottle

Mechanism of Action: Maralixibat is a reversible inhibitor of IBAT; inhibition of IBAT results in reduced reabsorption of bile acids from the terminal ileum. The complete mechanism by which maralixibat improves pruritus in patients with ALGS 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 ALGS may have abnormal liver tests at baseline. During the Phase 2 study of maralixibat, 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 maralixibat and should be monitored during treatment. Dose reductions or treatment interruptions should be considered if liver test abnormalities occur in the absence of other causes, and treatment discontinuation should be considered for persistent or recurrent liver test abnormalities. Maralixibat was not studied in ALGS patients with cirrhosis. Liver tests should be closely monitored and maralixibat should be permanently discontinued if the patient progresses to portal hypertension or experiences a hepatic decompensation event during treatment.
- Gastrointestinal (GI) Adverse Reactions: Diarrhea, abdominal pain, and vomiting were the most commonly reported adverse reactions in the clinical studies of maralixibat. Serious vomiting requiring hospitalization or intravenous (IV) fluid administration occurred in 3 patients (3%) treated with maralixibat. If diarrhea, abdominal pain, and/or vomiting occur and no other etiologies are found, dose reduction or interruption of maralixibat should be considered. Patients who experience diarrhea or vomiting during treatment with maralixibat should be monitored for dehydration, and dehydration should be promptly treated if it occurs. If a patient experiences persistent diarrhea, diarrhea with bloody stool, vomiting, dehydration requiring treatment, or fever, treatment with maralixibat should be interrupted. Treatment with maralixibat may be restarted at the initial 190mcg/kg/day dose when GI symptoms resolve. If GI symptoms recur upon re-challenge, discontinuation of maralixibat should be considered.
- FSV Deficiency: Patients with ALGS may have FSV deficiency at baseline, and treatment with maralixibat may affect absorption of FSVs.

In the Phase 2 study of maralixibat, treatment emergent FSV deficiency was reported in 3 patients (10%) during 48 weeks of treatment. Baseline serum FSV levels should be obtained before initiating treatment with maralixibat and during treatment. If FSV deficiency is diagnosed during treatment, FSV supplementation should be given. If FSV deficiency persists or worsens despite adequate FSV supplementation, discontinuation of maralixibat should be considered.

- Pregnancy: Maternal use at the recommended clinical dose of maralixibat is not expected to result in measurable fetal exposure because systemic absorption following oral administration is low. No developmental effects were observed in animal reproduction studies. Because maralixibat may inhibit the absorption of FSV, increased FSV supplementation may be needed during pregnancy.
- Lactation: Systemic absorption of maralixibat following oral administration is low, and breastfeeding is not expected to result in exposure of the infant to maralixibat at the recommended dose. There are no data available on the presence of maralixibat in human milk, the effects on the breastfed child, or the effects of the drug on milk production. Because maralixibat 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 maralixibat have been established in pediatric patients 1 to 15 years of age for the treatment of cholestatic pruritus in patients with ALGS. Use of maralixibat in this age range is supported by evidence from a Phase 2 study in 31 pediatric patients with ALGS, including 18 weeks of open-label treatment followed by a 4-week placebo-controlled randomized withdrawal period and a subsequent 26-week open-label treatment period. The safety and efficacy of maralixibat have not been established in patients younger than 1 year of age.
- Geriatric Use: The safety and efficacy of maralixibat for the treatment of pruritus in ALGS in adult patients, including those 65 years of age and older, have not been established.
- Hepatic Impairment: Patients with ALGS may have impaired hepatic function at baseline. The efficacy and safety of maralixibat in patients with clinically significant portal hypertension and in patients with decompensated cirrhosis have not been established.

Adverse Reactions: The most common adverse reactions (≥5%) in the clinical studies of maralixibat were diarrhea (55.8%), abdominal pain (53.5%), vomiting (40.7%), FSV deficiency (25.6%), elevated transaminases (18.6%), GI bleeding (10.4%), bone fractures (9.3%), and nausea (8.1%).

Efficacy: The efficacy of maralixibat for the treatment of cholestatic pruritus in ALGS was assessed in the Phase 2b ICONIC study, which was divided into 4 segments: (1) an 18-week open-label treatment period during which all patients received maralixibat 380mcg/kg once daily (following an initial titration); (2) a 4-week randomized, double-blind, placebo-controlled withdrawal period; (3) a 26-week open-label treatment period; and (4) an open-label long-term extension period. The study enrolled 31 pediatric patients with a genetically confirmed diagnosis of ALGS, all of whom had mutations in the *JAG1* gene. Two patients discontinued treatment during the initial 18-weeks of open-label treatment. The remaining 29 patients were randomized approximately 1:1 to receive maralixibat 380mcg/kg or placebo once daily during the 4-week drug withdrawal period. Following the 4-week drug-withdrawal period, all 29 patients again received open-label maralixibat 380mcg/kg once daily for an additional 26 weeks. The median age of patients in the study was 5 years (range: 1 to 15 years of age).

- Inclusion Criteria: All patients had a diagnosis of ALGS, evidence of cholestasis, and the presence of significant pruritus at baseline (average caregiver-reported observed scratching score >2 on a scale from 0 to 4, with higher scores indicating worse itching). At study entry, 90.3% of patients were receiving ≥1 additional medication(s) for the treatment of pruritus. Pre-existing anti-pruritic medications were allowed to be continued throughout the study at stable dosing (with the exception of bile-acid binding resins). The included patients had a history of previous treatment for pruritus utilizing UDCA (81% of patients), rifampin (74% of patients), naltrexone (3% of patients), and sertraline (3% of patients).
- Exclusion Criteria: Patients were excluded if they had previous surgical interruption of the enterohepatic circulation, previous liver transplantation, hepatic decompensation events, or other concomitant liver disease. Additionally, the use of bile acid-binding resins was prohibited during the study.
- Pruritus Endpoint: Pruritus symptoms were assessed by a caregiver twice daily (once in the morning and once in the evening) on a 5-point scale ranging from 0 (no scratching) to 4 (very severe scratching). The main efficacy endpoint for pruritus was the change in the weekly average of the worst daily pruritus score from week 18 (at the end of the open-label treatment period) to week 22 (at the end of the 4-week randomized withdrawal period).

- Results: At baseline (pre-treatment), the average of the worst daily pruritus score was 3.1. At week 18, at the end of the open-label treatment period, the average of the worst daily pruritus score had decreased to 1.4. At week 22, following the 4-week randomized, placebo-controlled withdrawal period, the average of the worst daily pruritus score was 1.6 in the maralixibat group and 3.0 in the placebo group [mean difference: -1.4; 95% confidence interval (CI): -2.1, -0.8]. The difference between the maralixibat group and the placebo group was statistically significant and demonstrated worsening pruritus symptoms in patients who received placebo compared to patients who continued to receive treatment with maralixibat during the 4-week withdrawal period.

Cost: The Wholesale Acquisition Cost (WAC) of Livmarli™ is $1,550 per milliliter (mL), resulting in a cost of $46,500 per 30mL bottle. For a member weighing 17kg, the estimated cost of Livmarli™ is $28,752.50 for the first 30 days of treatment based on the recommended dosing of 190mcg/kg once daily for the first 7 days, followed by 380mcg/kg once daily thereafter. For subsequent treatment, the estimated cost of Livmarli™ for a member weighing 17kg is $32,550 per 30 days or $390,600 per year.

Recommendations

The College of Pharmacy recommends the prior authorization of Livmarli™ (maralixibat) with the following criteria:

Livmarli™ (Maralixibat) Approval Criteria:

1. An FDA approved indication for the treatment of cholestatic pruritus in members with Alagille Syndrome (ALGS); and
    a. Diagnosis must be confirmed by genetic testing identifying mutations in the *JAG1* or *NOTCH2* genes; and
2. Member must be 1 year of age or older; and
3. Livmarli™ must be prescribed by a gastroenterologist, hepatologist, geneticist, or other specialist with expertise in the treatment of ALGS (or an advanced care practitioner with a supervising physician who is a gastroenterologist, hepatologist, geneticist, or other specialist with expertise in the treatment of ALGS); and
4. Prescriber must verify member has a history of significant pruritus that is unresponsive to treatment with at least 3 of the following, unless contraindicated:
    a. Ursodeoxycholic acid (UDCA); or
    b. Cholestyramine; or
    c. Rifampin; or
    d. Sertraline; or
    e. Naltrexone; and

5. Member must have evidence of cholestasis demonstrated by ≥1 of the following:
    a. Total serum bile acid >3x upper limit of normal (ULN) for age; or
    b. Conjugated bilirubin >1mg/dL; or
    c. Fat soluble vitamin deficiency otherwise unexplainable; or
    d. Gamma-glutamyl transferase (GGT) >3x ULN for age; or
    e. Intractable pruritus explainable only by liver disease; and
6. Members with a history of liver transplantation will not generally be approved for Livmarli™;
7. Prescriber must verify surgical intervention (e.g., biliary diversion, liver transplantation) is not currently clinically appropriate for the member; and
8. 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 Livmarli™; and
9. Prescriber must verify the member and/or member's caregiver has been counseled on appropriate storage, dosing, and administration of Livmarli™, including the use of a calibrated oral dosing dispenser for accurate measurement; 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 a duration of 3 months. After 3 months of treatment, further approval may be granted for a duration of 1 year if the prescriber documents the member is responding well to treatment and surgical intervention is still not clinically appropriate.

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Appendix L

30-Day Notice to Prior Authorize Byooviz™ (Ranibizumab-nuna Intravitreal Injection) and Susvimo™ (Ranibizumab Intravitreal Implant)

Oklahoma Health Care Authority
December 2021

Introduction[1,2]

Age-related macular degeneration (AMD) is the leading cause of adult blindness in industrialized countries. AMD is a degenerative disease of the central portion of the retina which results primarily in loss of central vision. Central vision is required for activities such as driving, reading, watching television, and performing activities of daily living. AMD is classified as dry (atrophic) or wet (neovascular or exudative). Wet AMD is characterized by growth of abnormal vessels into the subretinal space. These abnormal blood vessels leak, leading to collections of subretinal fluid and/or blood beneath the retina. Wet AMD is found in only 10-15% of patients with AMD; however, wet AMD accounts for ≥80% of cases with severe visual loss or legal blindness. In contrast to dry AMD, in which vision loss is slow and gradual, wet AMD is characterized by rapid distortion and loss of central vision over a period of days to weeks. Effective therapies for wet AMD include intravitreous injection of a vascular endothelial growth factor (VEGF) inhibitor, photodynamic therapy (PDT), and supplementation with zinc and antioxidant vitamins.

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

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

- **September 2021:** The FDA approved Byooviz™ (ranibizumab-nuna intravitreal injection), a biosimilar to Lucentis® (ranibizumab intravitreal injection) for the treatment of wet AMD, macular edema following retinal vein occlusion (RVO), and myopic choroidal neovascularization (mCNV). Ranibizumab is an anti-VEGF therapy that prevents vision loss in patients with retinal vascular disorders which can cause irreversible blindness or visual impairments in adults. Byooviz™ is the first ophthalmology biosimilar approved in the United States. The FDA approval was based on analytical, non-clinical, and clinical data from a phase 3 study evaluating Byooviz™ in wet AMD patients. The study compared the efficacy, safety, pharmacokinetics, and immunogenicity of Byooviz™ with the reference drug, Lucentis®, over 48 weeks of treatment. Data on all key endpoints from the study of Byooviz™ were comparable to Lucentis®. An agreement is in place to allow the start of commercialization of Byooviz™ in the United States in June 2022.

- **October 2021:** The FDA approved Susvimo™ (ranibizumab 100mg/mL intravitreal implant) for intravitreal use via ocular implant for the treatment of patients with wet AMD who have previously responded to at least 2 anti-VEGF injections. Susvimo™, previously called Port Delivery System with ranibizumab, is the first and only FDA-approved treatment for wet AMD that offers as few as 2 treatments per year. Susvimo™ delivers ranibizumab continuously, offering patients living with wet AMD a more convenient alternative to anti-VEGF intravitreal injections needed as often as once a month. The implant is surgically inserted into the eye during a 1-time, outpatient procedure and refilled every 6 months in an office-based setting under aseptic conditions. If necessary, supplemental intravitreal ranibizumab injections can be administered to the affected eye while the Susvimo™ implant is in place.

Susvimo™ (Ranibizumab Intravitreal Implant) Product Summary[7,8,9,10,11]

Indication(s): Susvimo™ (ranibizumab intravitreal implant) is indicated for the treatment of patients with neovascular (wet) AMD who have previously responded to ≥2 intravitreal injections of a VEGF inhibitor.

Boxed Warning: Endophthalmitis

- The Susvimo™ implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab. In clinical trials, 2% of patients receiving an implant experienced an episode of endophthalmitis.

How Supplied: 100mg/mL solution in a single-dose vial

Dosing and Administration:

- Susvimo™ is for intravitreal use via the Susvimo™ implant.
- The recommended dose of Susvimo™ is 2mg (0.02mL of 100mg/mL solution) continuously delivered via the Susvimo™ implant with refills every 24 weeks (approximately 6 months).
- Supplemental treatment with 0.5mg intravitreal ranibizumab injections may be administered in the affected eye if clinically necessary.
- The initial implantation, refill-exchange, and implant removal (if necessary) should be performed under strict aseptic conditions.

Mechanism of Action:

- Ranibizumab binds to the receptor binding site of multiple biologically active forms of VEGF-A, including VEGF110. VEGF-A has been shown to cause neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular AMD. The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on

the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.

Contraindication(s):

- Ocular or periocular infections
- Active intraocular inflammation
- Hypersensitivity to ranibizumab products or any of the excipients in Susvimo™

Adverse Reactions: The most common adverse reactions were conjunctival hemorrhage (72%), conjunctival hyperemia (26%), iritis (23%), and eye pain (10%).

Efficacy: The clinical efficacy and safety of Susvimo™ were assessed in a randomized, visual assessor-masked, active treatment-controlled study in patients with wet AMD. A total of 415 patients (248 in the Susvimo™ arm and 167 in the intravitreal ranibizumab arm) were enrolled and treated in this study. Inclusion criteria required that patients were diagnosed with wet AMD within the 9 months prior to screening and received ≥3 doses of anti-VEGF intravitreal agents in the study eye within the last 6 months prior to screening. Each patient was required to have demonstrated a response to an anti-VEGF intravitreal agent prior to randomization. Patients were randomized in a 3:2 ratio to receive continuous delivery of Susvimo™ via the Susvimo™ implant every 24 weeks or 0.5mg intravitreal ranibizumab injections every 4 weeks. For patients randomized to the Susvimo™ arm, supplemental treatment with 0.5mg intravitreal ranibizumab injections was available at weeks 16, 20, 40, 44, 64, 68, 88, and 92, if needed. In the first 24 weeks, 1.6% of patients assessed for supplemental treatment received 1 or more supplemental treatment(s) and in the following 24 weeks, 5.4% of patients assessed for supplemental treatment received 1 or more supplemental treatment(s). The primary efficacy endpoint of change from baseline in distance Best Corrected Visual Acuity (BCVA) score, as assessed using the Early Treatment Diabetic Retinopathy Study Visual Acuity Chart at a starting distance of 4 meters, averaged over week 36 and week 40 demonstrated that Susvimo™ was equivalent to intravitreal ranibizumab injections administered every 4 weeks.

Cost Comparison

Product	Cost Per Dose	Cost Per Year
Susvimo™ (ranibizumab implant) 10mg/0.1mL*	**$16,000 per 0.2mL**	**$32,000.00**
Lucentis® (ranibizumab injection) 0.5mg/0.5mL±	$1,950 per 0.05mL	$23,400.00
Eylea® (aflibercept injection) 2mg/0.05mL+	$1,850 per 0.05mL	$14,800.00
Beovu® (brolucizumab-dbll injection) 6mg/0.05mL≠	$1,850 per 0.05mL	$14,800.00

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).
*Susvimo™ cost is based on 2mg (0.02mL) via implant with refills every 6 months and does not include the surgical costs for implantation.
±Lucentis® cost is based on 0.5mg once monthly.
+Eylea® cost is based on 2mg every 4 weeks for the first 3 months, followed by 2mg every 8 weeks.
≠Beovu® cost is based on 6mg monthly for 3 doses, followed by 6mg every 8 weeks.

Recommendations

The College of Pharmacy recommends the prior authorization of Byooviz™ (ranibizumab-nuna intravitreal injection) and Susvimo™ (ranibizumab intravitreal implant) with the following criteria:

Byooviz™ (Ranibizumab-nuna Intravitreal Injection) Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Neovascular (wet) age-related macular degeneration (AMD); or
    b. Macular edema following retinal vein occlusion (RVO); or
    c. Myopic choroidal neovascularization (mCNV); and
2. A patient-specific, clinically significant reason why the member cannot use Lucentis® (ranibizumab intravitreal injection) 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.

Susvimo™ (Ranibizumab Intravitreal Implant) Approval Criteria:

1. An FDA approved indication for the treatment of adults with neovascular (wet) age-related macular degeneration (AMD); and
2. Member must have previously responded to ≥2 intravitreal injections of a vascular endothelial growth factor (VEGF) inhibitor; and
3. Member must not have ocular or periocular infections or active intraocular inflammation; and
4. Susvimo™ must be prescribed and administered by an ophthalmologist or a physician experienced in vitreoretinal surgery; and
5. Prescriber must verify the member will be monitored for endophthalmitis, rhegmatogenous retinal detachment, implant

dislocation, vitreous hemorrhage, conjunctival erosion, conjunctival retraction, and conjunctival blebs; and

6. A patient-specific, clinically significant reason why the member cannot use Lucentis® (ranibizumab intravitreal injection) or other VEGF inhibitor injection products (appropriate to disease state) must be provided; and
7. Susvimo™ will have a quantity limit of 0.2mL every 180 days.

Utilization Details of Ophthalmic VEGF Inhibitor Medications: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	% COST
MEDICAL CLAIMS					
AFLIBERCEPT INJ (J0178)	191	62*	$356,322.83	$1,865.56	98.57%
RANIBIZUMAB INJ (J2778)	5	4*	$3,305.44	$661.09	0.91%
BROLUCIZUMAB-DBLL INJ (J0179)	1	1*	$1,889.70	$1,899.70	0.52%
TOTAL	**197⁺**	**67***	**$361,517.97**	**$1,835.12**	**100.00%**

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

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[10] Eylea® (aflibercept injection) Prescribing Information. Regeneron Pharmaceuticals, Inc. Available online at: https://www.regeneron.com/downloads/eylea_fpi.pdf. Last updated 06/2021. Last accessed 11/21/2021.

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Appendix M

Fiscal Year 2021 Annual Review of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon) and 30-Day Notice to Prior Authorize Empaveli™ (Pegcetacoplan)

Oklahoma Health Care Authority
December 2021

Current Prior Authorization Criteria

Enspryng™ (Satralizumab-mwge) Approval Criteria:

1. An FDA approved indication of neuromyelitis optica spectrum disorder (NMOSD) in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have experienced at least 1 acute NMOSD attack in the prior 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤6.5; and
5. Prescriber must verify hepatitis B virus (HBV) and tuberculosis (TB) screening are negative before the first dose; and
6. Approvals will not be granted for members with active hepatitis B virus infection or active or untreated latent tuberculosis; and
7. Prescriber must verify liver function tests have been assessed prior to initiation of treatment with Enspryng™ and levels are acceptable to prescriber; and
8. Prescriber must agree to counsel the member to monitor for clinically significant active infection(s) prior to each dose (for active infections, the dose should be delayed until the infection resolves); and
9. Prescriber must agree to monitor neutrophil counts 4 to 8 weeks after initiation of therapy and thereafter as clinically appropriate; and
10. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
11. Member and/or caregiver must be trained by a health care professional on subcutaneous administration and storage of Enspryng™; and
12. A quantity limit override for the loading dose will be approved upon meeting the Enspryng™ approval criteria. A quantity limit of 1 syringe per 28 days will apply for the maintenance dose, according to the package labeling; and

13. 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.

Soliris® (Eculizumab) Approval Criteria [Atypical Hemolytic Uremic Syndrome (aHUS) or Paroxysmal Nocturnal Hemoglobinuria (PNH) Diagnosis]:

1. Member must have an established diagnosis of aHUS or PNH via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply; and
3. For members younger than 18 years of age, approval can be granted with a documented diagnosis of aHUS.

Soliris® (Eculizumab) Approval Criteria [Generalized Myasthenia Gravis (gMG) Diagnosis]:

1. An FDA approved diagnosis of gMG; and
2. Positive serologic test for anti-AChR antibodies; and
3. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV; and
4. MG-Activities of Daily Living (MG-ADL) total score ≥6; and
5. Member must meet 1 of the following:
    a. Failed treatment over 1 year or more with 2 or more immunosuppressive therapies (ISTs) either in combination or as monotherapy; or
    b. Failed at least 1 IST and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIg); and
6. Initial approvals will be for the duration of 6 months at which time an updated MG-ADL score must be provided. Continued authorization requires improvement in the MG-ADL score from baseline. Subsequent approvals will be for the duration of 1 year.

Soliris® (Eculizumab) Approval Criteria [Neuromyelitis Optica Spectrum Disorder (NMOSD) Diagnosis]:

1. An FDA approved indication of NMOSD in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have a history of at least 2 NMOSD attacks in last 12 months or 3 attacks in the last 24 months, with at least 1 attack in the past 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤7; and
5. 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.

Ultomiris® (Ravulizumab-cwvz) Approval Criteria [Atypical Hemolytic Uremic Syndrome (aHUS) Diagnosis]:

1. Member must have a documented diagnosis of aHUS.

Ultomiris® (Ravulizumab-cwvz) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria (PNH) Diagnosis]:

1. Member must have an established diagnosis of PNH via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply.

Uplizna® (Inebilizumab-cdon) Approval Criteria:

1. An FDA approved indication of neuromyelitis optica spectrum disorder (NMOSD) in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have experienced at least 1 acute NMOSD attack in the prior 12 months, or at least 2 attacks in the prior 24 months, requiring rescue therapy; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤8; and
5. Prescriber must verify hepatitis B virus (HBV) and tuberculosis (TB) screening are negative before the first dose; and
6. Approvals will not be granted for members with active HBV infection or active or untreated latent TB; and
7. Prescriber must agree to monitor member for clinically significant active infection(s) prior to each dose (for active infections, the dose should be delayed until the infection resolves); and
8. Prescriber must verify testing for quantitative serum immunoglobulins has been performed before the first dose and levels are acceptable to prescriber; and
9. Prescriber must agree to monitor the level of serum immunoglobulins during and after discontinuation of treatment with Uplizna® until B-cell repletion; and
10. The infusion must be administered under the supervision of a health care professional with access to appropriate medical support to manage potential severe reactions, and the patient must be observed for at least 1 hour after the completion of each infusion; and
11. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of treatment; and
12. Female members of reproductive potential must use contraception while receiving Uplizna® and for 6 months after the last infusion; and

13. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
14. A quantity limit override for the loading dose will be approved upon meeting the Uplizna® approval criteria. A quantity limit of 30mL per 180 days will apply for the maintenance dose; and
15. 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.

Utilization of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon): 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	7	107	$2,432,880.77	$22,737.20	$1,649.41	24,160	1,475
2021	5	100	$2,373,069.81	$23,730.70	$1,734.70	22,746	1,368
% Change	**-28.6%**	**-6.5%**	**-2.5%**	**4.4%**	**5.2%**	**-5.9%**	**-7.3%**
Change	**-2**	**-7**	**-$59,810.96**	**$993.50**	**$85.29**	**-1,414**	**-107**

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

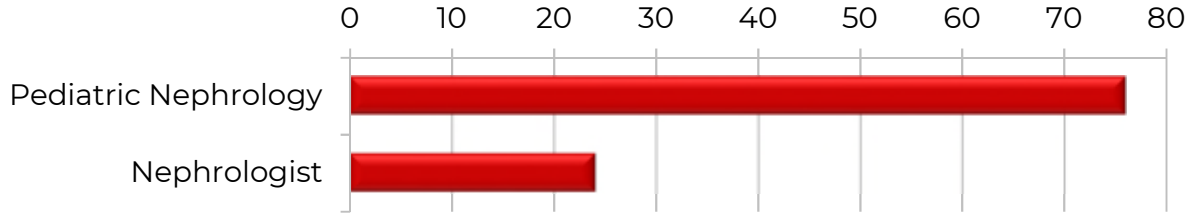
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2020	5	17	$780,254.40	$45,897.32	3,660
2021	4	14	$776,477.40	$55,462.67	3,510
% Change	**-20%**	**-17.65%**	**-0.48%**	**20.84%**	**-4.10%**
Change	**-1**	**-3**	**-$3,807.00**	**$9,565.35**	**-150**

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 Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon): Pharmacy Claims

- Due to the limited number of members utilizing Enspryng™, Soliris®, Ultomiris®, and Uplizna® during fiscal year 2021, detailed demographic information could not be provided.

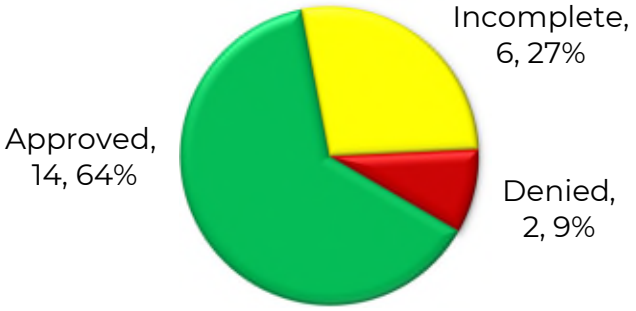
Top Prescriber Specialties of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon) by Number of Claims: Pharmacy Claims



Prior Authorization of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon)

There were 22 prior authorization requests submitted for Enspryng™, Soliris®, Ultomiris®, and Uplizna® 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]

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

- **May 2021:** The FDA approved Empaveli™ (pegcetacoplan) as the first complement protein C3 targeted therapy approved for adults with paroxysmal nocturnal hemoglobinuria (PNH). Patients with PNH have uncontrolled complement activation and destruction of red blood cells through intravascular and extravascular hemolysis. These patients will often have low levels of hemoglobin (Hb) and require blood transfusions. Empaveli™ is approved in patients with PNH who are either treatment naïve or switching from a C5 inhibitor such as Soliris® or Ultomiris®. The approval of Empaveli™ was based on a head-to-head Phase 3 study, known as PEGASUS, which compared Empaveli™ to Soliris®. Empaveli™ was shown to be superior to Soliris® for the change

in baseline Hb level at week 16 with an adjusted mean increase of 3.84g/dL (P<0.0001). Eighty-five percent of Empaveli™-treated patients were transfusion free over 16 weeks versus 15% of Soliris®-treated patients. The most common adverse reactions (≥10%) with Empaveli™ were injection-site reactions, infections, diarrhea, and abdominal pain.

Pipeline:

- **Crovalimab (RG6107):** Roche has initiated a Phase 3 study evaluating the use of crovalimab for the treatment of PNH in treatment-naïve patients. Crovalimab is a monoclonal antibody that blocks the cleavage of C5 to C5a to C5b, causing the inhibition of complement activation. The expected FDA filing date for crovalimab is in 2022.
- **Iptacopan (LNP023):** Iptacopan is an oral Factor B inhibitor of the alternative complement pathway. It acts upstream of the C5 terminal pathway, preventing both intravascular and extravascular hemolysis in patients with PNH. Results from a 12-week Phase 2 study of iptacopan monotherapy demonstrated the medication was well tolerated and resulted in rapid and durable transfusion-free improvement of Hb levels in the majority of patients.

Empaveli™ (Pegcetacoplan) Product Summary[4]

Indication(s): Empaveli™ (pegcetacoplan) is a complement inhibitor indicated for the treatment of adult patients with PNH.

Boxed Warning: Serious Infections Caused by Encapsulated Bacteria

- The use of Empaveli™ may predispose patients to serious infections caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y, and B, and *Haemophilus influenzae* type B. Patients should be vaccinated at least 2 weeks prior to initiating the first dose of Empaveli™ unless the risk of delaying therapy outweighs the risk of developing a serious infection.
- Empaveli™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

How Supplied: 1,080mg/20mL (54mg/mL) solution in a 20mL single-dose vial (SDV) for subcutaneous (sub-Q) infusion

Dosing and Administration:

- The recommended dosage is 1,080mg by sub-Q infusion twice weekly via a commercially available pump.
- For patients currently stable on a C5 inhibitor (Soliris® or Ultomiris®), bridging from C5 to C3 therapy should occur to reduce the risk of hemolysis from abrupt treatment discontinuation:

- For patients switching from Soliris®, Empaveli™ should be initiated while continuing Soliris® at its current dose. After 4 weeks, Soliris® should be discontinued before continuing on monotherapy with Empaveli™.
- For patients switching from Ultomiris®, Empaveli™ should be initiated no more than 4 weeks after the last dose of Ultomiris®.

Mechanism of Action: Pegcetacoplan binds to complement protein C3 and its activation fragment C3b, thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation. This decrease in complement activation leads to a decrease in intravascular and extravascular hemolysis.

Warnings and Precautions:

- **Serious Infections Caused by Encapsulated Bacteria:** Due to the serious risk of life-threatening or fatal infections caused by encapsulated bacteria, all patients must be vaccinated against the bacteria listed in the *Boxed Warning* at least 2 weeks prior to initiating therapy with pegcetacoplan. If immediate therapy is required, vaccinations should be administered immediately and 2 weeks of prophylactic antibiotics should be provided.

Contraindication(s):

- Patients with a hypersensitivity to pegcetacoplan or any of the excipients
- Patients who are not currently vaccinated against certain encapsulated bacteria unless the risks of delaying treatment outweigh the risk of developing a serious bacterial infection with an encapsulated organism
- Patients with unresolved serious infections caused by encapsulated bacteria

Adverse Reactions: The most common adverse reactions in patients with PNH (incidence ≥10%) were injection-site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, viral infection, and fatigue.

Efficacy: The safety and efficacy of pegcetacoplan were established in a 16-week, randomized (1:1), head-to-head study comparing pegcetacoplan versus eculizumab in 80 eculizumab-treated patients with PNH. Patients in this study had to be on a current stable dose of eculizumab for ≥3 months. Prior to entering the randomized controlled period (RCP), a 4-week run-in period was initiated, in which all patients continued their current dose of eculizumab with the addition of pegcetacoplan. After the 4-week run-in period, patients were then randomized to monotherapy with pegcetacoplan or eculizumab and followed for 16 weeks.

- Primary Endpoint: The change in Hb levels from baseline to week 16 (during the RCP) between pegcetacoplan and eculizumab. A key secondary endpoint was the number of patients who were transfusion free at 16 weeks.
- Results: Pegcetacoplan was superior to eculizumab in the change from baseline in Hb level at week 16 (2.37g/dL vs. -1.47g/dL; P<0.0001) with an adjusted mean increase of 3.84g/dL [95% confidence interval (CI): 2.33, 5.34]. For the secondary endpoint of transfusion avoidance, 85% (N=41) of pegcetacoplan-treated patients did not have a blood transfusion compared to 15% (N=6) of eculizumab-treated patients.

Cost: The Wholesale Acquisition Cost (WAC) of Empaveli™ is $4,403.84 per 1,080mg/20mL SDV, resulting in an estimated annual cost of $458,000 based on the recommended dose of 1,080mg twice weekly.

Cost Comparison: PNH Therapies

Medication	Cost for First Year	Cost per Year for Maintenance
Empaveli™ (pegcetacoplan)	**$458,000**	**$458,000**
Ultomiris® (ravulizumab-cwvz)*	$550,745	$493,109
Soliris® (eculizumab)	$521,832	$508,786

Costs do not reflect rebated prices or net costs.
Cost of therapy calculated based on wholesale acquisition cost (WAC).
*Costs based on recommended dosing for patients weighing 60kg to <100kg with PNH.

Recommendations

The College of Pharmacy recommends the prior authorization of Empaveli™ (pegcetacoplan) with the following criteria:

Empaveli™ (Pegcetacoplan) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria (PNH) Diagnosis]:

1. An FDA approved diagnosis of PNH; and
2. Must have an established diagnosis of PNH via international classification of disease (ICD) coding in member's medical claims history; and
3. An age restriction of 18 years and older will apply; and
4. For member self-administration or caregiver administration, the prescriber must verify the member or caregiver has been trained by a health care provider on proper administration and storage of Empaveli™; and
5. Prescriber and pharmacy must be enrolled in the Empaveli™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and

6. For members switching from Soliris® to Empaveli™, prescriber must verify the member will continue the current dose of Soliris® for 4 weeks before switching to Empaveli™ as monotherapy; and
7. For members switching from Ultomiris® to Empaveli™, prescriber must verify that Empaveli™ will be initiated no more than 4 weeks after the last dose of Ultomiris®.

Utilization Details of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon): Fiscal Year 2021

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
SOLIRIS INJ 10MG/ML	91	4	$1,910,608.14	$20,995.69	22.75
ULTOMIRIS INJ 300MG/30ML	9	3	$462,461.67	$51,384.63	3
TOTAL	**100**	**5***	**$2,373,069.81**	**$23,730.70**	**20**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
SOLIRIS INJ 10MG/ML (J1300)	5	2	$104,630.40	$20,926.08	2.5
ULTOMIRIS INJ 300/30ML (J1303)	9	2	$671,847.00	$74,649.67	4.5
TOTAL	**14⁺**	**4***	**$776,477.40**	**$55,462.67**	**3.5**

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

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[1] Apellis Pharmaceuticals, Inc. Apellis Announces U.S. Food and Drug Administration (FDA) Approval of EMPAVELI™ (Pegcetacoplan) for Adults with Paroxysmal Nocturnal Hemoglobinuria (PNH). *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2021/05/14/2230226/0/en/Apellis-Announces-U-S-Food-and-Drug-Administration-FDA-Approval-of-EMPAVELI-pegcetacoplan-for-Adults-with-Paroxysmal-Nocturnal-Hemoglobinuria-PNH.html. Issued 05/14/2021. Last Accessed 11/09/2021.

[2] F. Hoffmann-La Roche Ltd. Product Development Portfolio. Available online at: https://www.roche.com/research_and_development/who_we_are_how_we_work/pipeline.htm. Last revised 10/20/2021. Last accessed 11/15/2021.

[3] Novartis. Novartis Investigational Oral Therapy Iptacopan (LNP023) Shows Benefit as Monotherapy in Treatment-Naïve Patients with Rare and Life-Threatening Blood Disorder Paroxysmal Nocturnal Hemoglobinuria. Available online at: https://www.novartis.com/news/media-releases/novartis-investigational-oral-therapy-iptacopan-lnp023-shows-benefit-monotherapy-treatment-naive-patients-rare-and-life-threatening-blood-disorder-paroxysmal-nocturnal-hemoglobinuria. Issued 06/11/2021. Last accessed 11/15/2021.

[4] Empaveli™ (Pegcetacoplan) Prescribing Information. Apellis Pharmaceuticals, Inc. Available online at: https://pi.apellis.com/files/PI_Empaveli.pdf. Last revised 05/2021. Last accessed 11/08/2021.

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: November 12, 2021

FDA Approves Treatment for Rare Blood Disease

The FDA approved Besremi® (ropeginterferon alfa-2b-njft) injection to treat adults with polycythemia vera, a blood disease that causes the overproduction of red blood cells (RBCs). The excess cells thicken the blood, slowing blood flow and increasing the chance of blood clots. Besremi® is the first FDA-approved medication for polycythemia vera that patients can take regardless of their treatment history and the first interferon therapy specifically approved for polycythemia vera.

Treatment for polycythemia vera includes phlebotomies as well as medications to reduce the number of RBCs. Besremi® is thought to work by binding to interferon alfa receptor, setting off a chain reaction that makes the bone marrow reduce RBC production. Besremi® is a long-acting drug that patients take by subcutaneous (sub-Q) injection once every 2 weeks. If Besremi® can reduce excess RBCs and maintain normal levels for at least 1 year, the dosing frequency may be reduced to once every 4 weeks.

The safety and efficacy of Besremi® were evaluated in a multicenter, single-arm study that lasted 7.5 years. In this study, 51 adults with polycythemia vera received Besremi® for an average of about 5 years. The effectiveness of Besremi® was assessed by looking at how many patients achieved a complete hematological response, which meant that patients had a RBC volume of <45% without a recent phlebotomy, normal white cell and platelet counts, normal spleen size, and no blood clots. Overall, 61% of patients had a complete hematological response.

Besremi® can cause liver enzyme elevations, low levels of white blood cells, low levels of platelets, joint pain, fatigue, itching, upper airway infection, muscle pain, and flu-like illness. Side effects may also include urinary tract infection, depression, and transient ischemic attacks. Besremi® should not be taken by patients who are allergic to the drug, have a severe psychiatric disorder or a history of a severe psychiatric disorder, are immunosuppressed transplant recipients, have an autoimmune disease or a history of autoimmune disease, or have liver disease. Patients who could be pregnant should be tested for pregnancy prior to starting Besremi® due to the risk of fetal harm.

FDA NEWS RELEASE

For Immediate Release: October 29, 2021

FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age

The FDA authorized the emergency use of the Pfizer-BioNTech COVID-19 vaccine for the prevention of COVID-19 to include children 5 to 11 years of age. The authorization was based on the FDA's thorough and transparent evaluation of the data that included input from independent advisory committee experts who overwhelmingly voted in favor of making the vaccine available to children in this age group.

Key points for parents and caregivers:

- Effectiveness: Immune responses of children 5 to 11 years of age were comparable to those of individuals 16 to 25 years of age. In addition, the vaccine

was found to be 90.7% effective in preventing COVID-19 in children 5 to 11 years of age.
- Safety: The vaccine's safety was studied in approximately 3,100 children 5 to 11 years of age who received the vaccine and no serious side effects have been detected in the ongoing study.
- The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices will meet next week to discuss further clinical recommendations.

The Pfizer-BioNTech COVID-19 vaccine for children 5 to 11 years of age is administered as a 2 dose primary series, 3 weeks apart, but is a lower dose (10mcg) than that used for individuals 12 years of age and older (30mcg).

In the United States, COVID-19 cases in children 5 to 11 years of age make up 39% of cases in individuals younger than 18 years of age. According to the CDC, approximately 8,300 COVID-19 cases in children 5 to 11 years of age resulted in hospitalization. As of October 17, 2021, 691 deaths from COVID-19 have been reported in the United States in individuals younger than 18 years of age, with 146 deaths in the 5 to 11 years age group.

The FDA has determined this Pfizer vaccine has met the criteria for emergency use authorization (EUA). Based on the totality of scientific evidence available, the known and potential benefits of the Pfizer-BioNTech COVID-19 vaccine in individuals down to 5 years of age outweigh the known and potential risks.

FDA Evaluation of Available Effectiveness Data

The effectiveness data to support the EUA in children as young as 5 years of age is based on an ongoing randomized, placebo-controlled study that has enrolled approximately 4,700 children 5 to 11 years of age. The study is being conducted in the United States, Finland, Poland, and Spain. Children in the vaccine group received 2 doses of the Pfizer-BioNTech COVID-19 vaccine containing 10mcg of messenger ribonucleic acid (mRNA) per dose. The FDA analyzed data that compared the immune response of 264 participants from this study to 253 participants 16 to 25 years of age who had 2 higher doses of the vaccine in a previous study which determined the vaccine to be effective in preventing COVID-19. The immune responses of the younger age participants were comparable to the older participants.

The FDA also conducted a preliminary analysis of cases of COVID-19 occurring 7 days after the second dose. In this analysis, among participants without evidence of prior infection with SARS-CoV-2, 3 cases of COVID-19 occurred among 1,305 vaccine recipients and 16 cases of COVID-19 occurred among 663 placebo recipients; the vaccine was 90.7% effective in preventing COVID-19.

FDA Evaluation of Available Safety Data

The available safety data to support the EUA include more than 4,600 participants (3,100 vaccine, 1,538 placebo) 5 to 11 years of age enrolled in the ongoing study. In this study, a total of 1,444 vaccine recipients were followed for safety for at least 2 months after the second dose.

Commonly reported side effects in the clinical study included injection site pain, redness and swelling, fatigue, headache, muscle and/or joint pain, chills, fever, swollen lymph nodes, nausea, and decreased appetite. More children reported side effects after the second dose than after the first dose. Side effects were generally mild-to-moderate in severity and occurred within 2 days after vaccination, and most went away within 1 to 2 days.

The FDA and CDC safety surveillance systems have previously identified increased risks of myocarditis and pericarditis following vaccination with Pfizer-BioNTech COVID-19

vaccine, particularly following the second dose, and with the observed risk highest in males 12 to 17 years of age. Therefore, the FDA conducted its own benefit-risk assessment using modelling to predict how many symptomatic COVID-19 cases, hospitalizations, intensive care unit (ICU) admissions, and deaths from COVID-19 the vaccine in children 5 to 11 years of age would prevent versus the number of potential myocarditis cases, hospitalizations, ICU admissions, and deaths that the vaccine might cause. The FDA's model predicts that overall, the benefits of the vaccine would outweigh its risks in children 5 to 11 years of age.

Ongoing Safety Monitoring

Pfizer has updated its safety monitoring plan to include evaluation of myocarditis, pericarditis, and other events of interest in children 5 to 11 years of age. In addition, the FDA and the CDC have several systems in place to continually monitor COVID-19 vaccine safety and allow for the rapid detection and investigation of potential safety problems.

It is mandatory for Pfizer and vaccination providers to report any serious adverse events, cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death in vaccinated individuals. It is also mandatory for vaccination providers to report all vaccine administration errors to Vaccine Adverse Event Reporting System (VAERS) for which they become aware and for Pfizer to include a summary and analysis of all identified vaccine administration errors in monthly safety reports to the FDA.

Data Supports New Vaccine Formulation to Improve Stability and Storage Conditions

The FDA also authorized a manufacturing change for the vaccine to include a formulation that uses a different buffer to help maintain the vaccine's pH and stability. This new formulation is more stable at refrigerated temperatures for longer periods of time, permitting greater flexibility for vaccination providers.

The new formulation of the vaccine developed by Pfizer contains Tris buffer, a commonly used buffer in a variety of other FDA-approved vaccines and other biologics, including products for use in children. The FDA evaluated manufacturing data to support the use of Pfizer-BioNTech COVID-19 vaccine containing Tris buffer and concluded it does not present safety or effectiveness concerns.

FDA NEWS RELEASE

For Immediate Release: October 27, 2021

FDA, NIH, and 15 Private Organizations Join Forces to Increase Effective Gene Therapies for Rare Diseases

The FDA, the National Institutes of Health (NIH), 10 pharmaceutical companies, and 5 non-profit organizations have partnered to accelerate development of gene therapies for the 30 million Americans who suffer from a rare disease. While there are approximately 7,000 rare diseases, only 2 heritable diseases currently have FDA-approved gene therapies. The newly launched Bespoke Gene Therapy Consortium (BGTC), part of the NIH Accelerating Medicines Partnership (AMP) program and project-managed by the Foundation for the National Institutes of Health (FNIH), aims to optimize and streamline the gene therapy development process to help fill the unmet medical needs of people with rare diseases.

A single rare disease affects small numbers of people, but rare diseases collectively affect millions. Most rare inherited diseases stem from a specific gene mutation that is already known, making gene therapy a promising therapeutic approach. However, gene therapy development for rare diseases is highly complex, time consuming, and expensive. Moreover, the development process is stymied by limited access to tools and

technologies, lack of standards across the field, and a one-disease-at-a-time approach to therapeutic development. A standardized therapeutic development model that includes a common gene delivery technology (a vector) could allow for a more efficient approach to specific gene therapies, saving time and cost.

A primary aim of BGTC is to improve understanding of the basic biology of a common gene delivery vector known as the adeno-associated virus (AAV). BGTC researchers will examine the biological and mechanistic steps involved in AAV vector production, vector delivery of genes into human cells, and how therapeutic genes are activated in target cells. These results will provide important information for improving the efficiency of vector manufacturing and enhancing the overall therapeutic benefit of AAV gene therapy.

To improve and accelerate gene and vector manufacturing and production processes, the BGTC program will develop a standard set of analytic tests to apply to the manufacture of viral vectors made by consortium researchers. Such tests could be broadly applicable to different manufacturing methods and make the process of developing gene therapies for very rare conditions much more efficient.

A clinical component of BGTC-funded research will support between 4 and 6 clinical studies, each focused on a different rare disease. These diseases are expected to be rare, single-gene diseases with no gene therapies or commercial programs in development and that already have substantial groundwork in place to rapidly initiate preclinical and clinical studies. The studies will employ different types of AAV vectors that have been used before in clinical studies. For these studies, the BGTC will aim to shorten the path from studies in animal models of disease to human clinical studies.

The BGTC also will explore methods to streamline regulatory requirements and processes for the FDA approval of safe and effective gene therapies, including developing standardized approaches to preclinical testing (e.g., toxicology studies).

NIH and private partners will contribute approximately $76 million over 5 years to support BGTC-funded projects. This includes about $39.5 million from the participating NIH institutes and centers, pending availability of funds. National Center for Advancing Translational Sciences (NCATS), which developed the related Platform Vector Gene Therapy (PaVe-GT) program and is the NIH lead institute for BGTC, expects to contribute approximately $8 million over 5 years.

Private partners include Biogen Inc., Janssen Research & Development, LLC, Novartis Institutes for BioMedical Research, Pfizer Inc., REGENXBIO Inc., Spark Therapeutics, Takeda Pharmaceutical Company Limited, Taysha Gene Therapies, Thermo Fisher Scientific Inc., and Ultragenyx Pharmaceutical. Several non-profit partners also are involved, including the Alliance for Regenerative Medicine (ARM), the American Society of Gene and Cell Therapy, CureDuchenne, National Organization for Rare Disorders (NORD), and The National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL).

In addition to NCATS, participating NIH institutes include the Eunice Kennedy Shriver National Institute of Child Health and Human Development; National Eye Institute; National Heart, Lung, and Blood Institute; National Human Genome Research Institute; National Institute of Arthritis and Musculoskeletal and Skin Diseases; National Institute of Dental and Craniofacial Research; National Institute of Mental Health; National Institute of Neurological Disorders and Stroke; and National Institute on Deafness and Other Communication Disorders.

The BGTC is the first AMP initiative focused on rare diseases. Other ongoing AMP projects bring together scientific talent and financial resources from academia, industry, philanthropy, and government, and focus on improving the productivity of therapeutic

development for common metabolic diseases, schizophrenia, Parkinson's disease, Alzheimer's disease, type 2 diabetes, and autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus.

FDA NEWS RELEASE

For Immediate Release: October 20, 2021

Coronavirus (COVID-19) Update: FDA Takes Additional Actions on the Use of a Booster Dose for COVID-19 Vaccines

The FDA took action to expand the use of a booster dose for COVID-19 vaccines in eligible populations. The agency is amending the EUA for COVID-19 vaccines to allow for the use of a single booster dose as follows:

- The use of a single booster dose of the Moderna COVID-19 vaccine that may be administered at least 6 months after completion of the primary series to individuals:
  - 65 years of age and older
  - 18 to 64 years of age at high risk of severe COVID-19
  - 18 to 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2
- The use of a single booster dose of the Janssen (Johnson and Johnson) COVID-19 vaccine may be administered at least 2 months after completion of the single-dose primary regimen to individuals 18 years of age and older.
- The use of each of the available COVID-19 vaccines as a heterologous booster dose in eligible individuals following completion of primary vaccination with a different available COVID-19 vaccine.
- To clarify that a single booster dose of the Pfizer-BioNTech COVID-19 vaccine may be administered at least 6 months after completion of the primary series to individuals 18 to 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2.

Authorization of Moderna COVID-19 Vaccine Booster Dose

To support the EUA of a single booster dose of the Moderna COVID-19 vaccine, the FDA analyzed immune response data from 149 participants 18 years of age and older from the original clinical studies who received a booster dose at least 6 months after their second dose and compared it to the immune responses of 1,055 study participants after completing their 2 dose series. The antibody response of the 149 participants against SARS-CoV-2 virus 29 days after a booster dose of the vaccine demonstrated a booster response.

The FDA also evaluated an additional analysis from Moderna comparing the rates of COVID-19 accrued during the Delta variant surge during July and August 2021, which suggest that there is a waning of vaccine effectiveness over time.

Safety was evaluated in 171 participants 18 years of age and older who were followed for an average of approximately 6 months. The most commonly reported side effects by the clinical study participants who received the booster dose of the vaccine were pain at the injection site, tiredness, headache, muscle and/or joint pain, chills, swollen lymph nodes in same arm as the injection, nausea and vomiting, and fever. Of note, swollen lymph nodes in the underarm were observed more frequently following the booster dose than after the primary 2-dose series.

Ongoing analyses from the FDA and the CDC safety surveillance systems have identified increased risks of inflammatory heart conditions, myocarditis and pericarditis, following vaccination with the Moderna COVID-19 vaccine, particularly following the

second dose. Typically, onset of symptoms has been a few days following vaccination. The observed risk is higher among males younger than 40 years of age, particularly males 18 to 24 years of age, than among females and older males.

The Moderna COVID-19 single booster dose is half of the dose that is administered for a primary series dose and is administered at least 6 months after completion of a primary series of the vaccine.

Authorization of Janssen (Johnson and Johnson) COVID-19 Vaccine Booster Dose

The EUA of a single booster dose of the Janssen COVID-19 Vaccine is based on the FDA's evaluation of immune response data in 39 participants from a clinical study including 24 participants who were 18 to 55 years of age and 15 participants who were 65 years of age and older. The study participants received a booster dose approximately 2 months after their first dose, and the results demonstrated a booster response.

Overall, approximately 9,000 clinical study participants have received 2 doses of Janssen COVID-19 vaccine administered at least 2 months apart and of these, approximately 2,700 have had at least 2 months of safety follow-up after the booster dose. Janssen's safety analyses from these studies have not identified new safety concerns.

Earlier analyses from the FDA and CDC safety surveillance systems suggest an increased risk of a serious and rare type of blood clot in combination with low blood platelets following administration of the Janssen COVID-19 vaccine. This serious condition is called thrombocytopenia syndrome (TTS). People who developed TTS after receiving the vaccine had symptoms that began about 1 to 2 weeks after vaccination. Reporting of TTS has been highest in females 18 to 49 years of age. In addition, safety surveillance suggests an increased risk of a specific serious neurological disorder called Guillain-Barré syndrome within 42 days following receipt of the Janssen COVID-19 vaccine.

Authorization of "Mix and Match" Booster Dose

The FDA is also authorizing the use of heterologous booster dose for currently available (i.e., FDA-authorized or approved) COVID-19 vaccines. Following a presentation of clinical study data from the National Institute of Allergy and Infectious Diseases, the Vaccines and Related Biological Products Advisory Committee's discussion of information submitted for consideration, along with the agency's evaluation of the available data, the FDA has determined that the known and potential benefits of the use of a single heterologous booster dose outweigh the known and potential risks of their use in eligible populations.

A single booster dose of any of the available COVID-19 vaccines may be administered as a heterologous booster dose following completion of primary vaccination with a different available COVID-19 vaccine. The eligible population(s) and dosing interval for a heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

For example, Janssen COVID-19 vaccine recipients 18 years of age and older may receive a single booster dose of Janssen COVID-19 vaccine, Moderna COVID-19 vaccine (half dose), or Pfizer-BioNTech COVID-19 vaccine at least 2 months after receiving their Janssen COVID-19 vaccine primary vaccination.

In another example, Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine recipients falling into 1 of the authorized categories for boosters (65 years of age and older, 18 to 64 years of age at high-risk of severe COVID-19, and 18 to 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2) may receive a booster dose of Moderna COVID-19 vaccine (half dose), Pfizer-BioNTech COVID-19 vaccine, or Janssen COVID-19 vaccine at least 6 months after completing their primary vaccination.

The FDA recognizes that health care providers and COVID-19 vaccine recipients will have questions about booster doses. The individual fact sheets for each available vaccine provide relevant information for health care providers and the vaccine recipients. The FDA encourages health care providers to also follow the recommendations that will be provided by the CDC following a meeting of their Advisory Committee on Immunization Practices and formal recommendations signed by the CDC director.

FDA NEWS RELEASE

For Immediate Release: October 18, 2021

FDA Approves Cyltezo®, the First Interchangeable Biosimilar to Humira®

The FDA approved the first interchangeable biosimilar product to treat certain inflammatory diseases. Cyltezo® (adalimumab-adbm), originally approved in August 2017, is both biosimilar to, and interchangeable with its reference product Humira® (adalimumab). Cyltezo® is the second interchangeable biosimilar product approved by the agency and the first interchangeable monoclonal antibody. Once on the market, approved biosimilar and interchangeable biosimilar products can play a role in facilitating access to treatments for many serious health conditions.

Cyltezo® is approved for the following indications in adult patients:

- Moderately-to-severely active rheumatoid arthritis;
- Active psoriatic arthritis;
- Active ankylosing spondylitis ;
- Moderately-to-severely active Crohn's disease (CD);
- Moderately-to-severely active ulcerative colitis; and
- Moderate-to-severe chronic plaque psoriasis.

Cyltezo® is also indicated for moderately-to-severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older, and pediatric patients 6 years of age or older with CD.

Biological products, generally derived from a living organism, include medications for treating many serious illnesses and chronic health conditions. A biosimilar is a biological product that is highly similar to, and has no clinically meaningful differences from, a biological product already approved by the FDA (also called the reference product). Patients can expect the same safety and effectiveness from the biosimilar as they can from the reference product. Interchangeable biosimilar products can be expected to produce the same clinical result as the reference product in any given patient and, for biological products administered more than once to an individual, the risk in terms of safety or diminished efficacy of switching between the 2 products is not greater than the risk of using the reference product without such switching.

An interchangeable biosimilar product may be substituted for the reference product without the prescriber having to change the prescription. The substitution may occur at the pharmacy, subject to state pharmacy laws which vary by state, a practice commonly called "pharmacy-level substitution" – similar to how generic drugs are substituted for brand name drugs. Biosimilar and interchangeable biosimilar products may cost less than the brand-name medicine.

Cyltezo®, offered in a single-dose, pre-filled glass syringe (40mg/0.8mL, 20mg/0.4mL), is administered sub-Q under the guidance of a physician. The most serious known side effects with Cyltezo® are infections and malignancies. The most common expected adverse reactions are upper respiratory and sinus infections, injection site reactions, headache, and rash.

Like Humira®, the labeling for Cyltezo® contains a *Boxed Warning* to alert health care professionals and patients about an increased risk of serious infections that may lead to hospitalization or death. The *Boxed Warning* also notes that lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor blockers, including adalimumab products. The drug must be dispensed with a patient Medication Guide that describes important information about its uses and risks.

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

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

Acetazolamide Injection	***Currently in Shortage***
Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azacitidine for Injection	***Currently in Shortage***
Belatacept (Nulojix®) Lyophilized Powder 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***
Dacarbazine 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***
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***
Lipid Injection	***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***
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***
Potassium Chloride Concentrate 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***
Vitamin A Palmitate (Aquasol A®) Injection	***Currently in Shortage***