OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
September 14, 2022
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 – September 14, 2022

DATE: September 7, 2022

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 September 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/Nonalcoholic Fatty Liver Disease (NAFLD) Overview – Appendix B

Action Item – Vote to Update the Approval Criteria for the Ophthalmic Anti-Inflammatory Products – Appendix C

Action Item – Vote to Prior Authorize Recorlev® (Levoketoconazole) and Update the Approval Criteria for Isturisa® (Osilodrostat) – Appendix D

Action Item – Vote to Prior Authorize Tlando® (Testosterone Undecanoate) and Update the Approval Criteria for the Testosterone Products – Appendix E

Action Item – Vote to Update the Approval Criteria for the Opioid Analgesics and Medication-Assisted Treatment (MAT) Medications – Appendix F

Action Item – Vote to Prior Authorize Adlarity® (Donepezil Transdermal System) and Aduhelm™ (Aducanumab-avwa) – Appendix G

Action Item – Vote to Update the Approval Criteria for the Topical Corticosteroids – Appendix H

Action Item – Vote to Prior Authorize Camzyos™ (Mavacamten) – Appendix I

Action Item – Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications – Appendix J

Action Item – Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators – Appendix K

Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk) – Appendix L

Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Amvuttra™ (Vutrisiran) – Appendix M

Annual Review of Synagis® (Palivizumab) – Appendix N

Annual Review of Nulibry® (Fosdenopterin) – Appendix O

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – September 14, 2022 @ 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. Megan Hanner –	participating in person
Dr. Lynn Mitchell –	participating in person
Dr. John Muchmore –	participating in person
Dr. Lee Muñoz –	participating in person
Dr. James Osborne –	participating in person

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

Or join by phone:
Dial: +1-602-753-0140 or +1-669-219-2599
Webinar ID: 952 7560 1667
Passcode: 69395211

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. July 13, 2022 DUR Board Meeting Minutes
   B. July 13, 2022 DUR Board Recommendations Memorandum
   C. August 10, 2022 DUR Board Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Nonalcoholic Fatty Liver Disease (NAFLD) Overview – See Appendix B**
   A. Pharmacy Helpdesk Activity for August 2022
   B. Medication Coverage Activity for August 2022
   C. NAFLD Overview

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

5. **Action Item – Vote to Update the Approval Criteria for the Ophthalmic Anti-Inflammatory Products – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Recorlev® (Levoketoconazole) and Update the Approval Criteria for Isturisa® (Osilodrostat) – See Appendix D**
   A. Market News and Updates
   B. Recorlev® (Levoketoconazole) Product Summary

C. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Tlando® (Testosterone Undecanoate) and Update the Approval Criteria for the Testosterone Products – See Appendix E**
   A. Market News and Updates
   B. Cost Comparison
   C. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Update the Approval Criteria for the Opioid Analgesics and Medication-Assisted Treatment (MAT) Medications – See Appendix F**
   A. Market News and Updates
   B. College of Pharmacy Recommendations

Items to be presented by Dr. O'Halloran, Dr. Muchmore, Chairman:

9. **Action Item – Vote to Prior Authorize Adlarity® (Donepezil Transdermal System) and Aduhelm® (Aducanumab-avwa) – See Appendix G**
   A. Market News and Updates
   B. Aduhelm® (Aducanumab-avwa) Product Summary
   C. College of Pharmacy Recommendations

Items to be presented by Dr. O'Halloran, Dr. Muchmore, Chairman:

10. **Action Item – Vote to Update the Approval Criteria for the Topical Corticosteroids – See Appendix H**
    A. College of Pharmacy Recommendations

Items to be presented by Dr. O'Halloran, Dr. Muchmore, Chairman:

11. **Action Item – Vote to Prior Authorize Camzyos™ (Mavacamten) – See Appendix I**
    A. Market News and Updates
    B. Camzyos™ (Mavacamten) Product Summary
    C. College of Pharmacy Recommendations

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

12. **Action Item – Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications – See Appendix J**
    A. Market News and Updates
    B. Product Summaries
    C. College of Pharmacy Recommendations

Items to be presented by Dr. O'Halloran, Dr. Muchmore, Chairman:

13. **Action Item – Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators – See Appendix K**
    A. Current Prior Authorization Criteria
    B. Utilization of CFTR Modulators
    C. Prior Authorization of CFTR Modulators
    D. Market News and Updates
    E. College of Pharmacy Recommendations
    F. Utilization Details of CFTR Modulators

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

14. **Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk) – See Appendix L**
    A. Introduction
    B. Current Prior Authorization Criteria
    C. Utilization of Breast Cancer Medications
    D. Prior Authorization of Breast Cancer Medications
    E. Market News and Updates
    F. Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk) Product Summary
    G. College of Pharmacy Recommendations
    H. Utilization Details of Breast Cancer Medications

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

15. **Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Amvuttra™ (Vutrisiran) – See Appendix M**
    A. Current Prior Authorization Criteria
    B. Utilization of Amyloidosis Medications
    C. Prior Authorization of Amyloidosis Medications
    D. Market News and Updates
    E. Amvuttra™ (Vutrisiran) Product Summary
    F. College of Pharmacy Recommendations
    G. Utilization Details of Amyloidosis Medications

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

16. **Annual Review of Synagis® (Palivizumab) – See Appendix N**
    A. Current Prior Authorization Criteria
    B. Utilization of Synagis® (Palivizumab)
    C. Prior Authorization of Synagis® (Palivizumab)
    D. Respiratory Syncytial Virus (RSV) Season Comparison
    E. Market News and Updates
    F. College of Pharmacy Recommendations

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

17. Annual Review of Nulibry® (Fosdenopterin) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Nulibry® (Fosdenopterin)
C. Prior Authorization of Nulibry® (Fosdenopterin)
D. Market News and Updates
E. College of Pharmacy Recommendations

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

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

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

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

A. Anemia Medications
B. Hepatitis C Medications
C. Spinal Muscular Atrophy (SMA) Medications
D. Targeted Immunomodulator Agents

*Future product and class reviews subject to change.

20. 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 JULY 13, 2022

DUR BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.		X
Jennifer de los Angeles, Pharm.D., BCOP	X	
Jennifer Boyett, MHS; PA-C	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
Thara Kottoor, Pharm.D.; Pharmacy Resident	X	
Morgan Masterson, Pharm.D; Clinical Pharmacist		X
Regan Moss, 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
Ashley Teel, Pharm.D.; Clinical Pharmacist		X
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	X	
Devin Wilcox, D.Ph.; Pharmacy Director	X	
Justin Wilson, Pharm.D.; Clinical Pharmacist		X
PA Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		X
Emily Borders, Pharm.D., BCOP	X	
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 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	
Josh Holloway, J.D.; Deputy General Counsel	X	

Debra Montgomery, D.O.; Medical Director		X
Traylor Rains; State Medicaid Director		X
Jill Ratterman, D.Ph.; Clinical Pharmacist	X	
Paula Root, M.D.; Senior Medical Director, Interim Chief Medical Officer	X	
Shanna Simmons, Pharm.D.; Program Integrity Pharmacist	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:	
Kenneth Berry, Alkermes	Audrey Rattan, Alkermes
Robert Greely, Biogen	Christopher Ngai, Calliditas
Ed Eldridge, Gilead	Frank Alvarado, Johnson & Johnson
Ed Clasby, Medtronic	Christy Olson, Medtronic
Shellie Keast, Mercer	Brent Parker, Merck
Mark Kaiser, Otsuka	Marc Parker, Sunovion
Bob Atkins, Biogen	Heather Higgins, Jazz
Sheri Jepsen, Seagen	Steven Angelcyk, Embecta
Tom Seignious, Azurity	Robin Selsor, Aimmune
Evie Knisely, Novartis	Bettina Buob, Neurelis
Maggie Shaffer, Alzheimer's Association	Burl Beasley, OMES
Aaron Austin, Takeda	Rhonda Clark, Indivior
Gina Heinen, Novo Nordisk	Himanshu Patel, McDermott, Will, & Emery
Jeff Knappen, Spark	Craig Irwin, Acadia
Raquel Jordan, Takeda	Tracey Maravilla, Ascendis
Chrystal Mayes, Sanofi	

PRESENT FOR PUBLIC COMMENT:	
Kenneth Berry, Alkermes	Christopher Ngai, Calliditas Therapeutics
Robert Greely, Biogen	

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

1A: ROLL CALL

Dr. Muchmore called the meeting to order at 4:01pm. Roll call by Dr. Wilcox established the presence of a quorum.

ACTION: NONE REQUIRED

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

2A: AGENDA ITEM NO. 8 KENNETH BERRY
2B: AGENDA ITEM NO. 10 CHRISTOPHER NGAI
2C: AGENDA ITEM NO. 14 ROBERT GREELY
ACTION: NONE REQUIRED

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

3A: JUNE 8, 2022 DUR MINUTES – VOTE

Materials included in agenda packet; presented by Dr. Muchmore
Dr. Muñoz moved to approve; seconded by Ms. Boyett

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/CHRONIC MEDICATION ADHERENCE (CMA) PROGRAM UPDATE**

4A: PHARMACY HELPDESK ACTIVITY FOR JUNE 2022
4B: MEDICATION COVERAGE ACTIVITY FOR JUNE 2022
4C: CMA PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. O'Halloran, Dr. Travers
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE XELSTRYM™ (DEXTROAMPHETAMINE TRANSDERMAL SYSTEM) AND UPDATE THE APPROVAL CRITERIA FOR THE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND NARCOLEPSY MEDICATIONS**

5A: MARKET NEWS AND UPDATES
5B: XELSTRYM™ (DEXTROAMPHETAMINE TRANDSERMAL SYSTEM) PRODUCT SUMMARY
5C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Travers
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE LIVTENCITY™ (MARIBAVIR)**

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

Materials included in agenda packet; presented by Dr. Ha
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE QUVIVIQ™ (DARIDOREXANT) AND UPDATE THE APPROVAL CRITERIA FOR THE INSOMNIA MEDICATIONS**

7A: MARKET NEWS AND UPDATES
7B: QUVIVIQ™ (DARIDOREXANT) PRODUCT SUMMARY
7C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ha
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE INVEGA HAFYERA™ (PALIPERIDONE PALMITATE INJECTION) AND UPDATE THE APPROVAL CRITERIA FOR THE ATYPICAL ANTIPSYCHOTIC MEDICATIONS**

8A: MARKET NEWS AND UPDATES
8B: INVEGA HAFYERA™ (PALIPERIDONE PALMITATE) PRODUCT SUMMARY
8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. O'Halloran
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE RYPLAZIM® (PLASMINOGEN, HUMAN-TVMH)**

9A: MARKET NEWS AND UPDATE
9B: RYPLAZIM® (PLASMINOGEN, HUMAN-TVMH) PRODUCT SUMMARY

9C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. O'Halloran
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE CITALOPRAM CAPSULE, DARTISLA ODT™ (GLYCOPYRROLATE ORALLY DISINTEGRATING TABLET), FLEQSUVY™ (BACLOFEN ORAL SUSPENSION), LOFENA™ (DICLOFENAC POTASSIUM TABLET), LOREEV XR™ (LORAZEPAM EXTENDED-RELEASE CAPSULE), NORLIQVA® (AMLODIPINE BESYLATE ORAL SOLUTION), SEGLENTIS® (CELECOXIB/TRAMADOL TABLET), SUTAB® (SODIUM SULFATE/MAGNESIUM SULFATE/POTASSIUM CHLORIDE TABLET), TARPEYO™ (BUDESONIDE DELAYED-RELEASE CAPSULE), VUITY™ (PILOCARPINE 1.25% OPHTHALMIC SOLUTION), AND XIPERE™ (TRIAMCINOLONE ACETONIDE INJECTION)
10A: INTRODUCTION
10B: PRODUCT SUMMARIES AND COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE CAMCEVI™ (LEUPROLIDE), PLUVICTO® (LUTETIUM LU 177 VIPIVOTIDE TETRAXETAN), TIVDAK® (TISOTUMAB VEDOTIN-TFTV), AND WELIREG™ (BELZUTIFAN) AND UPDATE THE APPROVAL CRITERIA FOR THE GENITOURINARY AND CERVICAL/ENDOMETRIAL CANCER MEDICATIONS
11A: MARKET NEWS AND UPDATES
11B: PRODUCT SUMMARIES
11C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Muñoz moved to approve; seconded by Ms. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF COLORECTAL CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ALYMSYS® (BEVACIZUMAB-MALY), LONSURF® (TRIFLURIDINE/TIPIRACIL), AND STIVARGA® (REGORAFENIB)
12A: INTRODUCTION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF COLORECTAL CANCER MEDICATIONS
12D: PRIOR AUTHORIZATION OF COLORECTAL CANCER MEDICATIONS
12E: MARKET NEWS AND UPDATES
12F: PRODUCT SUMMARIES
12G: COLLEGE OF PHARMACY RECOMMENDATIONS
12H: UTILIZATION DETAILS OF COLORECTAL CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER

AGENDA ITEM NO. 13: ANNUAL REVIEW OF DANYELZA® (NAXITAMAB-GQGK), KOSELUGO® (SELUMETINIB), PEMAZYRE® (PEMIGATINIB), QINLOCK™ (RIPRETINIB), AND TRUSELTIQ™ (INFIGRATINIB)
13A: INTRODUCTION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA

13C: UTILIZATION OF DANYELZA® (NAXITAMAB-GQGK), KOSELUGO® (SELUMETINIB), PEMAZYRE® (PEMIGATINIB), QINLOCK™ (RIPRETINIB), AND TRUSELTIQ™ (INFIGRATINIB)
13D: PRIOR AUTHORIZATION OF DANYELZA® (NAXITAMAB-GQGK), KOSELUGO® (SELUMETINIB), PEMAZYRE® (PEMIGATINIB), QINLOCK™ (RIPRETINIB), AND TRUSELTIQ™ (INFIGRATINIB)
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF DANYELZA® (NAXITAMAB-GQGK), KOSELUGO® (SELUMETINIB), PEMAZYRE® (PEMIGATINIB), QINLOCK™ (RIPRETINIB), AND TRUSELTIQ™ (INFIGRATINIB)
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ALZHEIMER'S DISEASE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ADLARITY® (DONEPEZIL TRANSDERMAL SYSTEM) AND ADUHELM™ (ADUCANUMAB-AVWA)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF ALZHEIMER'S DISEASE MEDICATIONS
14C: PRIOR AUTHORIZATION OF ALZHEIMER'S DISEASE MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: ADUHELM™ (ADUCANUMAB-AVWA) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF ALZHEIMER'S DISEASE MEDICATIONS
Materials included in agenda packet; presented by Dr. O'Halloran
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER

AGENDA ITEM NO. 15: ANNUAL REVIEW OF TESTOSTERONE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TLANDO® (TESTOSTERONE UNDECANOATE)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF TESTOSTERONE PRODUCTS
15C: PRIOR AUTHORIZATION OF TESTOSTERONE PRODUCTS
15D: MARKET NEWS AND UPDATES
15E: COST COMPARISON
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF TESTOSTERONE PRODUCTS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER

AGENDA ITEM NO. 16: ANNUAL REVIEW OF VARIOUS SYSTEMIC ANTIBIOTICS
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF VARIOUS SYSTEMIC ANTIBIOTICS
16C: PRIOR AUTHORIZATION OF VARIOUS SYSTEMIC ANTIBIOTICS
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS
16F: UTILIZATION DETAILS OF VARIOUS SYSTEMIC ANTIBIOTICS
Materials included in agenda packet; presented by Dr. Ha
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF ISTURISA® (OSILODROSTAT) AND 30-DAY NOTICE TO PRIOR AUTHORIZE RECORLEV® (LEVOKETOCONAZOLE)
17A: CURRENT PRIOR AUTHORIZATION CRITERIA

17B: UTILIZATION OF ISTURISA® (OSILODROSTAT)
17C: PRIOR AUTHORIZATION OF ISTURISA® (OSILODROSTAT)
17D: MARKET NEWS AND UPDATES
17E: RECORLEV® (LEVOKETOCONAZOLE) PRODUCT SUMMARY
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Ha
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER

AGENDA ITEM NO. 18: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. O'Halloran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
No live DUR Board meeting scheduled for August 2022. August 2022 will be a packet-only meeting.
19A: INTRAVENOUS (IV) IRON PRODUCTS
19B: OPHTHALMIC ANTI-INFLAMMATORY PRODUCTS
19C: OPIOID ANALGESICS AND MEDICATION-ASSISTED TREATMENT (MAT) MEDICATIONS
19D: TOPICAL CORTICOSTEROIDS
*Future product and class reviews subject to change.
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: ADJOURNMENT
The meeting was adjourned at 5:40pm.

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

Memorandum

Date: July 15, 2022

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 July 13, 2022

Recommendation 1: Chronic Medication Adherence (CMA) Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Xelstrym™ (Dextroamphetamine Transdermal System) and Update the Approval Criteria for Attention-Deficit/Hyperactivity Disorder (ADHD) and Narcolepsy Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the ADHD and Narcolepsy Medications Product Based Prior Authorization (PBPA) category (changes shown in red):

1. Updating the approval criteria for Qelbree® (viloxazine) based on the recent FDA approved age expansion
2. Updating the approval criteria for Xywav® (calcium/magnesium/ potassium/sodium oxybates) based on the recent FDA approval for idiopathic hypersomnia
3. The prior authorization of Dyanavel XR® [amphetamine extended-release (ER) tablets] and placement into Tier-2 of the Long-Acting Stimulants category of the ADHD Medications PBPA Tier chart

4. The prior authorization of Xelstrym™ (dextroamphetamine transdermal system) and placement into the Special PA Tier of the ADHD Medications PBPA Tier chart with the following additional criteria

ADHD Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			amphetamine ER susp (Adzenys ER™) amphetamine ER ODT (Adenyls XR-ODT®) amphetamine (Evekeo®) amphetamine ODT (Evekeo ODT™) amphetamine/ dextroamphetamine ER (Mydayis®) dextroamphetamine (Dexedrine®) dextroamphetamine ER (Dexedrine Spansules®) dextroamphetamine soln (ProCentra®) **dextroamphetamine (Xelstrym™)** dextroamphetamine (Zenzedi®) lisdexamfetamine chew tab (Vyvanse®)+ methamphetamine (Desoxyn®) methylphenidate ER ODT (Cotempla XR-ODT®) methylphenidate chew tab (Methylin®)
Short-Acting			
amphetamine/ dextroamphetamine (Adderall®)			
Long-Acting			
amphetamine/ dextroamphetamine ER (Adderall XR®) lisdexamfetamine cap (Vyvanse®)+	amphetamine ER susp **and tab** (Dyanavel® XR)		
Methylphenidate			
Short-Acting			
dexmethylphenidate (Focalin®) methylphenidate tab and soln (Methylin®) methylphenidate (Ritalin®)			
Long-Acting			
dexmethylphenidate ER (Focalin XR®) – **Brand Preferred** methylphenidate ER (Concerta®) methylphenidate ER (Daytrana®) methylphenidate ER (Metadate CD®) methylphenidate ER (Metadate ER®) methylphenidate ER (Methylin ER®) methylphenidate ER (Ritalin LA®) methylphenidate ER (Ritalin SR®)	dexmethylphenidate ER (generic Focalin XR®) methylphenidate ER (Aptensio XR®) methylphenidate ER susp (Quillivant XR®)	methylphenidate ER 72mg methylphenidate ER (Adhansia XR®) methylphenidate ER (Jornay PM®) serdexmethylphen-idate/dexmethylphen-idate (Azstarys™)	

ADHD Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Non-Stimulants			methylphenidate ER chew tab (QuilliChew ER®) viloxazine (Qelbree®)
atomoxetine (Strattera®) guanfacine ER (Intuniv®)	clonidine ER (Kapvay®)Δ		

*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). Placement of products shown in blue is based on net cost after federal and/or supplemental rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.

+Unique criteria applies for the diagnosis of binge eating disorder (BED).

ΔUnique criteria applies in addition to tier trial requirements.

ADHD = attention-deficit/hyperactivity disorder; cap = capsule; chew tab = chewable tablet; ER = extended-release; ODT = orally disintegrating tablet; PA = prior authorization; soln = solution; susp = suspension; tab = tablet

ADHD Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least 1 long-acting Tier-1 stimulant that resulted in an inadequate response:
   a. Trials should have been within the last 180 days; and
   b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician; and
3. For Dyanavel® XR oral suspension and Quillivant XR®, an age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
4. Kapvay® [Clonidine Extended-Release (ER) Tablet] Approval Criteria:
   a. An FDA approved diagnosis; and
   b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
   c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets must be provided.

ADHD Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least 1 long-acting Tier-1 stimulant that resulted in an inadequate response; and
3. A previously failed trial with at least 1 long-acting Tier-2 stimulant that resulted in an inadequate response:
   a. Trials should have been within the last 365 days; and

b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

ADHD Medications Special Prior Authorization (PA) Approval Criteria:

1. Adzenys XR-ODT®, Adzenys ER™, Cotempla XR-ODT®, Evekeo ODT™, QuilliChew ER®, Vyvanse® Chewable Tablets, and Xelstrym™ Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of stimulant medications that can be used for members who cannot swallow capsules or tablets must be provided; and
   c. An age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
2. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra®, and Zenzedi® Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications must be provided.
3. Methylin® Chewable Tablets Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use methylphenidate immediate-release tablets or oral solution must be provided; and
   c. An age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
4. Mydayis® Approval Criteria:
   a. A covered diagnosis; and
   b. Member must be 13 years of age or older; and
   c. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications must be provided.
5. Qelbree® [Viloxazine Extended-Release (ER) Capsule] Approval Criteria:
   a. An FDA approved diagnosis; and
   b. Member must be 6 ~~to 17~~ years of age or older; and
   c. Previously failed trials (within the last 180 days) with any 2 Tier-1 or Tier-2 ADHD medications, unless contraindicated, that did not yield adequate results; and

i. Qelbree® will not require a prior authorization and claims will pay at the point of sale if the member has paid claims for 2 Tier-1 or Tier-2 ADHD medications within the past 180 days of claims history; and

d. Member must not be taking a monoamine oxidase inhibitor (MAOI) or have taken an MAOI within the last 14 days; and
e. Member must not be taking sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range (e.g., alosetron, duloxetine, ramelteon, tasimelteon, tizanidine, theophylline) concomitantly with Qelbree®; and
f. A quantity limit of 30 capsules per 30 days will apply for the 100mg strengths and 60 capsules per 30 days will apply for the 150mg and 200mg strength.

ADHD Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum dose are not covered.
2. Prior authorization is required for all tiers for members older than 20 years of age and for members younger than 5 years of age. All prior authorization requests for members younger than 5 years of age must be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted psychiatrist.
3. For Daytrana® patches and Methylin® oral solution, an age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
4. Vyvanse® (Lisdexamfetamine) Approval Criteria [Binge Eating Disorder (BED) Diagnosis]:
   a. An FDA approved diagnosis of moderate-to-severe BED; and
   b. Member must be 18 years of age or older; and
   c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
   d. Authorizations will not be granted for the purpose of weight loss without the diagnosis of BED or for the diagnosis of obesity alone. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
   e. A quantity limit of 30 capsules or chewable tablets per 30 days will apply; and
   f. Initial approvals will be for the duration of 3 months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

Narcolepsy Medications Approval Criteria:

1. An FDA approved diagnosis; and
2. Use of Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and

a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; or
3. Use of Provigil® (modafinil) requires a previously failed trial (within the last 180 days) with Nuvigil® and a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; or
4. Use of Sunosi® (solriamfetol), Wakix® (pitolisant), Xyrem® (sodium oxybate), or Xywav® (calcium/magnesium/potassium/sodium oxybates) requires previously failed trials (within the last 180 days) with Tier-1 and Tier-2 stimulants from different chemical categories, Provigil®, and Nuvigil®, unless contraindicated, that did not yield adequate results; and
5. Additionally, use of Xywav® (calcium/magnesium/potassium/sodium oxybates) requires a patient-specific, clinically significant reason why the member cannot use Xyrem®; and
   a. For members requesting Xywav® due to lower sodium content in comparison to Xyrem®, a patient-specific, clinically significant reason why the member requires a low-sodium product must be provided; and
6. The diagnosis of obstructive sleep apnea requires concurrent treatment for obstructive sleep apnea; and
7. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

Idiopathic Hypersomnia (IH) Medications Approval Criteria:

1. Diagnosis of IH meeting the following ICSD-3 (International Classification of Sleep Disorders) criteria:
   a. Daily periods of irresistible need to sleep or daytime lapses into sleep for >3 months; and
   b. Absence of cataplexy; and
   c. Multiple sleep latency test (MSLT) results showing 1 of the following:
      i. <2 sleep-onset rapid eye movement (REM) periods (SOREMPs); or
      ii. No SOREMPs if the REM sleep latency on the preceding polysomnogram is ≤15 minutes; and
   d. At least 1 of the following:
      i. MSLT showing mean sleep latency ≤8 minutes; or
      ii. Total 24-hour sleep time ≥660 minutes on 24-hour polysomnography monitoring (performed after the correction of chronic sleep deprivation) or by wrist actigraphy in association with a sleep log (averaged over ≥7 days with unrestricted sleep); and
   e. Insufficient sleep syndrome has been ruled out; and

    f. Hypersomnolence or MSLT findings are not better explained by any other sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance abuse; and
2. Diagnosis must be confirmed by a sleep specialist; and
3. Use of Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
    a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; and
4. Use of Provigil® (modafinil) requires a previously failed trial (within the last 180 days) with Nuvigil® and a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
5. Use of Xyrem® (sodium oxybate) or Xywav® (calcium/magnesium/potassium/sodium oxybates) requires previously failed trials (within the last 180 days) with at least 4 of the following, unless contraindicated, that did not yield adequate results:
    a. Tier-1 stimulant; or
    b. Tier-2 stimulant; or
    c. Nuvigil®; or
    d. Provigil®; or
    e. Clarithromycin; and
6. Xywav® (calcium/magnesium/potassium/sodium oxybates) additionally requires a patient-specific, clinically significant reason why the member cannot use Xyrem®; and
    a. For members requesting Xywav® due to lower sodium content in comparison to Xyrem®, a patient-specific, clinically significant reason why the member requires a low-sodium product must be provided.

Recommendation 3: Vote to Prior Authorize Livtencity™ (Maribavir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Livtencity™ (maribavir) with the following criteria:

Livtencity™ (Maribavir) Approval Criteria:

1. An FDA approved indication of the treatment of post-transplant cytomegalovirus (CMV) infection and disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir, or foscarnet in adults and pediatric members (12 years of age and older weighing ≥35kg); and

2. A previously failed trial at least 14 days in duration with ganciclovir, valganciclovir, cidofovir, or foscarnet; and
3. Prescriber must verify the member does not have CMV disease involving the central nervous system including the retina (CMV retinitis); and
4. Prescriber must verify member will not receive concurrent treatment with ganciclovir and/or valganciclovir while taking Livtencity™; and
5. Prescriber must verify the member will be monitored for virologic failure during and after treatment with Livtencity™; and
6. Livtencity™ must be prescribed by an oncology, hematology, infectious disease, or transplant specialist (or advanced care practitioner with a supervising physician who is an oncology, hematology, infectious disease, or transplant specialist); and
7. Prescriber must verify Livtencity™ will not be used concomitantly with strong inducers of CYP3A4 (e.g., rifampin, rifabutin, St. John's wort) except carbamazepine, phenobarbital, or phenytoin. Use of carbamazepine, phenobarbital, or phenytoin concomitantly with Livtencity™ will require dose adjustment according to package labeling; and
8. Prescriber must agree to monitor drug concentrations of immunosuppressant drugs that are CYP3A4 and/or P-glycoprotein (P-gp) substrates (e.g., tacrolimus, cyclosporine, sirolimus, everolimus) throughout treatment with Livtencity™ and adjust the dose of immunosuppressant drug(s) as needed; and
9. Approvals will be for a maximum duration of 8 weeks, and a quantity limit of 112 tablets per 28 days will apply.

Recommendation 4: Vote to Prior Authorize Quviviq™ (Daridorexant) and Update the Approval Criteria for the Insomnia Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends following changes to the Insomnia Medications Product Based Prior Authorization (PBPA) category (changes noted in red in the following PBPA Tier chart and approval criteria):

1. Updating the approval criteria for Hetlioz® (tasimelteon capsules) based on the new FDA approved indication
2. The prior authorization of Hetlioz LQ™ (tasimelteon oral suspension) and placement into the Special Prior Authorization (PA) Tier of the Insomnia Medications PBPA Tier chart with the following additional criteria
3. The prior authorization of Quviviq™ (daridorexant) and placement into the Special PA category of the Insomnia Medications PBPA category

Insomnia Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA***
estazolam (ProSom®)	zolpidem CR (Ambien® CR)	lemborexant (Dayvigo®)	**daridorexant (Quviviq™)**
eszopiclone (Lunesta®)		suvorexant (Belsomra®)	doxepin (Silenor®)
flurazepam (Dalmane®)			tasimelteon (Hetlioz®, **Hetlioz LQ™**)+
ramelteon (Rozerem®) – **Brand Preferred**			temazepam (Restoril®) 7.5mg and 22.5mg
temazepam (Restoril®) 15mg and 30mg			zolpidem SL tablets (Edluar®)
triazolam (Halcion®)			zolpidem SL tablets (Intermezzo®)
zaleplon (Sonata®)			zolpidem oral spray (Zolpimist®)
zolpidem (Ambien®)			

CR = controlled release; PA = prior authorization; SL = sublingual
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Medications in the Special PA Tier, including unique dosage formulations, require a special reason for use in place of ~~Tier-1 formulations~~ lower-tiered medications.
+Individual criteria specific to tasimelteon applies.

Hetlioz® (Tasimelteon Capsule) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. ~~An FDA approved diagnosis of~~ Non-24-Hour Sleep-Wake Disorder (Non-24) confirmed by a sleep specialist; ~~and~~ or
   b. Nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) confirmed by a sleep specialist; and
2. Member must be 18 years of age or older for a diagnosis of Non-24 or 16 years of age or older for a diagnosis of SMS; and
3. Member must have a failed trial of appropriately timed doses of melatonin; and
4. Initial approvals will be for the duration of 12 weeks. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
5. A quantity limit of 30 capsules for 30 days will apply.

Hetlioz LQ™ (Tasimelteon Oral Suspension) Approval Criteria:

1. An FDA approved diagnosis of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) confirmed by a sleep specialist; and
2. Member must be 3 to 15 years of age; and
3. Member must have a failed trial of appropriately timed doses of melatonin; and

4. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to the Hetlioz LQ™ *Prescribing Information*; and
5. Initial approvals will be for the duration of 12 weeks. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication.

Recommendation 5: Vote to Prior Authorize Invega Hafyera™ (Paliperidone Palmitate Injection) and Update the Approval Criteria for the Atypical Antipsychotic Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Invega Hafyera™ (paliperidone palmitate IM injection) into Tier-1 of the Atypical Antipsychotic Medications Product Based Prior Authorization (PBPA) category based on net costs (changes noted in red):

Atypical Antipsychotic Medications*		
Tier-1	**Tier-2**	**Tier-3**
aripiprazole (Abilify®)¥	asenapine (Saphris®)	aripiprazole tablets with sensor (Abilify MyCite®)~
aripiprazole IM inj (Abilify Maintena®)	lurasidone (Latuda®)	asenapine transdermal system (Secuado®)+
aripiprazole lauroxil IM inj (Aristada®)		brexpiprazole (Rexulti®)
aripiprazole lauroxil IM inj (Aristada Initio®)		cariprazine (Vraylar®)
clozapine (Clozaril®)◊		clozapine ODT (Fazaclo®)+
olanzapine (Zyprexa®)		clozapine oral susp (Versacloz®)+
paliperidone palmitate IM inj (Invega Hafyera™)^		iloperidone (Fanapt®)
paliperidone palmitate IM inj (Invega Sustenna®)		lumateperone (Caplyta®)
paliperidone palmitate IM inj (Invega Trinza®)**		olanzapine/fluoxetine (Symbyax®)+
quetiapine (Seroquel®)		olanzapine/samidorphan (Lybalvi™)+
quetiapine ER (Seroquel XR®)		paliperidone (Invega®)
risperidone (Risperdal®)		
risperidone IM inj (Risperdal Consta®)		
risperidone ER sub-Q inj (Perseris®)		

Atypical Antipsychotic Medications*		
ziprasidone (Geodon®)		

*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). Placement of products shown in blue is based on net cost after federal and/or supplemental rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.
ER = extended-release; IM = intramuscular; inj = injection; ODT = orally disintegrating tablet; susp = suspension; sub-Q = subcutaneous
¥Aripiprazole (Abilify®) orally disintegrating tablet (ODT) is considered a special formulation and requires a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation.
◊Clozapine does not count towards a Tier-1 trial.
^Use of Invega Hafyera™ requires members to have been adequately treated with the 1-month paliperidone palmitate injection (Invega Sustenna®) for at least 4 months or the 3-month paliperidone palmitate injection (Invega Trinza®) for at least one 3-month cycle.
**Use of Invega Trinza® requires members to have been adequately treated with the 1-month paliperidone palmitate injection (Invega Sustenna®) for at least 4 months.
~Unique criteria applies to Abilify MyCite® (aripiprazole tablets with sensor).
+Unique criteria applies in addition to tier trial requirements.

Additionally, the College of Pharmacy recommends adding the following criteria to Lybalvi™ (olanzapine/samidorphan):

Lybalvi™ (Olanzapine/Samidorphan) Approval Criteria:

1. An FDA approved diagnosis; and
2. Member must be 18 years of age or older; and
3. Member must be stable on olanzapine for at least 14 days and be experiencing significant weight gain (baseline and current weight must be provided); or
4. A patient specific, clinically significant reason why the member cannot use a lower-tiered product with a lower weight gain profile must be provided; and
5. Member must not be taking opioids or undergoing acute opioid withdrawal; and
6. Initial approvals will be for 3 months. For continuation consideration, documentation that the member is responding well to treatment and has had no excessive weight gain while on therapy must be provided.

Recommendation 6: Vote to Prior Authorize Ryplazim® (Plasminogen, Human-tvmh)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ryplazim® (plasminogen, human-tvmh) with the following criteria:

Ryplazim® (Plasminogen, Human-tvmh) Approval Criteria:

1. An FDA approved indication of plasminogen deficiency type 1 (hypoplasminogenemia) as confirmed by at least 2 of the following:

a. Genetic testing confirming biallelic mutations in the plasminogen (*PLG*) gene; or
b. Plasminogen activity level ≤45%; or
c. Documentation of clinical symptoms and lesions consistent with plasminogen deficiency type 1 (e.g., ligneous conjunctivitis, ligneous gingivitis or gingival overgrowth, vision abnormalities, respiratory distress and/or obstruction, abnormal wound healing); and

2. Ryplazim® must be prescribed by, or in consultation with, a hematologist, pulmonologist, ophthalmologist, geneticist, or other specialist with expertise in the treatment of plasminogen deficiency (or an advanced care practitioner with a supervising physician who is a hematologist, pulmonologist, ophthalmologist, geneticist, or other specialist with expertise in the treatment of plasminogen deficiency); and
3. Prescriber must verify that members at high risk for bleeding and/or confirmed or suspected airway disease will be monitored by a health care provider for 4 hours after receiving the first dose; and
4. Documented vaccination history to hepatitis A and B must be provided or provider must verify member has received the first vaccine dose and is scheduled to receive the second vaccine dose; and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
6. Initial approvals will be for 6 months, after which time the prescriber must document improvement in clinical symptoms, partial or complete lesion resolution, and increased plasminogen activity level; and
7. Subsequent approvals will be for the duration of 1 year and will require documentation from the prescriber that member has not developed new or recurrent lesions while on Ryplazim® and that adequate plasminogen activity trough levels are being maintained.

Recommendation 7: Vote to Prior Authorize Citalopram Capsule, Dartisla ODT™ [Glycopyrrolate Orally Disintegrating Tablet (ODT)], Fleqsuvy™ (Baclofen Oral Suspension), Lofena™ (Diclofenac Potassium Tablet), Loreev XR™ [Lorazepam Extended-Release (ER) Capsule], Norliqva® (Amlodipine Oral Solution), Seglentis® (Celecoxib/Tramadol Tablet), Sutab® (Sodium Sulfate/Magnesium Sulfate/Potassium Chloride Tablet), Tarpeyo™ [Budesonide Delayed-Release (DR) Capsule], Vuity™ (Pilocarpine 1.25% Ophthalmic Solution), and Xipere® (Triamcinolone Acetonide Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of citalopram capsules into the Special Prior Authorization (PA) Tier of the Antidepressants Product Based Prior Authorization (PBPA) category with the following additional criteria:

Citalopram Capsule Approval Criteria:

1. An FDA approved indication of major depressive disorder (MDD) in adults; and
2. Member must have initiated treatment with citalopram tablets for dose titration up to the 30mg dose; and
3. A patient-specific, clinically significant reason why the member cannot use citalopram tablets, which are available without prior authorization, in place of the capsule formulation must be provided; and
4. Citalopram capsules will not be approved for members 60 years of age or older; and
5. A quantity limit of 30 capsules per 30 days will apply.

The College of Pharmacy recommends the placement of Dartisla ODT™ (glycopyrrolate ODT) into the Special PA Tier of the Anti-Ulcer Medications PBPA category with the following additional criteria:

Dartisla ODT™ [Glycopyrrolate Orally Disintegrating Tablet (ODT)] Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of peptic ulcer disease (PUD) in members 18 years of age and older; and
2. A patient-specific, clinically significant reason why the member cannot use glycopyrrolate 1mg and 2mg tablets, which are available without prior authorization, must be provided; and
3. A quantity limit of 120 ODTs per 30 days will apply.

The College of Pharmacy recommends adding Fleqsuvy™ (baclofen oral suspension) to the current Ozobax® (baclofen oral solution) prior authorization with the changes shown in red:

Fleqsuvy™ 25mg/5mL (Baclofen Oral Suspension) and Ozobax® 5mg/5mL (Baclofen Oral Solution) Approval Criteria:

1. An FDA approved indication of spasticity resulting from multiple sclerosis (relief of flexor spasms and concomitant pain, clonus, and muscular rigidity) or spinal cord injuries/diseases; and
2. Members older than 10 years of age require a patient-specific, clinically significant reason why the member cannot use baclofen oral tablets, even when tablets are crushed.

The College of Pharmacy recommends the placement of Lofena™ (diclofenac potassium tablet) into the Special PA Tier of the NSAIDs PBPA category with the following additional criteria (changes shown in red):

NSAIDs Special Prior Authorization (PA) Approval Criteria:

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

The College of Pharmacy recommends the prior authorization of Loreev XR™ (lorazepam ER capsule) with the following criteria:

Loreev XR™ [Lorazepam Extended-Release (ER) Capsule] Approval Criteria:

1. An FDA approved indication for the treatment of anxiety disorders; and
2. Member must be 18 years of age or older; and
3. Member must be receiving a stable, evenly divided, 3 times daily dosing regimen of lorazepam tablets; and
4. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use the immediate-release formulation must be provided; and
5. A quantity limit of 30 capsules per 30 days will apply.

The College of Pharmacy recommends the placement of Norliqva® (amlodipine oral solution) into the Special PA Tier of the Calcium Channel Blockers (CCBs) PBPA category with criteria similar to Katerzia® (amlodipine oral suspension) as follows (changes shown in red):

Katerzia® (Amlodipine Oral Suspension) and Norliqva® (Amlodipine Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Hypertension in adults and pediatric members 6 years of age and older; or
   b. Coronary artery disease; or
   c. Chronic stable angina; or
   d. Vasospastic angina; and

2. A patient specific, clinically significant reason the member cannot use amlodipine oral tablets even when the tablets are crushed must be provided; and
3. A quantity limit of 300mL per 30 days will apply.

The College of Pharmacy recommends the placement of Seglentis® (celecoxib/tramadol) into the Special PA Tier of the Opioid Analgesics PBPA category with the following additional criteria:

Seglentis® (Celecoxib 56mg/Tramadol 44mg) Approval Criteria:

1. An FDA approved indication of acute pain in adults that is severe enough to require an opioid analgesic; and
2. A patient-specific, clinically significant reason why the member cannot use any other opioid medication for treatment of acute pain must be provided; and
3. A patient-specific, clinically significant reason why the member cannot use celecoxib and tramadol individual products in place of Seglentis® must be provided; and
4. An age restriction will apply for members younger than 12 years of age. For members younger than 12 years of age, the provider must submit patient-specific, clinically significant information supporting the use of tramadol despite the medication being contraindicated for the member's age; and
5. A quantity limit of 28 tablets for a 7-day supply will apply.

The College of Pharmacy recommends the prior authorization of Sutab® (sodium sulfate/magnesium sulfate/potassium chloride tablet) with the following criteria:

Clenpiq®, ColPrep Kit®, OsmoPrep®, Plenvu®, Prepopik®, SUPREP®, and Sutab® Approval Criteria:

1. An FDA approved indication for use in cleansing of the colon as a preparation for colonoscopy; and
2. A patient-specific, clinically significant reason other than convenience why the member cannot use other bowel preparation medications available without prior authorization must be provided.
3. If the member requires a low volume polyethylene glycol electrolyte lavage solution, MoviPrep® is available without prior authorization. Other medications currently available without a prior authorization include: Colyte®, Gavilyte®, Golytely®, and Trilyte®.

The College of Pharmacy recommends the prior authorization of Tarpeyo™ (budesonide DR capsule) with the following criteria [changes shown in red indicate updates made based on guideline recommendations and Drug Utilization Review (DUR) Board recommendations]:

Tarpeyo™ [Budesonide Delayed Release (DR) Capsule] Approval Criteria:

1. An FDA approved indication to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression; and
2. The diagnosis of primary IgAN must be confirmed by the following:
    a. Kidney biopsy; and
    b. Secondary causes of IgAN have been ruled out (i.e., IgA vasculitis; IgAN secondary to virus, inflammatory bowel disease, autoimmune disease, or liver cirrhosis; IgA-dominant infection-related glomerulonephritis); and
3. Member must be 18 years of age or older; and
4. Must be prescribed by a nephrologist (or advanced care practitioner with a supervising physician who is a nephrologist); and
5. Member must ~~have a~~ be at risk of rapid disease progression as demonstrated by ≥1 of the following, despite maximal supportive care:
    a. Urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g; or
    b. Proteinuria >0.75g/day; and
6. Member must be on a stable dose of a maximally-tolerated angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB), unless contraindicated or intolerant; and
7. A patient-specific, clinically significant reason why ~~the member cannot use~~ a 6-month trial of an alternative formulation of budesonide DR oral capsules (e.g., Entocort® EC) or alternative oral corticosteroids ~~available without prior authorization~~ is not appropriate for the member must be provided; and
8. Approval duration will be for 9 months; and
9. A quantity limit of 120 capsules per 30 days will apply.

The College of Pharmacy recommends the prior authorization of Vuity™ (pilocarpine 1.25% ophthalmic solution) with the following criteria:

Vuity™ (Pilocarpine 1.25% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication of the treatment of presbyopia in adults; and
2. Must be prescribed by an ophthalmologist or optometrist; and
3. Prescriber must verify the member does not have iritis; and
4. Prescriber must verify the member has been counseled on the risk of retinal detachment with use of Vuity™ and when to seek immediate medical care; and
5. Prescriber must verify the member has been advised to use caution with night driving and hazardous occupations in poor illumination as vision may not be clear in these conditions while using Vuity™; and
6. A patient-specific, clinically significant reason the member cannot use corrective lenses must be provided; and

7. A patient-specific, clinically significant reason the member cannot use generic pilocarpine ophthalmic solution (Isopto® Carpine) must be provided.

The College of Pharmacy recommends the prior authorization of Xipere® (triamcinolone acetonide injection) with the following criteria:

Xipere® (Triamcinolone Acetonide Injection) Approval Criteria:

1. An FDA approved indication for the treatment of macular edema associated with non-infectious uveitis; and
2. Member must be 18 years of age or older; and
3. Xipere® must be administered by an ophthalmologist; and
4. Prescriber must confirm that the member does not have an active ocular or periocular infection; and
5. Prescriber must confirm member does not have untreated ocular hypertension or uncontrolled glaucoma; and
6. A patient-specific, clinically significant reason why the member cannot use corticosteroid ophthalmic preparations, such as solution or suspension, must be provided; and
7. A patient-specific, clinically significant reason the member cannot use Triesence® (triamcinolone acetonide injection) must be provided; and
8. Initial authorization will be for 12 weeks, with an additional dose approved at or after 12 weeks if the prescriber documents improvement from baseline in visual acuity.

Recommendation 8: Vote to Prior Authorize Camcevi™ (Leuprolide), Pluvicto™ (Lutetium Lu 177 Vipivotide Tetraxetan), Tivdak® (Tisotumab Vedotin-tftv), and Welireg™ (Belzutifan) and Update the Approval Criteria for the Genitourinary and Cervical/Endometrial Cancer Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Camcevi™ (leuprolide), Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan), Tivdak® (tisotumab vedotin-tftv), and Welireg™ (belzutifan) with the following criteria listed in red:

Camcevi™ (Leuprolide) Approval Criteria [Prostate Cancer Diagnosis]:

1. Diagnosis of advanced prostate cancer; and
2. A patient-specific, clinically significant reason why the member cannot use Eligard® (leuprolide acetate), Firmagon® (degarelix), and Lupron Depot® (leuprolide acetate) must be provided [reason(s) must address each medication].

Pluvicto® (Lutetium Lu 177 Vipivotide Tetraxetan) Approval Criteria [Prostate Cancer Diagnosis]:

1. Diagnosis of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC); and
2. Member must have been treated with androgen receptor pathway inhibition and taxane-based chemotherapy.

Tivdak® (Tisotumab Vedotin-tftv) Approval Criteria [Cervical Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic cervical cancer; and
2. Disease has progressed on or after chemotherapy.

Welireg™ (Belzutifan) Approval Criteria:

1. Diagnosis of von Hippel-Landau (VHL) disease; and
2. Diagnosis of either renal cell carcinoma, central nervous system hemangioblastomas, or pancreatic neuroendocrine tumor; and
3. Does not require immediate surgery.

Additionally, the College of Pharmacy recommends updating the Cabometyx® (cabozantinib) prior authorization criteria based on the recent FDA approval (changes noted in red):

Cabometyx® (Cabozantinib) Approval Criteria:

1. For cabozantinib monotherapy:
    a. Diagnosis of advanced renal cell carcinoma (RCC); or
    b. Diagnosis of advanced hepatocellular carcinoma (HCC); and
        i. Member has previously received sorafenib; or
    c. Diagnosis of locally advanced or metastatic differentiated thyroid cancer (DTC) in adults and pediatric members 12 years of age and older; and
        i. Disease has progressed following prior vascular endothelial growth factor (VEGF)-targeted therapy; and
        ii. Disease is radioactive iodine-refractory or member is ineligible for radioactive iodine; or
2. For cabozantinib in combination with nivolumab:
    a. Diagnosis of relapsed or surgically unresectable stage 4 disease in the initial treatment of members with advanced RCC; and
    b. Nivolumab, when used in combination with cabozantinib for RCC, will be approved for a maximum duration of 2 years.

Recommendation 9: Annual Review of Colorectal Cancer Medications and 30-Day Notice to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 10: Annual Review of Danyelza® (Naxitamab-gqgk), Koselugo® (Selumetinib), Pemazyre® (Pemigatinib), Qinlock® (Ripretinib), and Truseltiq® (Infigratinib)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Alzheimer's Disease Medications and 30-Day Notice to Prior Authorize Adlarity® (Donepezil Transdermal System) and Aduhelm® (Aducanumab-avwa)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 12: Annual Review of Testosterone Products and 30-Day Notice to Prior Authorize Tlando® (Testosterone Undecanoate)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 13: Annual Review of Various Systemic Antibiotics

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Isturisa® (Osilodrostat) and 30-Day Notice to Prior Authorize Recorlev® (Levoketoconazole)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

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

NO ACTION REQUIRED.

Recommendation 16: Future Business

No live DUR Board meeting is scheduled for August 2022. August 2022 will be a packet-only meeting.

NO ACTION REQUIRED.

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

Memorandum

Date: August 12, 2022

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 Packet Meeting on August 10, 2022

Recommendation 1: Use of Statins in Members with Diabetes Mellitus (DM)

NO ACTION REQUIRED.

Recommendation 2: 30-Day Notice to Prior Authorize Camzyos™ (Mavacamten)

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 3: Annual Review of Intravenous (IV) Iron Products

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Ophthalmic Anti-Inflammatory Products

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 5: Annual Review of Opioid Analgesics and Opioid Medication Assisted Treatment (MAT) Medications

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 6: Annual Review of Topical Corticosteroids

NO ACTION REQUIRED; WILL BE AN ACTION ITEM IN SEPTEMBER 2022.

Recommendation 7: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

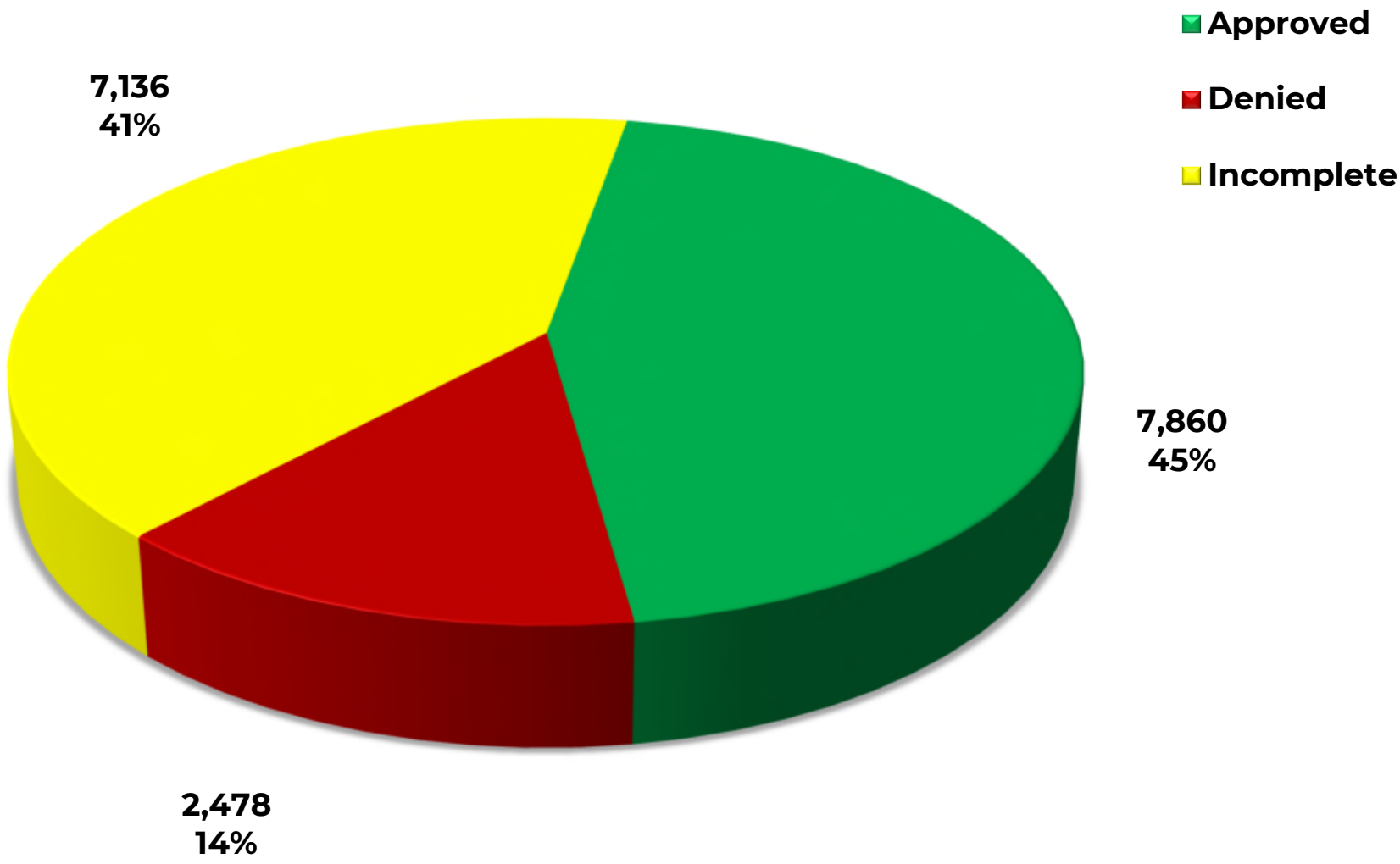
NO ACTION REQUIRED.

Recommendation 8: Future Business

NO ACTION REQUIRED.

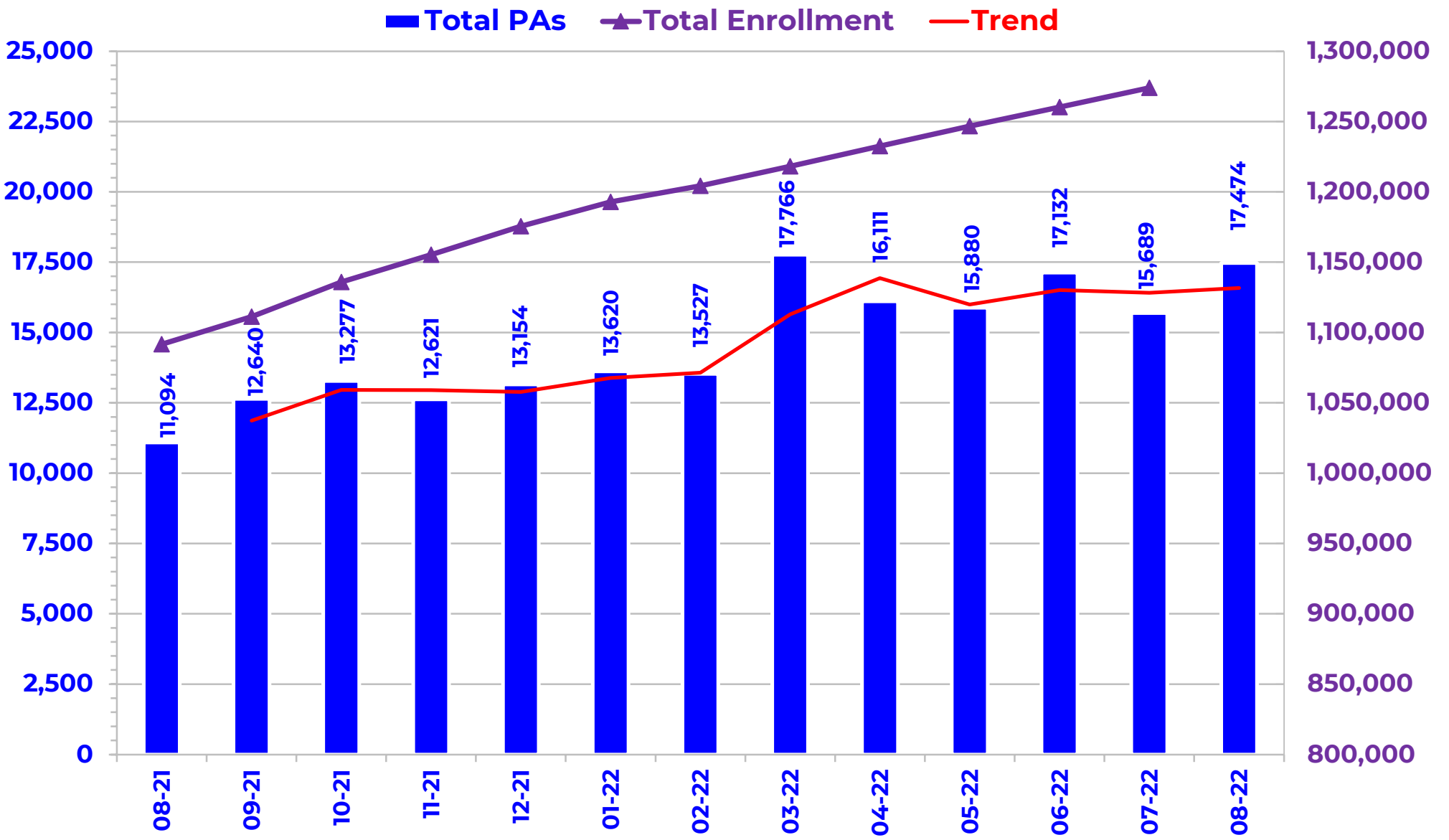
Appendix B

PRIOR AUTHORIZATION (PA) ACTIVITY REPORT: AUGUST 2022



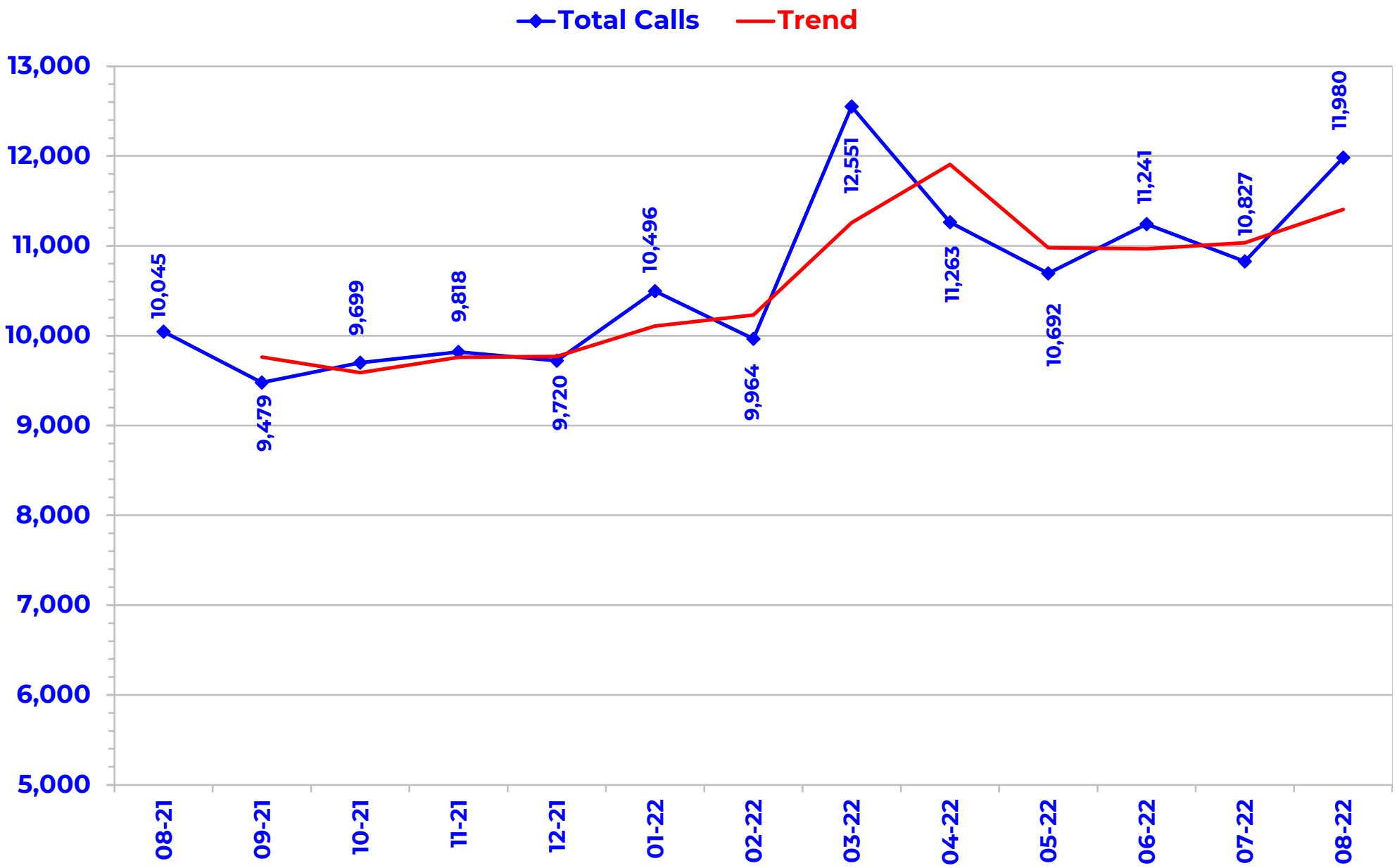
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION (PA) REPORT: AUGUST 2021 – AUGUST 2022



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
AUGUST 2021 – AUGUST 2022



Prior Authorization Activity

8/1/2022 Through 8/31/2022

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	101	26	8	67	353
Analgesic - NonNarcotic	37	1	6	30	179
Analgesic, Narcotic	442	149	45	248	150
Angiotensin Receptor Antagonist	18	2	3	13	360
Anorectal	17	1	10	6	35
Antiasthma	85	23	27	35	255
Antibiotic	63	31	1	31	258
Anticonvulsant	264	120	20	124	287
Antidepressant	447	89	68	290	334
Antidiabetic	1,683	669	313	701	354
Antifungal	25	2	7	16	24
Antigout	14	4	2	8	358
Antihemophilic Factor	25	20	0	5	234
Antihistamine	51	14	15	22	359
Antimalarial Agent	120	98	1	21	357
Antimigraine	744	110	263	371	248
Antineoplastic	290	195	11	84	176
Antiobesity	25	5	14	6	359
Antiparasitic	31	11	5	15	17
Antiparkinsons	15	0	7	8	0
Antiulcers	44	5	8	31	149
Anxiolytic	56	9	4	43	226
Atypical Antipsychotics	680	294	75	311	347
Benign Prostatic Hypertrophy	22	3	9	10	359
Biologics	359	196	37	126	236
Bladder Control	121	14	40	67	340
Blood Thinners	777	484	30	263	339
Botox	93	50	24	19	335
Buprenorphine Medications	148	63	16	69	82
Calcium Channel Blockers	28	10	5	13	199
Cardiovascular	132	46	27	59	340
Chronic Obstructive Pulmonary Disease	359	72	73	214	331
Constipation/Diarrhea Medications	296	58	83	155	234
Contraceptive	63	21	9	33	317
Corticosteroid	17	1	7	9	87
Dermatological	535	154	169	212	225
Diabetic Supplies	1,041	414	157	470	233
Endocrine & Metabolic Drugs	126	55	12	59	209
Erythropoietin Stimulating Agents	22	11	4	7	129

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Estrogen Derivative	16	2	5	9	359
Fibric Acid Derivatives	14	0	8	6	0
Fibromyalgia	20	2	4	14	357
Fish Oils	35	4	14	17	359
Gastrointestinal Agents	248	53	49	146	232
Genitourinary Agents	14	1	6	7	136
Glaucoma	21	2	3	16	51
Growth Hormones	103	77	8	18	152
Hematopoietic Agents	28	14	1	13	215
Hepatitis C	204	116	17	71	9
HFA Rescue Inhalers	22	0	1	21	0
Insomnia	140	14	33	93	205
Insulin	359	127	33	199	349
Miscellaneous Antibiotics	29	8	4	17	13
Multiple Sclerosis	119	51	17	51	193
Muscle Relaxant	71	8	20	43	57
Nasal Allergy	70	12	20	38	268
Neurological Agents	177	60	27	90	209
Neuromuscular Agents	10	8	1	1	270
Nsaids	54	2	9	43	360
Ocular Allergy	24	3	7	14	85
Ophthalmic	19	2	5	12	362
Ophthalmic Anti-infectives	35	13	3	19	17
Ophthalmic Corticosteroid	15	3	2	10	358
Osteoporosis	51	13	13	25	331
Other*	396	99	72	225	264
Otic Antibiotic	49	10	7	32	17
Pediculicide	23	4	2	17	16
Respiratory Agents	54	34	1	19	198
Statins	77	17	17	43	165
Stimulant	2,099	1,381	105	613	352
Synagis	67	35	17	15	21
Testosterone	252	70	62	120	350
Thyroid	25	11	5	9	283
Topical Antifungal	57	4	10	43	18
Topical Corticosteroids	85	9	41	35	151
Vitamin	158	20	73	65	114
Pharmacotherapy	89	76	0	13	258
Emergency PAs	0	0	0	0	
Total	**14,745**	**5,895**	**2,337**	**6,513**	

* 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	45	27	2	16	255
Compound	6	6	0	0	76
Diabetic Supplies	1	1	0	0	17
Dosage Change	484	443	1	40	15
High Dose	12	8	1	3	317
Ingredient Duplication	4	4	0	0	60
Lost/Broken Rx	142	133	3	6	19
MAT Override	323	254	10	59	72
NDC vs Age	414	259	50	105	235
NDC vs Sex	12	7	1	4	120
Nursing Home Issue	65	61	1	3	21
Opioid MME Limit	178	48	16	114	148
Opioid Quantity	55	38	3	14	154
Other	83	73	0	10	23
Quantity vs Days Supply	755	507	42	206	244
STBS/STBSM	11	8	1	2	121
Step Therapy Exception	24	15	3	6	357
Stolen	25	23	0	2	16
Third Brand Request	90	50	7	33	30
Overrides Total	**2,729**	**1,965**	**141**	**623**	
Total Regular PAs + Overrides	**17,474**	**7,860**	**2,478**	**7,136**	

Denial Reasons	
Unable to verify required trials.	6,006
Does not meet established criteria.	2,527
Lack required information to process request.	1,063
Other PA Activity	
Duplicate Requests	1,407
Letters	36,656
No Process	3
Changes to existing PAs	1,218
Helpdesk Initiated Prior Authorizations	1,304
PAs Missing Information	0

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

Nonalcoholic Fatty Liver Disease (NAFLD) Overview

Oklahoma Health Care Authority
September 2022

Introduction[1,2,3,4]

Nonalcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease and is closely associated with obesity, insulin resistance, type 2 diabetes mellitus (T2DM), hypertension (HTN), and atherogenic dyslipidemia. NAFLD occurs when there is evidence of hepatic steatosis on imaging or histology in the absence of secondary causes (e.g., significant alcohol consumption, chronic use of steatogenic medications, certain genetic disorders). NAFLD can be further classified as either nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis (NASH). NAFL is defined by hepatic steatosis present in ≥5% of hepatocytes without evidence of hepatocellular injury (e.g., hepatocyte ballooning). NASH is a more aggressive form of NAFLD defined by hepatic steatosis present in ≥5% of hepatocytes with the presence of inflammation and hepatocyte injury, with or without fibrosis. NASH can further progress to advanced liver fibrosis, cirrhosis, or hepatocellular carcinoma and is currently the second most common cause of hepatocellular carcinoma, after hepatitis C, among patients waiting for liver transplantation in the United States.

NAFLD is estimated to affect approximately 25% of people globally, of which 12-14% have NASH. The prevalence is even higher among patients with T2DM and obesity, with approximately 25-30% of obese people and 30-40% of people with T2DM having NASH. The prevalence of either form of NAFLD may be as high as 70% among people with T2DM. Despite this, fewer than 5% of patients with NAFLD are aware of their liver disease and many remain asymptomatic even with advanced liver disease related to NAFLD.

T2DM has been identified as a major driver of disease progression in NAFLD and may result in faster disease progression. Approximately one third of people with NAFLD will progress to NASH, 20% of whom will develop liver fibrosis and have a high risk of extrahepatic complications, cirrhosis, and liver failure. All stages of NAFLD are associated with an increased overall risk of mortality and the risk of mortality increases with increased severity of liver disease. Mortality in NAFLD is due primarily to extrahepatic cancer, cirrhosis, cardiovascular disease (CVD), and hepatocellular carcinoma.

Treatment of NAFLD involves treating the liver disease itself as well as the associated co-morbidities, including obesity, T2DM, HTN, and hyperlipidemia. There are currently no medications approved by the U.S. Food and Drug

Administration (FDA) for the treatment of NAFLD or NASH, but pioglitazone and vitamin E have been recommended for patients with biopsy-proven NASH in prior clinical guidelines. In May 2022, the American Association of Clinical Endocrinology (AACE) and American Association for the Study of Liver Diseases (AASLD) issued updated guidelines for the diagnosis and management of NAFLD in primary care and endocrinology clinical settings. Key recommendations from the guidelines for the management of adults with NAFLD include:

- Individuals with NAFLD should be managed for obesity, metabolic syndrome, prediabetes, diabetes mellitus, dyslipidemia, HTN, and CVD based on the current standards of care for those conditions (*Grade B; Intermediate/High Strength of Evidence*).
- Weight loss of ≥5% (and preferably ≥10%) is recommended, as more weight loss is associated with greater liver histologic and cardiometabolic benefit. Participation in a structured weight loss program is recommended, when possible, and should be tailored to individual lifestyles and personal preferences (*Grade B; Intermediate/ High Strength of Evidence*).
- Dietary modifications, including macronutrient content reductions to induce an energy deficit and adoption of healthier eating patterns, such as the Mediterranean diet, are recommended (*Grade A; Intermediate Strength of Evidence*).
- Pioglitazone and glucagon-like peptide-1 (GLP-1) receptor agonists are recommended for individuals with T2DM and biopsy-proven NASH or individuals with T2DM when there is elevated probability of NASH based on elevated plasma aminotransferase levels and noninvasive tests (*Grade A; High Strength of Evidence*).
- Metformin, acarbose, dipeptidyl peptidase-4 (DPP-4) inhibitors, and insulin are not recommended for the treatment of steatohepatitis but may be continued as needed for hyperglycemia in patients with T2DM and NAFLD or NASH (*Grade B; High Strength of Evidence*).
- Vitamin E can be considered for the treatment of NASH in patients without T2DM, but there is insufficient evidence to recommend its use in patients with T2DM or advanced cirrhosis (*Grade B; High Strength of Evidence*).
- Obesity pharmacotherapy is recommended as adjunctive therapy in patients with obesity and NAFLD or NASH to achieve weight loss of ≥5% (and preferably ≥10%) when not achieved by lifestyle modification alone (*Grade B; Intermediate Strength of Evidence*).
- Semaglutide 2.4mg/week or liraglutide 3mg/day are preferred for chronic weight management in patients with body mass index (BMI) ≥27kg/m^2 and NAFLD or NASH (*Grade B; High/Intermediate Strength of Evidence*).

Additionally, some key recommendations from the 2022 AACE/AASLD guidelines for the management of children with NAFLD include:

- Lifestyle changes are recommended to promote adoption of dietary changes to create an energy deficit, with reduction in sugar consumption as first-line lifestyle modifications and increased physical activity aiming for BMI optimization (*Grade B; Intermediate Strength of Evidence*).
- GLP-1 receptor agonists may be considered for the treatment of pediatric obesity and T2DM, which may also offer benefits for pediatric NAFLD, although not FDA-approved for this indication (*Grade D; Expert Opinion*).

SoonerCare Impact

The International Classification of Diseases, Tenth Revision (ICD-10) includes diagnosis codes K76.0 [Fatty (change of) liver, not elsewhere classified] for reporting NAFLD and K75.81 [Nonalcoholic steatohepatitis (NASH)] for reporting NASH. During fiscal year 2022 (07/01/2021 to 06/30/2022), there were 9,917 members with a reported diagnosis of NAFLD (using the K76.0 code), there were 1,022 members with a reported diagnosis of NASH, and there were 10,564 unique members with either diagnosis. Of the 9,917 members with a NAFLD diagnosis, 1,146 (11.56%) were younger than 21 years of age. Of the 1,022 members with a NASH diagnosis, 96 (9.39%) were younger than 21 years of age. Additionally, during fiscal year 2022, there were 33,051 unique members with paid claims for anti-diabetic medications, including insulin. Because T2DM has a significant impact on disease progression in NAFLD, the high prevalence of T2DM in Oklahoma suggests that the number of SoonerCare members with NAFLD or NASH is likely to increase.

Pipeline[5,6,7,8,9,10,11,12,13,14,15,16,17,18,19]

There is an active pipeline of candidate therapeutic agents for the treatment of NAFLD and NASH. These therapeutic candidates target a variety of mechanisms involved in the pathophysiology of NAFLD, including lipid carbohydrate metabolism, lipotoxicity and cell death, inflammation, and fibrosis. Some pipeline candidates in Phase 3 development for NAFLD include:

- **Aramchol:** Galmed Pharmaceuticals is developing aramchol for the treatment of NASH and fibrosis. Aramchol is a first-in-class, oral, synthetic small molecule conjugate of cholic acid and arachidic acid that modulates stearoyl-CoA desaturase 1 (SCD1), the rate-limiting step in the synthesis of monounsaturated fatty acids, which are the major fatty acid of triglycerides, cholesteryl esters, and membrane phospholipids. This results in a potentially beneficial effect on fibrosis by downregulating hepatic steatosis. A Phase 3 study in patients with

NASH and advanced fibrosis was initiated, but an open-label portion of the study has been discontinued and further plans for initiating the double-blinded portion of the study have not been announced.

- **Belapectin:** Galectin Therapeutics is developing belapectin for the treatment of advanced fibrosis or cirrhosis in NASH. Belapectin is a complex polymer of galacturonic acid, galactose, arabinose, rhamnose, and smaller amounts of other sugars. Belapectin binds to and inhibits galectin-3, which is a protein critical to the pathogenesis of NASH and fibrosis. The Phase 2b/3 NAVIGATE study was initiated in June 2020 and will evaluate the safety and efficacy of belapectin in adult patients with liver cirrhosis due to NASH, with the primary efficacy endpoint of preventing esophageal varices in these patients with advanced disease.
- **Cotadutide:** AstraZeneca is developing cotadutide, a dual GLP-1/glucagon receptor agonist, for the treatment of NASH with cirrhosis. Activation of GLP-1 receptors results in beneficial effects on food intake, insulin secretion, and weight loss. Activation of glucagon receptors results in increased energy expenditure and reduced lipid production in the liver. Preclinical models demonstrated reductions in steatosis and inflammation, reversed fibrosis, improved glucose control, decreased food intake, and induced weight loss with cotadutide. The Phase 2b/3 PROXYMO-ADV study is currently recruiting and will evaluate the efficacy and safety of cotadutide in adult patients with NASH and fibrosis.
- **Lanifibranor:** Inventiva is developing lanifibranor for the treatment of NASH. Lanifibranor is an oral small molecule agonist of peroxisome proliferator-activated receptor (PPAR) with the ability to activate all 3 isoforms of PPAR, including PPARα, PPARδ, and PPARγ, resulting in anti-fibrotic, anti-inflammatory, and beneficial metabolic changes in the body. The Phase 3 NaTiV3 study was initiated in September 2021 and will evaluate the safety and efficacy of lanifibranor in adults with biopsy-proven non-cirrhotic NASH and F2/F3 stage liver fibrosis, with the primary efficacy outcome being the resolution of NASH and improvement in fibrosis at week 72.
- **Obeticholic Acid:** Intercept Pharmaceuticals is developing obeticholic acid for 2 potential NASH-related indications: fibrosis due to NASH and compensated cirrhosis due to NASH. Obeticholic acid is an oral analog of the bile acid chenodeoxycholic acid which acts as an agonist of the farnesoid X receptor (FXR). FXR is a nuclear receptor expressed in the liver and intestines that regulates bile acid, inflammatory, fibrotic, and metabolic pathways. Obeticholic acid was previously approved by the FDA in 2016 for the treatment of primary biliary cholangitis. The Phase 3 REGENERATE study is evaluating the safety and efficacy of obeticholic acid in patients with liver fibrosis due to NASH. In June 2020, the FDA issued a Complete Response Letter (CRL) to Intercept regarding their

New Drug Application (NDA) for obeticholic acid for the treatment of fibrosis due to NASH. In July 2022, Intercept announced positive data from a new analysis from the REGENERATE study and stated they will be resubmitting the NDA for this indication by the end of 2022.

- **Resmetirom:** Madrigal Pharmaceuticals is developing resmetirom for the treatment of NASH. Resmetirom is an oral thyroid hormone receptor (THR) β-selective agonist. Resmetirom targets the underlying causes of NASH by reducing hepatic steatosis, inflammation, hepatocyte ballooning, and fibrosis. The Phase 3 MAESTRO-NASH and MAESTRO-NAFLD-1 studies are ongoing to evaluate the safety and efficacy of resmetirom both in patients with biopsy-proven NASH (in MAESTRO-NASH) and in patients with NAFLD with presumed NASH (in MAESTRO-NAFLD-1).
- **Semaglutide:** Novo Nordisk is developing semaglutide for the treatment of NASH. Semaglutide is a GLP-1 receptor agonist that was previously FDA approved in 2017 for the treatment of T2DM and in 2021 for obesity. The Phase 3 ESSENCE study is ongoing to evaluate the safety and efficacy of semaglutide for the treatment of adult patients with biopsy-proven NASH. The primary efficacy endpoints will evaluate the resolution of steatohepatitis (with no worsening of liver fibrosis) and improvement in fibrosis (with no worsening of steatohepatitis) through week 72 of treatment in part 1 of the study. In part 2 of the study, the primary efficacy endpoint will evaluate the time to first liver-related clinical event over 240 weeks of treatment.

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Appendix C

Vote to Update the Approval Criteria for the Ophthalmic Anti-Inflammatory Products

Oklahoma Health Care Authority
September 2022

Recommendations

The College of Pharmacy recommends making Durezol® (difluprednate 0.05%) brand preferred based on net costs (changes are shown in red in the following Tier chart):

Ophthalmic Corticosteroids	
Tier-1	**Tier-2**
dexamethasone 0.1% sus (Maxidex®)	fluorometholone 0.25% sus (FML Forte®)
dexamethasone sodium phosphate 0.1% sol	fluorometholone 0.1% oint (FML S.O.P®)
difluprednate 0.05% emu (Durezol®) **– Brand Preferred**	loteprednol 1% sus (Inveltys®)
fluorometholone 0.1% sus (Flarex®)	loteprednol 0.38% gel (Lotemax® SM)
fluorometholone 0.1% sus (FML Liquifilm®)	prednisolone acetate 1% sus (Pred Forte®)
loteprednol 0.5% gel, oint, sus (Lotemax®) – **Brand Preferred**	
prednisolone acetate 1% sus (Omnipred®)	
prednisolone acetate 0.12% sus (Pred Mild®)	
prednisolone sodium phosphate 1% sol	

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).
emu = emulsion; oint = ointment; sol = solution; sus = suspension

Ophthalmic Corticosteroids Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic corticosteroids (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication(s) to all lower-tiered medications; or
3. A unique indication for which the Tier-1 ophthalmic corticosteroids lack.

Appendix D

Vote to Prior Authorize Recorlev® (Levoketoconazole) and Update the Approval Criteria for Isturisa® (Osilodrostat)

Oklahoma Health Care Authority
September 2022

Market News and Updates[1]

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

- **December 2021:** The FDA approved Recorlev® (levoketoconazole) for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome (CS) for whom surgery is not an option or has not been curative. CS is a rare and serious endocrine disease caused by elevated cortisol level exposure often due to a benign tumor of the pituitary gland. This disease is most common in adults 30-50 years of age and affects women 3 times more than men. Metabolic changes such as diabetes, high blood pressure, high cholesterol, and psychological disturbances such as depression can occur in patients with CS. If untreated, the 5-year survival rate is approximately 50%. Recorlev® is a pure 2S, 4R enantiomer of ketoconazole and works by inhibiting cortisol synthesis. The approval of Recorlev® was based on 2 Phase 3 studies in 166 patients with CS. Both studies met their primary and key secondary endpoints which included reducing and normalizing mean urinary free cortisol concentrations without a dose increase and normalizing and maintaining therapeutic response compared to placebo.

Recorlev® (Levoketoconazole) Product Summary[2]

Indication(s): Treatment of endogenous hypercortisolemia in adult patients with CS for whom surgery is not an option or has not been curative

How Supplied: 150mg oral tablet

Dosing:

- The initial dosage is 150mg orally twice daily. Dosage may be titrated by 150mg daily, no more frequently than every 2-3 weeks.
- The maximum recommended dosage is 1,200mg daily, administered as 600mg [(4) 150mg tablets] twice daily.

Boxed Warning: Hepatotoxicity and QT Prolongation

- Hepatotoxicity:
  - Cases of hepatotoxicity with a fatal outcome or requiring liver transplantation have been reported with use of oral ketoconazole.
  - Liver enzymes should be evaluated prior to and during treatment.
- QT Prolongation:
  - Recorlev® is associated with a dose-related QT interval prolongation and may lead to life-threatening ventricular dysrhythmias.
  - A baseline electrocardiogram should be obtained prior to initiating therapy.
  - Hypokalemia and hypomagnesemia should be corrected prior to initiating therapy.

Warnings/Precautions:

- Hypocortisolism: Dosage reduction or interruption may be necessary if urine free cortisol or morning serum or plasma cortisol levels fall below the target range. Exogenous glucocorticoid replacement therapy should be administered if cortisol levels are below target range and signs and/or symptoms of adrenal insufficiency or hypocortisolism are present.
- Risks Related to Decreased Testosterone: Decreased testosterone may be seen in both men and women. Potential clinical manifestations of decreased testosterone concentrations in men may include gynecomastia, impotence, and oligospermia. Potential clinical manifestations of decreased testosterone in women include decreased libido and mood changes.

Mechanism of Action: Levoketoconazole inhibits key steps in the synthesis of cortisol and testosterone, principally mediated by CYP11B1, CYP11A1, and CYP17A1.

Contraindication(s):

- Cirrhosis, acute liver disease, or poorly controlled chronic liver disease, baseline AST or ALT >3 times the upper limit of normal (ULN), recurrent symptomatic cholelithiasis, a prior history of drug induced liver injury due to any azole antifungal therapy that required discontinuation of treatment, or extensive metastatic liver disease
- Taking drugs that cause QT prolongation associated with ventricular arrhythmias, including torsades de pointes
- Prolonged QTcF interval >470msec at baseline, history of torsades de pointes, ventricular tachycardia, ventricular fibrillation, or prolonged QT syndrome

- Taking certain drugs that are sensitive substrates of CYP3A4 and/or P-gp (e.g., ritonavir, mifepristone, isoniazid, carbamazepine, phenytoin)

Use in Specific Populations:

- Pregnancy: There is insufficient data to evaluate the drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproduction studies, embryotoxic effects were observed in pregnant mice, rats, and rabbits, and fetal malformations were observed in rats.
- Pediatric Use: The safety and efficacy of levoketoconazole have not been established in pediatric patients younger than 18 years of age.
- Geriatric Use: Of the 166 patients in the clinical studies, 12 patients (7%) were 65 years of age and older. There was an insufficient number of patients 65 years of age and older to determine whether they responded differently from younger adult patients.

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence >20%) were nausea/vomiting, hypokalemia, hemorrhage/ contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Year*
Recorlev® (levoketoconazole) 150mg tablet	**$270.00**	**$777,600.00**
Isturisa® (osilodrostat) 10mg tablet	$529.12	$1,142,899.20
Metopirone® (metyrapone) 250mg capsule	$40.26	$347,846.40
ketoconazole 200mg tablet	$0.78	$1,684.80

Costs do not reflect rebated prices or net costs.
Cost of therapy calculated based on wholesale acquisition cost (WAC).
Unit = tablet or capsule
*Cost per year based on maximum recommended dosage of 1,200mg per day for levoketoconazole and ketoconazole, 60mg per day for osilodrostat, and 6g per day for metyrapone.

Recommendations[3]

The College of Pharmacy recommends the prior authorization of Recorlev® (levoketoconazole) with the following criteria [changes shown in red indicate updates made based on Drug Utilization Review (DUR) Board recommendations and consistent with current treatment guidelines]:

Recorlev® (Levoketoconazole) Approval Criteria:

1. An FDA approved indication for the treatment of adult members with Cushing's disease for whom pituitary or adrenal surgery is not an option or has not been curative; and
2. Member must be 18 years of age or older; and
3. Recorlev® must be prescribed by, or in consultation with, an endocrinologist (or an advanced care practitioner with a supervising physician who is an endocrinologist); and
4. Prescriber must document that the member has had an inadequate response to pituitary or adrenal surgery or is not a candidate for pituitary or adrenal surgery; and
5. Prescriber agrees to obtain baseline liver test and electrocardiogram (ECG) prior to initiating treatment; and
6. Prescriber agrees to monitor liver enzymes and bilirubin weekly for at least 6 weeks after initiating treatment, every 2 weeks for the next 6 weeks, monthly for the next 3 months, and then as clinically indicated; and
7. Prescriber must verify that hypokalemia and hypomagnesemia are corrected prior to starting Recorlev®; and
8. Member must not be taking medications that cause QT prolongation associated with ventricular arrhythmias, including torsades de pointes (e.g., dofetilide, dronedarone, methadone, quinidine, ranolazine); and
9. Member must not be taking medications that are sensitive substrates of CYP3A4 and/or P-gp (e.g., digoxin, lovastatin, simvastatin, tacrolimus, triazolam); and
10. If the member is taking medications that are strong CYP3A4 inhibitors (e.g., ritonavir, mifepristone) or strong CYP3A4 inducers (e.g. isoniazid, carbamazepine, rifampicin, phenytoin), the prescriber must verify the medication will be stopped 2 weeks before and during treatment with Recorlev® per package labeling; and
11. For female members, prescriber must verify that the member is not breastfeeding; and
12. A patient-specific, clinically significant reason why the member cannot use ketoconazole tablets and metyrapone capsules must be provided; and
13. Initial authorizations will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide a recent 24-hour urine free cortisol (UFC) level within the normal range to demonstrate the effectiveness of this medication, and compliance will also be checked at that time. Subsequent approvals will be for the duration of 1 year and will require the prescriber to verify the member is still not a candidate for pituitary or adrenal surgery.

Additionally, the College of Pharmacy recommends updating the approval criteria for Isturisa® based on Drug Utilization Review (DUR) Board recommendations and consistent with current treatment guidelines (updates shown in red):

Isturisa® (Osilodrostat) Approval Criteria:

1. An FDA approved indication for the treatment of adult members with Cushing's disease for whom pituitary or adrenal surgery is not an option or has not been curative;
2. Member must be 18 years of age or older; and
3. Prescriber must document that the member has had an inadequate response to pituitary or adrenal surgery or is not a candidate for pituitary or adrenal surgery; and
4. Prescriber must verify that hypokalemia and hypomagnesemia are corrected prior to starting Isturisa®; and
5. Prescriber must agree to perform and monitor electrocardiogram (ECG) at baseline, 1 week after treatment initiation, and as clinically indicated thereafter; and
6. Prescriber must verify that dose titration will be followed according to package labeling; and
7. If the member is taking strong CYP3A4 inhibitors (e.g., itraconazole, clarithromycin) or strong CYP3A4 and/or CYP2B6 inducers (e.g., carbamazepine, rifampin, phenobarbital), the prescriber must verify that the Isturisa® dose will be adjusted according to the package labeling; and
8. For female members, prescriber must verify that the member is not breastfeeding; and
9. Isturisa® must be prescribed by, or in consultation with, an endocrinologist (or an advanced care practitioner with a supervising physician who is an endocrinologist); and
10. A patient-specific, clinically significant reason why the member cannot use ketoconazole tablets and metyrapone capsules must be provided; and
11. Initial authorizations will be for the duration of 3 months after which time, compliance and 24-hour urine free cortisol levels within the normal range (to demonstrate the effectiveness of this medication) will be required for continued approval. Subsequent approvals will be for the duration of 1 year and will require the prescriber to verify the member is still not a candidate for pituitary or adrenal surgery.

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[2] Recorlev® (Levoketoconazole) Prescribing Information. Xeris Pharmaceuticals. Available online at: https://www.recorlev.com/full-prescribing-information.pdf. Last revised 12/2021. Last accessed 08/29/2022.

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Appendix E

Vote to Prior Authorize Tlando® (Testosterone Undecanoate) and Update the Approval Criteria for the Testosterone Products

Oklahoma Health Care Authority
September 2022

Market News and Updates[1,2,3]

Product Discontinuation(s):

- Androgel® (testosterone topical gel 1.62% packet)
- Androgel® (testosterone topical gel 1% packet)

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

- **March 2022:** The FDA approved Tlando® (testosterone undecanoate), an oral testosterone replacement therapy, for conditions associated with a deficiency or absence of endogenous testosterone or hypogonadism in adult males. Tlando® is supplied as 112.5mg testosterone undecanoate oral capsules and is not substitutable with other oral testosterone undecanoate products. The recommended dosing is 225mg twice daily with food. The approval of Tlando® was based on data from a multicenter, open-label, single-arm Phase 3 study, which evaluated the efficacy and safety of Tlando® in 95 adult hypogonadal male patients. Patients received 225mg orally twice daily with food for approximately 24 days; no titration was performed to adjust the dosage. Results demonstrated that the trial met the primary endpoint with 80% (95% confidence interval: 72, 88) of patients achieving a 24-hour average serum testosterone concentration (Cavg0-24h) within the normal range of 300-1080ng/dL on the final visit of the study. The safety and efficacy of Tlando® in males younger than 18 years of age have not been established.

Cost Comparison

Product	Cost Per Unit	Cost Per Month*
Tlando® (testosterone undecanoate 112.5mg cap)	**$5.79**	**$694.80**
Jatenzo® (testosterone undecanoate 198mg cap)	$8.02	$962.40
testosterone cypionate 200mg/mL inj (Depo-Testosterone®)	$14.64	$58.56

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 30 days based on the maximum FDA recommended dosing for each product.
cap = capsule; inj = injection; Unit = mL or capsule

Recommendations

The College of Pharmacy recommends the following changes to the testosterone products Product Based Prior Authorization (PBPA) category based on new FDA approvals, product discontinuations, net costs, and recommendations from the Drug Utilization Review (DUR) Board (changes shown in red in the following Tier chart and approval criteria):

1. Placement of Tlando® (testosterone undecanoate) into the Special Prior Authorization (PA) Tier; and
2. Moving Androgel® (testosterone topical gel 1% packet and 1.62% packet) from Tier-1 to Tier-2; and
3. Moving Testim® (testosterone topical gel 1% tube) and Vogelxo® (testosterone topical gel 1% packet, 1% pump, and 1% tube) from Tier-2 to Tier-1; and
4. Updating the initial approval criteria for all testosterone products to verify evaluation of the member for a pituitary tumor as the potential cause of low testosterone prior to starting treatment with a testosterone product.

Testosterone Products		
Tier-1	**Tier-2**	**Special PA**
methyltestosterone powder	testosterone enanthate sub-Q auto-injector (Xyosted®)	fluoxymesterone oral tab (Androxy®)
testosterone cypionate IM inj (Depo-Testosterone®)	testosterone nasal gel (Natesto®)	methyltestosterone oral tab/cap (Android®, Methitest®, Testred®)
testosterone enanthate IM inj (Delatestryl®)	testosterone patch (Androderm®)	testosterone buccal tab (Striant®)
testosterone topical gel 1% (Testim®, Vogelxo®)	**testosterone topical gel 1%, 1.62% packet (Androgel®)**	testosterone pellets (Testopel®)
testosterone topical gel **1.62% pump** (Androgel® ~~**1%, 1.62%**~~) – **Brand Preferred**	testosterone topical gel **2% pump** (Fortesta®~~**, Testim®, Vogelxo®**~~)	testosterone undecanoate oral cap (Jatenzo®**, Tlando®)**
	testosterone topical solution (Axiron®)	
	testosterone undecanoate IM inj (Aveed®)	

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)
cap = capsule; IM = intramuscular; inj = injection; PA = prior authorization; sub-Q = subcutaneous; tab = tablet

Initial Approval Criteria for All Testosterone Products:

1. An FDA approved diagnosis of 1 of the following:
   a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome, or orchiectomy; or
   b. Idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation; or

    c. Delayed puberty; or
    d. Advanced inoperable metastatic mammary cancer in females 1 to 5 years postmenopausal, or premenopausal females with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and
2. The prescriber must verify the member has been evaluated for the presence of a pituitary tumor as the potential cause of low testosterone and the member will receive appropriate follow-up and/or treatment as necessary; and
3. Must include 2 labs showing pre-medication, morning testosterone (total testosterone) levels <300ng/dL; and
4. Must include 1 lab showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis; or
5. Testosterone and gonadotropin labs are not required for authorization of testosterone therapy if documentation is provided for established hypothalamic pituitary or gonadal disease, if the pituitary gland or testes has/have been removed, or for postmenopausal females with advanced inoperable metastatic mammary cancer or premenopausal females with breast cancer benefitting from oophorectomy and that have been determined to have a hormone-responsive tumor.

Testosterone Products Tier-2 Approval Criteria:

1. All diagnoses and laboratory requirements listed in the initial approval criteria for all testosterone products must be met; and
2. Member must have a trial of at least 2 Tier-1 products (must include at least 1 injectable and 1 topical formulation) at least 12 weeks in duration; or
3. A patient-specific, clinically significant reason why member cannot use all available Tier-1 products must be provided; or
4. Prior stabilization on a Tier-2 product (within the past 180 days); and
5. Approvals will be for the duration of 1 year; and
6. For Xyosted® [testosterone enanthate subcutaneous (sub-Q) auto-injector]:
    a. Member must be trained by a health care professional on sub-Q administration and storage of Xyosted® sub-Q auto-injector.

Testosterone Products Special Prior Authorization (PA) Approval Criteria:

1. All diagnoses and laboratory requirements listed in the initial approval criteria for all testosterone products must be met; and
2. A patient-specific, clinically significant reason why member cannot use all other available formulations of testosterone must be provided; and
3. Approvals will be for the duration of 1 year.

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 09/2022. Last Accessed 09/07/2022.
[2] Park B. FDA Approves Oral Testosterone Replacement Therapy Tlando®. *MPR*. Available online at: https://www.empr.com/home/news/fda-approves-oral-testosterone-replacement-therapy-tlando/. Issued 03/30/2022. Last accessed 08/25/2022.
[3] Tlando® Prescribing Information. Antares Pharma, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208088s000lbl.pdf. Last revised 03/2022. Last accessed 08/25/2022.

Appendix F

Vote to Update the Approval Criteria for the Opioid Analgesics and Medication-Assisted Treatment (MAT) Medications

Oklahoma Health Care Authority
September 2022

Market News and Updates[1,2]

News:

- **March 2020:** BioDelivery Sciences International, Inc., announced it was discontinuing Bunavail® in the United States. This was a marketing decision; Bunavail® was not discontinued due to side effects or lack of effectiveness. Given the competition with other similar drugs on the market, the company decided to concentrate on its other products instead.

Recommendations

The College of Pharmacy recommends the following changes to the Opioid Analgesics Product Based Prior Authorization (PBPA) category (changes noted in red in the following Tier chart and approval criteria; only criteria with changes are listed):

1. Moving hydrocodone/ibuprofen 10/200mg tablet (Ibudone®, Reprexain™) from Tier-1 to Tier-2 of the Short-Acting Opioid Analgesics category based on net cost

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting			
buprenorphine patch (Butrans®) – **Brand Preferred**	fentanyl patch (Duragesic®)	buprenorphine ER buccal film (Belbuca®)	oxycodone/APAP ER tab (Xartemis® XR)
oxycodone ER tab 10mg, 15mg, 20mg only (OxyContin®) – **Brand Preferred**	morphine ER tab (MS Contin®)	hydrocodone ER cap (Zohydro® ER)	oxymorphone ER tab
	oxycodone ER tab 30mg, 40mg, 60mg, 80mg (OxyContin®) – **Brand Preferred**	hydrocodone ER tab (Hysingla® ER)	tramadol ER cap (ConZip®)

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting			
	tramadol ER tab (Ultram ER®, Ryzolt®)	hydromorphone ER tab (Exalgo®)	
		methadone tab and oral soln (Dolophine®)	
		morphine ER cap (Avinza®, Kadian®)	
		morphine ER tab (Arymo™ ER)	
		morphine ER tab (MorphaBond™)	
		oxycodone ER cap (Xtampza® ER)	
		oxycodone/ naltrexone ER cap (Troxyca® ER)	
Short-Acting			
APAP/butalbital/ caff/codeine cap (Fioricet® with Codeine)	**hydrocodone/IBU tab 10/200mg (Ibudone®, Reprexain™)**	benzhydrocodone/ APAP tab (Apadaz®)	levorphanol tab
ASA/butalbital/caff/ codeine cap (Fiorinal® with Codeine)	oxymorphone IR tab (Opana®)	dihydrocodeine/ APAP/caff cap (Trezix®)	tramadol 100mg tab
codeine tab	tapentadol IR tab (Nucynta®)	hydrocodone/ APAP oral soln (Zamicet®, Liquicet®)	tramadol oral soln (Qdolo™)

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Short-Acting			
codeine/APAP tab (Tylenol® with Codeine)		hydrocodone/ APAP tab (Xodol®)	
dihydrocodeine/ ASA/caff cap (Synalgos-DC®)		oxycodone tab (Oxaydo®)	
hydrocodone/ APAP tab (Norco®)		oxycodone tab (RoxyBond™)	
hydrocodone/IBU tab **5/200mg, 7.5/200mg only** (Vicoprofen®, Ibudone®, Reprexain™)			
hydromorphone tab (Dilaudid®)			
morphine IR tab (MSIR®)			***Oncology Only:***
oxycodone/APAP tab (Percocet®)			fentanyl buccal film (Onsolis®)
oxycodone/ASA tab (Percodan®)			fentanyl buccal tab (Fentora®)
oxycodone IR cap (Oxy IR®)			fentanyl nasal spray (Lazanda®)
oxycodone IR tab (Roxicodone®)			fentanyl SL spray (Subsys®)
tramadol 50mg tab (Ultram®)			fentanyl SL tab (Abstral®)
tramadol/APAP tab (Ultracet®)			fentanyl transmucosal lozenge (Actiq®)

*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).
APAP = acetaminophen; ASA = aspirin; caff = caffeine; cap = capsule; ER = extended-release; IBU = ibuprofen; IR = immediate-release; PA = prior authorization; SL = sublingual; soln = solution; tab = tablet

Additionally, the College of Pharmacy recommends the following changes to the MAT medications approval criteria (changes noted in red in the following criteria; only criteria with changes are listed):

1. Removal of Bunavail® (buprenorphine/naloxone buccal film) based on product discontinuation

~~Bunavail® (Buprenorphine/Naloxone Buccal Film),~~ Suboxone® [Buprenorphine/Naloxone Sublingual (SL) Tablet and Film], Subutex® (Buprenorphine SL Tablet), and Zubsolv® (Buprenorphine/Naloxone SL Tablet) Approval Criteria:

1. Generic buprenorphine/naloxone SL tablet is the preferred product. Authorization consideration of ~~Bunavail®,~~ Suboxone® films (brand and generic)~~,~~ and Zubsolv® requires a patient-specific, clinically significant reason why generic buprenorphine/naloxone SL tablets are not appropriate.
2. Subutex® (buprenorphine) 2mg and 8mg SL tablets will only be approved if the member is pregnant or has a documented serious allergy or adverse reaction to naloxone; and
3. Buprenorphine products FDA approved for a diagnosis of opioid abuse/dependence must be prescribed by a licensed practitioner who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
4. Member must have an FDA approved diagnosis of opioid abuse/dependence; and
5. Concomitant treatment with opioid analgesics (including tramadol) will be denied; and
6. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
7. The following limitations will apply:
    a. Suboxone® 2mg/0.5mg and 4mg/1mg SL tablets and films: A quantity limit of 90 SL units per 30 days will apply.
    b. Suboxone® 8mg/2mg SL tablets and films: A quantity limit of 60 SL units per 30 days will apply.
    c. Suboxone® 12mg/3mg SL films: A quantity limit of 30 SL films per 30 days will apply.
    d. Subutex® 2mg SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.
    e. Subutex® 8mg SL tablets: A quantity limit of 60 SL tablets per 30 days will apply.
    f. Zubsolv® 0.7mg/0.18mg, 1.4mg/0.36mg, and 2.9mg/0.71mg SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.

g. Zubsolv® 5.7mg/1.4mg SL tablets: A quantity limit of 60 SL tablets per 30 days will apply.
h. Zubsolv® 8.6mg/2.1mg and 11.4mg/2.9mg SL tablets: A quantity limit of 30 SL tablets per 30 days will apply.
~~i. Bunavail® 2.1mg/0.3mg buccal films: A quantity limit of 90 buccal films per 30 days will apply.~~
~~j. Bunavail® 4.2mg/0.7mg buccal films: A quantity limit of 60 buccal films per 30 days will apply.~~
~~k. Bunavail® 6.3mg/1mg buccal films: A quantity limit of 30 buccal films per 30 days will apply.~~

[1] Choa S. Why was Bunavail® Discontinued? *Drugs.com*. Available online at: https://www.drugs.com/medical-answers/bunavail-discontinued-3558339/#:~:text=The%20drug%20company%20that%20made,on%20its%20other%20products%20instead. Last revised 05/27/2021. Last accessed 08/10/2022.
[2] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 08/2022. Last accessed 08/10/2022.

Appendix G

Vote to Prior Authorize Adlarity® (Donepezil Transdermal System) and Aduhelm® (Aducanumab-avwa)

Oklahoma Health Care Authority
September 2022

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

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

- **June 2021:** The FDA approved Aduhelm® (aducanumab-avwa) for the treatment of Alzheimer's disease through the accelerated approval pathway. Aduhelm® is the first new treatment approved for Alzheimer's disease since 2003 and the first therapy that targets the fundamental pathophysiology of the disease by reducing amyloid beta plaques in the brain. The efficacy of Aduhelm® was evaluated in 3 Phase 3 clinical studies, EMERGE (study 1), ENGAGE (study 2), and PRIME (study 3), in patients with early stages of Alzheimer's disease (mild cognitive impairment and mild dementia) with confirmed presence of amyloid pathology. In these studies, Aduhelm® consistently showed a dose- and time-dependent effect on the lowering of amyloid beta plaques [by 59% (P<0.0001) in ENGAGE, 71% (P<0.0001) in EMERGE, and 61% (P<0.0001) in PRIME]. Continued approval for Aduhelm® may be contingent upon verification of clinical benefit in confirmatory studies.
- **March 2022:** The FDA approved Adlarity® (donepezil transdermal system) as a treatment for patients with mild, moderate, or severe dementia of the Alzheimer's type. This is the first and only once-weekly patch of donepezil. It uses Corium's proprietary CORPLEX transdermal technology that was developed to deliver continuous, controlled, and sustained release of a drug over a defined time. Adlarity® was approved through the FDA 505(b)(2) regulatory pathway and was shown to have bioequivalence to donepezil tablets. It will be supplied as a 5mg/day and 10mg/day patch and should be applied to the patient's back, thigh, or buttocks. Adlarity® is expected to be available in early fall 2022.

News:

- **March 2022:** New data released by Biogen showed that long-term treatment with Aduhelm® continues to reduce the underlying pathologies of Alzheimer's disease after more than 2 years of treatment. Patients receiving Aduhelm® in the long-term extension phase of 2 Phase 3 studies (ENGAGE and EMERGE) continued to experience significant reductions in amyloid beta plaque levels (P<0.001) out to

week 132 and plasma p-tau181 levels (P<0.001) out to week 128. In both studies, at 78 weeks, patients with a reduction in plasma p-tau181, an exploratory endpoint, had less clinical progression across all 4 clinical endpoints measuring cognition and function than patients whose plasma p-tau181 levels were not reduced. Biogen started screening patients in May 2022 for the Phase 4 confirmatory study with the primary readout of data expected 4 years later.

Aduhelm® (Aducanumab-avwa) Product Summary[5]

Indication(s): An amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical studies

- Continued approval for this indication is contingent upon verification of clinical benefit in confirmatory studies.

How Supplied: 170mg/1.7mL and 300mg/3mL solution in a single dose vial

Dosing and Administration:

- The presence of amyloid beta pathology should be confirmed prior to initiating treatment.
- A recent (within 1 year) magnetic resonance imaging (MRI) should be obtained prior to treatment initiation.
- The recommended maintenance dosage is 10mg/kg via intravenous (IV) infusion over 1 hour every 4 weeks following a dose titration.
- An MRI should be obtained prior to the 5th, 7th, 9th, and 12th infusions. If amyloid-related imaging abnormalities (ARIA) occur, treatment recommendations are based on type, severity, and presence of symptoms.
- Refer to the full Aduhelm® *Prescribing Information* for the recommended dose titration and recommendations for patients with occurrence of ARIA.

Mechanism of Action: Aducanumab-avwa is a human, immunoglobulin gamma (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta and thereby reduces amyloid beta plaques in the brain. The accumulation of amyloid beta plaques is a defining pathophysiological feature of Alzheimer's disease.

Contraindication(s): None

Warnings and Precautions:

- ARIA: Enhanced clinical vigilance for ARIA should be performed during the first 8 doses of treatment with Aduhelm®, particularly during titration. If a patient experiences symptoms which could be suggestive

of ARIA, clinical evaluation should be performed, including MRI testing if indicated.

- Hypersensitivity Reactions: Angioedema and urticaria have occurred. If a hypersensitivity reaction occurs, the infusion of Aduhelm® should be discontinued and appropriate therapy should be initiated.

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence ≥10%) were ARIA-edema (ARIA-E), headache, ARIA-hemosiderin deposition (ARIA-H) microhemorrhage, ARIA-H superficial siderosis, and fall.

Efficacy: The efficacy of Aduhelm® was evaluated in 3 double-blind, randomized, placebo-controlled studies in patients with Alzheimer's disease confirmed by the presence of amyloid pathology and mild cognitive impairment or mild dementia stage of disease. In studies 1 and 2, patients were randomized to receive Aduhelm® low dose [3 or 6mg/kg for apolipoprotein E (ApoE) 4 carriers and noncarriers, respectively], Aduhelm® high dose (10mg/kg), or placebo every 4 weeks for 18 months, followed by an optional, dose-blind, long-term extension period. In study 3, 197 patients were randomized to receive a fixed dose of Aduhelm® 1mg/kg, 3mg/kg, 6mg/kg, 10mg/kg, titration to 10mg/kg over 44 weeks, or placebo for 12 months.

- **Study 1:**
  - Primary Endpoint: The primary efficacy endpoint was the change from baseline on the Clinical Dementia Rating-Sum of Boxes (CDR-SB) at week 78. Additionally, sub-studies were conducted to assess the reduction of amyloid beta plaques biomarkers.
  - Results: Treatment with Aduhelm® high dose reduced clinical decline, as shown by a statistically significant treatment effect on change from baseline in CDR-SB compared to placebo [-0.39 (-22%), P=0.0120]. Differences from placebo observed in the low dose group numerically favored Aduhelm® but were not statistically significant. Biomarker results for Aduhelm® showed a significant dose- and time-dependent reduction of amyloid beta plaques [-60.8 (-71%), P<0.0001].
- **Study 2:**
  - Primary Endpoint: The primary efficacy endpoint was the change from baseline on the CDR-SB at week 78. Additionally, sub-studies were conducted to assess the reduction of amyloid beta plaques biomarkers.
  - Results: No statistically significant differences were seen between Aduhelm®-treated and placebo-treated patients on the primary efficacy endpoint. Biomarker results for Aduhelm® showed a statistically significant dose- and time-dependent reduction of amyloid beta plaques [-54.0 (-59%), P<0.0001].

- **Study 3:**
  - Primary Endpoint: The primary outcome was the number of patients with adverse effects from baseline to week 518 and to evaluate the safety and tolerability of multiple doses. A key exploratory endpoint was the measure of clinical decline on the CDR-SB and Mini-Mental State Examination (MMSE) scores.
  - Results: Results for clinical assessments were exploratory and directionally aligned with the findings from study 1, with less change from baseline in CDR-SB and MMSE scores at 1 year in the Aduhelm® 10mg/kg fixed-dose group than in patients on placebo [CDR-SB: -1.26, 95% confidence interval (CI): -2.356, -0.163; MMSE: 1.9, 95% CI: 0.06, 3.75]. The most common adverse events seen in the long-term extension study were fall, headache, and ARIA. The majority of ARIA events occurred early during treatment and were typically mild, asymptomatic, and resolved or stabilized within 4-12 weeks, with most patients continuing treatment.

Cost: The Wholesale Acquisition Cost (WAC) of Aduhelm® is $282 per mL, or $846 per 300mg/3mL single dose vial. A member weighing 80kg would have an annual cost of $32,994 at the recommended dosage of 10mg/kg every 4 weeks.

Recommendations

The College of Pharmacy recommends the prior authorization of Adlarity® (donepezil transdermal system) as a special formulation product. The following criteria will apply:

Alzheimer's Disease Medications Approval Criteria:

1. Special formulation products including oral solutions, transdermal patches, and other convenience formulations require prior authorization with the following approval criteria:
   a. A patient-specific, clinically significant reason why the special formulation is necessary in place of the standard formulation.

Additionally, the College of Pharmacy recommends the prior authorization of Aduhelm® (aducanumab-avwa) with the following criteria:

Aduhelm® (Aducanumab-avwa) Approval Criteria:

1. An FDA approved diagnosis of mild cognitive impairment or mild dementia stage of Alzheimer's disease [stage 3 or stage 4 Alzheimer's disease based on the Global Deterioration Scale (GDS)]. Diagnosis must be confirmed by at least 2 of the following:
   a. Mini-Mental State Exam (MMSE) score between 24 and 30; or
   b. Clinical Dementia Rating Global Score (CDR-GS) equal to 0.5; or
   c. Montreal Cognitive Assessment (MoCA) score ≥19; or

   d. Quick Dementia Rating System (QDRS) score ≤5; and
2. Member must have presence of amyloid pathology confirmed by a positive amyloid positron emission tomography (PET) scan or cerebral spinal fluid (CSF) test; and
3. Aduhelm® must be prescribed by, or in consultation with, a neurologist (or an advanced care practitioner with a supervising physician who is a neurologist); and
4. Other known medical or neurological causes of dementia have been ruled out (i.e., vascular dementia, dementia with Lewy bodies, frontotemporal dementia, Parkinson's disease dementia); and
5. Member must not have brain hemorrhage, bleeding disorder, or cerebrovascular abnormalities that increase the risk of hemorrhage; and
6. Member must not be taking anticoagulant or antiplatelet agents except for aspirin 325mg per day or less; and
7. Member must not have had a stroke or transient ischemic attack (TIA) or unexplained loss of consciousness in the past year; and
8. Member must not have any contraindications to brain magnetic resonance imaging (MRI) or PET scans; and
9. Member must not have any pre-treatment localized superficial siderosis, ≥10 brain microhemorrhages, or a brain hemorrhage >1cm within 1 year of treatment initiation as safety with Aduhelm® has not been established in patients with these conditions; and
10. Member must have a recent (within 1 year) brain MRI prior to initiating treatment with Aduhelm® and prior to the 7th infusion (1st dose of 10mg/kg) and 12th infusion (6th dose of 10mg/kg); and
11. The prescriber must confirm that the member will be monitored for amyloid-related imaging abnormalities (ARIA) during the first 8 doses of treatment with Aduhelm®, particularly during titration, and also throughout treatment; and
12. If ≥10 new incident microhemorrhages or >2 focal areas of superficial siderosis [radiographic severe amyloid related imaging abnormalities-hemosiderin deposition (ARIA-H)] are observed on MRI, prescriber must confirm that treatment will be continued with caution and only after a clinical evaluation and a follow-up MRI demonstrating radiographic stabilization (i.e., no increase in size or number of ARIA-H); and
13. Aduhelm® must be administered by a health care provider; and
14. Aduhelm® must be shipped via cold chain supply shipping and stored in a refrigerator; and
15. Member's weight must be provided and have been taken within the last 4 weeks to ensure accurate weight-based dosing; and
16. Initial approvals will be for 6 months. Confirmation that MRI has been completed and is acceptable to the provider prior to 7th infusion is required for continuation; and

17. Subsequent approvals will be for 6 months and prescriber must document that the member has responded well to therapy compared to pretreatment baseline status as evidenced by improvement, stability, or slowing in cognitive and/or functional impairment using the same baseline test(s) performed at initiation of therapy; and
18. Approval quantities will be dependent on the member's weight and dosing based on the Aduhelm® *Prescribing Information*; and
19. The maximum dose approvable is 10mg/kg per 28 days.

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[1] U.S. Food and Drug Administration (FDA). FDA Grants Accelerated Approval for Alzheimer's Drug. Available online at: https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug. Issued 06/07/2021. Last accessed 08/02/2022.
[2] Biogen. FDA Grants Accelerated Approval for Aduhelm® as the First and Only Alzheimer's Disease Treatment to Address a Defining Pathology of the Disease. Available online at: https://investors.biogen.com/news-releases/news-release-details/fda-grants-accelerated-approval-aduhelmtm-first-and-only. Issued 06/07/2021. Last accessed 08/02/2022.
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[4] Brauser D. Aducanumab Reduces Amyloid Plaques in Early Alzheimer's: PRIME Published. *Medscape*. Available online at: https://www.medscape.com/viewarticle/868438#vp_2. Issued 09/06/2016. Last accessed 08/02/2022.
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Appendix H

Vote to Update the Approval Criteria for the Topical Corticosteroids

Oklahoma Health Care Authority
September 2022

Recommendations

The College of Pharmacy recommends the following changes to the topical corticosteroids Product Based Prior Authorization (PBPA) Tier chart based on net costs (changes shown in red in the following Tier chart):

1. Ultra-High to High Potency:
    a. Augmented betamethasone 0.05% gel from Tier-1 to Tier-2; and
    b. Augmented betamethasone 0.05% ointment from Tier-2 to Tier-1; and
    c. Betamethasone dipropionate 0.05% cream and ointment from Tier-2 to Tier-1; and
    d. Clobetasol propionate 0.05% lotion from Tier-1 to Tier-2; and
    e. Desoximetasone 0.25% cream and ointment from Tier-3 to Tier-1; and
    f. Fluocinonide 0.1% cream from Tier-2 to Tier-1; and
    g. Halobetasol 0.05% ointment from Tier-2 to Tier-1.
2. Medium-High to Medium Potency:
    a. Betamethasone valerate 0.1% lotion from Tier-1 to Tier-2; and
    b. Desoximetasone 0.05% cream and ointment from Tier-2 to Tier-3.
3. Low Potency:
    a. Alclometasone 0.05% ointment from Tier-2 to Tier-3.
    b. Desonate® (desonide 0.05%) gel from Tier-1 to Tier-3; and
    c. Desonide emollient 0.05% cream and ointment from Tier-3 to Tier-1; and
    d. Fluocinolone 0.01% solution from Tier-2 to Tier-1; and
    e. Fluocinolone 0.01% oil from Tier-3 to Tier-2.

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% (**Diprolene®,** Diprolene AF®)	C,~~G,~~**O**	amcinonide 0.1%	C,L	clobetasol propionate 0.05% (Clobex®)	Sh,Spr

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
betamethasone dipropionate 0.05% (Diprosone®)	**C,O**	augmented betamethasone dipropionate 0.05% (Diprolene®, **Diprolene AF®**)	**G**,L,~~**O**~~	clobetasol propionate 0.05% (Olux®, Olux-E®, Tovet®)	F
~~**clobetasol propionate 0.05% (Clobex®)**~~	~~**L**~~	~~**betamethasone dipropionate 0.05% (Diprosone®)**~~	~~**C,O**~~	clobetasol propionate 0.05% (Impeklo™)	L
clobetasol propionate 0.05% (Temovate®)	C,O,So	**clobetasol propionate 0.05% (Clobex®)**	**L**	desoximetasone 0.25% (Topicort®)	~~**C,O**~~,Spr
desoximetasone 0.25% (Topicort®)	**C,O**	clobetasol propionate 0.05% (Temovate®)	G	diflorasone diacetate 0.05% (Apexicon®)	C,O
fluocinonide 0.05%	C,O,So	desoximetasone 0.05% (Topicort®)	G	diflorasone diacetate 0.05% (Apexicon E®)	C
fluocinonide 0.1% (Vanos®)	**C**	fluocinonide 0.05%	G	halobetasol propionate 0.01% (Bryhali®)	L
halobetasol propionate 0.05% (Ultravate®)	C,**O**	~~**fluocinonide 0.1% (Vanos®)**~~	~~**C**~~	halobetasol propionate 0.05% (Lexette®)	F
		flurandrenolide tape 0.05% (Cordran®)	Tape		
		halcinonide 0.1% (Halog®)	C,O,So		
		halobetasol propionate 0.05% (Ultravate®)	L,~~**O**~~		
Medium-High to Medium Potency					
betamethasone dipropionate 0.05%	L	betamethasone dipropionate/ calcipotriene 0.064%/ 0.005% (Taclonex®)	O,Spr, Sus	**desoximetasone 0.05% (Topicort LP®)**	**C,O**
betamethasone valerate 0.1% (Beta-Val®)	C,~~**L**~~,O	betamethasone valerate 0.12% (Luxiq®)	F	hydrocortisone valerate 0.2% (Westcort®)	C,O
fluticasone propionate 0.005% (Cutivate®)	O	**betamethasone valerate 0.1% (Beta-Val®)**	**L**		
fluticasone propionate 0.05% (Cutivate®)	C	calcipotriene/ betamethasone dipropionate 0.064%/0.005% (Enstilar®)	F		

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
mometasone furoate 0.1% (Elocon®)	C,L,O, So	clocortolone pivalate 0.1% (Cloderm®)	C		
triamcinolone acetonide 0.025%	O	~~**desoximetasone 0.05% (Topicort LP®)**~~	~~**C,O**~~		
triamcinolone acetonide 0.1%	C,L,O	fluocinolone acetonide 0.025% (Synalar®)	C,O		
triamcinolone acetonide 0.5%	C,O	fluocinonide emollient 0.05% (Lidex E®)	C		
		flurandrenolide 0.05%	C,LO		
		fluticasone propionate 0.05% (Cutivate®)	L		
		hydrocortisone butyrate 0.1%	C,L,O, So		
		hydrocortisone probutate 0.1% (Pandel®)	C		
		prednicarbate 0.1% (Dermatop®)	C,O		
		triamcinolone acetonide 0.147mg/g (Kenalog®)	Spr		
Low Potency					
~~**desonide 0.05% (Desonate®)**~~	~~**G**~~	alclometasone dipropionate 0.05% (Aclovate®)	C,~~**O**~~	**alclometasone dipropionate 0.05% (Aclovate®)**	**O**
desonide emollient 0.05%	**C,O**	fluocinolone acetonide 0.01% (Synalar®)	C,~~**So**~~	~~**fluocinolone acetonide 0.01% (Derma-Smoothe®; Derma-Smoothe FS®)**~~	~~**Oil**~~
fluocinolone acetonide 0.01% (Capex®)	Sh	**fluocinolone acetonide 0.01% (Derma-Smoothe®; Derma-Smoothe FS®)**	**Oil**	desonide 0.05%	L
fluocinolone acetonide 0.01% (Synalar®)	**So**	hydrocortisone 2.5% (Texacort®)	So	~~**desonide emollient 0.05%**~~	~~**C,O**~~
hydrocortisone acetate 1%	C,O	hydrocortisone/ pramoxine 1%/1% (Pramosone®)	C,L	**desonide 0.05% (Desonate®)**	**G**

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
hydrocortisone acetate 2.5%	C,L,O				

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).
C = cream; F = foam; G = gel; L= lotion; O = ointment; Sh = shampoo; So = solution; Spr = spray; Sus = suspension

Topical Corticosteroids Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief; and
2. If Tier-1 trials are completed and do not yield adequate relief, the member must also provide a patient-specific, clinically significant reason for requesting a Tier-2 in the same potency instead of trying a higher potency; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (foams, shampoos, sprays, kits, etc.); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over standard formulations.

Topical Corticosteroids Tier-3 Approval Criteria:

1. Documented trials of all Tier-1 and Tier-2 topical corticosteroids of similar potency in the past 90 days that did not yield adequate relief; and
2. If Tier-1 and Tier-2 trials are completed and do not yield adequate relief, the member must also provide a patient-specific, clinically significant reason for requesting a Tier-3 in the same potency instead of trying a higher potency; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-3 (foams, shampoos, sprays, kits, etc.); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Appendix I

Vote to Prior Authorize Camzyos™ (Mavacamten)

Oklahoma Health Care Authority
September 2022

Market News and Updates[1,2]

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

- **April 2022:** The FDA approved Camzyos™ (mavacamten) to treat adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms. HCM is the most common form of genetic heart disease and is most often caused by abnormal genes in the heart muscle that cause the walls of the heart chamber to become thicker than normal. The most common form is obstructive HCM, where the thickened walls block or reduce the blood flow from the left ventricle to the aorta. It is estimated that 1 in every 500 people have HCM, but most are undiagnosed; of those diagnosed, about two-thirds of patients have obstructive HCM. The current treatment for obstructive HCM is dependent on the patient's severity of symptoms and is focused on symptom relief and prevention of sudden cardiac death. First-line therapies typically consist of beta blockers and nondihydropyridine calcium channel blockers; however, these current pharmacological options only provide symptomatic relief and do not target the underlying pathophysiology of HCM. Camzyos™ is the first FDA approved cardiac myosin inhibitor that targets the underlying pathophysiology of obstructive HCM.

Camzyos™ (Mavacamten) Product Summary[3]

Indication(s): A cardiac myosin inhibitor indicated for the treatment of adults with symptomatic NYHA class II-III obstructive HCM to improve functional capacity and symptoms

How Supplied: 2.5mg, 5mg, 10mg, and 15mg oral capsules

Dosing and Administration:

- Dosage should be individualized based on clinical status and echocardiogram assessment of patient response.
- The recommended starting dose is 5mg once daily without regard to food.
- Regular left ventricular ejection fraction (LVEF) and Valsalva left ventricular outflow tract (LVOT) gradient assessment should be performed for careful titration of mavacamten.

- Refer to the full *Prescribing Information* for the recommended initiation and maintenance dosing algorithm.

Boxed Warning: Risk of Heart Failure

- Mavacamten can cause heart failure due to systolic dysfunction.
  - Echocardiogram assessments of LVEF are required before and during use.
  - Initiation in patients with LVEF <55% is not recommended.
  - Treatment should be interrupted if LVEF is <50% or if worsening clinical status occurs.
- Concomitant use of mavacamten with certain cytochrome P450 inhibitors or discontinuation of certain cytochrome P450 inducers may increase the risk of heart failure due to systolic dysfunction; therefore, the use of mavacamten is contraindicated with the following:
  - Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors
  - Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers
- Mavacamten is only available through the Risk Evaluation and Mitigation Strategy (REMS) program.

Warnings and Precautions:

- Heart Failure: Mavacamten reduces systolic contraction and can cause heart failure or totally block ventricular function. Patients who experience a serious intercurrent illness (e.g., serious infection) or arrhythmia (e.g., atrial fibrillation or other uncontrolled tachyarrhythmia) are at greater risk of developing systolic dysfunction and heart failure. Interruption of mavacamten should be considered in patients with serious infections or arrhythmias.
- Drug Interactions Leading to Heart Failure or Loss of Effectiveness: Patients should be advised of potential drug interactions including over-the-counter medications (e.g., omeprazole, esomeprazole, cimetidine, St. John's wort).
- Embryo-Fetal Toxicity: Females of reproductive potential should be advised to use effective contraception until 4 months after the last dose. A contraceptive not affected by CYP450 enzyme induction [e.g., intrauterine device (IUD)] or nonhormonal contraception should be used.

Mechanism of Action: Mavacamten is an allosteric and reversible inhibitor selective for cardiac myosin. It modulates the number of myosin heads that can enter "on actin" (power-generating) states, thus reducing the probability of force-producing (systolic) and residual (diastolic) cross-bridge formation. Excess myosin actin cross-bridge formation and dysregulation of the super-relaxed state are mechanistic hallmarks of HCM. Mavacamten shifts the

overall myosin population towards an energy-sparing, recruitable, super-relaxed state. In HCM patients, myosin inhibition with mavacamten reduces dynamic LVOT obstruction and improves cardiac filling pressures.

Contraindication(s):

- Moderate to strong CYP2C19 (e.g., proton pump inhibitors, clopidogrel, voriconazole, fluvoxamine) or strong CYP3A4 (e.g., itraconazole, ketoconazole, ritonavir) inhibitors
- Moderate to strong CYP2C19 (e.g., rifampicin, carbamazepine) or CYP3A4 (e.g., rifampin, carbamazepine, phenytoin) inducers

Use in Specific Populations:

- Pregnancy: Based on animal data, mavacamten may cause fetal harm when administered to a pregnant female. There is no human data on the use of mavacamten during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.
- Lactation: The presence of mavacamten in human or animal milk, the drug's effects on the breastfed infant, and the effects on milk production are unknown.
- Females and Males of Reproductive Potential: Mavacamten may cause fetal harm when administered to a pregnant female. Absence of pregnancy should be confirmed in females of reproductive potential prior to initiation. Females of reproductive potential should use effective contraception during treatment and for 4 months after the last dose.
- Pediatric Use: The safety and effectiveness of mavacamten have not been established in pediatric patients.
- Geriatric Use: Clinical trials of mavacamten included 263 patients 65 years of age and older. Safety, effectiveness, and pharmacokinetics were similar between elderly patients and younger patients.

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence >5%) were dizziness and syncope.

Efficacy: The approval of mavacamten was based on a Phase 3, double-blind, randomized study in 251 adults. Patients were randomized 1:1 to receive either mavacamten 5mg or placebo once daily for 30 weeks. All patients were initiated on 5mg once daily of mavacamten or placebo and the dose was adjusted periodically to optimize patient response and maintain LVEF ≥50%.

- Primary Endpoint: The primary composite functional endpoint was defined as the proportion of patients who achieved either improvement of peak oxygen consumption (pVO2) by ≥1.5mL/kg/min plus improvement in NYHA class by at least 1 class or improvement of pVO2 by ≥3.0 mL/kg/min plus no worsening in NYHA class.

- Results: A greater proportion of patients met the primary endpoint at week 30 in the mavacamten group compared to the placebo group [37% vs. 17%, respectively; difference of 19% (95% confidence interval: 9, 30; P=0.0005)].

Cost: The Wholesale Acquisition Cost (WAC) of Camzyos™ is $245.21 per capsule regardless of strength, resulting in an annual cost of $88,275.60 for the recommended dosage of 1 capsule once daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Camzyos™ (mavacamten) with the following criteria:

Camzyos™ (Mavacamten) Approval Criteria:

1. An FDA approved diagnosis of obstructive hypertrophic cardiomyopathy (HCM); and
2. Member must be 18 years of age or older; and
3. Member must have New York Heart Association (NYHA) class II to III heart failure; and
4. Camzyos™ must be prescribed by, or in consultation with, a cardiologist (or an advanced care practitioner with a supervising physician who is a cardiologist); and
5. Member must have left ventricular ejection fraction (LVEF) ≥55%; and
6. Member must be on current treatment with or have a documented failure, contraindication, or intolerance to beta blockers or nondihydropyridine calcium channel blockers; and
7. Member must not be taking concurrent moderate to strong CYP2C19 inhibitors (e.g., proton pump inhibitors, clopidogrel, voriconazole, fluvoxamine), strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, ritonavir), moderate to strong CYP2C19 inducers (e.g., rifampicin, carbamazepine), or moderate to strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin); and
8. Member must not be taking or planning to take disopyramide, ranolazine, or a combination of a beta blocker and a calcium channel blocker concomitantly with Camzyos™; and
9. Female members of reproductive potential must have a negative pregnancy test prior to initiation of therapy and must agree to use effective contraception during treatment and for 4 months after the final dose of Camzyos™; and
10. Prescriber, pharmacy, and member must be enrolled in the Camzyos™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; 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; and
12. Subsequent approvals will be for the duration of 1 year.

[1] Bristol Myers Squibb. U.S. Food and Drug Administration Approves Camzyos™ (Mavacamten) for the Treatment of Adults With Symptomatic New York Heart Association Class II-III Obstructive Hypertrophic Cardiomyopathy (HCM) to Improve Functional Capacity and Symptoms. Available online at: https://news.bms.com/news/corporate-financial/2022/U.S.-Food-and-Drug-Administration-Approves-Camzyos-mavacamten-for-the-Treatment-of-Adults-With-Symptomatic-New-York-Heart-Association-Class-II-III-ObstructiveHypertrophic-Cardiomyopathy-HCM-to-Improve-Functional-Capacity-and-Symptoms/default.aspx. Issued 04/28/2022. Last accessed 08/04/2022.
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Appendix J

Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications

Oklahoma Health Care Authority
September 2022

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

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

- **April 2017:** The FDA approved Stivarga® (regorafenib) for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with the drug sorafenib. Stivarga® was first FDA approved in 2012 and is also indicated to treat colorectal cancer (CRC) and gastrointestinal stromal tumors (GIST) that are no longer responding to previous treatments.
- **August 2017:** The FDA approved Opdivo® (nivolumab) for the treatment of adult and pediatric patients 12 years of age and older with microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. Approval for this indication was granted under accelerated approval based on overall response rate (ORR) and duration of response (DOR). In 2018, the combination of Opdivo® and Yervoy® (ipilimumab) was granted an expanded indication for the treatment of adult and pediatric patients 12 years of age and older with MSI-H or dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- **February 2019:** The FDA approved Lonsurf® (trifluridine/tipiracil tablets) for the treatment of adults with metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma previously treated with at least 2 prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, human epidermal receptor type 2 (HER2)/neu-targeted therapy. This approval expands the indication for Lonsurf® which includes the treatment of adults with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, anti-vascular endothelial growth factor (VEGF) biological therapy, and if RAS wild-type, an anti-epidermal growth factor receptor (EGFR) therapy. Lonsurf® was originally FDA approved in 2015.

- **June 2020:** The FDA approved Keytruda® (pembrolizumab) for the treatment of unresectable or metastatic MSI-H or dMMR CRC based on improved progression-free survival (PFS) in the frontline setting.
- **April 2022:** The FDA approved Alymsys® (bevacizumab-maly), a biosimilar to Avastin® (bevacizumab). The approval was based on data demonstrating the biosimilar product and the reference product were highly similar, and there were no clinically meaningful differences between the agents. Alymsys® is a VEGF inhibitor indicated for the treatment of mCRC; unresectable, locally advanced, recurrent, or metastatic non-squamous non-small cell lung cancer (NSCLC); recurrent glioblastoma in adults; metastatic renal cell carcinoma (RCC); persistent, recurrent, or metastatic cervical cancer; and epithelial ovarian, fallopian tube, or primary peritoneal cancer. Alymsys® is not indicated for the adjuvant treatment of colon cancer.
- **May 2022:** The FDA approved Opdivo® (nivolumab) in combination with fluoropyrimidine- and platinum-based chemotherapy or in combination with ipilimumab for the first-line treatment of patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC).

Guideline Update(s):

- **February 2022:** The National Comprehensive Caner Network (NCCN) Guidelines for colon cancer recommend the use of Herceptin® (trastuzumab) or its biosimilars in combination with Perjeta® (pertuzumab) or Tykerb® (lapatinib) for use in colon cancer patients with HER2/neu amplified disease who do not have BRAF or RAS mutations. The combination regimens produced a 30% objective response rate in this patient population. Additionally, Enhertu® (fam-trastuzumab deruxtecan-nxki) is now recommended in patients with HER2/ neu positive and BRAF/RAS wild-type disease in the second-line setting. Median PFS in patients with strong HER2/neu expressing tumors was 6.9 months and overall survival (OS) has not yet been reached.

Product Summaries[9,10,11]

Alymsys® (Bevacizumab-maly):

- **Therapeutic Class:** VEGF inhibitor, biosimilar to Avastin® (bevacizumab)
- **Indication(s):**
  - mCRC:
    - In combination with intravenous (IV) fluorouracil-based chemotherapy for first- or second-line treatment
    - In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-

line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen
    - Unresectable locally advanced, recurrent, or metastatic non-squamous NSCLC, in combination with carboplatin and paclitaxel for first-line treatment
    - Recurrent glioblastoma in adults
    - Metastatic RCC in combination with interferon alfa
    - Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and either cisplatin or topotecan
    - Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
    - Limitation(s) of Use: Alymsys® is not indicated for the adjuvant treatment of colon cancer.
- **How Supplied:** 100mg/4mL (25mg/mL) or 400mg/16mL (25mg/mL) sterile solution for IV infusion in single-dose vials
- **Dose:** 5mg/kg to 15mg/kg every 2 to 3 weeks based on diagnosis (see Alymsys® *Prescribing Information* for diagnosis-dependent dosing regimens)
- **Cost:** The Wholesale Acquisition Cost (WAC) is $179.65 per mL, resulting in a monthly cost of $11,497.60 and annual cost of $149,468.80 based on the recommended dosing of 10mg/kg every 2 weeks for the treatment of mCRC for an 80kg adult.

Lonsurf® (Trifluridine/Tipiracil):
- **Therapeutic Class:** Combination nucleoside metabolic inhibitor and thymidine phosphorylase inhibitor
- **Indication(s):**
    - mCRC previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy
    - GEJ adenocarcinoma previously treated with at least 2 prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy
- **How Supplied:** 15mg/6.14mg and 20mg/8.19mg trifluridine/tipiracil oral tablets
- **Dose:** 35mg/m^2 per dose twice daily up to a maximum of 80mg per dose (based on the trifluridine component) on days 1 through 5 and days 8 through 12 of each 28-day cycle
- **Cost:** The WAC is $250.67 per 20mg/8.19mg trifluridine/tipiracil tablet resulting in a monthly cost of $20,053.60 and an annual cost of $260,696.80 based on the maximum recommended dosing.

Stivarga® (Regorafenib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - mCRC previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and if RAS wild-type, an anti-EGFR therapy
  - Locally advanced unresectable or metastatic GIST previously treated with imatinib mesylate and sunitinib malate
  - HCC previously treated with sorafenib
- **How Supplied:** 40mg oral tablet
- **Dose:** 160mg [(4) 40mg tablets] once daily for the first 21 days of each 28-day cycle
- **Cost:** The WAC is $243.48 per tablet resulting in a monthly cost of $20,452.32 and an annual cost of $265,880.16 based on the recommended dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Alymsys® (bevacizumab-maly), Lonsurf® (trifluridine/tipiracil), and Stivarga® (regorafenib) with the following criteria (new criteria and updates listed in red):

Alymsys® (Bevacizumab-maly) and Mvasi® (Bevacizumab-awwb) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Avastin® (bevacizumab) or Zirabev® (bevacizumab-bvzr), which are available without prior authorization, 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.

Lonsurf® (Trifluridine/Tipiracil) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]:

1. Diagnosis of metastatic, recurrent, or unresectable CRC; and
2. Previously treated with a fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; and
3. Previously treated with an anti-vascular endothelial growth factor (VEGF) therapy; and
   a. If RAS wild-type disease, previously treated with an anti-epidermal growth factor receptor (EGFR) therapy; and
4. Used as monotherapy or in combination with bevacizumab.

Lonsurf® (Trifluridine/Tipiracil) Approval Criteria [Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma Diagnosis]:

1. Diagnosis of metastatic gastric or GEJ adenocarcinoma; and
2. Previously treated with at least 2 prior lines of chemotherapy that included a fluoropyrimidine, a platinum, paclitaxel, docetaxel, or irinotecan; and
3. If human epidermal receptor type 2 (HER2) positive disease, prior treatment should have included HER2 targeted therapy.

Stivarga® (Regorafenib) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]:

1. Diagnosis of metastatic, recurrent, or unresectable CRC; and
2. Previous treatment with a fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; and
3. Previous treatment with an anti-vascular endothelial growth factor (VEGF) therapy; and
    a. If RAS wild-type disease, previously treated with an anti-epidermal growth factor receptor (EGFR) therapy.

Stivarga® (Regorafenib) Approval Criteria [Gastrointestinal Stromal Tumor (GIST) Diagnosis]:

1. Diagnosis of locally advanced unresectable or metastatic GIST; and
2. Previously treated with imatinib and sunitinib.

Stivarga® (Regorafenib) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Diagnosis of HCC; and
2. Previous treatment with sorafenib.

Additionally, the College of Pharmacy recommends updating the Enhertu® (fam-trastuzumab deruxtecan-nxki), Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), Kanjinti® (trastuzumab-anns), Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), Trazimera® (trastuzumab-qyyp), Keytruda® (pembrolizumab), Opdivo® (nivolumab), Perjeta® (pertuzumab), and Yervoy® (ipilimumab) prior authorization criteria based on FDA approvals, NCCN guideline recommendations, and net costs (changes noted in red):

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

1. Diagnosis of advanced or metastatic disease; and
2. Disease has progressed on prior therapy; and
3. Human epidermal receptor type 2 (HER2) amplified disease; and
4. RAS and BRAF mutation negative; and
5. Used as a single agent.

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

1. Diagnosis of human epidermal receptor type 2 (HER2)-positive CRC; and
2. RAS and BRAF mutation negative; and
3. Used in combination with ~~trastuzumab~~ pertuzumab or lapatinib; and
4. Used in 1 of the following settings:
    a. If first-line therapy, member should not be a candidate for intensive therapy; or
    b. For the treatment of advanced or metastatic disease following disease progression; and
5. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), ~~or~~ Kanjinti® (trastuzumab-anns), or Ogivri® (trastuzumab-dkst) will also require a patient-specific, clinically significant reason why the member cannot use ~~Ogivri® (trastuzumab-dkst),~~ Ontruzant® (trastuzumab-dttb)~~,~~ or Trazimera® (trastuzumab-qyyp). Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

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

1. Diagnosis of unresectable or metastatic CRC; and
2. ~~First-line treatment; and~~
3. Tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

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

1. Diagnosis of unresectable advanced or metastatic ESCC; and
    a. Used in the first-line setting; and
    b. Used in combination with 1 of the following:
        i. Fluoropyrimidine- and platinum-based chemotherapy; or
        ii. Ipilimumab; 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. Used in first-line setting; and
            1. Used in combination with oxaliplatin and fluorouracil or capecitabine; and
            2. Adenocarcinoma pathology; or
        ii. Used in the second-line or greater setting; and
            1. As a single agent; and
            2. Squamous cell pathology.

Opdivo® (Nivolumab) Approval Criteria [~~Metastatic~~ Colorectal Cancer (~~m~~CRC) Diagnosis]:

1. Diagnosis of unresectable or metastatic CRC; and
2. ~~Disease has progressed on treatment with 5-fluorouracil (5-FU), oxaliplatin, and irinotecan; and~~
3. Tumor is microsatellite-instability high (MSI-H) or mismatch repair deficient (dMMR).~~; and~~
4. ~~Used as a single agent or in combination with ipilimumab.~~

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

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

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

1. Diagnosis of human epidermal receptor type 2 (HER2)-positive CRC; and
2. RAS and BRAF mutation negative; and
3. Used in combination with trastuzumab; and
4. Used in 1 of the following settings:
    a. If first-line therapy, member should not be a candidate for intensive therapy; or
    b. For the treatment of advanced or metastatic disease following disease progression.

Yervoy® (Ipilimumab) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]:

1. Diagnosis of unresectable or metastatic CRC; and

~~2. Disease has progressed on treatment with 5-fluorouracil (5-FU), oxaliplatin, and irinotecan; and~~

3. Tumor is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
4. Used in combination with nivolumab.

Yervoy® (Ipilimumab) Approval Criteria [Esophageal Squamous Cell Carcinoma (ESCC) Diagnosis]:

1. Diagnosis of unresectable advanced or metastatic ESCC; and
   a. Used in the first-line setting; and
   b. Used in combination with nivolumab.

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Appendix K

Fiscal Year 2022 Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators

Oklahoma Health Care Authority
September 2022

Current Prior Authorization Criteria

Kalydeco® (Ivacaftor) Approval Criteria:

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

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene; and
3. Orkambi® will not be approved for members with CF other than those homozygous for the *F508del* mutation; and
4. Member must be 2 years of age or older; and
5. Members using Orkambi® must be supervised by a pulmonary disease specialist; and

6. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi®, every 3 months during the first year of treatment, and annually thereafter; and
7. Member must not be taking any of the following medications concomitantly with Orkambi®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
8. A quantity limit of 4 tablets per day or 112 tablets per 28 days will apply or a quantity limit of 2 granule packets per day or 56 packets per 28 days will apply; and
9. An age restriction of 2 years to younger than 6 years of age will apply to Orkambi® oral granule packets. Members 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
10. Initial approvals will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance, and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation or who have at least 1 mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 6 years of age or older; and
4. Members using Symdeko® must be supervised by a pulmonary disease specialist; and
5. If the member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) and experiencing adverse effects associated with Orkambi® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify the member has been counseled on proper administration of Symdeko® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter; and

8. Member must not be taking any of the following medications concomitantly with Symdeko®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
9. A quantity limit of 2 tablets per day or 56 tablets per 28 days will apply; and
10. Initial approvals will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance, and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally, after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events must be provided for members who switched from Orkambi® to Symdeko®.

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

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene or a mutation in the *CFTR* gene that is responsive based on *in vitro* data; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 6 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary disease specialist; and
5. If the member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify the member has been counseled on proper administration of Trikafta® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify the member does not have severe hepatic impairment; and
9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and

10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
11. For members 6 to 11 years of age, the member's recent weight must be provided on the prior authorization request in order to authorize the appropriate dose according to package labeling, as follows:
    a. Members 6 to 11 years of age weighing <30kg will be approved for Trikafta® (elexacaftor 50mg/tezacaftor 25mg/ivacaftor 37.5mg and ivacaftor 75mg) upon meeting approval criteria; or
    b. Members 6 to 11 years of age weighing ≥30kg and members 12 years of age and older will be approved for Trikafta® (elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg and ivacaftor 150mg) upon meeting approval criteria; and
12. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
13. Initial approvals will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance, and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally, after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events than with a previous CFTR therapy must be provided for members who switched from Orkambi® or Symdeko® to Trikafta®.

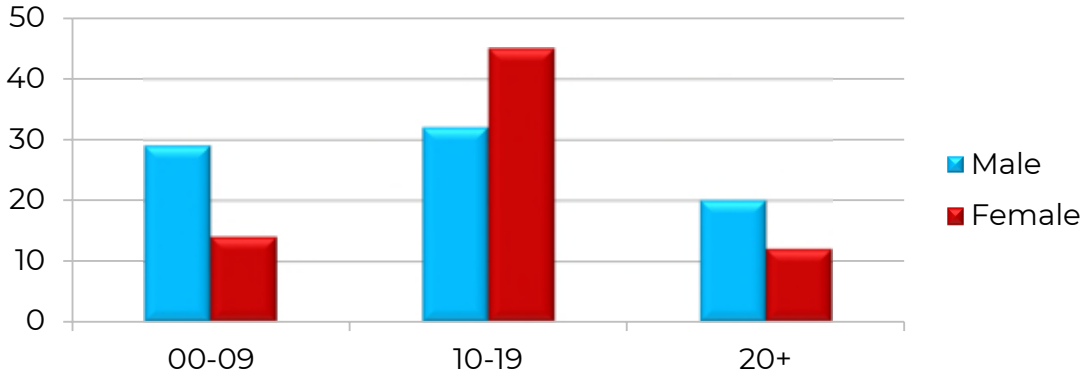
Utilization of CFTR Modulators: Fiscal Year 2022

Comparison of Fiscal Years

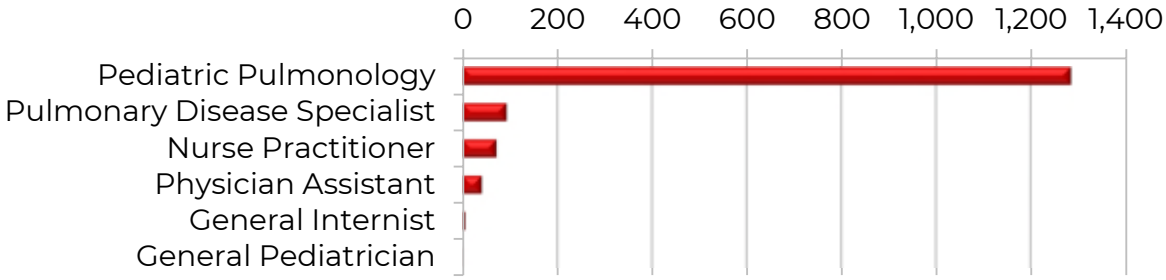
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2021	132	1,182	$26,612,806.14	$22,515.06	$804.11	88,060	33,096
2022	152	1,500	$34,769,675.50	$23,179.78	$825.33	120,064	42,128
% Change	**15.2%**	**26.9%**	**30.7%**	**3.0%**	**2.6%**	**36.3%**	**27.3%**
Change	**20**	**318**	**$8,156,869.36**	**$664.72**	**$21.22**	**32,004**	**9,032**

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; Fiscal Year 2022 = 07/01/2021 to 06/30/2022

Demographics of Members Utilizing CFTR Modulators



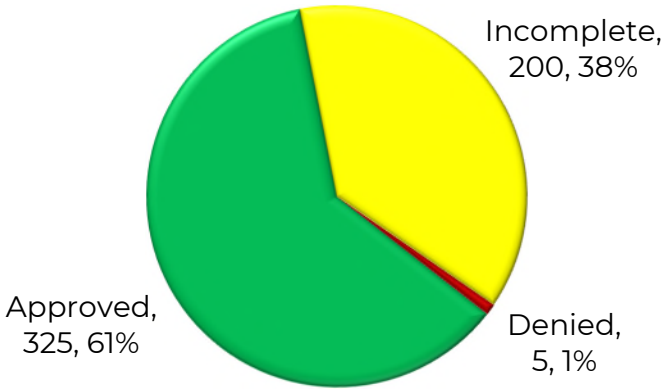
Top Prescriber Specialties of CFTR Modulators by Number of Claims



Prior Authorization of CFTR Modulators

There were 530 prior authorization requests submitted for CFTR modulators during fiscal year 2022. The following chart shows the status of the submitted petitions for fiscal year 2022.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Kalydeco® (ivacaftor tablets): August 2029
- Orkambi® (lumacaftor/ivacaftor tablets and granules): December 2030
- Kalydeco® (ivacaftor granules): February 2033
- Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets): April 2035
- Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor tablets): December 2037

News:

- **April 2022:** The Cystic Fibrosis Foundation announced its $5 million investment in Sionna Therapeutics. Sionna is developing a pipeline of potential modulators that could benefit the most common cystic fibrosis (CF) mutation, *F508del*, and could eventually offer an alternative to the current U.S. Food and Drug Administration (FDA) approved CFTR modulators. The novel modulators target the nucleotide-binding domain 1 (NBD1), the region of the gene where the *F508del* mutation occurs. No modulator currently on the market targets NBD1.
- **August 2022:** Vertex Pharmaceuticals announced the completion of a Phase 3 study of Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor tablets) in children 2 to 5 years of age with CF. Data from this study showed similar compelling efficacy to other age groups and no new safety findings. Vertex anticipates submitting regulatory filings to the FDA this year to expand the use of Trikafta® in children 2 to 5 years of age.
- **September 2022:** Vertex Pharmaceuticals announced FDA approval of their supplemental New Drug Application (sNDA) to expand the use of Orkambi® (lumacaftor/ivacaftor) to include children with CF ages 12 months to younger than 24 months who are homozygous for the *F508del* mutation. Orkambi® was previously approved for use in patients 2 years of age and older. The approval in children ages 12 months to less than 24 months is based on a 24-week, Phase 3, open-label, multi-center study in 46 children ages 12 months to younger than 24 months who were homozygous for the *F508del* mutation. With the sNDA approval, a new strength of granule packets was also approved, lumacaftor/ivacaftor 75mg/94mg per packet. Orkambi® was generally well tolerated, and the safety profile and pharmacokinetics were similar to that observed in studies in patients ages 2 years and older. Additional study results, including reductions in sweat chloride concentration, suggest the potential for CF disease modification with the use of Orkambi®.

Pipeline:

- **VX-121/Tezacaftor/VX-561:** Vertex Pharmaceuticals is conducting 2 Phase 3 clinical studies (SKYLINE 102 and SKYLINE 103) to evaluate the once daily triple combination of VX-121/tezacaftor/VX-561. VX-121 and tezacaftor are designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the CFTR protein. VX-561 is a potentiator designed to keep CFTR proteins at the cell surface open longer to improve the flow of salt and water across the cell membrane, which helps hydrate and clear mucus from the airways. Enrollment for both studies is expected to be completed in late 2022 or early 2023.

Recommendations

The College of Pharmacy recommends updating the current prior authorization criteria for the CFTR modulators to be consistent with clinical practice and updating the age restriction for Orkambi® based on the newly FDA approved age expansion (changes shown in red):

Kalydeco® (Ivacaftor) Approval Criteria:

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

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene; and
3. Orkambi® will not be approved for members with CF other than those homozygous for the *F508del* mutation; and
4. Member must be 12 months ~~2 years~~ of age or older; and
5. Members using Orkambi® must be supervised by a pulmonary disease specialist; and
6. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi®, every 3 months during the first year of treatment, and annually thereafter; and
7. Member must not be taking any of the following medications concomitantly with Orkambi®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
8. A quantity limit of 4 tablets per day or 112 tablets per 28 days will apply or a quantity limit of 2 granule packets per day or 56 packets per 28 days will apply; and
9. An age restriction of 12 months ~~2 years~~ to younger than 6 years of age will apply to Orkambi® oral granule packets. Members 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
10. Approvals will be based on the recommended dosing per package labeling based on the member's age and recent weight, if applicable. For members who require weight-based dosing, the member's recent weight must be provided on the prior authorization request; and
11. Initial approvals will be for the duration of 6 ~~3~~ months~~, after which time compliance will be required for continued approval~~. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval; and
12. Subsequent approvals will be for the duration of 1 year.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation or who have at least 1 mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed

by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 6 years of age or older; and
4. Members using Symdeko® must be supervised by a pulmonary disease specialist; and
5. If the member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) and experiencing adverse effects associated with Orkambi® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify the member has been counseled on proper administration of Symdeko® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter; and
8. Member must not be taking any of the following medications concomitantly with Symdeko®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
9. A quantity limit of 2 tablets per day or 56 tablets per 28 days will apply; and
10. Approvals will be based on the recommended dosing per package labeling based on the member's age and recent weight, if applicable. For members who require weight-based dosing, the member's recent weight must be provided on the prior authorization request; and
11. Initial approvals will be for the duration of 6 ~~3~~ months~~, after which time compliance will be required for continued approval~~. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally, after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events must be provided for members who switched from Orkambi® to Symdeko®; and
12. Subsequent approvals will be for the duration of 1 year.

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

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene or a mutation in the *CFTR* gene that is responsive based on *in vitro* data; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and

3. Member must be 6 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary disease specialist; and
5. If the member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify the member has been counseled on proper administration of Trikafta® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify the member does not have severe hepatic impairment; and
9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and
10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, or St. John's wort; and
11. ~~For members 6 to 11 years of age, the member's recent weight must be provided on the prior authorization request in order to authorize the appropriate dose according to package labeling, as follows:~~
    a. ~~Members 6 to 11 years of age weighing <30kg will be approved for Trikafta® (elexacaftor 50mg/tezacaftor 25mg/ivacaftor 37.5mg and ivacaftor 75mg) upon meeting approval criteria; or~~
    b. ~~Members 6 to 11 years of age weighing ≥30kg and members 12 years of age and older will be approved for Trikafta® (elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg and ivacaftor 150mg) upon meeting approval criteria; and~~
12. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
13. Approvals will be based on the recommended dosing per package labeling based on the member's age and recent weight, if applicable. For members who require weight-based dosing, the member's recent weight must be provided on the prior authorization request; and
14. Initial approvals will be for the duration of 6 ~~3~~ months~~, after which time compliance will be required for continued approval~~. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally, after 6 months of utilization, information regarding efficacy as previously mentioned or

fewer adverse events than with a previous CFTR therapy must be provided for members who switched from Orkambi® or Symdeko® to Trikafta®; and

15. Subsequent approvals will be for the duration of 1 year.

Utilization Details of CFTR Modulators: Fiscal Year 2022

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
ELEXACAFTOR/TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS						
TRIKAFTA TAB 100-50-75/150MG	993	104	$23,242,130.27	$23,405.97	9.55	66.85%
TRIKAFTA TAB 50-25-37.5/75MG	258	32	$6,297,095.74	$24,407.35	8.06	18.11%
SUBTOTAL	**1,251**	**136**	**$29,539,226.01**	**$23,612.49**	**9.20**	**84.96%**
LUMACAFTOR/IVACAFTOR COMBINATION PRODUCTS						
ORKAMBI GRA 150-188MG	109	11	$2,161,460.74	$19,829.92	9.91	6.22%
ORKAMBI GRA 100-125MG	36	5	$776,053.92	$21,557.05	7.2	2.23%
ORKAMBI TAB 100-125MG	25	3	$470,246.16	$18,809.85	8.33	1.35%
SUBTOTAL	**170**	**19**	**$3,407,760.82**	**$20,045.65**	**8.95**	**9.80%**
TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS						
SYMDEKO TAB 50-75MG	28	7	$618,458.82	$22,087.82	4	1.78%
SYMDEKO TAB 100-150MG	23	4	$523,145.63	$22,745.46	5.75	1.50%
SUBTOTAL	**51**	**11**	**$1,141,604.45**	**$22,384.40**	**4.64**	**3.28%**
IVACAFTOR PRODUCTS						
KALYDECO TAB 150MG	15	3	$363,260.74	$24,217.38	5	1.04%
KALYDECO PAK 75MG	13	1	$317,823.48	$24,447.96	13	0.91%
SUBTOTAL	**28**	**4**	**$681,084.22**	**$24,324.44**	**7**	**1.95%**
TOTAL	**1,500**	**152***	**$34,769,675.50**	**$23,179.78**	**9.87**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
GRA = granule; PAK = packet; TAB = tablet
Fiscal Year 2022 = 07/01/2021 to 06/30/2022

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[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 08/2022. Last accessed 08/09/2022.

[2] Cystic Fibrosis Foundation. Cystic Fibrosis Foundation Invests $5 Million in Sionna Therapeutics to Develop New CFTR Modulator Therapy. *BusinessWire*. Available online at: https://www.businesswire.com/news/home/20220419005056/en/Cystic-Fibrosis-Foundation-Invests-5-Million-in-Sionna-Therapeutics-to-Develop-New-CFTR-Modulator-Therapy. Issued 04/19/2022. Last accessed 08/10/2022.

[3] Vertex Pharmaceuticals Inc. Vertex Announces U.S. FDA Approval for Orkambi® (Lumacaftor/Ivacaftor) in Children with Cystic Fibrosis Ages 12 to <24 months. *BusinessWire*. Available online at: https://www.businesswire.com/news/home/20220902005252/en/Vertex-Announces-U.S.-FDA-Approval-for-ORKAMBI%C2%AE-lumacaftorivacaftor-in-Children-With-Cystic-Fibrosis-Ages-12-to-24-months. Issued 09/02/2022. Last accessed 09/06/2022.

[4] Orkambi® (Lumacaftor/Ivacaftor) Prescribing Information. Vertex Pharmaceutics. Available online at: uspi_lumacaftor_ivacaftor.pdf (vrtx.com). Last revised 09/2022. Last accessed 09/06/2022.

[5] Vertex Pharmaceuticals Inc. R&D Pipeline. Available online at: https://www.vrtx.com/our-science/pipeline/. Last accessed 08/10/2022.

Appendix L

Fiscal Year 2022 Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk)

Oklahoma Health Care Authority
September 2022

Introduction[1,2,3,4]

According to the National Cancer Institute, in 2022, there will be an estimated 287,850 new cases of breast cancer, making it the second most common cancer diagnosed in women in the United States after skin cancer. Additionally, it is estimated there will be 43,250 breast cancer deaths in 2022. The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Breast cancer can also begin in the cells of the lobules and in other tissues in the breast. Invasive breast cancer is breast cancer that has spread from where it began in the ducts or lobules to surrounding tissues. About 8 of 10 invasive breast cancers are invasive ductal carcinomas. There are several different types of treatments available for patients with breast cancer, including surgery, radiation, hormone therapy, and traditional chemotherapy. Additionally, targeted therapy using drugs or other substances (e.g., targeted radiation) to identify and attack specific cancer cells without harming normal cells is being used. Types of targeted therapy used for breast cancer include monoclonal antibodies, tyrosine kinase inhibitors, cyclin-dependent kinase (CDK) inhibitors, mammalian target of rapamycin (mTOR) inhibitors, and poly [adenosine diphosphate (ADP)-ribose] polymerase (PARP) inhibitors. Additionally, biosimilar agents for use in breast cancer have been approved by the U.S. Food and Drug Administration (FDA) in recent years.

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

Current Prior Authorization Criteria

Approval criteria for Keytruda® (pembrolizumab) for indications other than breast cancer diagnoses can be found in the December 2021 Drug Utilization Review (DUR) Board packet. Pembrolizumab approval criteria are reviewed annually with the skin cancer medications.

Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-negative; and
3. Hormone receptor (HR) positive; and
4. Used in combination with exemestane, fulvestrant, or tamoxifen; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.

Afinitor® (Everolimus) Approval Criteria [Neuroendocrine Tumors (NET) of Pancreatic (PNET), Gastrointestinal, or Lung Origin Diagnosis]:

1. Diagnosis of unresectable, locally advanced, or metastatic NET of pancreatic (PNET), gastrointestinal, or lung origin; and
2. Progressive disease from a previous treatment.

Afinitor® (Everolimus) Approval Criteria [Renal Angiomyolipoma (AML) and Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of renal AML and TSC; and
2. Not requiring immediate surgery; and
3. Used in pediatric and adult members 1 year of age and older.

Afinitor® (Everolimus) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of advanced RCC; and
2. Failure of treatment with sunitinib or sorafenib; and
3. Everolimus may also be approved to be used in combination with lenvatinib for advanced RCC.

Afinitor® (Everolimus) Approval Criteria [Subependymal Giant Cell Astrocytoma (SEGA) with Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of SEGA with TSC; and
2. Requires therapeutic intervention but cannot be curatively resected.

Afinitor® (Everolimus) Approval Criteria [Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures Diagnosis]:

1. Diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and
3. Failure of ≥3 other medications commonly used for seizures; and
4. Must be used as adjunctive treatment; and
5. Member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. Member must not be taking St. John's wort concurrently with Afinitor®; and

7. Prescriber must verify that Afinitor® trough levels and adverse reactions (e.g., non-infectious pneumonitis, stomatitis, hyperglycemia, dyslipidemia, thrombocytopenia, neutropenia, febrile neutropenia) will be monitored and dosing changes or discontinuations will correspond with recommendations in the drug labeling; and
8. Prescriber must verify that female members are not pregnant and will use contraception while receiving Afinitor® therapy and for 8 weeks after the last dose of Afinitor® and that male members with female partners of reproductive potential will use contraception while receiving Afinitor® therapy and for 4 weeks after the last dose of Afinitor®; and
9. The member's recent body surface area (BSA) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
10. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

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

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

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

1. Diagnosis of advanced or metastatic disease; and
2. Disease has progressed on prior therapy; and
3. Human epidermal receptor type 2 (HER2) amplified disease; and
4. RAS and BRAF mutation negative; and
5. Used as a single agent.

[v]Approval criteria for Enhertu® (fam-trastuzumab deruxtecan-nxki) for the indication of CRC can be found in the Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications report, which is also being presented at the September 2022 DUR Board meeting. Fam-trastuzumab deruxtecan-nxki approval criteria are reviewed annually with the breast cancer medications.

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

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

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

Halaven® (Eribulin) Approval Criteria [Recurrent or Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Used in 1 of the following settings:
    a. Previously received ≥2 chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting; or
    b. In combination with trastuzumab for human epidermal growth factor receptor 2 (HER2)-positive disease that is:
        i. Hormone receptor (HR) negative; or
        ii. HR positive with or without endocrine therapy; or
    c. As a single-agent for HER2-negative disease that is:
        i. HR negative; or
        ii. HR positive with visceral crisis or endocrine therapy refractory.

Halaven® (Eribulin) Approval Criteria [Liposarcoma Diagnosis]:

1. Diagnosis of unresectable or metastatic liposarcoma; and
2. Previously received an anthracycline-containing chemotherapy regimen.

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

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

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

1. Diagnosis of human epidermal receptor type 2 (HER2)-positive CRC; and
2. RAS and BRAF mutation negative; and
3. Used in combination with pertuzumab or lapatinib; and
4. Used in 1 of the following settings:
    a. If first-line therapy, patient should not be a candidate for intensive therapy; or
    b. For the treatment of advanced or metastatic disease following disease progression; and
5. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), Kanjinti® (trastuzumab-anns), or Ogivri® (trastuzumab-dkst) will also require a patient-specific, clinically significant reason why the member cannot use Ontruzant® (trastuzumab-dttb) and Trazimera® (trastuzumab-qyyp). Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

*Approval criteria for Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), Kanjinti® (trastuzumab-anns), Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), and Trazimera® (trastuzumab-qyyp) for the indication of CRC can be found in the Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications report, which is also being presented at the September 2022 DUR Board meeting. Trastuzumab approval criteria are reviewed annually with the breast cancer medications.

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

1. Diagnosis of human epidermal growth factor receptor 2 (HER2)-positive metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), or Kanjinti® (trastuzumab-anns) will also require a patient-specific, clinically significant reason why the member cannot use Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), or Trazimera™ (trastuzumab-qyyp). Biosimilars and/or reference products

are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

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

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

Ixempra® (Ixabepilone) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Used in 1 of the following settings:
    a. In combination with capecitabine after failure of an anthracycline and a taxane (must have failed combination taxane and anthracycline therapy unless anthracyclines not indicated); or
    b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine.

Kadcyla® (Ado-Trastuzumab Emtansine) Approval Criteria [Early Stage or Locally Advanced Breast Cancer Diagnosis]:

1. Diagnosis of early stage or locally advanced breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-positive; and
3. Used as adjuvant treatment in members with residual invasive disease after neoadjuvant therapy with taxane and trastuzumab-based treatment; and
4. Maximum duration of a total of 14 cycles.

Kadcyla® (Ado-Trastuzumab Emtansine) Approval Criteria [Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-positive; and
3. Previously received trastuzumab and a taxane, separately or in combination; and
4. Members should also have either:
    a. Received prior therapy for metastatic disease; or
    b. Developed disease recurrence during or within 6 months of completing adjuvant therapy.

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.

Kisqali® (Ribociclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Hormone receptor (HR) positive; and
2. Human epidermal growth factor receptor 2 (HER2)-negative; and
3. Used in 1 of the following settings:
    a. Diagnosis of advanced or metastatic breast cancer, as initial therapy; and
        i. In combination with an aromatase inhibitor; or
    b. Diagnosis of advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on endocrine therapy; and
        i. In combination with fulvestrant; and
        ii. Must be used in postmenopausal women only.

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer, as initial therapy; and
2. Hormone receptor (HR) positive; and
3. Human epidermal growth factor receptor 2 (HER2)-negative.

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

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

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

1. **Treatment of Advanced Recurrent/Refractory Ovarian Cancer:**
    a. Diagnosis of deleterious or suspected deleterious germline BRCA mutated (*gBRCAm*), advanced ovarian cancer; and
    b. Previous treatment with ≥2 prior lines of chemotherapy. Prior chemotherapy regimens should be documented on the prior authorization request; and

c. A quantity limit based on FDA approved dosing will apply; or

2. **Maintenance Treatment of Advanced Ovarian Cancer:**
    a. Disease must be in complete or partial response to primary chemotherapy; and
        i. Used as a single agent in members with a diagnosis of deleterious or suspected deleterious *gBRCAm*, advanced ovarian cancer; or
        ii. Used in combination with bevacizumab following a primary therapy regimen that included bevacizumab; or
    b. Complete or partial response to second-line or greater platinum-based based chemotherapy (no mutation required); and
    c. A quantity limit based on FDA approved dosing will apply.

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

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

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

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

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

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

Nerlynx® (Neratinib) Approval Criteria [Non-Metastatic Breast Cancer Diagnosis]:

1. For adjuvant treatment in early-stage breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
3. Neratinib must be used to follow adjuvant trastuzumab-based therapy.

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

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

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

1. Human epidermal growth factor receptor 2 (HER2)-positive; and
2. Used in 1 of the following settings:
    a. Metastatic breast cancer in members who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
        i. Used in combination with trastuzumab and docetaxel; or
    b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):
        i. Used in combination with trastuzumab and docetaxel or paclitaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel or paclitaxel); or
    c. Adjuvant systemic therapy for members with node positive, HER2-positive tumors or members with high-risk node negative tumors [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or younger than 35 years of age]:
        i. Used in combination with trastuzumab and paclitaxel following doxorubicin/cyclophosphamide (AC); or
        ii. Used in combination with trastuzumab and docetaxel following AC; or
        iii. Used in combination with docetaxel/carboplatin/trastuzumab (TCH).

Perjeta® (Pertuzumab) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]†:

1. Diagnosis of human epidermal receptor type 2 (HER2)-positive CRC; and
2. RAS and BRAF mutation-negative; and
3. Used in combination with trastuzumab; and
4. Used in 1 of the following settings:
    a. If first-line therapy, patient should not be a candidate for intensive therapy; or

b. For the treatment of advanced or metastatic disease following disease progression.

[+]Approval criteria for Perjeta® (pertuzumab) for the indication of CRC can be found in the Vote to Prior Authorize Alymsys® (Bevacizumab-maly), Lonsurf® (Trifluridine/Tipiracil), and Stivarga® (Regorafenib) and Update the Approval Criteria for the Colorectal Cancer Medications report, which is also being presented at the September 2022 DUR Board meeting. Pertuzumab approval criteria are reviewed annually with the breast cancer medications.

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

1. Human epidermal growth factor receptor 2 (HER2)-positive disease; and
2. Used in 1 of the following settings:
   a. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer; or
   b. Adjuvant treatment of members with early breast cancer; or
   c. In combination with docetaxel for members with metastatic disease.

Piqray® (Alpelisib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer that has progressed on or after an endocrine-based regimen in men or in postmenopausal women; and
2. Hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2)-negative; and
3. PIK3CA-mutated; and
4. In combination with fulvestrant.

Talzenna® (Talazoparib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-negative; and
3. Presence of BRCA1/BRCA2-germline mutated disease; and
4. Disease is hormone receptor (HR) negative or is HR positive and endocrine therapy refractory; and
5. Patient has symptomatic visceral disease; and
6. Must be used as a single-agent.

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

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

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

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

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

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

Tykerb® (Lapatinib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic or recurrent breast cancer; and
2. Human epidermal growth factor receptor 2 (HER2)-positive; and
3. Lapatinib must be used in combination with 1 of the following:
    a. Trastuzumab; or
    b. Capecitabine; or
    c. An aromatase inhibitor (e.g., exemestane, letrozole, anastrozole) if also estrogen receptor (ER) positive.

Verzenio® (Abemaciclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Used in 1 of the following settings:
    a. In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women; or
    b. In combination with fulvestrant with disease progression following endocrine therapy in advanced or metastatic breast cancer; or
    c. As monotherapy for disease progression following endocrine therapy and prior chemotherapy in metastatic breast cancer; and
2. All of the following criteria must be present:
    a. Advanced or metastatic breast cancer; and
    b. Progressed after endocrine therapy when used with fulvestrant or as initial therapy in combination with an aromatase inhibitor; and
    c. Hormone receptor (HR) positive; and
    d. Human epidermal growth factor receptor 2 (HER2)-negative.

Utilization of Breast Cancer Medications: Fiscal Year 2022

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

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2021	85	548	$8,945,030.17	$16,323.05	$584.68	24,645	15,299
2022	112	725	$11,858,177.99	$16,356.11	$573.69	35,767	20,670
% Change	**31.80%**	**32.30%**	**32.60%**	**0.20%**	**-1.90%**	**45.10%**	**35.10%**
Change	**27**	**177**	**$2,913,147.82**	**$33.06**	**-$10.99**	**11,122**	**5,371**

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; Fiscal Year 2022 = 07/01/2021 to 06/30/2022

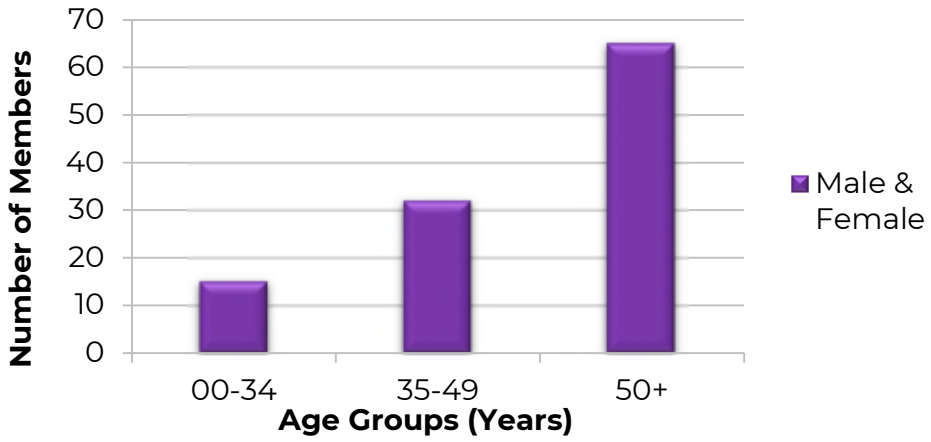
Fiscal Year Comparison: Medical Claims

Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2021	228	1,273	$12,910,175.19	$10,141.54	5.58
2022	412	1,846	$16,241,063.72	$8,797.98	4.48
% Change	**80.70%**	**45.01%**	**25.80%**	**-13.25%**	**-19.71%**
Change	**184**	**573**	**$3,330,888.53**	**-$1,343.56**	**-1.1**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Please note: Some members may be utilizing medications concomitantly.
Fiscal Year 2021 = 07/01/2020 to 06/30/2021; Fiscal Year 2022 = 07/01/2021 to 06/30/2022

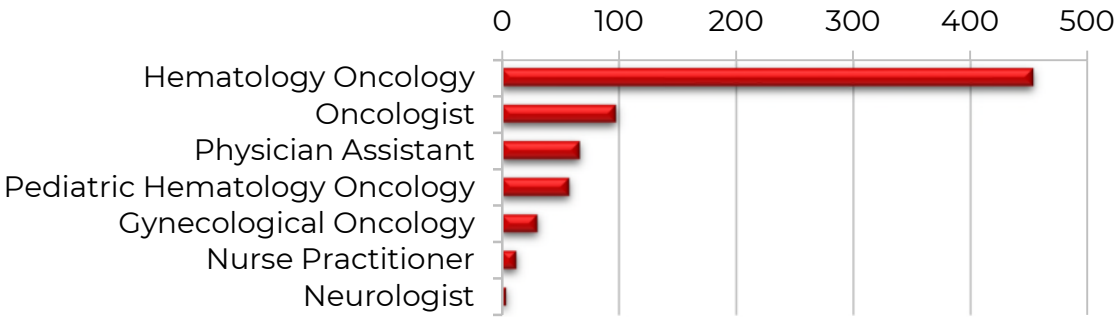
- Aggregate drug rebates collected during fiscal year 2022 for Breast Cancer Medications: $3,225,231.25.[Δ] These rebates are collected after reimbursement for the medication and are not reflected in this report. The costs included in this report do not reflect net costs.

Demographics of Members Utilizing Breast Cancer Medications: Pharmacy Claims



[Δ] Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed.

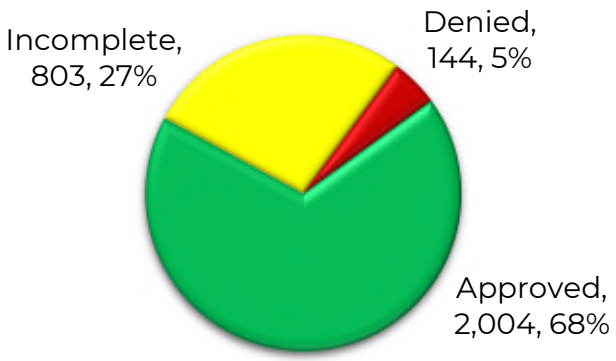
Top Prescriber Specialties of Breast Cancer Medications by Number of Claims: Pharmacy Claims



Prior Authorization of Breast Cancer Medications

There were 2,951 prior authorization requests submitted for breast cancer medications during fiscal year 2022. The following chart shows the status of the submitted petitions for fiscal year 2022.

Status of Petitions



Market News and Updates[4,5,6]

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

- **February 2019:** The FDA approved Herceptin Hylecta™ (trastuzumab/hyaluronidase-oysk) for subcutaneous (sub-Q) injection. Herceptin Hylecta™ is a combination of trastuzumab, a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist, and hyaluronidase, an endoglycosidase, for the treatment of HER2-overexpressing breast cancer.
- **October 2021:** The FDA approved Verzenio® (abemaciclib) with endocrine therapy (tamoxifen or an aromatase inhibitor) for adjuvant treatment of adult patients with hormone receptor (HR)-positive, HER2-negative, node-positive, early breast cancer at high risk of recurrence

and a Ki-67 score ≥20%. This is the first CDK 4/6 inhibitor approved for adjuvant treatment of breast cancer.

- **March 2022:** The FDA approved Lynparza® (olaparib) for the adjuvant treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative, high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy.
- **May 2022:** The FDA granted regular approval to Enhertu® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy. Previously, in December 2019, Enhertu® received accelerated approval for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received 2 or more prior anti-HER2-based regimens in the metastatic setting.
- **August 2022:** The FDA approved Enhertu® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients with unresectable or metastatic HER2-low [immunohistochemistry (IHC) 1+ or IHC 2+/in situ hybridization (ISH)-] breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
- **August 2022:** The FDA granted accelerated approval to Enhertu® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations and who have received a prior systemic therapy. This is the first drug approved for HER2-mutant NSCLC.

Guideline Update(s):

- **Ixempra® (Ixabepilone):** Based on several Phase 2 trial results, ixabepilone now has a role as monotherapy in the treatment of metastatic breast cancer. In these trials, objective response rates ranged from 11.5% in refractory patients to 41.5% in the first-line setting. The NCCN guidelines were updated to reflect the use of ixabepilone in these settings.

Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk) Product Summary[7]

- **Therapeutic Class:** Combination HER2/neu receptor antagonist and endoglycosidase
- **Indication(s):** HER2-overexpressing breast cancer

- **How Supplied:** 600mg trastuzumab/10,000 units hyaluronidase/5mL (120mg/2,000 units/mL) solution in a single-dose vial
- **Dose:** 600mg trastuzumab/10,000 units hyaluronidase via sub-Q administration once every 3 weeks
- **Cost:** The Wholesale Acquisition Cost (WAC) is $935.05 per mL, resulting in a cost per dose of $4,675.25 and an annual cost of $84,154.50 based on the recommended dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Herceptin Hylecta™ (trastuzumab/hyaluronidase-oysk) and updating the prior authorization criteria for Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), Kanjinti® (trastuzumab-anns), Ogivri® (trastuzumab-dkst), Ontruzant® (trastuzumab-dttb), and Trazimera™ (trastuzumab-qyyp) based on net costs (changes noted in red):

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

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

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

1. Diagnosis of human epidermal growth factor receptor 2 (HER2)-positive metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. Authorization of Herceptin® (trastuzumab), Herzuma® (trastuzumab-pkrb), ~~or~~ Kanjinti® (trastuzumab-anns), or Ogivri® (trastuzumab-dkst) will also require a patient-specific, clinically significant reason why the

member cannot use ~~Ogivri® (trastuzumab-dkst),~~ Ontruzant® (trastuzumab-dttb)~~,~~ or Trazimera™ (trastuzumab-qyyp). Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

The College of Pharmacy also recommends updating the approval criteria for Enhertu® (fam-trastuzumab deruxtecan-nxki), Lynparza® (olaparib), and Verzenio® (abemaciclib) based on recent FDA approvals (changes and new criteria noted in red; only criteria with updates are listed):

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

1. Adult members with unresectable or metastatic disease ~~human epidermal growth factor receptor 2 (HER2)-positive breast cancer~~; and
    a. For human epidermal growth factor receptor 2 (HER2)-positive disease, must meet the following:
        i. Member received prior therapy in the metastatic, neoadjuvant, or adjuvant setting and developed disease recurrence during or within 6 months of completing therapy; and
        ii. Member has received ≥~~2~~ 1 prior anti-HER2-based regimen~~s in the metastatic setting.~~; or
    b. For HER-2 low [immunohistochemistry (IHC) 1+ or IHC 2+/in situ hybridization (ISH)-] disease, must meet the following:
        i. Member received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.

Enhertu® (Fam-Trastuzumab Deruxtecan-nxki) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Unresectable or metastatic NSCLC; and
2. Disease is human epidermal growth factor receptor 2 (HER2)-positive; and
3. Member must have received a prior systemic therapy.

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

1. Diagnosis of human epidermal growth factor receptor 2 (HER2)-negative, high-risk early breast cancer previously treated with neoadjuvant or adjuvant chemotherapy; and
    a. Used in the adjuvant setting; and
    b. Positive test for a germline BRCA-mutation (gBRCAm); and
    c. Maximum treatment duration of 1 year; or
2. Diagnosis of metastatic breast cancer; and

a. Member must have shown progression on previous chemotherapy ~~in any setting~~; and
b. Members with hormone receptor positive disease must have failed prior endocrine therapy or are considered to not be a candidate for endocrine therapy.

Verzenio® (Abemaciclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer; and
   a. Hormone receptor positive disease; and
   b. Human epidermal receptor 2 (HER2)-negative disease; and
      i. Used in 1 of the following settings:
         1. In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women; or
         2. In combination with fulvestrant with disease progression following endocrine therapy; or
         3. As monotherapy for disease progression following endocrine therapy and prior chemotherapy; or
2. Diagnosis of early-stage breast cancer; and
   a. Hormone receptor positive disease; and
   b. HER2-negative disease; and
   c. Node-positive disease high risk for recurrence with Ki-67 ≥20%; and
   d. Used as adjuvant treatment in combination with endocrine therapy.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Ixempra® (ixabepilone) based on NCCN compendium approval (changes noted in red):

Ixempra® (Ixabepilone) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Used in combination with capecitabine; and
   a. After failure of an anthracycline and a taxane unless anthracycline contraindicated; or
3. Used as a single agent; and
   a. Used in 1 of the following settings:
      i. After failure of capecitabine, an anthracycline, and a taxane; or
      ii. In members with no response to preoperative systemic therapy; or
      iii. After at least 1 line of therapy for recurrent unresectable (local or regional) disease; or
      iv. Disease is human epidermal growth factor receptor 2 (HER2)-negative; or
4. Used in combination with trastuzumab; and
   a. Disease is HER2-positive; and

b. Third-line or subsequent therapy.

Finally, the College of Pharmacy also recommends updating the prior authorization criteria for Perjeta® (pertuzumab) to more closely reflect the FDA approval granted to pertuzumab for this indication (changes noted in red):

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

1. Human epidermal growth factor receptor 2 (HER2)-positive; and
2. Used in 1 of the following settings:
   a. Metastatic breast cancer in members who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
      i. Used in combination with trastuzumab and ~~docetaxel~~ chemotherapy; or
   b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):
      i. Used in combination with trastuzumab and ~~docetaxel or paclitaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel or paclitaxel~~ chemotherapy; or
   c. Adjuvant systemic therapy for members with node positive, HER2-positive tumors or members with high-risk node negative tumors [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or younger than 35 years of age]:
      i. Used in combination with trastuzumab and chemotherapy ~~paclitaxel following doxorubicin/cyclophosphamide (AC)~~; or
      ii. Used in combination with trastuzumab and docetaxel following doxorubicin/cyclophosphamide (AC); or
      iii. Used in combination with docetaxel/carboplatin/trastuzumab (TCH); or
      iv. Used in combination with trastuzumab following neoadjuvant therapy with paclitaxel/docetaxel/carboplatin/trastuzumab/pertuzumab (pTCHP).

Utilization Details of Breast Cancer Medications: Fiscal Year 2022

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
PALBOCICLIB PRODUCTS					
IBRANCE TAB 125MG	185	30	$2,505,709.80	6.17	$13,544.38
IBRANCE TAB 100MG	75	8	$1,017,252.15	9.38	$13,563.36
IBRANCE CAP 100MG	34	5	$463,654.63	6.8	$13,636.90
IBRANCE CAP 125MG	24	5	$323,891.56	4.8	$13,495.48
IBRANCE TAB 75MG	13	3	$176,355.97	4.33	$13,565.84
IBRANCE CAP 75MG	2	1	$27,970.42	2	$13,985.21
SUBTOTAL	**333**	**52**	**$4,514,834.53**	**6.4**	**$13,558.06**
EVEROLIMUS PRODUCTS					
AFINITOR DIS TAB 3MG	30	5	$890,700.48	6	$29,690.02
AFINITOR DIS TAB 5MG	27	4	$1,256,844.87	6.75	$46,549.81
EVEROLIMUS TAB 5MG	21	6	$122,195.58	3.5	$5,818.84
EVEROLIMUS TAB 3MG	17	4	$742,569.95	4.25	$43,680.59
EVEROLIMUS TAB 10MG	14	4	$55,188.60	3.5	$3,942.04
EVEROLIMUS TAB 7.5MG	12	1	$81,870.00	12	$6,822.50
EVEROLIMUS TAB 5MG	8	5	$244,090.64	1.6	$30,511.33
AFINITOR TAB 10MG	7	3	$110,018.84	2.33	$15,716.98
AFINITOR DIS TAB 2MG	6	2	$104,657.84	3	$17,442.97
EVEROLIMUS TAB 2MG	2	1	$38,707.76	2	$19,353.88
SUBTOTAL	**144**	**35**	**$3,646,844.56**	**4.11**	**$25,325.31**
ABEMACICLIB PRODUCTS					
VERZENIO TAB 150MG	58	15	$748,248.98	3.87	$12,900.84
VERZENIO TAB 100MG	13	5	$174,897.81	2.6	$13,453.68
VERZENIO TAB 50MG	12	2	$159,665.56	6	$13,305.46
SUBTOTAL	**83**	**22**	**$1,082,812.35**	**3.77**	**$13,045.93**
OLAPARIB PRODUCTS					
LYNPARZA TAB 150MG	47	13	$684,262.58	3.62	$14,558.78
LYNPARZA TAB 100MG	15	2	$213,364.55	7.5	$14,224.30
SUBTOTAL	**62**	**15**	**$897,627.13**	**4.13**	**$14,477.86**
TUCATINIB PRODUCTS					
TUKYSA TAB 150MG	28	6	$493,137.48	4.67	$17,612.05
TUKYSA TAB 50MG	7	1	$72,531.87	7	$10,361.70
SUBTOTAL	**35**	**7**	**$565,669.35**	**5**	**$16,161.98**
ALPELISIB PRODUCTS					
PIQRAY TAB 300MG	26	6	$468,620.14	4.33	$18,023.85
PIQRAY TAB 250MG	6	2	$108,707.44	3	$18,117.91
SUBTOTAL	**32**	**8**	**$577,327.58**	**4**	**$18,041.49**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
RIBOCICLIB PRODUCTS					
KISQALI TAB 600MG DOSE PACK	26	5	$385,558.39	5.2	$14,829.17
SUBTOTAL	**26**	**5**	**$385,558.39**	**5.2**	**$14,829.17**
NERATINIB PRODUCTS					
NERLYNX TAB 40MG	10	1	$187,504.10	10	$18,750.41
SUBTOTAL	**10**	**1**	**$187,504.10**	**10**	**$18,750.41**
TOTAL	**725**	**112***	**$11,858,177.99**	**6.47**	**$16,356.11**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
CAP = capsule; DIS = Disperz (oral tablet for suspension); TAB = tablet
Fiscal Year 2022 = 07/01/2021 to 06/30/2022

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBERS	COST/ CLAIM
J9271 PEMBROLIZUMAB INJ	835	203	$10,656,236.00	4.11	$12,761.96
J9355 TRASTUZUMAB INJ	343	53	$1,375,180.00	6.47	$4,009.27
J9306 PERTUZUMAB INJ	309	60	$2,168,131.80	5.15	$7,016.61
J9354 ADO-TRASTUZUMAB INJ	132	21	$1,088,861.80	6.29	$8,248.95
Q5114 TRASTUZUMAB-DKST INJ	77	29	$212,368.32	2.66	$2,758.03
Q5116 TRASTUZUMAB-QYYP INJ	36	15	$88,560.77	2.4	$2,460.02
J9179 ERIBULIN MESYLATE INJ	27	8	$99,664.00	3.38	$3,691.26
J9317 SACITUZUMAB GOVITECAN-HZIY INJ	21	4	$228,588.12	5.25	$10,885.15
Q5112 TRASTUZUMAB-DTTB INJ	20	5	$40,493.19	4	$2,024.66
Q5117 TRASTUZUMAB-ANNS INJ	19	4	$47,259.32	4.75	$2,487.33
J9358 FAM-TRASTUZUMAB INJ	17	5	$137,357.98	3.4	$8,079.88
J9207 IXABEPILONE INJ	9	4	$89,859.22	2.25	$9,984.36
J9316 PERTUZUMAB/TRASTUZUMAB/ HYALURONIDASE-ZZXF INJ	1	1	$8,503.20	1	$8,503.20
TOTAL	**1,846**	**412**	**$16,241,063.72**	**4.48**	**$8,797.98**

Costs do not reflect rebated prices or net costs.
+Total number of unduplicated claims.
*Total number of unduplicated utilizing members. Please note: Some members may be utilizing medications concomitantly.
INJ = injection
Fiscal Year 2022 = 07/01/2021 to 06/30/2022

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[7] Herceptin Hylecta™ (Trastuzumab/Hyaluronidase-oysk) Prescribing Information. Genentech. Available online at: https://www.gene.com/download/pdf/herceptin_hylecta_prescribing.pdf. Last revised 02/2019. Last accessed 08/31/2022.

Appendix M

Fiscal Year 2022 Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Amvuttra™ (Vutrisiran)

Oklahoma Health Care Authority
September 2022

Current Prior Authorization Criteria

Onpattro® (Patisiran) Approval Criteria:

1. An FDA approved indication for the treatment of polyneuropathy associated with hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
   a. Tissue (fat pad) biopsy confirming amyloid deposits; and
   b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Onpattro® must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist); and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
5. Prescriber must confirm the member will be pre-medicated with intravenous (IV) corticosteroid, oral acetaminophen, IV histamine-1 (H_1) antagonist, and IV histamine-2 (H_2) antagonist 60 minutes prior to Onpattro® administration to reduce the risk of infusion-related reaction(s); and
6. Onpattro® will not be approved for concomitant use with Tegsedi® (inotersen), Vyndaqel® (tafamidis meglumine), or Vyndamax® (tafamidis); and
7. Member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
8. Onpattro® approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Tegsedi® (Inotersen) Approval Criteria:

1. An FDA approved indication for the treatment of polyneuropathy associated with hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:

    a. Tissue (fat pad) biopsy confirming amyloid deposits; and
    b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Tegsedi® must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist); and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
5. Prescriber must agree to monitor ALT, AST, and total bilirubin prior to initiation of Tegsedi® and every 4 months during treatment; and
6. Prescriber must confirm the first injection of Tegsedi® administered by the member or caregiver will be performed under the guidance of a health care professional; and
7. Prescriber must confirm the member or caregiver has been trained by a health care professional on the subcutaneous (sub-Q) administration and proper storage of Tegsedi®; and
8. Tegsedi® will not be approved for concomitant use with Onpattro® (patisiran), Vyndaqel® (tafamidis meglumine), or Vyndamax® (tafamidis); and
9. Prescriber, pharmacy, and member must be enrolled in the Tegsedi® Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
10. Tegsedi® approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
11. A quantity limit of 4 syringes per 28 days will apply.

Vyndamax® (Tafamidis) and Vyndaqel® (Tafamidis Meglumine) Approval Criteria:

1. An FDA approved indication for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular (CV) mortality and CV-related hospitalization; and
2. Diagnosis confirmed by:
    a. Genetic confirmation of transthyretin (*TTR*) mutation (e.g., Val122Ile) or wild-type amyloidosis; and
    b. Cardiac imaging (e.g., ultrasound, MRI) confirming cardiac involvement; and
3. Presence of amyloid deposits confirmed by:
    a. Nuclear scintigraphy; or
    b. Endomyocardial biopsy; and
4. Member must have medical history of heart failure (NYHA Class I to III); and

5. Prescriber must confirm light-chain amyloidosis (AL) has been ruled out; and
6. Vyndamax® or Vyndaqel® must be prescribed by or in consultation with a cardiologist or geneticist (or an advanced care practitioner with a supervising physician who is a cardiologist or geneticist); and
7. Vyndamax® or Vyndaqel® will not be approved for concomitant use with Onpattro® (patisiran) or Tegsedi® (inotersen); and
8. 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; and
9. A quantity limit of 1 Vyndamax® capsule or 4 Vyndaqel® capsules per day will apply.

Utilization of Amyloidosis Medications: Fiscal Year 2022

There was no SoonerCare utilization of amyloidosis medications during fiscal year 2022 (07/01/2021 to 06/30/2022).

Prior Authorization of Amyloidosis Medications

There were no prior authorization requests submitted for amyloidosis medications during fiscal year 2022 (07/01/2021 to 06/30/2022).

Market News and Updates[1,2]

Anticipated Patent Expiration(s):

- Vyndaqel® (tafamidis meglumine): April 2024
- Tegsedi® (inotersen): April 2031
- Onpattro® (patisiran): August 2035
- Vyndamax® (tafamidis): August 2035
- Amvuttra™ (vutrisiran): July 2036

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

- **June 2022:** Alnylam Pharmaceuticals, Inc. announced FDA approval of Amvuttra™ (vutrisiran), a small interfering ribonucleic acid (siRNA) administered via subcutaneous (sub-Q) injection once every 3 months for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. The FDA approval is based on positive 9-month results from the HELIOS-A Phase 3 study, where Amvuttra™ significantly improved the signs and symptoms of polyneuropathy, with more than 50% of patients experiencing halting or reversal of their disease manifestations.

Amvuttra™ (Vutrisiran) Product Summary[3]

Indication(s): Amvuttra™ (vutrisiran) is a transthyretin (TTR)-siRNA indicated for the treatment of the polyneuropathy of hATTR amyloidosis in adults.

How Supplied: Amvuttra™ is supplied as 25mg/0.5mL solution in a single-dose prefilled syringe for sub-Q injection.

Dosing and Administration:

- The recommended dosing is 25mg via sub-Q injection once every 3 months.
- Amvuttra™ is for sub-Q use only and should be administered by a health care professional.

Contraindication(s): None

Mechanism of Action:

- Vutrisiran is a double-stranded siRNA-N-acetylgalactosamine conjugate that causes degradation of mutant and wild-type TTR messenger RNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

Safety:

- Reduced Serum Vitamin A Levels: Treatment with vutrisiran leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance of vitamin A is advised for patients taking vutrisiran (700-900mcg retinol activity equivalents for adults). Higher doses than the recommended daily allowance of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with vutrisiran, as serum vitamin A levels do not reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).
- Pregnancy: There are no available data on vutrisiran use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Treatment with vutrisiran leads to a decrease in serum vitamin A levels, and vitamin A supplementation is advised for patients taking vutrisiran. Vitamin A is essential for normal embryofetal development; however, excessive levels of vitamin A are associated with adverse developmental effects. The effects on the fetus of a reduction in maternal serum TTR caused by vutrisiran and of vitamin A supplementation are unknown. In animal studies, sub-Q administration of vutrisiran to pregnant rats resulted in developmental toxicity (reduced fetal body weight and embryofetal mortality) at doses associated with maternal toxicity.

- Lactation: There is no information regarding the presence of vutrisiran in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vutrisiran and any potential adverse effects on the breastfed infant from vutrisiran or from the underlying maternal condition.
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
- Geriatric Use: No dose adjustment is required in patients 65 years of age or older. A total of 46 (38%) patients 65 years of age or older, including 7 (6%) patients 75 years of age or older, received vutrisiran in the clinical study. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: No dose adjustment is recommended in patients with mild or moderate renal impairment [estimated glomerular filtration rate (eGFR) ≥30 to <90mL/min/1.73 m^2]. Vutrisiran has not been studied in patients with severe renal impairment or end-stage renal disease.
- Hepatic Impairment: No dose adjustment is recommended in patients with mild hepatic impairment [total bilirubin ≤1x upper limit of normal (ULN) and aspartate aminotransferase (AST) >1x ULN, or total bilirubin >1.0 to 1.5x ULN and any level of AST]. Vutrisiran has not been studied in patients with moderate or severe hepatic impairment.

Adverse Reactions: The most common adverse reactions (≥5%) were arthralgia, dyspnea, and reduced serum vitamin A levels.

Efficacy:

- Study: The efficacy of vutrisiran was evaluated in the Phase 3 HELIOS-A study, a randomized, open-label clinical study in adult patients with polyneuropathy caused by hATTR amyloidosis. Patients were randomized 3:1 to receive 25mg of vutrisiran sub-Q once every 3 months (N=122), or 0.3mg/kg patisiran intravenously every 3 weeks (N=42). The patisiran-treated group was a reference group and the differences between this group and the vutrisiran and placebo groups were not evaluated against the primary endpoint. Efficacy assessments were based on a comparison of the vutrisiran arm of the study with an external placebo group from the Phase 3 APOLLO study of patisiran which was composed of a comparable population of adult patients with polyneuropathy caused by hATTR amyloidosis.
- Primary Efficacy Endpoint: The primary endpoint was the change from baseline to month 9 in modified Neuropathy Impairment Score +7 (mNIS+7). The mNIS+7 is an objective assessment of neuropathy and

comprises the NIS and Modified +7 composite scores. In the version of the mNIS+7 used in the trial, the NIS objectively measures deficits in cranial nerve function, muscle strength, and reflexes, and the +7 assesses postural blood pressure, quantitative sensory testing, and peripheral nerve electrophysiology. The mNIS+7 has a total score range from 0 to 304 points, with higher scores representing a greater severity of disease.

- Results: Treatment with vutrisiran in HELIOS-A resulted in statistically significant improvements in the mNIS+7 (P<0.001) from baseline to month 9 compared to placebo. Additionally, treatment with vutrisiran in HELIOS-A resulted in statistically significant improvements in the Norfolk Quality of Life-Diabetic Neuropathy total score and 10-meter walk test at month 9 compared to placebo (P<0.001).

Cost Comparison:

Medication	Cost Per mL	Cost Per Year*
Amvuttra™ (vutrisiran) 25mg/0.5mL	**$231,750.00**	**$463,500.00**
Onpattro® (patisiran) 10mg/5mL	$1,957.00	$528,390.00
Tegsedi® (inotersen) 284mg/1.5mL	$6,117.86	$477,193.08

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 year based on maximum FDA recommended dosing for Amvuttra™ 25mg every 3 months, Onpattro® 30mg once every 3 weeks, and Tegsedi® 284mg once a week.

Recommendations[4]

The College of Pharmacy recommends the prior authorization of Amvuttra™ (vutrisiran) with criteria similar to Onpattro® (patisiran) as follows (changes shown in red):

Amvuttra™ (Vutrisiran) and Onpattro® (Patisiran) Approval Criteria:

1. An FDA approved indication for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
   a. Tissue (fat pad) biopsy confirming amyloid deposits; ~~and~~ or
   b. Genetic confirmation of transthyretin (TTR) gene mutation (e.g., Val30Met); and
3. Prescriber must verify member is currently experiencing signs and symptoms of polyneuropathy and other causes of polyneuropathy have been ruled out; and
4. Must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist); and
5. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and

6. Prescriber must confirm the member does not have severe renal impairment, end-stage renal disease, and/or moderate or severe hepatic impairment; and
7. Prescriber must confirm the member has not undergone a liver transplant; and
8. For Onpattro®, prescriber must confirm the member will be pre-medicated with intravenous (IV) corticosteroid, oral acetaminophen, IV histamine-1 (H_1) antagonist, and IV histamine-2 (H_2) antagonist 60 minutes prior to administration to reduce the risk of infusion-related reaction(s); and
9. Amvuttra™ will not be approved for concomitant use with Onpattro® (patisiran), Tegsedi® (inotersen), Vyndamax® (tafamidis), or Vyndaqel® (tafamidis meglumine); and
10. Authorization for Amvuttra™ will also require a patient-specific, clinically significant reason why the member cannot use Onpattro®; and
11. Onpattro® will not be approved for concomitant use with Amvuttra™ (vutrisiran), Tegsedi® (inotersen), Vyndamax® (tafamidis), or Vyndaqel® (tafamidis meglumine); and
12. For Onpattro®, member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
13. For Amvuttra™, a quantity limit of 0.5mL per 90 days will apply; and
14. Approvals will be for the duration of 1 year ~~6 months~~. Reauthorization may be granted if the prescriber documents the member is responding well to treatment and member has not undergone a liver transplant.

The College of Pharmacy also recommends updating the prior authorization criteria for Tegsedi® (inotersen), Vyndamax® (tafamidis), and Vyndaqel® (tafamidis meglumine) as follows (changes shown in red):

Tegsedi® (Inotersen) Approval Criteria:

1. An FDA approved indication for the treatment of polyneuropathy associated with hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
   a. ~~a.~~ Tissue (fat pad) biopsy confirming amyloid deposits; ~~and~~ or
   b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Prescriber must verify member is currently experiencing signs and symptoms of polyneuropathy and other causes of polyneuropathy have been ruled out; and
4. Tegsedi® must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a

supervising physician who is a cardiologist, geneticist, or neurologist); and
5. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
6. Prescriber must agree to monitor ALT, AST, and total bilirubin prior to initiation of Tegsedi® and every 4 months during treatment; and
7. Prescriber must confirm the first injection of Tegsedi® administered by the member or caregiver will be performed under the guidance of a health care professional; and
8. Prescriber must confirm the member or caregiver has been trained by a health care professional on the subcutaneous (sub-Q) administration and proper storage of Tegsedi®; and
9. Prescriber must confirm the member has not undergone a liver transplant; and
10. Tegsedi® will not be approved for concomitant use with Amvuttra™ (vutrisiran), Onpattro® (patisiran), Vyndamax® (tafamidis), or Vyndaqel® (tafamidis meglumine); and
11. Prescriber, pharmacy, and member must be enrolled in the Tegsedi® Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
12. Tegsedi® approvals will be for the duration of 1 year ~~6 months~~. Reauthorization may be granted if the prescriber documents the member is responding well to treatment and member has not undergone a liver transplant; and
13. A quantity limit of 4 syringes per 28 days will apply.

Vyndamax® (Tafamidis) and Vyndaqel® (Tafamidis Meglumine) Approval Criteria:

1. An FDA approved indication for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular (CV) mortality and CV-related hospitalization; and
2. Diagnosis confirmed by:
   a. Genetic confirmation of transthyretin (*TTR*) mutation (e.g., Val122Ile) or wild-type amyloidosis; and
   b. Cardiac imaging (e.g., ultrasound, MRI) confirming cardiac involvement; and
3. Presence of amyloid deposits confirmed by:
   a. Nuclear scintigraphy; or
   b. Endomyocardial biopsy; and
4. Member must have medical history of heart failure (NYHA Class I to III); and
5. Prescriber must confirm light-chain amyloidosis (AL) has been ruled out; and

6. Prescriber must confirm the member has not undergone a liver transplant; and
7. Vyndamax® or Vyndaqel® must be prescribed by or in consultation with a cardiologist or geneticist (or an advanced care practitioner with a supervising physician who is a cardiologist or geneticist); and
8. Vyndamax® or Vyndaqel® will not be approved for concomitant use Amvuttra™ (vutrisiran), Onpattro® (patisiran) or Tegsedi® (inotersen); and
9. 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 and member has not undergone a liver transplant; and
10. A quantity limit of 1 Vyndamax® capsule or 4 Vyndaqel® capsules per day will apply.

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Appendix N

Fiscal Year 2022 Annual Review of Synagis® (Palivizumab)

Oklahoma Health Care Authority
September 2022

Current Prior Authorization Criteria[1]

A prior authorization is required for all members who receive palivizumab in an outpatient setting. Palivizumab is approved for members who meet the established prior authorization criteria, which is based on the American Academy of Pediatrics (AAP) 2014 guidelines for palivizumab prophylaxis.

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection:
   1. Infants younger than 12 months of age at the start of respiratory syncytial virus (RSV) season:
      a. Born before 29 weeks, 0 days gestation; or
      b. Born before 32 weeks, 0 days gestation and develop chronic lung disease (CLD) of prematurity (require >21% oxygen supplementation for ≥28 days after birth); or
      c. Have hemodynamically significant congenital heart disease [acyanotic heart disease and receiving medication to control congestive heart failure (CHF) and will require surgical procedures, or have moderate-to-severe pulmonary hypertension]; or
      d. May be considered for:
         i. Infants with neuromuscular disease or a congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough; or
         ii. Infants who undergo cardiac transplantation during RSV season; or
         iii. Infants who are profoundly immunocompromised during RSV season; or
         iv. Infants with cystic fibrosis with clinical evidence of CLD and/or who are nutritionally compromised; or
   2. Infants 12 to 24 months of age at the start of RSV season:
      a. Born before 32 weeks, 0 days gestation and have CLD of prematurity (required ≥28 days of oxygen after birth) and continue to require medical support (i.e., chronic corticosteroid therapy, diuretic therapy, supplemental oxygen) during the 6 months before the start of the RSV season; or

b. May be considered for:
    i. Infants who undergo cardiac transplantation during RSV season; or
    ii. Infants who are profoundly immunocompromised during RSV season; or
    iii. Infants with cystic fibrosis with manifestations of severe lung disease or weight for length less than the 10th percentile.

B. Length of Treatment: Palivizumab is approved for use only during RSV season in Oklahoma as determined by the Oklahoma State Department of Health (OSDH) Viral Respiratory Illness Sentinel Surveillance System or other credible statewide monitoring system. The threshold for determining RSV seasonality is 10% of positive tests. RSV is determined to be in season once the percentage of positive tests is >10%; however, due to a potential lag in reporting data, palivizumab coverage will begin when the percentage of positive tests is consistently increasing and approaching the 10% threshold. RSV season is determined to be at an end when the percentage of positive tests is consistently <10%. Initial approvals will be for the duration of 3 months from the determined RSV season start date in Oklahoma. Subsequent approvals will be for the duration of 1 month until RSV season end. A separate prior authorization request will be required for consideration of initial approval and for each subsequent approval.
C. Units Authorized: The member's current weight (taken within the last 3 weeks) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling. Doses are to be administered no more often than every 30 days. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as 1 of the approved total.
D. Dose-Pooling: To avoid unnecessary risk to the member, multiple members are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Utilization of Synagis® (Palivizumab): Fiscal Year 2022

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2021	291	1,283	$3,186,343.30	$2,483.51	$82.78	1,108	38,490
2022	312	1,214	$3,161,700.09	$2,604.37	$86.83	1,052	36,414
% Change	**7.20%**	**-5.40%**	**-0.80%**	**4.90%**	**4.90%**	**-5.10%**	**-5.40%**
Change	**21**	**-69**	**-$24,643.21**	**$120.86**	**$4.05**	**-56**	**-2,076**

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; Fiscal Year 2022 = 07/01/2021 to 06/30/2022

Pharmacy Claim Details for Fiscal Year 2022

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PALIVIZUMAB PRODUCTS						
SYNAGIS INJ 100MG/ML	851	281	$2,586,625.91	$3,039.51	3.03	81.81%
SYNAGIS INJ 50MG/0.5ML	363	220	$575,074.18	$1,584.23	1.65	18.19%
TOTAL	**1,214**	**312***	**$3,161,700.09**	**$2,604.37**	**3.89**	**100%**

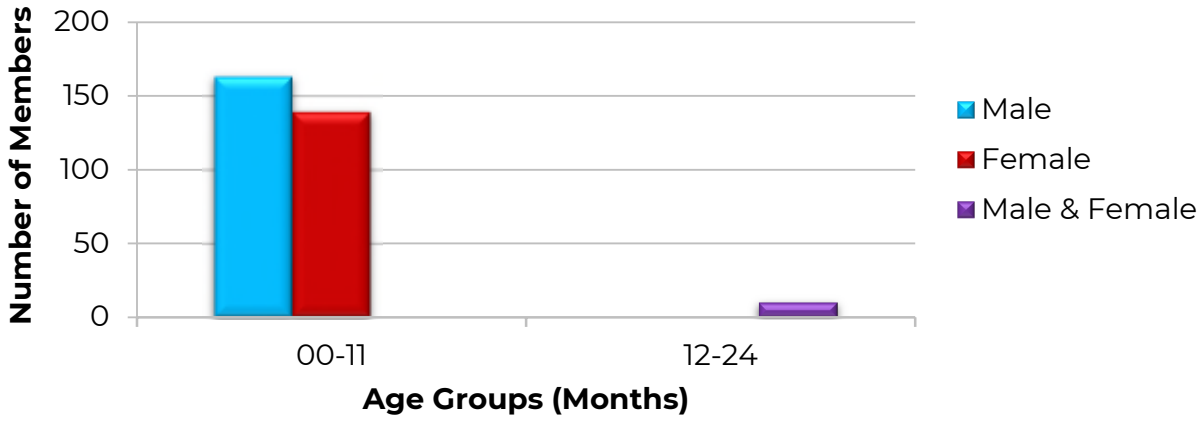
Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
INJ = injection
Fiscal Year 2022 = 07/01/2021 to 06/30/2022

Cost Per Vial

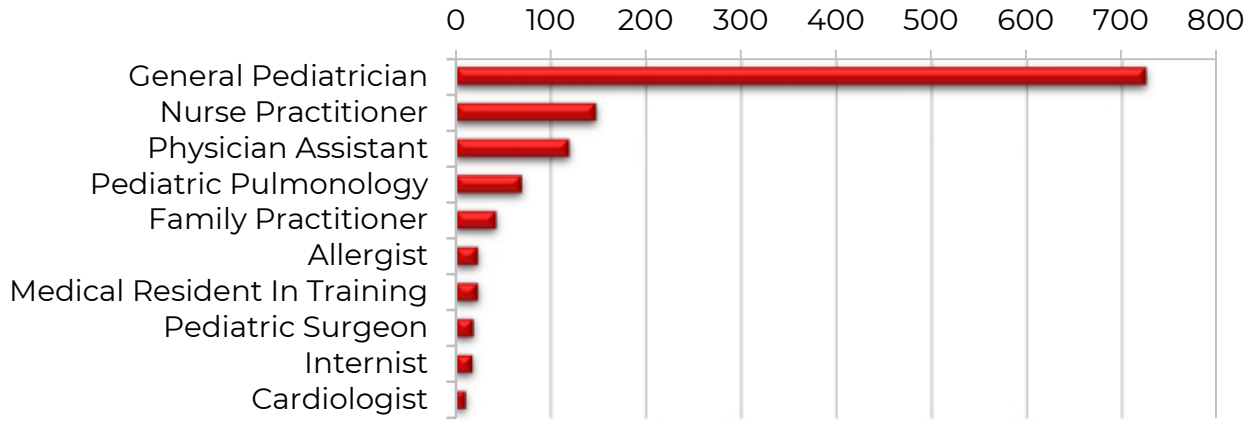
Vial Size	Cost Per Vial
Synagis® (palivizumab) 100mg/mL vial	$3,224.08
Synagis® (palivizumab) 50mg/0.5mL vial	$1,707.41

Costs do not reflect rebated prices or net costs.
Costs based on specialty pharmaceutical allowable cost (SPAC).

Demographics of Members Utilizing Synagis® (Palivizumab)



Top Prescriber Specialties of Synagis® (Palivizumab) by Number of Claims

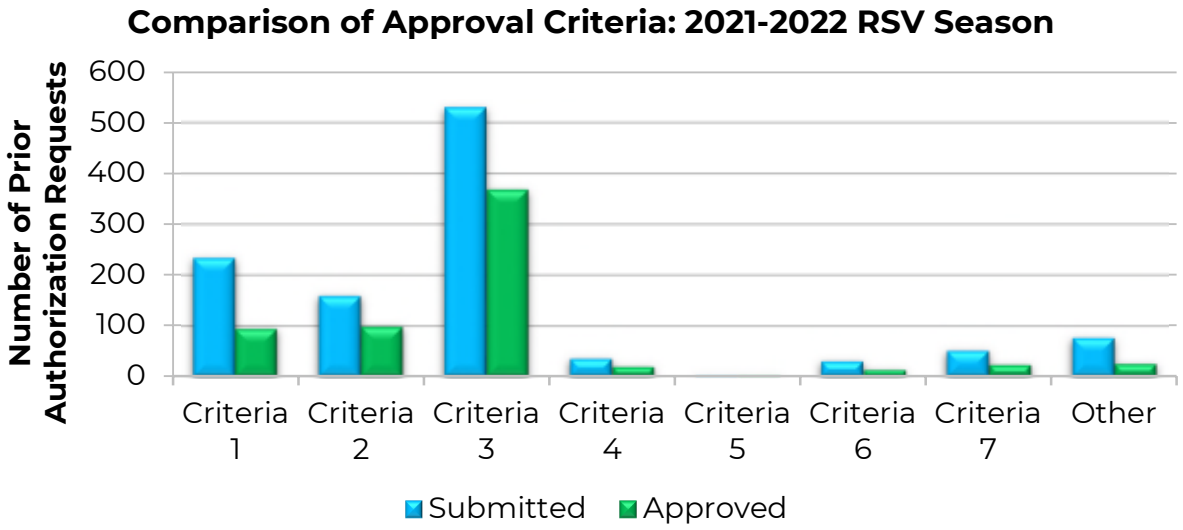


Prior Authorization of Synagis® (Palivizumab)

There were 1,299 palivizumab prior authorization requests submitted for 461 unique members during fiscal year 2022. This is an increase in both submitted petitions and number of members requesting palivizumab compared to fiscal year 2021 when there were 805 palivizumab prior authorization requests submitted for 444 unique members. The following chart shows the status of the submitted petitions for fiscal year 2022.

Status of Petitions

The following graph shows the number of submissions and approvals for each prior authorization criteria. The graph is followed by a numbered list in which the list number corresponds to the criteria number in the graph. The most commonly requested and approved criteria selection during the 2021 to 2022 respiratory syncytial virus (RSV) season was criteria number 3: infants born before 29 weeks, 0 days gestation. Infants born before 32 weeks, 0 days gestation and who had chronic lung disease (CLD) of prematurity was also a commonly requested and approved criteria selection (criteria number 1).



Criteria List:

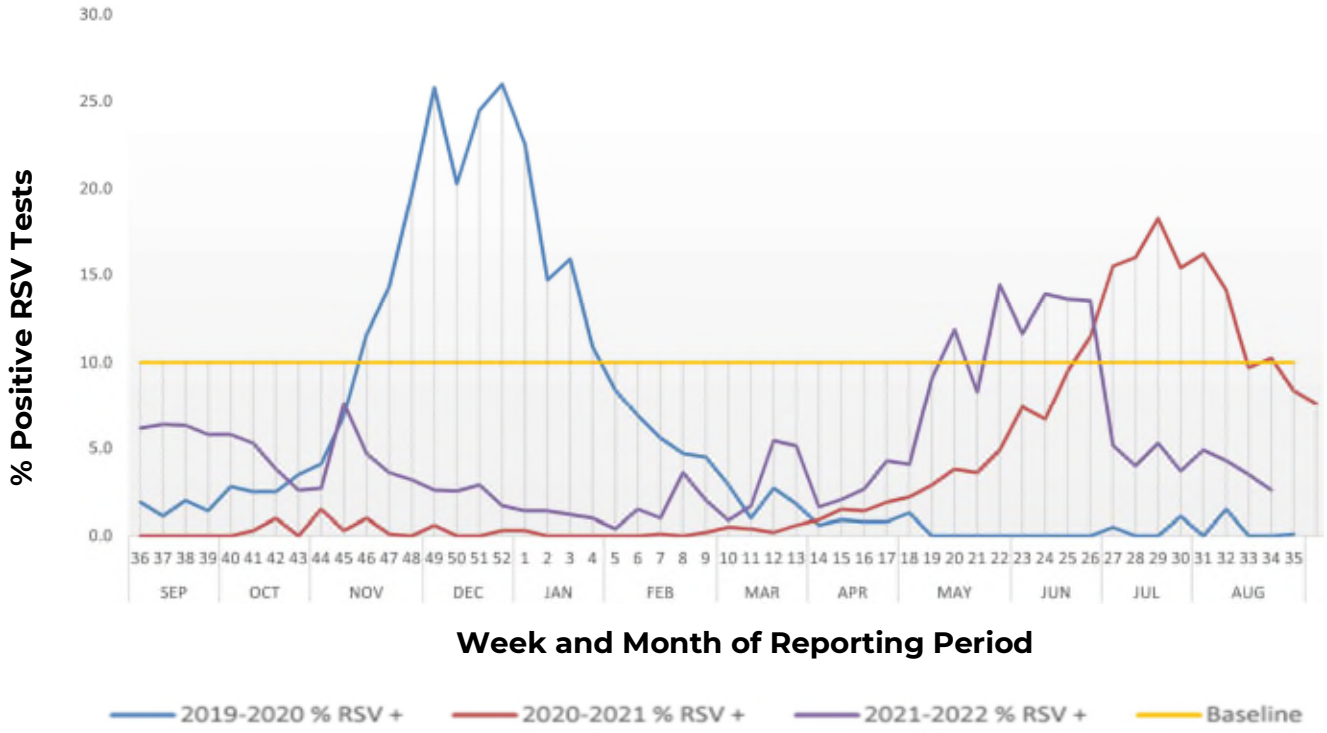
1. Infants 0 to 24 months of age at the start of RSV season born before 32 weeks, 0 days gestation and have CLD of prematurity
2. Infants who have hemodynamically significant congenital heart disease and will require surgical procedures, or have moderate-to-severe pulmonary hypertension
3. Infants born before 29 weeks, 0 days gestation
4. Infants with neuromuscular disease or a congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough
5. Infants who undergo cardiac transplantation during RSV season
6. Infants who are profoundly immunocompromised during RSV season
7. Infants with cystic fibrosis with clinical evidence of CLD and/or are nutritionally compromised

RSV Season Comparison[2,3,4,5,6,7]

The following chart contains the weekly percentage of laboratory positive RSV tests in Oklahoma as reported by the Oklahoma State Department of Health (OSDH) Viral Respiratory Illness Sentinel Surveillance System. The chart is included to compare RSV seasons since 2019. RSV is determined to be in season once the percentage of positive tests is >10% for 2 consecutive weeks. Similarly, the season is determined to be at an end when the percentage of positive tests is <10% for 2 consecutive weeks. Historically, RSV seasons were similar with a peak typically in December or January and a season end by late March. Beginning in 2020, the percentage of positive tests did not exceed 10% during the typical RSV season months, likely due to nonpharmacological interventions (e.g., masking, social distancing, decreased travel) related to the COVID-19 pandemic, resulting in atypical onset and offset of the RSV season. Currently, SoonerCare coverage of

palivizumab is determined based on the percentage of positive tests, as reported by the OSDH. During fiscal year 2022 in Oklahoma, the percentage of positive antigen detection tests exceeded the 10% threshold during portions of July 2021, August 2021, May 2022, and June 2022.

OSDH: Weekly Percentage of Laboratory Positive RSV Tests 2019-2022

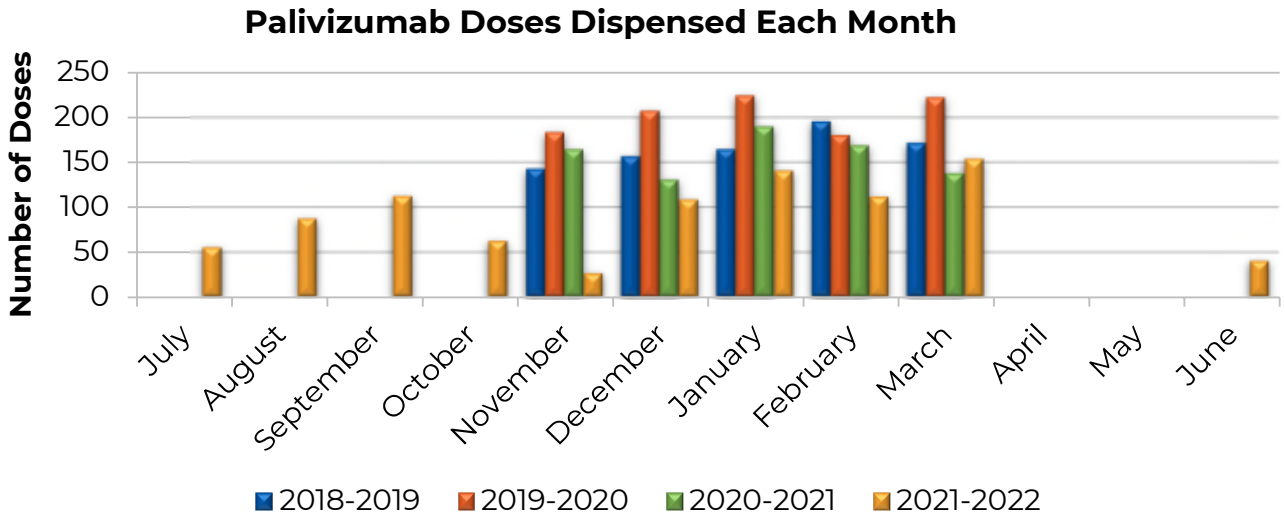


The CDC reported seasonality by using RSV polymerase chain reaction (PCR) laboratory detections. Laboratories are shifting away from antigen-based RSV testing, and since 2014, the majority of RSV detections among reporting laboratories were determined by PCR. RSV season onset, when evaluated by PCR detections and a new statistical method determined by the CDC, was defined as the second of 2 consecutive weeks when the slope, or normalized 5-week moving average of RSV detections between subsequent weeks, exceeded 10 standardized detections per week. Season offset was determined as the last week when the standardized detections exceeded the standardized detections at onset. These changes were done to reflect the adoption of a statistical method rather than a threshold or percentage positive which can be influenced by volume of tests performed. The CDC cautioned that the statistical detection method used captures a high proportion of RSV detection for retrospectively determining seasonality but cannot be used to determine seasonal onset and offset in real time and can only be used after the season is at an end. The CDC advises that surveillance data collected by state and local health departments might be more accurate to describe local RSV circulation trends. RSV PCR testing is not currently

reported by the OSDH to evaluate local trends specific to the state of Oklahoma. The *Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection* released by the AAP in 2014 states the following with regard to RSV seasonality:

> "During the 6 RSV seasons from July 2007 to January 2013, the median duration of the RSV season ranged from 13 to 23 weeks, with median peak activity from mid-December to early February, with the exception of Florida and Alaska. Within the 10 Health and Human Services Regions, in the few regions when the RSV season began in October, the season ended in March or early April. In regions where the RSV season began in November or December, the season ended by April or early May. Because 5 monthly doses of palivizumab at 15mg/kg per dose will provide more than 6 months of serum palivizumab concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States."

The following bar graph shows the number of palivizumab doses reimbursed for by SoonerCare for each month during the last 4 RSV seasons. Notably, the use of palivizumab outside the typical RSV season months (November through March) was allowed for the first time during fiscal year 2022, due to atypical RSV season onset and offset. Although the number of doses dispensed each month was lower during most months of fiscal year 2022 compared to previous fiscal years, the overall number of doses increased, corresponding with the increased number of prior authorization requests submitted during fiscal year 2022. As a result of the atypical RSV season onset and offset, the palivizumab approval criteria was updated by the Drug Utilization Review (DUR) Board in September 2021 to allow coverage based on RSV positivity in Oklahoma, rather than only during specific months.



Market News and Updates[8,9,10,11,12,13,14,15,16,17,18,19]

News:

- **July 2022:** The AAP released updated guidance for the use of palivizumab prophylaxis to prevent hospitalization from severe RSV infection during the 2022-2023 RSV season. Because of the changing patterns of RSV circulation observed since 2020, likely due to nonpharmacologic interventions aimed at preventing COVID-19, the AAP continues to strongly support consideration for use of palivizumab in eligible patients during the interseasonal spread of RSV in regions experiencing high rates of RSV circulation. The AAP will continue to monitor the interseason RSV trends and provide updated guidance as needed if the RSV season extends longer than 6 months.

Pipeline:

- **Ad26.RSV.preF:** Janssen Pharmaceutical Companies is developing Ad26.RSV.preF, a vaccine candidate for the prevention of RSV in adults. The investigational vaccine was previously granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) in September 2019. In September 2021, the Phase 3 EVERGREEN study was initiated and will enroll approximately 23,000 adults 60 years of age and older to compare the efficacy, safety, and immunogenicity of the vaccine vs. placebo.
- **GSK3844766A:** GlaxoSmithKline (GSK) is developing GSK3844766A, a vaccine candidate for the prevention of RSV in older adults. GSK3844766A contains a recombinant subunit pre-fusion RSV antigen (RSVPreF3) combined with a proprietary adjuvant (AS01), which is also used in GSK's shingles vaccine. In June 2022, GSK announced positive interim data from the Phase 3 AReSVi 006 study in adults 60 years of age and older. The pre-specified interim analysis showed the primary endpoint was met with no unexpected safety concerns identified. The study is ongoing, and GSK expects possible regulatory submission in the second half of 2022.
- **mRNA-1345:** Moderna is developing mRNA-1345 as a vaccine against RSV in vulnerable populations, including young children and older adults. mRNA-1345 encodes for a prefusion F glycoprotein, which elicits a higher neutralizing antibody response compared to the postfusion state and is developed using the same lipid nanoparticle (LNP) as Moderna's COVID-19 vaccine. In August 2021, the FDA granted Fast Track designation to mRNA-1435 as a vaccine against RSV in adults older than 60 years of age. In February 2022, Moderna announced the initiation of the Phase 3 ConquerRSV study of mRNA-1345 in adults 60 years of age and older after the Data and Safety Monitoring Board review of Phase 2 data suggested the vaccine had an acceptable safety

profile in older adults at the selected dose. Moderna plans to enroll approximately 34,000 participants in the Phase 3 study.

- **MVA-BN® RSV:** Bavarian Nordic is developing MVA-BN® RSV, a universal RSV vaccine. The vaccine incorporates 5 different RSV antigens to stimulate a broad immune response against both RSV subtypes (A and B), thus mimicking the immune response observed following a natural response to an RSV infection. In February 2022, the FDA granted Breakthrough Therapy designation to MVA-BN® RSV for the prevention of lower respiratory tract disease caused by RSV in adults 60 years of age and older. The Phase 3 VANIR study, originally planned to start in 2021, was previously postponed due to the lower prevalence of RSV seen during the COVID-19 pandemic; however, in April 2022, Bavarian Nordic announced the study has been initiated and the first participant has been vaccinated. The study is expected to enroll approximately 20,000 participants, with topline results expected in mid-2023.
- **Nirsevimab (MEDI8897):** AstraZeneca is developing nirsevimab, an extended half-life RSV F monoclonal antibody (mAb) for the prevention of lower respiratory tract infection (LRTI) caused by RSV. Nirsevimab is being developed for use in late preterm and healthy full-term infants and is being developed so that it may only require 1 dose during a typical 5-month RSV season. The FDA previously granted nirsevimab Breakthrough Therapy and Fast Track designations. In March 2022, the results of the Phase 3 MELODY study in late preterm and healthy term infants were published in *The New England Journal of Medicine*. The results showed that a single dose of nirsevimab resulted in a significantly lower rate of medically attended LRTI compared to placebo but did not result in a statistically significant reduction in hospitalizations for RSV LRTI. However, in May 2022, a pre-specified pooled analysis of data from MELODY and prior Phase 2b studies did demonstrate a statistically significant reduction in hospitalizations for RSV LRTI in the pooled analysis. The results from MELODY, MEDLEY (a Phase 2/3 study in high-risk infants), and the previous Phase 2b studies will form the basis of regulatory submissions which AstraZeneca plans to submit during 2022.

  RSVpreF (PF-06928316): Pfizer is developing RSVpreF, a bivalent protein-based vaccine candidate for the prevention of RSV in adults 60 years of age and older and for the prevention of RSV LRTI in infants by active immunization of pregnant women. A Phase 3 study evaluating the efficacy, immunogenicity, and safety of RSVpreF when administered to pregnant women to provide protection against RSV to the infants after birth was initiated in June 2020 and is ongoing. Additionally, the Phase 3 RENOIR study in older adults was initiated in September 2021. In March 2022, the FDA granted Breakthrough Therapy designation for RSVpreF for both indications.

Recommendations

The College of Pharmacy does not recommend any changes to the current Synagis® (palivizumab) prior authorization criteria at this time.

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[11] GSK. GSK Announces Positive Pivotal Phase III Data for its Respiratory Syncytial Virus (RSV) Vaccine Candidate for Older Adults. Available online at: https://www.gsk.com/en-gb/media/press-releases/gsk-announces-positive-pivotal-phase-iii-data-for-its-respiratory-syncytial-virus-rsv-vaccine-candidate-for-older-adults/. Issued 06/10/2022. Last accessed 08/23/2022.
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Appendix O

Fiscal Year 2022 Annual Review of Nulibry® (Fosdenopterin)

Oklahoma Health Care Authority
September 2022

Current Prior Authorization Criteria

Nulibry® (Fosdenopterin) Approval Criteria:

1. An FDA approved indication to reduce the risk of mortality in members with molybdenum cofactor deficiency (MoCD) Type A; and
2. MoCD Type A must be confirmed by genetic testing; and
    a. If the member is presumed to have MoCD Type A, Nulibry® can be approved for 1 month until genetic testing can be performed; and
    b. Nulibry® will be discontinued if genetic testing results do not confirm MoCD Type A; and
3. Nulibry® must be administered by a health care provider, or the prescriber must verify the member or member's caregiver has been trained by a health care professional on proper storage, preparation, and intravenous (IV) administration of Nulibry®; and
4. Member's weight (kg) must be provided and must have been taken within the last 4 weeks to ensure accurate weight-based dosing according to package labeling; and
5. Approval quantities will be dependent on the member's age, weight, and dosing based on the Nulibry® *Prescribing Information*.

Utilization of Nulibry® (Fosdenopterin): Fiscal Year 2022

There was no utilization of Nulibry® (fosdenopterin) during fiscal year 2022 (07/01/2021 to 06/30/2022).

Prior Authorization of Nulibry® (Fosdenopterin)

There were no prior authorization requests submitted for Nulibry® (fosdenopterin) during fiscal year 2022 (07/01/2021 to 06/30/2022).

Market News and Updates[1]

Anticipated Patent Expiration(s):

- Nulibry® (fosdenopterin): January 2025

Recommendations

The College of Pharmacy does not recommend any changes to the current Nulibry® (fosdenopterin) prior authorization criteria at this time.

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 08/2022. Last accessed 08/19/2022.

Appendix P

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

FDA NEWS RELEASE

For Immediate Release: August 31, 2022

FDA Approves First Treatment for Acid Sphingomyelinase Deficiency, a Rare Genetic Disease.

The FDA approved Xenpozyme™ (olipudase alfa) for intravenous infusion in pediatric and adult patients with Acid Sphingomyelinase Deficiency (ASMD), a rare genetic disease that causes premature death. Xenpozyme™ is the first approved medication to treat symptoms that are not related to the central nervous system in patients with ASMD.

ASMD is caused by the lack of an enzyme needed to break down a complex lipid, called sphingomyelin, that accumulates in the liver, spleen, lung, and brain. Patients with ASMD have enlarged abdomens that can cause pain, vomiting, feeding difficulties, and falls. They also have abnormal liver and blood tests. The most severely affected patients have profound neurologic symptoms and rarely survive beyond two to three years of age. Other patients may survive into adulthood but die prematurely from respiratory failure.

Xenpozyme™ is an enzyme replacement therapy that helps reduce sphingomyelin accumulation in the liver, spleen, and lung. The efficacy of Xenpozyme™ for the treatment of ASMD was demonstrated in a randomized, double-blind, placebo-controlled study of 31 patients randomized to take Xenpozyme™ or placebo. Because the study had the placebo comparator and measured treatment benefits that could be detected during the study's duration, the FDA was able to conclude that Xenpozyme™ is effective. Overall, treatment with Xenpozyme™ improved lung function and reduced liver and spleen size.

The most common side effects of Xenpozyme™ include headache, cough, fever, joint pain, diarrhea, and low blood pressure. Xenpozyme™ carries a *Boxed Warning* for severe hypersensitivity reactions including anaphylaxis. Some patients treated with Xenpozyme™ developed laboratory test abnormalities, such as abnormal liver blood tests. Routine blood laboratory testing should be obtained periodically. Xenpozyme™ should not be started during pregnancy due to the potential for fetal harm, which was observed during animal studies. Additionally, in the clinical trials, 75% of pediatric patients and 50% of adult patients experienced reactions including headaches, nausea, and vomiting while receiving Xenpozyme™ through intravenous infusion.

Xenpozyme™ received Fast Track, Breakthrough Therapy, and Priority Review designations. It also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA awarded the sponsor a Rare Pediatric Disease Priority Review voucher, an incentive to encourage development of new drugs and biologics that prevent and treat rare diseases in children.

More than 7,000 rare diseases affect more than 30 million people in the United States. Many rare conditions are life threatening and most do not have treatments. The FDA estimates that half of these serious or life-threatening diseases affect children.

The FDA granted the approval of Xenpozyme™ to Genzyme.

FDA NEWS RELEASE

For Immediate Release: August 31, 2022

Coronavirus (COVID-19) Update: FDA Authorizes Moderna, Pfizer-BioNTech Bivalent COVID-19 Vaccines for Use as a Booster Dose.

The FDA amended the emergency use authorizations (EUAs) of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine to authorize bivalent formulations of the vaccines for use as a single booster dose at least two months following primary or booster vaccination. The bivalent vaccines, which we will also refer to as "updated boosters," contain two messenger RNA (mRNA) components of SARS-CoV-2 virus, one of the original strain of SARS-CoV-2 and the other one in common between the BA.4 and BA.5 lineages of the omicron variant of SARS-CoV-2.

The Moderna COVID-19 Vaccine, Bivalent, is authorized for use as a single booster dose in individuals 18 years of age and older. The Pfizer-BioNTech COVID-19 Vaccine, Bivalent, is authorized for use as a single booster dose in individuals 12 years of age and older.

The monovalent COVID-19 vaccines that are authorized or approved by the FDA and have been administered to millions of people in the United States since December 2020 contain a component from the original strain of SARS-CoV-2.

What You Need to Know

The authorized bivalent COVID-19 vaccines, or updated boosters, include an mRNA component of the original strain to provide an immune response that is broadly protective against COVID-19 and an mRNA component in common between the omicron variant BA.4 and BA.5 lineages to provide better protection against COVID-19 caused by the omicron variant.

The BA.4 and BA.5 lineages of the omicron variant are currently causing most cases of COVID-19 in the U.S. and are predicted to circulate this fall and winter. In June, the agency's Vaccines and Related Biological Products Advisory Committee voted overwhelmingly to include an omicron component in COVID-19 booster vaccines.

For each bivalent COVID-19 vaccine, the FDA based its decision on the totality of available evidence, including extensive safety and effectiveness data for each of the monovalent mRNA COVID-19 vaccines, safety and immunogenicity data obtained from a clinical study of a bivalent COVID-19 vaccine that contained mRNA from omicron variant BA.1 lineage that is similar to each of the vaccines being authorized, and nonclinical data obtained using a bivalent COVID-19 vaccine that contained mRNA of the original strain and mRNA in common between the BA.4 and BA.5 lineages of the omicron variant.

Based on the data supporting each of these authorizations, the bivalent COVID-19 vaccines are expected to provide increased protection against the currently circulating omicron variant. Individuals who receive a bivalent COVID-19 vaccine may experience side effects commonly reported by individuals who receive authorized or approved monovalent mRNA COVID-19 vaccines.

With authorization of the bivalent vaccines, the monovalent mRNA COVID-19 vaccines are not authorized as booster doses for individuals 12 years of age and older.

The agency will work quickly to evaluate future data and submissions to support authorization of bivalent COVID-19 boosters for additional age groups as we receive them.

Who is Eligible to Receive a Single Booster Dose and When

Individuals 18 years of age and older are eligible for a single booster dose of the Moderna COVID-19 Vaccine, Bivalent if it has been at least two months since they have

completed primary vaccination or have received the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine.

Individuals 12 years of age and older are eligible for a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent if it has been at least two months since they have completed primary vaccination or have received the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine.

The Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent contain mRNA from the SARS-CoV-2 virus. The mRNA in these vaccines is a specific piece of genetic material that instructs cells in the body to make the distinctive "spike" protein of the original virus strain and the omicron variant lineages BA.4 and BA.5. The spike proteins of BA.4 and BA.5 are identical.

For each of the bivalent COVID-19 vaccines authorized, the FDA evaluated immunogenicity and safety data from a clinical study of a booster dose of a bivalent COVID-19 vaccine that contained a component of the original strain of SARS-CoV-2 and a component of omicron lineage BA.1. The FDA considers such data as relevant and supportive of vaccines containing a component of the omicron variant BA.4 and BA.5 lineages. Furthermore, data pertaining to the safety and effectiveness of the current mRNA COVID-19 vaccines, which have been administered to millions of people, including during the omicron waves of COVID-19, contributed to the agency's evaluation.

Data Supporting the Moderna COVID-19 Vaccine, Bivalent Authorization

To evaluate the effectiveness of a single booster dose of the Moderna COVID-19 Vaccine, Bivalent for individuals 18 years of age and older, the FDA analyzed immune response data among approximately 600 individuals 18 years of age and older who had previously received a two-dose primary series and one booster dose of monovalent Moderna COVID-19 Vaccine. These participants received a second booster dose of either the monovalent Moderna COVID-19 Vaccine or Moderna's investigational bivalent COVID-19 vaccine (original and omicron BA.1) at least 3 months after the first booster dose. After 28 days, the immune response against BA.1 of the participants who received the bivalent vaccine was better than the immune response of those who had received the monovalent Moderna COVID-19 Vaccine.

The safety of a single booster dose of the Moderna COVID-19 Vaccine, Bivalent for individuals 18 years of age and older is supported by safety data from a clinical study which evaluated a booster dose of Moderna's investigational bivalent COVID-19 vaccine (original and omicron BA.1), safety data from clinical trials which evaluated primary and booster vaccination with the monovalent Moderna COVID-19 Vaccine, and post marketing safety data with the monovalent Moderna COVID-19 Vaccine.

The safety data accrued with the bivalent vaccine (original and omicron BA.1) and with the monovalent Moderna COVID-19 Vaccine are relevant to the Moderna COVID-19 Vaccine, Bivalent because these vaccines are manufactured using the same process.

The clinical study that evaluated the safety of a booster dose of the bivalent vaccine (original and omicron BA.1) included approximately 800 participants 18 years of age and older who had previously received a two dose primary series and one booster dose of the monovalent Moderna COVID-19 Vaccine, and then at least 3 months later, received a second booster dose with either the monovalent Moderna COVID-19 Vaccine or Moderna's investigational bivalent COVID-19 vaccine (original and omicron BA.1).

Among the study participants who received the bivalent vaccine, the most commonly reported side effects included pain, redness and swelling at the injection site,

fatigue, headache, muscle pain, joint pain, chills, swelling of the lymph nodes in the same arm of the injection, nausea/vomiting and fever.

Data Supporting the Pfizer-BioNTech COVID-19 Vaccine, Bivalent Authorization

To evaluate the effectiveness of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for individuals 12 years of age and older, the FDA analyzed immune response data among approximately 600 adults greater than 55 years of age who had previously received a 2-dose primary series and one booster dose with the monovalent Pfizer-BioNTech COVID-19 Vaccine. These participants received a second booster dose of either the monovalent Pfizer-BioNTech COVID-19 Vaccine or Pfizer-BioNTech's investigational bivalent COVID-19 vaccine (original and omicron BA.1) 4.7 to 13.1 months after the first booster dose. After one month, the immune response against BA.1 of the participants who received the bivalent vaccine was better than the immune response of those who had received the monovalent Pfizer-BioNTech COVID-19 Vaccine.

The safety of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for individuals 12 years of age and older is based on safety data from a clinical study which evaluated a booster dose of Pfizer-BioNTech's investigational bivalent COVID-19 vaccine (original and omicron BA.1), safety data from clinical trials which evaluated primary and booster vaccination with the monovalent Pfizer-BioNTech COVID-19 Vaccine, and post marketing safety data with the monovalent Pfizer-BioNTech COVID-19 Vaccine.

The safety data accrued with the bivalent vaccine (original and omicron BA.1) and with the monovalent Pfizer-BioNTech COVID-19 Vaccine are relevant to Pfizer-BioNTech COVID 19 Vaccine, Bivalent because these vaccines are manufactured using the same process.

The clinical study that evaluated the safety of a booster dose of the bivalent vaccine (original and omicron BA.1) included approximately 600 participants greater than 55 years of age who had previously received a 2-dose primary series, one booster dose of the monovalent Pfizer-BioNTech COVID-19 Vaccine, and then 4.7 to 13.1 months later, received a second booster dose of either the monovalent Pfizer-BioNTech COVID-19 Vaccine or Pfizer-BioNTech's investigational bivalent COVID-19 vaccine (original and omicron BA.1). Among the study participants who received the bivalent vaccine, the most commonly reported side effects included pain, redness and swelling at the injection site, fatigue, headache, muscle pain, chills, joint pain, and fever.

The fact sheets for both bivalent COVID-19 vaccines for recipients and caregivers and for healthcare providers include information about the potential side effects, as well as the risks of myocarditis and pericarditis.

With this authorization, the FDA has also revised the EUA of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine to remove the use of the monovalent Moderna and Pfizer-BioNTech COVID-19 vaccines for booster administration for individuals 18 years of age and older and 12 years of age and older, respectively. These monovalent vaccines continue to be authorized for use for administration of a primary series for individuals 6 months of age and older as described in the letters of authorization. At this time, the Pfizer-BioNTech COVID-19 Vaccine remains authorized for administration of a single booster dose for individuals 5 through 11 years of age at least five months after completing a primary series of the Pfizer-BioNTech COVID-19 Vaccine.

FDA NEWS RELEASE

For Immediate Release: August 18, 2022

FDA Warns Manufacturer for Marketing Illegal Flavored Nicotine Gummies

The FDA issued a warning letter for marketing illegal flavored nicotine gummies – the first warning letter for this type of product. These types of gummies are of particular public concern because of their resemblance to kid-friendly food or candy products and the potential to cause severe nicotine toxicity or even death among young children.

The manufacturer, VPR Brands LP (doing business as, "Krave Nic"), markets gummies that have 1mg of nicotine each and are available in three flavors – Blueraz, Cherry Bomb, and Pineapple. The packaging claims that the products contain tobacco-free nicotine. This firm has not submitted a premarket tobacco product application (PMTA) to the FDA and does not have a marketing authorization order to manufacture, sell, or distribute these products in the U.S.

The manufacturer states that each gummy contains 1mg of nicotine with 12 gummies (12mg) per tin. Research indicates that ingesting 1 to 4mg of nicotine could be severely toxic to a child younger than 6 years of age depending on the child's body weight. However, nicotine toxicity among youth of any age may lead to nausea, vomiting, abdominal pain, increased blood pressure and heart rate, seizures, respiratory failure, coma, and even death. Nicotine is also highly addictive and exposure during adolescence can harm the developing brain.

In a recent study published in the journal *Pediatrics*, researchers found that flavored non-tobacco oral nicotine products, including gummies and lozenges, were among the most commonly used tobacco product among youth in southern California – second only to e-cigarettes. Use was particularly high among certain racial or ethnic, sexual or gender minority groups, and those with a history of nicotine use. These flavored non-tobacco oral nicotine products present an increased risk to youth due to their resemblance to kid-friendly food or candy products, such as gummies or gum, the availability in youth-appealing flavors, and the ability for teenagers to conceal use from adults.

The warning letter issued requests a written response from the manufacturer describing how the firm intends to address any violations and bring their products into compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act). Failure to promptly correct violations can result in further action such as civil money penalties, seizure, and/or injunction. Additionally, the firm must not sell or distribute violative products. The firm must submit a PMTA and receive marketing authorization from the FDA before selling or distributing the product in the U.S.

In response to the increase of non-tobacco nicotine in tobacco products, including in some of the e-cigarette brands that are most popular with youth, Congress passed a federal law that went into effect on April 14, 2022, clarifying the FDA's authority to regulate tobacco products containing nicotine from any source. This law gives the FDA authority over products made with non-tobacco nicotine, including synthetic nicotine, and imposes requirements under the FD&C Act for manufacturers, importers, retailers, and distributors of non-tobacco nicotine products. To date, no non-tobacco nicotine product has received a marketing granted order.

Efforts such as these support the FDA's commitment to using a science-based approach to protect youth from initiating tobacco use. In addition to the FDA's regulatory oversight, the agency recognizes the critical need for targeted youth tobacco prevention efforts designed to protect America's kids, including mass media campaigns such as "The Real Cost." The FDA also collaborates with the Centers for Disease Control and Prevention

(CDC) on the National Youth Tobacco Survey, the only nationally representative survey of middle and high school students that focuses exclusively on tobacco product use.

FDA NEWS RELEASE

For Immediate Release: August 17, 2022

FDA Approves First Cell-Based Gene Therapy to Treat Adult and Pediatric Patients with Beta-thalassemia Who Require Regular Blood Transfusions

The FDA approved Zynteglo® (betibeglogene autotemcel), the first cell-based gene therapy for the treatment of adult and pediatric patients with beta-thalassemia who require regular red blood cell transfusions.

Beta-thalassemia is a type of inherited blood disorder that causes a reduction of normal hemoglobin and red blood cells in the blood, through mutations in the beta-globin subunit, leading to insufficient delivery of oxygen in the body. The reduced levels of red blood cells can lead to several health issues including dizziness, weakness, fatigue, bone abnormalities and more serious complications. Transfusion-dependent beta-thalassemia, the most severe form of the condition, generally requires life-long red blood cell transfusions as the standard course of treatment. These regular transfusions can be associated with multiple health complications of their own, including problems in the heart, liver and other organs due to an excessive build-up of iron in the body.

Zynteglo® is a one-time gene therapy product administered as a single dose. Each dose of Zynteglo® is a customized treatment created using the patient's own bone marrow stem cells that are genetically modified to produce functional beta-globin.

The safety and effectiveness of Zynteglo® were established in 2 multicenter clinical studies that included adult and pediatric patients with beta-thalassemia requiring regular transfusions. Effectiveness was established based on achievement of transfusion independence, which is attained when the patient maintains a pre-determined level of hemoglobin without needing any red blood cell transfusions for at least 12 months. Of 41 patients receiving Zynteglo®, 89% achieved transfusion independence.

The most common adverse reactions associated with Zynteglo® included reduced platelet and other blood cell levels, as well as mucositis, febrile neutropenia, vomiting, pyrexia, alopecia, epistaxis, abdominal pain, musculoskeletal pain, cough, headache, diarrhea, rash, constipation, nausea, decreased appetite, pigmentation disorder, and pruritus.

There is a potential risk of blood cancer associated with this treatment; however, no cases have been seen in studies of Zynteglo®. Patients who receive Zynteglo® should have their blood monitored for at least 15 years for any evidence of cancer. Patients should also be monitored for hypersensitivity reactions during Zynteglo® administration and should be monitored for thrombocytopenia and bleeding.

This application was granted a Rare Pediatric Disease voucher, in addition to receiving Priority Review, Fast Track, Breakthrough Therapy, and Orphan Drug designations. The FDA granted approval of Zynteglo® to Bluebird Bio, Inc.

FDA NEWS RELEASE

For Immediate Release: August 9, 2022

Monkeypox Update: FDA Authorizes Emergency Use of Jynneos® Vaccine to Increase Vaccine Supply

The FDA issued an emergency use authorization (EUA) for the Jynneos® vaccine to allow health care providers to use the vaccine by intradermal injection for individuals 18 years of age and older who are determined to be at high risk for monkeypox infection.

This will increase the total number of doses available for use by up to five-fold. The EUA also allows for use of the vaccine in individuals younger than 18 years of age determined to be at high risk of monkeypox infection; in these individuals Jynneos® is administered by subcutaneous (sub-Q) injection.

Jynneos®, the Modified Vaccinia Ankara (MVA) vaccine, was approved in 2019 for prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection. Jynneos® is administered sub-Q as 2 doses, 4 weeks (28 days) apart. For individuals 18 years of age and older determined to be at high risk of monkeypox infection, the EUA now allows for a fraction of the Jynneos® dose to be administered intradermally. Two doses of the vaccine given 4 weeks (28 days) apart will still be needed. There are no data available to indicate that 1 dose of Jynneos® will provide long-lasting protection, which will be needed to control the current monkeypox outbreak.

Data from a 2015 clinical study of the MVA vaccine evaluated a 2-dose series given intradermally compared to sub-Q. Individuals who received the vaccine intradermally received a lower volume (one fifth) than individuals who received the vaccine sub-Q. The results of this study demonstrated that intradermal administration produced a similar immune response to sub-Q administration. Administration by the intradermal route resulted in more redness, firmness, itchiness, and swelling at the injection site, but less pain, and these side effects were manageable. The FDA has determined that the known and potential benefits of Jynneos® outweigh the known and potential risks for the authorized uses.

To support the FDA's authorization of 2 doses of Jynneos® administered by the sub-Q route of administration in individuals younger than 18 years of age, the FDA considered the available Jynneos® safety and immune response data in adults as well as the historical data with use of live virus smallpox vaccine in pediatric populations.

Jynneos® has been tested in individuals with immunocompromising conditions and has been found to be safe and effective in the trials that were performed to support approval. It was initially developed specifically as an alternative for use in immunocompromised individuals in the event of a smallpox outbreak.

Based on the determination by the Secretary of the Department of Health and Human Services on August 9, 2022, that there is a public health emergency, or the significant potential for a public health emergency, that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that circumstances exist justifying the emergency use of vaccines, the FDA may issue an EUA to allow emergency use of unapproved vaccines or unapproved uses of approved vaccines.

The FDA will provide updates as developments occur and will continue to work with federal public health partners and industry to ensure timely access to all available medical countermeasures. More information can be found on the FDA's monkeypox webpage.

FDA NEWS RELEASE

For Immediate Release: August 9, 2022

FDA Issues Warning Letters to 3 Companies for Selling Unapproved New Drugs for Mole and Skin Tag Removal

The FDA announced it issued 3 warning letters to companies for introducing mole and skin tag removal products into interstate commerce that are unapproved new drugs,

in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act). There are no FDA approved over-the-counter drug products for the removal of moles and skin tags.

Moles should be evaluated by a health care practitioner. Self-diagnosis and treatment of moles could lead to delayed cancer diagnosis and treatment, and even cancer progression. The FDA has issued a consumer warning noting that products marketed for removing moles and other skin lesions can cause injuries and scarring. The sale of these products risks public health and may jeopardize consumers' health when used without consulting a health care professional.

The FDA issued the warning letters to: Amazon.com, Ariella Naturals, and Justified Laboratories.

The mole and skin tag removal products sold by these firms have not been evaluated by the FDA for safety, effectiveness, or quality and require FDA approval. The introduction or delivery for introduction of these products into interstate commerce without an approved application is an additional violation of the FD&C Act.

The warning letters alert the companies that failure to adequately address the violations cited by the FDA may result in legal action including seizure and/or injunction. The companies have 15 days from receipt of the warning letter to respond to the agency with actions they have taken to address any violations. The FDA will continue to use all tools available to protect public health and remove fraudulent or unproven drug products from the United States marketplace. Warning letters are not meant to be final agency action.

The FDA encourages consumers and health care professionals to report any adverse events to the FDA's MedWatch Adverse Event Reporting program so action can be taken to protect the public from any unsafe products. The FDA works to protect consumers by informing about the risks and how to buy online safely.

FDA NEWS RELEASE

For Immediate Release: August 5, 2022

FDA Approves First Targeted Therapy for HER2-Low Breast Cancer

The FDA approved Enhertu® (fam-trastuzumab deruxtecan-nxki), an intravenous (IV) infusion for the treatment of patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-low breast cancer. This is the first approved therapy targeted to patients with the HER2-low breast cancer subtype, which is a newly defined subset of HER2-negative breast cancer.

It is estimated that 287,850 new cases of female breast cancer will be diagnosed in 2022 in the United States. Approximately 80-85% of those new cases were previously considered to be HER2-negative subtype [including hormone receptor positive (HR+) and triple negative breast cancer]. Of that proportion of breast cancer diagnoses, about 60% of patients previously classified as having HER2-negative subtype can now be considered as HER2-low. Prior to this approval, HER2-low patients received endocrine therapy or chemotherapy.

As part of the FDA's Cancer Moonshot program, President Biden tapped federal agencies to develop ways to reduce the rate of cancer deaths and improve the lives of cancer patients and their families through advancements in cancer research and technology, and development of new programs. The approval of Enhertu® further illustrates how the FDA's efforts align with the Cancer Moonshot goals of targeting the right treatments to the right patients, speeding the progress against the most deadly and rare cancers, and learning from the experience of all patients.

HER2 receptors, which are proteins made by the HER2 gene, are important in determining a patient's treatment. HER2-negative includes HR+ and triple negative breast cancers. HER2-low is a new classification of the HER2 subtype. It describes a new subtype of breast cancer that has some HER2 proteins on the cell surface, but not enough to be classified as HER2-positive.

Patients with HER2-low breast cancer are eligible for Enhertu® if they have received a prior chemotherapy in the metastatic setting or if their cancer returned during or within 6 months of completing adjuvant chemotherapy.

This approval is based on DESTINY-Breast04, a randomized, multicenter, open label clinical trial that enrolled 557 adult patients with unresectable or metastatic HER2-low breast cancer. The trial included 2 cohorts: 494 HR+ patients and 63 hormone receptor negative (HR-) patients. Of these patients, 373 randomly received Enhertu® by IV infusion every 3 weeks and 184 randomly received physician's choice of chemotherapy (eribulin, capecitabine, gemcitabine, nab-paclitaxel, or paclitaxel). The results showed improvement in both progression-free survival and overall survival in patients with unresectable or metastatic HER2-low breast cancer.

The median age of trial participants was 57 years, ranging from 28 to 81 years of age. Among the 557 patients, 24% were 65 years of age or older. Females comprised 99.6% of the trial population. Trial participants' race was reported as 48% white, 40% Asian, 2% black or African American, and 3.8% Hispanic/Latino.

The most common adverse reactions in patients receiving Enhertu® in DESTINY-Breast04 are nausea, fatigue, alopecia, vomiting, constipation, decreased appetite, musculoskeletal pain, and diarrhea. The *Prescribing Information* includes a *Boxed Warning* to advise health care professionals of the risk of interstitial lung disease and embryo-fetal toxicity. Enhertu® is not recommended for women who are pregnant.

Enhertu® received Priority Review and Breakthrough Therapy designations for this indication. The FDA granted the approval of Enhertu® to Daiichi Sankyo 4 months ahead of the Prescription Drug User Fee Act (PDUFA) deadline.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with the Australian Therapeutic Goods Administration, Health Canada, and Switzerland's Swissmedic. The application reviews may be ongoing at the other regulatory agencies.

Current Drug Shortages Index (as of August 29, 2022):

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

Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azacitidine for Injection	***Currently in Shortage***
Azithromycin (Azasite) Ophthalmic Solution 1%	***Currently in Shortage***
Bacteriostatic 0.9% Sodium Chloride Injection	***Currently in Shortage***
Bacteriostatic Water for Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***

Belladonna and Opium Suppositories	***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***
Cefixime Oral Capsules	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chlordiazepoxide Hydrochloride Capsules	***Currently in Shortage***
Chloroprocaine Hydrochloride Injection	***Currently in Shortage***
Conivaptan Hydrochloride (Vaprisol) in 5% Dextrose Plastic Container	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cortisone Acetate Tablets	***Currently in Shortage***
Cyclopentolate 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***
Dextrose 10% Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 5% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Rectal Gel	***Currently in Shortage***
Diflunisal Tablets	***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***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Floxuridine for Injection	***Currently in Shortage***
Fludarabine Phosphate Injection	***Currently in Shortage***

Fluorescein Injection	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection	***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***
Hydromorphone Hydrochloride Injection	***Currently in Shortage***
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert	***Currently in Shortage***
Ibutilide Fumarate Injection	***Currently in Shortage***
Indigotindisulfonate Sodium Injection	***Currently in Shortage***
Iodixanol Injection	***Currently in Shortage***
Iohexol Injection	***Currently in Shortage***
Iomeprol injection	***Currently in Shortage***
Iopromide (Ultravist) 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***
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***
Mannitol Injection	***Currently in Shortage***
Mepivacaine Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylprednisolone Acetate Injection	***Currently in Shortage***
Metronidazole Injection	***Currently in Shortage***
Midazolam Injection	***Currently in Shortage***
Morphine Sulfate Injection	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nizatidine Capsules	***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***
Pentostatin Injection	***Currently in Shortage***

Physostigmine Salicylate Injection	***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***
Remifentanil Injection	***Currently in Shortage***
Rifampin Capsules	***Currently in Shortage***
Rifampin Injection	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Semaglutide (Ozempic) Injection	***Currently in Shortage***
Semaglutide (Wegovy) Injection	***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 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 14.6% 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***
Sterile Water for Injection	***Currently in Shortage***
Streptozocin (Zanosar) Sterile Powder	***Currently in Shortage***
Sufentanil Citrate Injection	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Technetium TC-99M Mebrofenin Injection	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Teprotumumab-trbw	***Currently in Shortage***
Thiothixene Capsules	***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***
Vandetanib Tablets	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***