OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
February 9, 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 – February 2, 2022

DATE: February 9, 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 February 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/Use of Glucagon-Like Peptide-1 (GLP-1) Agonists or Sodium-Glucose Co-Transporter-2 (SGLT-2) Inhibitors with Cardiovascular (CV) Benefit in Members with

Type 2 Diabetes (T2D) and High CV Risk or Established Atherosclerotic CV Disease (ASCVD) Mailing Update – Appendix B

Narrow Therapeutic Index (NTI) List – Appendix C

Action Item – Vote to Prior Authorize Livmarli™ (Maralixibat) – Appendix D

Action Item – Vote to Prior Authorize Myfembree® (Relugolix/Estradiol/ Norethindrone) – Appendix E

Action Item – Vote to Prior Authorize Sertraline Capsules and Update the Approval Criteria for the Antidepressants – Appendix F

Action Item – Vote to Prior Authorize Tyrvana™ (Varenicline Nasal Spray) and Update the Approval Criteria for the Dry Eye Disease (DED) Medications – Appendix G

Action Item – Vote to Prior Authorize Byooviz™ (Ranibizumab-nuna Intravitreal Injection) and Susvimo™ (Ranibizumab Intravitreal Implant) – Appendix H

Action Item – Vote to Update the Approval Criteria for the Glaucoma Medications – Appendix I

Action Item – Vote to Prior Authorize Empaveli™ (Pegcetacoplan) – Appendix J

Action Item – Vote to Prior Authorize Evkeeza® (Evinacumab-dgnb) and Leqvio® (Inclisiran) and Update the Approval Criteria for the Antihyperlipidemics – Appendix K

Action Item – Annual Review of Arcalyst® (Rilonacept) – Appendix L

Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Erwinase® (Crisantaspase), Erwinaze® (Asparaginase *Erwinia Chrysanthemi*), Oncaspar® (Pegaspargase), Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn], and Scemblix® (Asciminib) – Appendix M

Annual Review of Azedra® (Iobenguane I-131) – Appendix N

Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Elepsia™ XR [Levetiracetam Extended-Release (ER) Tablet] and Eprontia™ (Topiramate Oral Solution) – Appendix O

Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Qulipta™ (Atogepant) and Trudhesa™ (Dihydroergotamine Nasal Spray) – Appendix P

Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Winlevi® (Clascoterone 1% Cream) – Appendix Q

30-Day Notice to Prior Authorize Dojolvi® (Triheptanoin) – Appendix R

Annual Review of Zokinvy™ (Lonafarnib) – Appendix S

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – February 9, 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. Markita Broyles –	participating in person
Dr. Megan Hanner –	participating in person
Dr. Lynn Mitchell –	participating in person
Dr. John Muchmore –	participating in person
Dr. Lee Muñoz –	participating in person
Dr. James Osborne –	participating in person

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

Or join by phone:
Dial: +1-602-753-0140 or +1-669-219-2599
Webinar ID: 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. December 8, 2021 DUR Board Meeting Minutes
   B. December 8, 2021 DUR Board Recommendations Memorandum
   C. January 12, 2022 DUR Board Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Use of Glucagon-Like Peptide-1 (GLP-1) Agonists or Sodium-Glucose Co-Transporter-2 (SGLT-2) Inhibitors with Cardiovascular (CV) Benefit in Members with Type 2 Diabetes (T2D) and High CV Risk or Established Atherosclerotic CV Disease (ASCVD) Mailing Update – See Appendix B**
   A. Pharmacy Helpdesk Activity for January 2022
   B. Medication Coverage Activity for January 2022
   C. Use of GLP-1 Agonists or SGLT-2 Inhibitors with CV Benefit in Members with T2D and High CV Risk or Established ASCVD Mailing Update

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

5. **Narrow Therapeutic Index (NTI) List – See Appendix C**
   A. Introduction
   B. SoonerCare NTI Drug List
   C. College of Pharmacy Recommendations

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

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

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

7. **Action Item – Vote to Prior Authorize Myfembree® (Relugolix/Estradiol/ Norethindrone) – See Appendix E**
   A. Market News and Updates
   B. Myfembree® (Relugolix/Estradiol/Norethindrone) Product Summary
   C. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Sertraline Capsules and Update the Approval Criteria for the Antidepressants – See Appendix F**
   A. Market News and Updates
   B. Sertraline Capsules Product Summary
   C. College of Pharmacy Recommendations

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

9. **Action Item – Vote to Prior Authorize Tyrvana™ (Varenicline Nasal Spray) and Update the Approval Criteria for the Dry Eye Disease (DED) Medications – See Appendix G**
   A. Market News and Updates
   B. Tyrvana™ (Varenicline Nasal Spray) Product Summary
   C. College of Pharmacy Recommendations

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

10. **Action Item – Vote to Prior Authorize Byooviz™ (Ranibizumab-nuna Intravitreal Injection) and Susvimo™ (Ranibizumab Intravitreal Implant) – See Appendix H**
    A. Market News and Updates
    B. Byooviz™ (Ranibizumab-nuna Intravitreal Injection) Product Summary
    C. Susvimo™ (Ranibizumab Intravitreal Implant) Product Summary
    D. College of Pharmacy Recommendations

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

11. **Action Item – Vote to Update the Approval Criteria for the Glaucoma Medications – See Appendix I**
    A. College of Pharmacy Recommendations

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

12. **Action Item – Vote to Prior Authorize Empaveli™ (Pegcetacoplan) – See Appendix J**
    A. Market News and Updates
    B. Empaveli™ (Pegcetacoplan) Product Summary
    C. College of Pharmacy Recommendations

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

13. **Action Item – Vote to Prior Authorize Evkeeza® (Evinacumab-dgnb) and Leqvio® (Inclisiran) and Update the Approval Criteria for the Antihyperlipidemics – See Appendix K**
    A. Market News and Updates
    B. Evkeeza® (Evinacumab-dgnb) Product Summary
    C. Leqvio® (Inclisiran) Product Summary
    D. College of Pharmacy Recommendations

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

14. **Action Item – Annual Review of Arcalyst® (Rilonacept) – See Appendix L**
    A. Current Prior Authorization Criteria
    B. Utilization of Arcalyst® (Rilonacept)
    C. Prior Authorization of Arcalyst® (Rilonacept)
    D. Market News and Updates
    E. Cryopyrin-Associated Periodic Syndromes (CAPS)
    F. Arcalyst® (Rilonacept) Product Summary
    G. College of Pharmacy Recommendations

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

15. **Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Erwinase® (Crisantaspase), Erwinaze® (Asparaginase *Erwinia Chrysanthemi*), Oncaspar® (Pegaspargase), Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn], and Scemblix® (Asciminib) – See Appendix M**
    A. Current Prior Authorization Criteria
    B. Utilization of Leukemia Medications
    C. Prior Authorization of Leukemia Medications
    D. Market News and Updates
    E. Product Summaries
    F. College of Pharmacy Recommendations
    G. Utilization Details of Leukemia Medications

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

16. **Annual Review of Azedra® (Iobenguane I-131) – See Appendix N**
    A. Current Prior Authorization Criteria
    B. Utilization of Azedra® (Iobenguane I-131)
    C. Prior Authorization of Azedra® (Iobenguane I-131)

D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Azedra® (Iobenguane I-131)

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

17. Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Elepsia™ XR [Levetiracetam Extended-Release (ER) Tablet] and Eprontia™ (Topiramate Oral Solution) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Anticonvulsants
C. Prior Authorization of Anticonvulsants
D. Market News and Updates
E. Elepsia™ XR (Levetiracetam ER) Product Summary
F. Eprontia™ (Topiramate Oral Solution) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Anticonvulsants

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

18. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Qulipta™ (Atogepant) and Trudhesa™ (Dihydroergotamine Nasal Spray) – See Appendix P

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Qulipta™ (Atogepant) Product Summary
F. Trudhesa™ (Dihydroergotamine Nasal Spray) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Anti-Migraine Medications

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

19. Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Winlevi® (Clascoterone 1% Cream) – See Appendix Q

A. Current Prior Authorization Criteria
B. Utilization of Topical Acne and Rosacea Products
C. Prior Authorization of Topical Acne and Rosacea Products
D. Market News and Updates
E. Winlevi® (Clascoterone 1% Cream) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Topical Acne and Rosacea Products

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

20. 30-Day Notice to Prior Authorize Dojolvi® (Triheptanoin) – See Appendix R

A. Introduction
B. Dojolvi® (Triheptanoin) Product Summary

C. College of Pharmacy Recommendations

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

21. Annual Review of Zokinvy™ (Lonafarnib) – See Appendix S

A. Current Prior Authorization Criteria
B. Utilization of Zokinvy™ (Lonafarnib)
C. Prior Authorization of Zokinvy™ (Lonafarnib)
D. Market News and Updates
E. College of Pharmacy Recommendations

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

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

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

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

A. Granulocyte Colony-Stimulating Factors (G-CSFs)
B. Growth Hormone Products
C. Hemophilia Medications
D. Lymphoma Medications

*Future product and class reviews subject to change.

24. 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 DECEMBER 8, 2021

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; DUR Manager	X	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	X	
Erin Ford, Pharm.D.; Clinical Pharmacist		X
Beth Galloway; Business Analyst	X	
Thomas Ha, Pharm.D.; Clinical Pharmacist	X	
Katrina Harris, Pharm.D.; Clinical Pharmacist		X
Robert Klatt, Pharm.D.; Clinical Pharmacist		X
Morgan Masterson, Pharm.D; Clinical Pharmacist		X
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	X	
Alicia O'Halloran, Pharm.D.; Clinical Pharmacist		X
Wynn Phung, Pharm.D.; Clinical Pharmacist		X
Grant H. Skrepnek, Ph.D.; Associate Professor		X
Regan Smith, Pharm.D.; Clinical Pharmacist		X
Ashley Teel, Pharm.D.; Clinical Pharmacist		X
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	X	
Devin Wilcox, D.Ph.; Pharmacy Director	X	
Justin Wilson, Pharm.D.; Clinical Pharmacist	X	
Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		X
Emily Borders, Pharm.D., BCOP	X	
Sarah Schmidt, Pharm.D., BCPS, BCOP		X
Graduate Students: Matthew Dickson, Pharm.D.	X	
Michael Nguyen, Pharm.D.		X
Corby Thompson, Pharm.D.	X	
Laura Tidmore, Pharm.D.	X	
Visiting Pharmacy Student(s): N/A		

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

Josh Holloway, J.D.; Deputy General Counsel	X	
Debra Montgomery, D.O.; Medical Director	X	
Jill Ratterman, D.Ph.; Clinical Pharmacist	X	
Paula Root, M.D.; Senior Medical Director, Interim Chief Medical Officer		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:	
Camille Kerr, Regeneron	Stormy Cameron, Artia Solutions
Chrystal Mayes, Sanofi	John Churnetski, Alexion
Garth Wright, Genentech	Kirk Culotta, Merck
Marie Abrego, Sumaira Foundation	Shellie Keast, Mercer
Robert Greely, Biogen	Gina Heinen, Novo Nordisk
Andrew Delgado, BMS	Leah Campbell, Sumaira Foundation
Kenneth Berry, Alkermes	Brian Maves, Pfizer
Nima Nabavi, Amgen	Ronald Cain, Pfizer
Bob Firnberg, Gilead	Don Napper, Apellis
Jamie Tobitt, Apellis	Pratik Parikh, Mirum
Jody Legg, Mirum	Jeff Knappen, Spark
Paul Sparks, Horizon	Marc Parker, Sunovion
Scott Hylla, Sunovion	Clint Degner, Novartis
David Prather, Novo Nordisk	Brent Parker, Merck

PRESENT FOR PUBLIC COMMENT:	
Pratik Parikh, Mirum	Jamie Tobitt, Apellis

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

1A: ROLL CALL

Dr. Muchmore called the meeting to order at 4:00pm. 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. 13 PRATIK PARIKH

2B: AGENDA ITEM NO. 15 JAMIE TOBITT

ACTION: NONE REQUIRED

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

3A: NOVEMBER 10, 2021 DUR MINUTES – VOTE

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ACADEMIC DETAILING (AD) PROGRAM UPDATE**

4A: PHARMACY HELPDESK ACTIVITY FOR NOVEMBER 2021

4B: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2021

4C: AD PROGRAM UPDATE

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **MAINTENANCE DRUG LIST**

5A: INTRODUCTION

5B: SOONERCARE MAINTENANCE DRUG LIST

5C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ha

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE OPZELURA™ (RUXOLITINIB 1.5% CREAM)**

6A: MARKET NEWS AND UPDATES

6B: OPZELURA™ (RUXOLITINIB 1.5% CREAM) PRODUCT SUMMARY

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Wilson

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE ABECMA® (IDECABTAGENE VICLEUCEL), FARYDAK® (PANOBINOSTAT), AND PEPAXTO® (MELPHALAN FLUFENAMIDE) AND UPDATE THE APPROVAL CRITERIA FOR THE MULTIPLE MYELOMA MEDICATIONS**

7A: MARKET NEWS AND UPDATES

7B: ABECMA® (IDECABTAGENE VICLEUCEL) PRODUCT SUMMARY

7C: FARYDAK® (PANOBINOSTAT) PRODUCT SUMMARY

7D: PEPAXTO® (MELPHALAN FLUFENAMIDE) PRODUCT SUMMARY

7E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE JEMPERLI® (DOSTARLIMAB-GXLY) AND UPDATE THE RENAL CELL CARCINOMA (RCC) APPROVAL CRITERIA FOR KEYTRUDA® (PEMBROLIZUMAB) AND LENVIMA® (LENVATINIB)**

8A: MARKET NEWS AND UPDATES

8B: JEMPERLI® (DOSTARLIMAB-GXLY) PRODUCT SUMMARY

8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

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

ACTION: MOTION CARRIED

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

9A: INTRODUCTION

9B: CURRENT PRIOR AUTHORIZATION CRITERIA

9C: UTILIZATION OF SKIN CANCER MEDICATIONS

9D: PRIOR AUTHORIZATION OF SKIN CANCER MEDICATIONS

9E: MARKET NEWS AND UPDATES

9F: COLLEGE OF PHARMACY RECOMMENDATIONS

9G: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Borders

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF CROHN'S DISEASE AND ULCERATIVE COLITIS (UC) MEDICATIONS**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF CROHN'S DISEASE AND UC MEDICATIONS
10C: PRIOR AUTHORIZATION OF CROHN'S DISEASE AND UC MEDICATIONS
10D: MARKET NEWS AND UPDATES
10E: COLLEGE OF PHARMACY RECOMMENDATIONS
10F: UTILIZATION DETAILS OF CROHN'S DISEASE AND UC MEDICATIONS

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

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS**

11A: CURRENT PRIOR AUTHORIZTION CRITERIA
11B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
11C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
11F: UTILIZATION DETAILS OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS

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

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE SERTRALINE CAPSULES**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF ANTIDEPRESSANTS
12C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS
12D: MARKET NEWS AND UPDATES
12E: SERTRALINE CAPSULE PRODUCT SUMMARY
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
12G: UTILIZATION DETAILS OF ANTIDEPRESSANTS

Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2022

AGENDA ITEM NO. 13: **30-DAY NOTICE TO PRIOR AUTHORIZE LIVMARLI™ (MARALIXIBAT)**

13A: INTRODUCTION
13B: LIVMARLI™ (MARALIXIBAT) PRODUCT SUMMARY
13C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Wilson
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2022

AGENDA ITEM NO. 14: **30-DAY NOTICE TO PRIOR AUTHORIZE BYOOVIZ™ (RANIBIZUMAB-NUNA INJECTION) AND SUSVIMO™ (RANIBIZUMAB INTRAVITREAL IMPLANT)**

14A: INTRODUCTION
14B: MARKET NEWS AND UPDATES
14C: BYOOVIZ™ (RANIBIZUMAB-NUNA INJECTION) PRODUCT SUMMARY
14D: SUSVIMO™ (RANIBIZUMAB INTRAVITREAL IMPLANT) PRODUCT SUMMARY

14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF OPHTHALMIC VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) INHIBITOR MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2022

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ENSPRYNG™ (SATRALIZUMAB-MWGE), SOLIRIS® (ECULIZUMAB), ULTOMIRIS® (RAVULIZUMAB-CWVZ) AND UPLIZNA® (INEBILIZUMAB-CDON) AND 30-DAY NOTICE TO PRIOR AUTHORIZE EMPAVELI™ (PEGCETACOPLAN)

15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF ENSPRYNG™ (SATRALIZUMAB-MWGE), SOLIRIS® (ECULIZUMAB), ULTOMIRIS® (RAVULIZUMAB-CWVZ), AND UPLIZNA® (INEBILIZUMAB-CDON)
15C: PRIOR AUTHORIZATION OF ENSPRYNG™ (SATRALIZUMAB-MWGE), SOLIRIS® (ECULIZUMAB), ULTOMIRIS® (RAVULIZUMAB-CWVZ), AND UPLIZNA® (INEBILIZUMAB-CDON)
15D: MARKET NEWS AND UPDATES
15E: EMPAVELI™ (PEGCETACOPLAN) PRODUCT SUMMARY
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF ENSPRYNG™ (SATRALIZUMAB-MWGE), SOLIRIS® (ECULIZUMAB), ULTOMIRIS® (RAVULIZUMAB-CWVZ), AND UPLIZNA® (INEBILIZUMAB-CDON)

Materials included in agenda packet; presented by Dr. Ha

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2022

AGENDA ITEM NO. 16: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTATION (DEA) UPDATES

Materials included in agenda packet; presented by Dr. Ha

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)

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

17A: ANTIHYPERLIPIDEMICS
17B: DRY EYE DISEASE (DED) MEDICATIONS
17C: GLAUCOMA MEDICATIONS
17D: GONADOTROPIN-RELEASING HORMONE (GNRH) MEDICATIONS

*Future product and class reviews subject to change.

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ADJOURNMENT

The meeting was adjourned at 5:25pm.

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

Memorandum

Date: December 10, 2021

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

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

Subject: DUR Board Recommendations from Meeting on December 8, 2021

Recommendation 1: Academic Detailing Program Update

NO ACTION REQUIRED.

Recommendation 2: Maintenance Drug List

MOTION CARRIED by unanimous approval.

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

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

- Hyperlipidemia Medications
- Parkinson's Medications
- Thyroid Medications

Recommendation 3: Vote to Prior Authorize Opzelura™ (Ruxolitinib 1.5% Cream)

MOTION CARRIED by unanimous approval.

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

Opzelura™ (Ruxolitinib 1.5% Cream) Approval Criteria:

1. An FDA approved indication for short-term and non-continuous treatment of mild-to-moderate atopic dermatitis; and
2. Member must be 12 years of age or older; and
3. Member must not be immunocompromised; and
4. Member must have a body surface area (BSA) involvement ≤20%; and
5. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with all of the following therapies (or have a contraindication or documented intolerance):
   a. One medium potency to very-high potency Tier-1 topical corticosteroid (TCS); and
   b. One topical calcineurin inhibitor (TCI) [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
   c. Eucrisa® (crisaborole); and
6. Concurrent use with therapeutic biologics, other Janus kinase (JAK) inhibitors, or potent immunosuppressants (e.g., azathioprine, cyclosporine) will not generally be approved; and
7. Prescriber must verify female members are not breastfeeding; and
8. If the member is pregnant or becomes pregnant, prescriber must verify member has been counseled on potential risks of this medication and will report the exposure to the Opzelura™ pregnancy registry; and
9. Approvals will be for a maximum duration of 8 weeks of treatment; and
10. Reauthorization may be considered if member has a recent TCS, TCI, or Eucrisa® trial (or a contraindication or documented intolerance); and
    a. Additionally, the prescriber must document the member had a positive response to and tolerated previous treatment with Opzelura™; and
11. Subsequent approvals will only be considered once each 90-day period to ensure appropriate short-term and non-continuous utilization.

Recommendation 4: Vote to Prior Authorize Abecma® (Idecabtagene Vicleucel), Farydak® (Panobinostat), and Pepaxto® (Melphalan Flufenamide) and Update the Approval Criteria for the Multiple Myeloma Medications

MOTION CARRIED by unanimous approval.

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

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

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM):
    a. Member has received ≥4 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody; and
        i. Induction with or without autologous hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen; and
        ii. Must have undergone ≥2 consecutive cycles of treatment for each regimen unless progressive disease was seen after 1 cycle; and
    b. Member must have measurable disease, including at least 1 of the following:
        i. Serum M-protein ≥0.5g/dL; or
        ii. Urine M-protein ≥200mg/24hr; or
        iii. Serum free light chain (FLC) assay: involved FLC ≥10mg/dL (100mg/L); or
        iv. Bone marrow plasma cells >30% of total bone marrow cells; and
    c. Member must not have any central nervous system involvement with multiple myeloma.

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

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

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

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and

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

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

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

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

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

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

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

h. After at least 1 prior therapy in combination with 1 of the following:
    i. Dexamethasone and bortezomib; or
    ii. Carfilzomib and dexamethasone; or
    iii. Dexamethasone and lenalidomide; or
    iv. Cyclophosphamide, bortezomib, and dexamethasone; or
    v. Pomalidomide and dexamethasone* [*previous therapy for this combination must include lenalidomide and a protease inhibitor (PI)]; or
    vi. Selinexor and dexamethasone; or
i. In combination with lenalidomide and dexamethasone for members who are ineligible for ASCT or with cyclophosphamide, bortezomib, and dexamethasone as primary therapy or for disease relapse after 6 months following primary induction therapy with the same regimen; or
j. As a single-agent in members who have received ≥3 prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.

Recommendation 5: Vote to Prior Authorize Jemperli® (Dostarlimab-gxly) and Update the Renal Cell Carcinoma (RCC) Approval Criteria for Keytruda® (Pembrolizumab) and Lenvima® (Lenvatinib)

MOTION CARRIED by unanimous approval.

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

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

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

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

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

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

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

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

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

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

Recommendation 6: Annual Review of Skin Cancer Medications

MOTION CARRIED by unanimous approval.

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

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

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

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

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

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

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

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

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

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

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

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

~~1. Diagnosis of unresectable, advanced, recurrent or metastatic esophageal squamous cell carcinoma disease; and~~
   ~~a. Following prior fluoropyrimidine- and platinum-based chemotherapy; or~~

2. Diagnosis of esophageal or GEJ cancer; and
   a. Member has received preoperative chemoradiation; and

b. Member underwent R0 (complete) resection and has residual disease; and
c. As a single agent; or

3. Palliative therapy for members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease; and
   a. Human epidermal receptor 2 (HER2)-negative disease; and
      i. In first-line therapy; and
         1. In combination with oxaliplatin and fluorouracil or capecitabine; and
         2. Adenocarcinoma pathology; or
      ii. In second-line or greater therapy; and
         1. As a single agent; and
         2. Squamous cell pathology.

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

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

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

1. Diagnosis of non-squamous NSCLC; and
   a. First-line therapy for metastatic disease; and
   b. Member does not have epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF, MET exon 14 skipping mutation, or RET mutations; and
   c. In combination with bevacizumab, paclitaxel, and carboplatin (maximum of 6 cycles) or in combination with paclitaxel (protein bound) and carboplatin; and
   d. Atezolizumab and bevacizumab may be continued after the above combination in members without disease progression (applies to the bevacizumab/paclitaxel/carboplatin regimen); or
2. Diagnosis of NSCLC; and
   a. For first-line therapy for metastatic disease:
      i. As a single-agent; and
      ii. Member does not have epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF, MET exon 14 skipping, or RET mutations; and
      iii. High programmed death ligand-1 (PD-L1) expression determined by 1 of the following:
         1. PD-L1 stained ≥50% of tumor cells (TC≥50%); or
         2. PD-L1 stained tumor-infiltrating immune cells (IC) covering ≥10% of the tumor area (IC≥10%); or
   b. For subsequent therapy for metastatic disease:
      i. As a single-agent; or
3. Diagnosis of stage 2 or 3A NSCLC; and

a. Member has undergone resection and completed platinum-based chemotherapy; and
b. PD-L1 expression of ≥1% of TC.

Recommendation 7: Annual Review of Crohn's Disease (CD) and Ulcerative Colitis (UC) Medications

MOTION CARRIED by unanimous approval.

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

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

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

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

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

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

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

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

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

Recommendation 8: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

MOTION CARRIED by unanimous approval.

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

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

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

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

Pradaxa® (Dabigatran) Approval Criteria:

1. Pradaxa® (dabigatran) capsules require the following:
    a. An FDA approved indication of 1 of the following:
        i. Non-valvular atrial fibrillation; or
        ii. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with a parenteral anticoagulant for 5 to 10 days; or
        iii. To reduce the risk of recurrent DVT or PE in members who have been previously treated; or
        iv. For the prophylaxis of DVT and PE in members who have undergone hip replacement surgery; or
        v. For the treatment of venous thromboembolic events (VTE) in pediatric members 8 to 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days; or
        vi. To reduce the risk of recurrent VTE in pediatric members 8 to 18 years of age who have been previously treated.
2. Pradaxa® (dabigatran) oral pellets require the following:
    a. An FDA approved indication of 1 of the following:
        i. Treatment of VTE in members who have been treated with a parenteral anticoagulant for at least 5 days; or
        ii. To reduce the risk of recurrent VTE in members who have been previously treated; and
    b. Member must be 3 months of age or older; and
    c. Members older than 10 years of age require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used.

Recommendation 9: Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Sertraline Capsules

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

Recommendation 10: 30-Day Notice to Prior Authorize Livmarli™ (Maralixibat)

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

Recommendation 11: 30-Day Notice to Prior Authorize Byooviz™ (Ranibizumab-nuna Intravitreal Injection) and Susvimo™ (Ranibizumab Intravitreal Implant)

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

Recommendation 12: Annual Review of Enspryng™ (Satralizumab-mwge), Soliris® (Eculizumab), Ultomiris® (Ravulizumab-cwvz), and Uplizna® (Inebilizumab-cdon) and 30-Day Notice to Prior Authorize Empaveli™ (Pegcetacoplan)

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

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

NO ACTION REQUIRED.

Recommendation 14: Future Business

No live DUR Board meeting is scheduled for January 2022. January 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: January 13, 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 January 12, 2022

Recommendation 1: SoonerCare Opioid Initiative Update

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Evkeeza® (Evinacumab-dgnb) and Leqvio® (Inclisiran)

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

Recommendation 3: Annual Review of Glaucoma Medications

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

Recommendation 4: Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Myfembree® (Relugolix/Estradiol/Norethindrone)

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

Recommendation 5: Annual Review of Oxlumo™ (Lumasiran)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Dry Eye Disease (DED) Medications and 30-Day Notice to Prior Authorize Tyrvaya™ (Varenicline Nasal Spray)

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

Recommendation 7: Annual Review of Imcivree™ (Setmelanotide)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Turalio® (Pexidartinib)

NO ACTION REQUIRED.

Recommendation 10: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

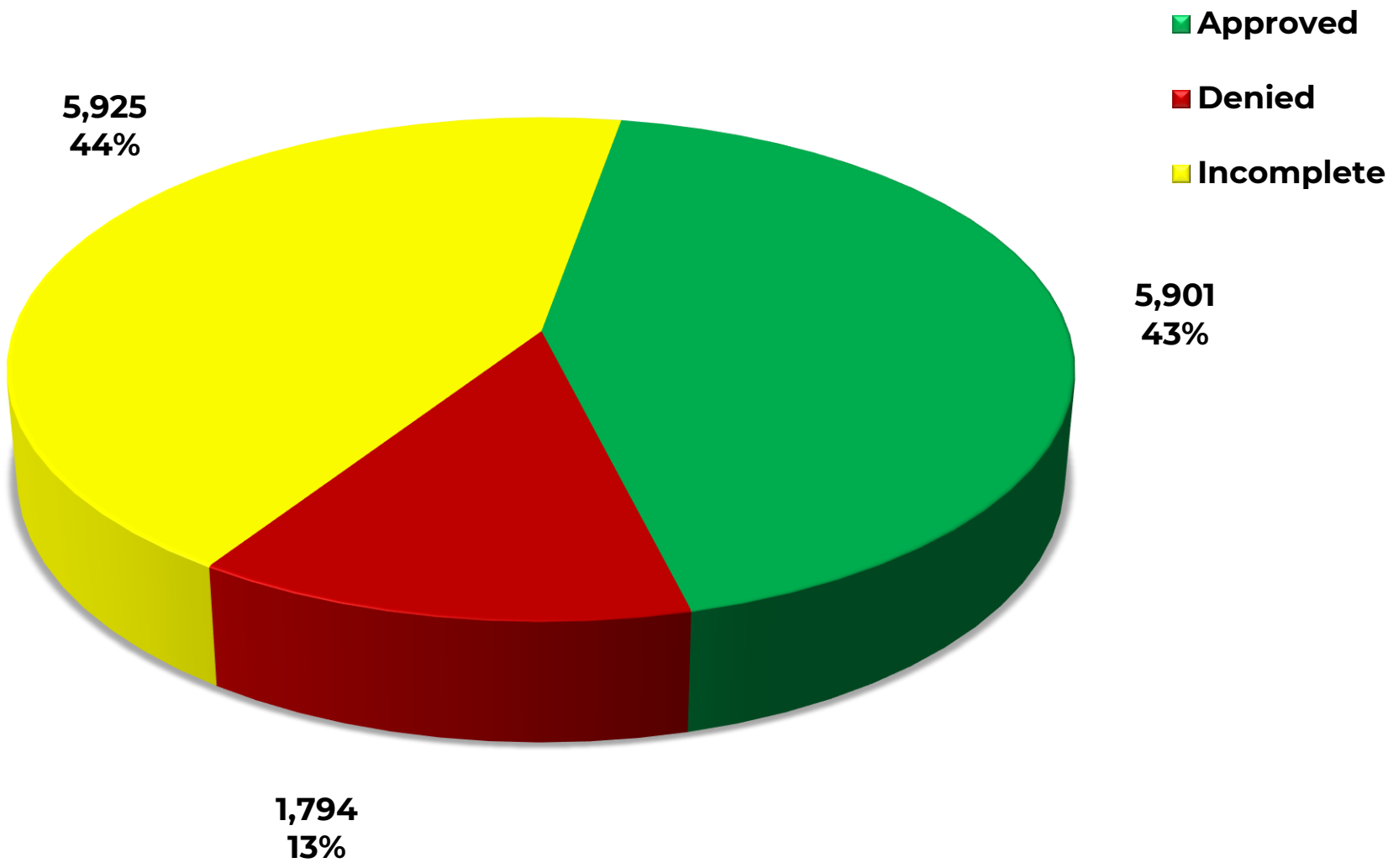
NO ACTION REQUIRED.

Recommendation 11: Future Business

NO ACTION REQUIRED.

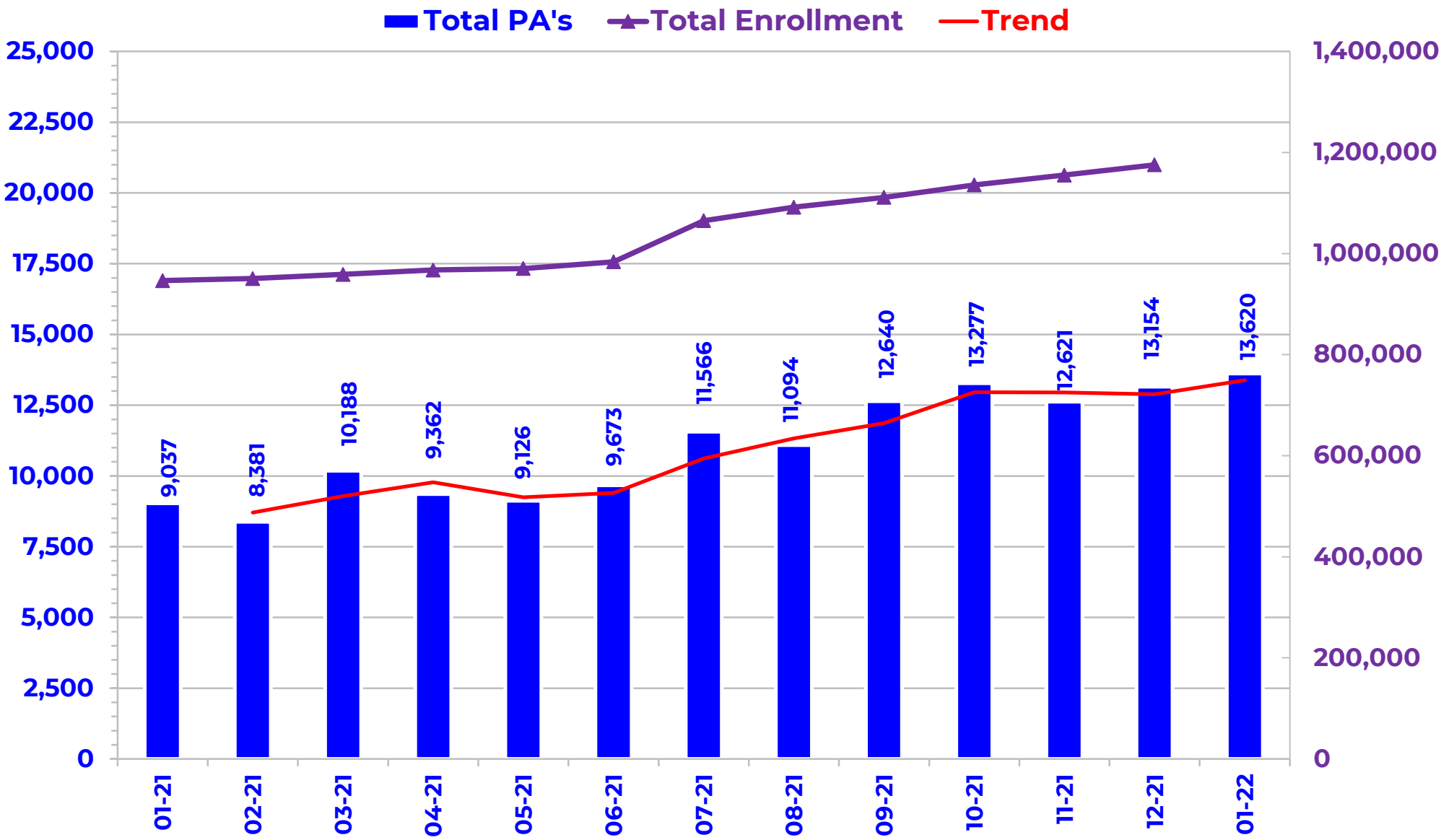
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY 2022



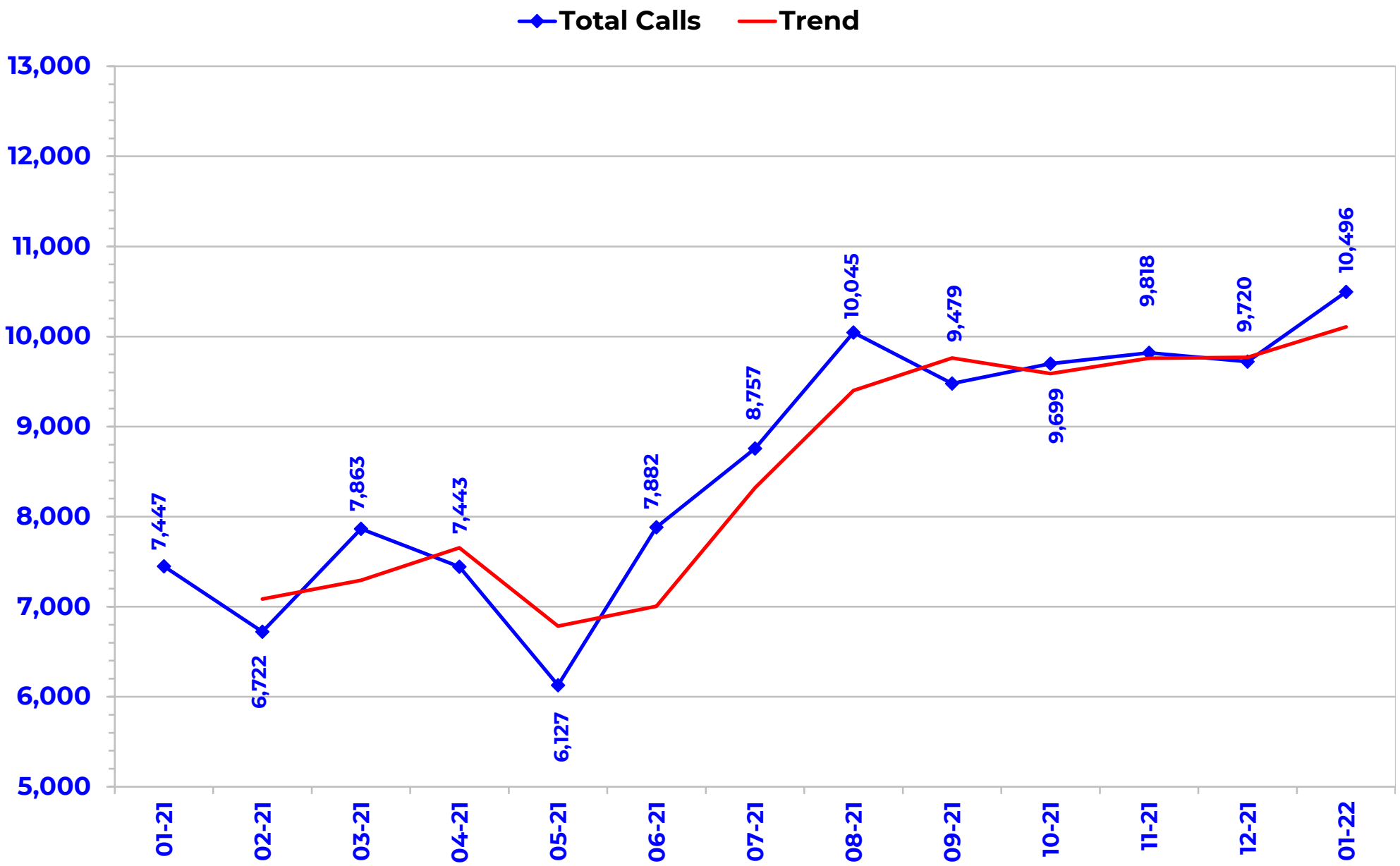
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2021 – JANUARY 2022



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: JANUARY 2021 – JANUARY 2022



Prior Authorization Activity

1/1/2022 Through 1/31/2022

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	109	29	10	70	359
Analgesic - NonNarcotic	25	2	7	16	268
Analgesic, Narcotic	359	108	44	207	140
Angiotensin Receptor Antagonist	12	0	1	11	0
Antiasthma	61	21	10	30	254
Antibiotic	63	27	8	28	227
Anticonvulsant	200	90	11	99	327
Antidepressant	328	66	36	226	343
Antidiabetic	1,168	392	203	573	353
Antigout	12	7	2	3	272
Antihemophilic Factor	12	8	0	4	317
Antihistamine	45	10	14	21	359
Antimigraine	435	66	133	236	222
Antineoplastic	253	173	12	68	169
Antiparasitic	61	16	19	26	41
Antiulcers	49	5	13	31	183
Anxiolytic	34	3	0	31	138
Atypical Antipsychotics	471	207	44	220	351
Benign Prostatic Hypertrophy	13	1	6	6	358
Biologics	235	116	28	91	273
Bladder Control	94	11	29	54	334
Blood Thinners	644	351	43	250	341
Botox	71	46	15	10	316
Buprenorphine Medications	117	41	15	61	95
Calcium Channel Blockers	19	2	1	16	192
Cardiovascular	92	40	4	48	330
Chronic Obstructive Pulmonary Disease	353	60	84	209	295
Constipation/Diarrhea Medications	210	35	49	126	254
Contraceptive	32	9	3	20	324
Corticosteroid	18	1	5	12	54
Dermatological	352	127	72	153	202
Diabetic Supplies	1,100	417	141	542	243
Endocrine & Metabolic Drugs	99	45	13	41	160
Erythropoietin Stimulating Agents	22	12	4	6	113
Fibromyalgia	14	2	2	10	19
Fish Oils	29	3	9	17	358
Gastrointestinal Agents	150	46	30	74	188
Genitourinary Agents	14	1	4	9	360
Glaucoma	31	7	6	18	266
Growth Hormones	118	74	12	32	143
Hematopoietic Agents	17	6	2	9	179

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Hepatitis C	234	143	31	60	9
Insomnia	117	15	22	80	224
Insulin	282	80	31	171	353
Miscellaneous Antibiotics	32	6	1	25	14
Multiple Sclerosis	79	34	8	37	196
Muscle Relaxant	53	4	13	36	123
Nasal Allergy	125	15	35	75	158
Neurological Agents	106	36	21	49	233
Neuromuscular Agents	10	7	0	3	227
NSAIDs	39	2	7	30	359
Ocular Allergy	14	2	5	7	87
Ophthalmic	18	2	4	12	205
Ophthalmic Anti-infectives	18	7	1	10	13
Ophthalmic Corticosteroid	11	3	3	5	359
Osteoporosis	23	4	6	13	357
Other*	342	75	55	212	285
Otic Antibiotic	28	5	7	16	11
Pediculicide	18	6	1	11	16
Respiratory Agents	66	36	1	29	256
Smoking Cess.	34	3	28	3	61
Statins	27	2	5	20	83
Stimulant	1,354	850	88	416	351
Synagis	147	62	30	55	42
Testosterone	145	45	28	72	317
Thyroid	32	16	2	14	328
Topical Antibiotic	10	0	1	9	0
Topical Antifungal	21	5	1	15	13
Topical Corticosteroids	94	4	46	44	121
Vitamin	110	17	54	39	227
Pharmacotherapy	67	57	1	9	312
Emergency PAs	1	1	0	0	
Total	**11,198**	**4,227**	**1,680**	**5,291**	

* 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	34	19	1	14	334
Compound	6	6	0	0	8
Cumulative Early Refill	3	2	1	0	18
Diabetic Supplies	20	20	0	0	114
Dosage Change	362	331	0	31	14
High Dose	3	2	1	0	189
IHS-Brand	1	1	0	0	26
Ingredient Duplication	6	2	0	4	18
Lost/Broken Rx	118	112	1	5	15
MAT Override	310	229	5	76	87
NDC vs. Age	412	219	47	146	255
NDC vs. Sex	13	8	3	2	122
Nursing Home Issue	99	84	1	14	14
Opioid MME Limit	123	32	8	83	120
Opioid Quantity	58	33	3	22	162
Other	74	61	0	13	13
Quantity vs. Days Supply	694	448	40	206	242
STBS/STBSM	19	18	0	1	91
Step Therapy Exception	7	4	1	2	358
Stolen	13	9	0	4	18
Third Brand Request	47	34	2	11	13
Overrides Total	**2,422**	**1,674**	**114**	**634**	
Total Regular PAs + Overrides	**13,620**	**5,901**	**1,794**	**5,925**	

Denial Reasons	
Unable to verify required trials.	4,942
Does not meet established criteria.	1,820
Lack required information to process request.	951
Other PA Activity	
Duplicate Requests	1,552
Letters	27,791
No Process	3
Changes to existing PAs	1,049
Helpdesk Initiated Prior Authorizations	1,049
PAs Missing Information	1

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

Use of Glucagon-Like Peptide-1 (GLP-1) Agonists or Sodium-Glucose Co-Transporter-2 (SGLT-2) Inhibitors with Cardiovascular (CV) Benefit in Members with Type 2 Diabetes (T2D) and High CV Risk or Established Atherosclerotic CV Disease (ASCVD) Mailing Update

Oklahoma Health Care Authority
February 2022

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

ASCVD is the leading cause of morbidity and mortality for individuals with diabetes, and an estimated $37.3 billion is spent annually on CV-related issues associated with diabetes. Co-existing conditions like hypertension (HTN) and hyperlipidemia (HLD) are risk factors for ASCVD, while diabetes itself confers independent risk. The 2021 and 2022 American Diabetes Association (ADA) *Standards of Medical Care in Diabetes* guidelines include a dedicated decision pathway for individuals with indicators of high CV risk or established ASCVD. For these individuals, either a GLP-1 agonist or an SGLT-2 inhibitor with known CV benefit should be considered independent of baseline hemoglobin A1C target or metformin use. Per the ADA guidelines, indicators of high CV risk include ≥55 years of age with left ventricular hypertrophy or with >50% coronary, carotid, or lower-extremity artery stenosis. The GLP-1 agonists with U.S. Food and Drug Administration (FDA) approved CV benefit include Victoza® (liraglutide), Trulicity® (dulaglutide), and Ozempic® (injectable semaglutide). The SGLT-2 inhibitors with FDA approved CV benefit include Jardiance® (empagliflozin), Farxiga® (dapagliflozin), and Invokana® (canagliflozin).

Mailing Summary

In late February 2021, the College of Pharmacy (COP) and the Oklahoma Health Care Authority (OHCA) sent an educational letter to 120 providers regarding 944 unique members with a diagnosis of type 2 diabetes (T2D) with high CV risk or established ASCVD who were not receiving treatment with 1 of the above GLP-1 agonists or SGLT-2 inhibitors based on their SoonerCare pharmacy claims history. The number of members associated with these top 120 providers ranged from 39 members to 3 members per provider. High CV risk was determined using the indicators suggested in the ADA guidelines (≥55 years of age with left ventricular hypertrophy or with >50% coronary, carotid, or lower-extremity artery stenosis) or a diagnosis of HTN and HLD as evidenced in the member's SoonerCare claims history. The

purpose of the educational mailing was to encourage providers to evaluate evidence-based prescribing practices for SoonerCare members with diabetes and high CV risk or established ASCVD and determine if they may benefit from therapy with a GLP-1 agonist or SGLT-2 inhibitor with FDA approved CV benefit. Providers were selected for this mailing if they were the most recent prescriber for at least 1 SoonerCare member with concurrent diagnoses of T2D and ASCVD or high CV risk factors in the last year who did not have any SoonerCare pharmacy paid claims for a GLP-1 agonist or SGLT-2 inhibitor with CV benefit. Members with a diagnosis of end-stage renal disease (ESRD), heart failure (HF), or pregnancy were excluded.

Mailing Results

In May 2021, 2.5 months after the letters were sent out, the first post-mailing claims analysis was performed and results presented to the OHCA Drug Utilization Review (DUR) Board in June 2021. The claims analysis found 23 members (2.44%) included in the mailing had a paid claim for a GLP-1 agonist or SGLT-2 inhibitor with CV benefit.

A second post-mailing claims analysis was performed in January 2022, 11 months after the letters were sent out to providers. This claims analysis found 132 members (13.98%) included in the mailing had a paid claim for a GLP-1 agonist or SGLT-2 inhibitor with CV benefit resulting in an 11.54% increase compared to the May 2021 analysis. Of the 120 providers included in the February 2021 educational mailing, 70 providers had at least 1 member who was previously included for evaluation of therapy with a GLP-1 agonist or an SGLT-2 inhibitor with FDA approved CV benefit who has now started on therapy with one of the indicated medications.

Conclusions

The second post-mailing claims analysis showed 13.98% of members with a diagnosis of T2D with high CV risk or established ASCVD who were not previously receiving treatment with a GLP-1 agonist or SGLT-2 inhibitor with CV benefit before the mailing in February 2021 were now receiving treatment at 11 months after the initial mailing. This follow-up analysis demonstrates an anticipated increase of 11.54% compared to the first post-mailing analysis performed in May 2021.

In October 2021, the COP started incorporating members meeting the inclusion criteria used for the mailing (diagnosis of T2D with high CV risk or established ASCVD who are lacking treatment with a GLP-1 agonist or SGLT-2 inhibitor with established CV benefit) into the SoonerCare Medication Therapy Management (MTM) program which, in addition to other variables, may have contributed to the increase seen between analyses. The MTM program uses a data-driven approach to perform medication reconciliation,

evaluate any opportunities to further optimize medications, address barriers to access, and improve quality measures.

The May 2021 post-mailing analysis performed had limitations including only 2.5 months had passed between the letter being mailed out and the claims analysis which is shorter than a 90-day medication supply; therefore, some members may not have been due for a prescription refill. A limitation both analyses have in common is that they occurred during a global pandemic in which members may not have been seen by their primary care provider. Additionally, it is important to note that the recommended GLP-1 agonists and SGLT-2 inhibitors with CV benefit require prior authorization that could delay the time to filling the medication. However, while these medications do require prior authorization, there is a clinical exception that applies for members who require the medication for its CV benefit (tier structure still applies).

Overall, the purpose of this mailing was not to see all of the members started on therapy with a GLP-1 agonist or SGLT-2 inhibitor with CV benefit, but rather to ensure the providers were evaluating these members for appropriate therapy. As of January 2022, there are currently 5,341 unique SoonerCare members with a diagnosis of T2D with high CV risk or established ASCVD who are not receiving treatment with a GLP-1 agonist or SGLT-2 inhibitor with CV benefit. The COP will continue to work with OHCA to improve the quality of care for SoonerCare members with T2D including educational mailings, inclusion in the MTM program when appropriate, and the future addition of system edits to detect T2D and high-risk CV diagnoses in the member's SoonerCare claims history to generate automated prior authorizations where possible for GLP-1 agonist or SGLT-2 inhibitor medications with CV benefit to prevent further delay of treatment caused by the requirement for submission of a manual prior authorization request. New interventions will be implemented where appropriate, and results will be reported to the DUR Board when available.

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[4] Gerstein HC, Colhoun HM, Dagenais GR, et al; REWIND Investigators. Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes (REWIND): A Double-blind, Randomized Placebo-controlled Trial. *Lancet* 2019; 394:121-130.
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[7] Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med* 2019; 380:347-357.
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Appendix C

Narrow Therapeutic Index (NTI) Drug List

Oklahoma Health Care Authority
February 2022

Introduction[1,2,3]

The U.S. Food and Drug Administration (FDA) defines narrow therapeutic index (NTI) drugs as drugs where small differences in dose or blood concentration may lead to serious therapeutic failures or adverse drug reactions. NTI drugs generally have the following characteristics:

- Little separation between therapeutic and toxic doses
- Sub-therapeutic concentration may lead to serious therapeutic failure
- Drugs are subject to therapeutic drug monitoring based on pharmacokinetic (PK) or pharmacodynamic (PD) measures
- In clinical practice, doses are often adjusted in very small increments (<20%)

The FDA Office of Generic Drugs assesses brand/generic interchangeability standards for NTI drugs. NTI drugs analyzed for bioequivalence by the FDA include warfarin, lithium, digoxin, theophylline, tacrolimus, phenytoin, levothyroxine, and carbamazepine. Other groups, including Health Canada, also include cyclosporine and sirolimus in their NTI drug classification group.

The Oklahoma Health Care Authority (OHCA) policy and rules state the following regarding brand necessary certification (317:30-5-77):

> "For certain narrow therapeutic index drugs, a prior authorization will not be required. The DUR Board will select and maintain the list of narrow therapeutic index drugs."

The purpose of this report is to provide the Drug Utilization Review (DUR) Board with the current SoonerCare NTI drug list for review, which is to be maintained by the DUR Board. Medications included in the NTI list are set up to bypass brand/generic substitution requirements in the claims processing system. Action by the DUR Board is not required unless the DUR Board recommends changes to the current NTI drug list.

SoonerCare NTI Drug List

- Carbamazepine
- Clozapine
- Cyclosporine
- Desipramine
- Digoxin
- Levothyroxine
- Lithium
- Nortriptyline
- Phenytoin
- Sirolimus
- Tacrolimus
- Theophylline
- Warfarin

Recommendations

The College of Pharmacy does not recommend any changes to the current SoonerCare NTI Drug List at this time.

[1] U.S. Food and Drug Administration (FDA). FY2015 Regulatory Science Research Report: Narrow Therapeutic Index Drugs. Available online at: https://www.fda.gov/industry/generic-drug-user-fee-amendments/fy2015-regulatory-science-research-report-narrow-therapeutic-index-drugs. Last revised 05/09/2017. Last accessed 01/05/2022.
[2] Yu LX. Quality and Bioequivalence Standards for Narrow Therapeutic Index Drugs. *FDA*. Available online at: https://www.fda.gov/media/82940/download. Issued 2011. Last accessed 01/05/2022.
[3] U.S. FDA. Building Confidence in Generic Narrow Therapeutic Index (NTI) Drugs. Available online at: https://www.fda.gov/about-fda/fda-pharmacy-student-experiential-program/building-confidence-generic-narrow-therapeutic-index-nti-drugs. Last revised 04/10/2020. Last accessed 01/05/2022.

Appendix D

Vote to Prior Authorize Livmarli™ (Maralixibat)

Oklahoma Health Care Authority
February 2022

Market News and Updates[1]

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

- **September 2021:** The FDA approved Livmarli™ (maralixibat) for the treatment of cholestatic pruritus in patients 1 year of age and older with Alagille Syndrome (ALGS). Maralixibat is a reversible inhibitor of the ileal bile acid transporter (IBAT) and is the first medication to be FDA approved for this indication. Pruritus is one of the most common and distressing symptoms of ALGS. In some ALGS patients, severe, intractable pruritus can have a major impact on quality of life and may be an indication for liver transplantation even in the absence of liver failure.

Livmarli™ (Maralixibat) Product Summary[2,3,4]

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

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

Dosing and Administration:

- The initiation dose is 190mcg/kg by mouth once daily for 7 days
- After 1 week, the dose should be increased to 380mcg/kg once daily, as tolerated
- Livmarli™ should be taken 30 minutes before the first meal of the day
- The maximum daily dose is 28.5mg (3mL)
- A calibrated measuring device (0.5mL, 1mL, or 3mL oral dosing dispenser) should be provided by the pharmacy to measure and deliver the prescribed dose accurately
- Livmarli™ should be stored between 20°C and 25°C (68°F and 77°F) and any remaining medication should be discarded 45 days after first opening the bottle

Mechanism of Action: Maralixibat is a reversible inhibitor of IBAT; inhibition of IBAT results in reduced reabsorption of bile acids from the terminal ileum. The complete mechanism by which maralixibat improves pruritus in patients

with ALGS is unknown; however, it may involve inhibition of IBAT leading to reduced reuptake of bile salts and decreased serum bile acids.

Contraindication(s): None

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

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

Recommendations

The College of Pharmacy recommends the prior authorization of Livmarli™ (maralixibat) with the following criteria, along with the recommended changes from the Drug Utilization Review (DUR) Board (proposed changes shown in red):

Livmarli™ (Maralixibat) Approval Criteria:

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

5. Member must have evidence of cholestasis demonstrated by ≥1 of the following:
    a. Total serum bile acid >3x upper limit of normal (ULN) for age; or
    b. Conjugated bilirubin >1mg/dL; or
    c. Fat soluble vitamin deficiency otherwise unexplainable; or
    d. Gamma-glutamyl transferase (GGT) >3x ULN for age; or
    e. Intractable pruritus explainable only by liver disease; and
6. Members with a history of liver transplantation will not generally be approved for Livmarli™; and
7. Prescriber must verify surgical intervention (e.g., biliary diversion, liver transplantation) is not currently clinically appropriate for the member; and
8. Prescriber must agree to monitor alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, and international normalized ratio (INR) at baseline and during treatment with Livmarli™; and
9. Prescriber must verify the member and/or member's caregiver has been counseled on appropriate storage, dosing, and administration of Livmarli™, including the use of a calibrated oral dosing dispenser for accurate measurement; and
10. Member's current weight (taken within the past 3 weeks) must be provided on initial and subsequent prior authorization requests in order to authorize the appropriate amount of drug required according to package labeling; and
11. Initial approvals will be for a duration of 3 months. After 3 months of treatment, further approval may be granted for a duration of 1 year if the prescriber documents the member is responding well to treatment and surgical intervention is still not clinically appropriate.

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[2] Livmarli™ (Maralixibat) Prescribing Information. Mirum Pharmaceuticals, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214662s000lbl.pdf. Last revised 09/2021. Last accessed 01/05/2022.
[3] Safety and Efficacy Study of LUM001 (Maralixibat) With a Drug Withdrawal Period in Participants with Alagille Syndrome (ALGS) (ICONIC). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02160782. Last revised 07/14/2021. Last accessed 01/05/2022.
[4] Gonzales E, Hardikar W, Stormon M, et al. Efficacy and Safety of Maralixibat Treatment in Patients with Alagille Syndrome and Cholestatic Pruritus (ICONIC): A Randomised Phase 2 Study. *Lancet* 2021; 398:1581-1592.

Appendix E

Vote to Prior Authorize Myfembree® (Relugolix/ Estradiol/Norethindrone)

Oklahoma Health Care Authority
February 2022

Market News and Updates[1]

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

- **May 2021:** The FDA approved Myfembree® (relugolix/estradiol/ norethindrone) for the management of heavy menstrual bleeding associated with uterine leiomyomas, also known as fibroids, in premenopausal women. Myfembree® is a combination of relugolix [a gonadotropin-releasing hormone (GnRH) receptor antagonist], estradiol (an estrogen), and norethindrone (a progestin) and is available in a fixed-dose oral tablet formulation. Myfembree® is the first once-daily treatment option to be FDA approved for this indication.

Myfembree® (Relugolix/Estradiol/Norethindrone) Product Summary[2,3]

Indication(s): Myfembree® (relugolix/estradiol/norethindrone) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

- Limitation(s) of Use: Use should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

Boxed Warning: Thromboembolic Disorders and Vascular Events

- Estrogen and progestin combinations, including Myfembree®, increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events
- Myfembree® is contraindicated in women with current or history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women older than 35 years of age who smoke or women with uncontrolled hypertension (HTN)

How Supplied:

- Relugolix/estradiol/norethindrone 40mg/1mg/0.5mg oral tablets

Dosing:

- 1 tablet by mouth once daily for up to 24 months

Mechanism of Action: Myfembree® contains a combination of relugolix (a GnRH receptor antagonist), estradiol (an estrogen), and norethindrone acetate (a progestin):

- Relugolix binds competitively to GnRH receptors in the pituitary gland, causing suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and a subsequent decrease in the blood concentrations of ovarian sex hormones, estradiol and progesterone. This ultimately reduces bleeding associated with uterine fibroids.
- Estradiol binds to nuclear receptors in estrogen-responsive tissues. The addition of estradiol may help to decrease bone loss that could occur due to a decrease in circulating estrogen from using relugolix alone.
- Norethindrone binds to nuclear receptors in progesterone-responsive tissues. The addition of norethindrone may help protect the uterus from potential adverse endometrial effects of unopposed estrogen.

Contraindication(s):

- High risk of arterial, venous thrombotic, or thromboembolic disorder
- Pregnancy
- Known osteoporosis
- Current or history of breast cancer or other hormonally-sensitive malignancies
- Known hepatic impairment or disease
- Undiagnosed abnormal uterine bleeding
- Known hypersensitivity to ingredients in Myfembree®

Adverse Reactions: The most common adverse reactions in clinical studies with Myfembree® (occurring in ≥3% of patients and at a greater frequency than placebo) were hot flush, hyperhidrosis, or night sweats (10.6%); abnormal uterine bleeding (6.3%); alopecia (3.5%); and decreased libido (3.1%). Additionally, in 1 of the 2 Phase 3 studies, new or worsening HTN was observed in 7% of patients treated with Myfembree® vs. 0.8% in the placebo group.

Cost Comparison:

Product	Cost Per Unit*	Cost Per Year†
Myfembree® (relugolix/estradiol/norethindrone) 40mg/1mg/0.5mg tablet	**$34.81**	**$12,531.60**
Lupron Depot® (leuprolide) 11.25mg injection (3-month kit)	$4,334.37	$17,337.48
Lupron Depot® (leuprolide) 3.75mg injection (1-month kit)	$1,435.16	$17,221.92
Oriahnn® (elagolix/estradiol/norethindrone and elagolix) 300mg/1mg/0.5mg and 300mg capsule	$16.84	$12,124.80
norgestimate/ethinyl estradiol 0.25mg/0.035mg tablet	$0.21	$75.60

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Unit = each capsule for Oriahnn®, each tablet for Myfembree® and norgestimate/ethinyl estradiol, and each package for Lupron Depot®
†Cost per year based on 1 capsule twice daily for Oriahnn®, 1 tablet daily for Myfembree® and norgestimate/ethinyl estradiol, 1 injection monthly for Lupron® Depot 1-month kit, and 1 injection every 3 months for Lupron® Depot 3-month kit

Recommendations

The College of Pharmacy recommends the prior authorization of Myfembree® (relugolix/estradiol/norethindrone) with criteria similar to Oriahnn® (elagolix/estradiol/norethindrone and elagolix) (updates and new criteria shown in red):

Myfembree® (Relugolix/Estradiol/Norethindrone) and Oriahnn® (Elagolix/Estradiol/Norethindrone and Elagolix) Approval Criteria:

1. An FDA approved diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women; and
2. Member must be 18 years of age or older; and
3. Member must not have any contraindications to therapy including:
    a. Osteoporosis; and
    b. Pregnancy; and
        i. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
        ii. Female members of reproductive potential must be willing to use effective non-hormonal contraception during treatment and for at least 1 week after discontinuing treatment; and
    c. Hepatic impairment or disease; and
    d. Undiagnosed abnormal uterine bleeding; and
    e. High risk of arterial, venous thrombotic, or thromboembolic disease, including uncontrolled hypertension; and
    f. Current or history of breast cancer or other hormonally-sensitive malignancies; and
    g. Known hypersensitivity to ingredients in Myfembree® or Oriahnn®; and
    ~~h. Concomitant use with an organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and~~
4. Must be prescribed by, or in consultation with, an obstetrician/gynecologist or a specialist with expertise in the treatment of uterine leiomyomas (fibroids); and
5. A failed trial at least 1 month in duration with nonsteroidal anti-inflammatory drugs (NSAIDs) or a patient-specific, clinically significant reason why the member cannot use NSAIDs must be provided; and
6. A failed trial at least 3 months in duration of hormonal contraceptives or a patient-specific, clinically significant reason why the member cannot use hormonal contraceptives must be provided; and
7. For Myfembree®, a patient-specific, clinically significant reason why the member cannot use leuprolide depot formulations available without prior authorization must be provided; and
8. For Myfembree®, a patient-specific, clinically significant reason (beyond convenience) why the member cannot use Oriahnn® must be provided; and

9. For Oriahnn®, prescriber must verify the member will not use Oriahnn® concomitantly with an organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and
10. Quantity limits will apply based on FDA approved dosing:
    a. For Myfembree®, a quantity limit of 28 tablets per 28 days will apply; and
    b. For Oriahnn®, a quantity limit of 56 tablets per 28 days will apply; and
11. Lifetime approval duration will be limited to a maximum of 24 months. For members previously approved for Myfembree® or Oriahnn®, a combined cumulative maximum treatment duration of 24 months will apply.

[1] Myovant Sciences. Myovant Sciences and Pfizer Receive FDA Approval for Myfembree®, the First Once-Daily Treatment for Heavy Menstrual Bleeding Associated with Uterine Fibroids. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2021/05/26/2236871/0/en/Myovant-Sciences-and-Pfizer-Receive-FDA-Approval-for-MYFEMBREE-the-First-Once-Daily-Treatment-for-Heavy-Menstrual-Bleeding-Associated-With-Uterine-Fibroids.html. Issued 05/26/2021. Last accessed 01/10/2022.

[2] Myfembree® (Relugolix/Estradiol/Norethindrone) Prescribing Information. Myovant Sciences, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214846s000lbl.pdf. Last revised 05/2021. Last accessed 01/10/2022.

[3] Al-Hendy A, Lukes AS, Poindexter AN, et al. Treatment of Uterine Fibroid Symptoms with Relugolix Combination Therapy. *N Engl J Med* 2021; 384:630-642.

Appendix F

Vote to Prior Authorize Sertraline Capsules and Update the Approval Criteria for the Antidepressants

Oklahoma Health Care Authority
February 2022

Market News and Updates[1,2,3]

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

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

Sertraline Capsule Product Summary[2]

Therapeutic Class: Selective serotonin reuptake inhibitor (SSRI)

Indication(s):

- MDD in adults
- OCD in adults and pediatric patients 6 years of age and older

How Supplied: 150mg and 200mg oral capsules

Dosing and Administration:

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

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

Cost Comparison:

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

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

Recommendations

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

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			citalopram 20mg/10mL soln (UDC)
escitalopram (Lexapro®)			escitalopram 10mg/10mL soln (UDC)
fluoxetine caps (Prozac®)			fluoxetine 20mg/5mL soln (UDC)
fluvoxamine (Luvox®)			fluoxetine tabs
paroxetine (Paxil®)			fluoxetine DR (Prozac® Weekly™)
sertraline tabs (Zoloft®)			fluvoxamine CR (Luvox CR®)
			paroxetine CR (Paxil CR®)
			paroxetine (Pexeva®)
			sertraline 150mg & 200mg caps

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	desvenlafaxine (Pristiq®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron SolTab®)		nefazodone (Serzone®)	duloxetine (Drizalma Sprinkle™)
trazodone 50mg, 100mg, & 150mg tabs (Desyrel®)		vilazodone (Viibryd®)	duloxetine 40mg (Irenka™)
venlafaxine (Effexor®, Effexor XR® caps)			trazodone 300mg tabs (Desyrel®)
			venlafaxine ER tabs (Effexor XR® tabs)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	isocarboxazid (Marplan®)
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	esketamine nasal spray (Spravato®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
caps = capsules; CR = controlled-release; DR = delayed-release; ER = extended-release; PA = prior authorization; soln = solution; tabs = tablets; UDC = unit dose cups

Antidepressants Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists; and
3. Tier structure rules still apply.
4. **Citalopram 20mg/10mL Solution, Escitalopram 10mg/10mL Solution, and Fluoxetine 20mg/5mL Solution Unit Dose Cup (UDC) Approval Criteria:**
    a. An FDA approved indication; and

b. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.

5. **Desyrel® (Trazodone 300mg Tablet) Approval Criteria:**
   a. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including 2 trazodone 150mg tablets or 3 trazodone 100mg tablets to achieve a 300mg dose must be provided.
6. **Drizalma Sprinkle™ (Duloxetine Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
   a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
   b. A patient-specific, clinically significant reason why the member cannot use generic duloxetine 20mg, 30mg, or 60mg capsules, which are available without prior authorization, in place of Drizalma Sprinkle™ must be provided; and
   c. A quantity limit of 30 capsules per 30 days will apply.
7. **Fluoxetine Tablet Approval Criteria:**
   a. Fluoxetine capsules are available without a prior authorization. The tablet formulation will require prior authorization and a patient-specific, clinically significant reason why the tablet formulation is required in place of the capsule formulation.
8. **Irenka™ (Duloxetine 40mg Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
   a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
   b. A patient-specific, clinically significant reason why the member cannot use 2 duloxetine 20mg capsules in place of Irenka™ 40mg capsules must be provided; and
   c. A quantity limit of 30 capsules per 30 days will apply.
9. **Marplan® (Isocarboxazid) Approval Criteria:**
   a. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan® must be provided.
10. **Sertraline Capsule Approval Criteria:**
    a. An FDA approved indication of major depressive disorder (MDD) in adults or obsessive-compulsive disorder (OCD) in adults and pediatric patients 6 years of age and older; and
    b. Member must have initiated treatment with sertraline tablets for dose titration up to the 150mg or 200mg dose; and
    c. A patient-specific, clinically significant reason why the member cannot use sertraline tablets, which are available without a prior

authorization, in place of the capsule formulation must be provided; and

d. A quantity limit of 30 capsules per 30 days will apply.

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

Antidepressants Tier-2 Approval Criteria:

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

Antidepressants Tier-3 Approval Criteria:

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

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

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

[1] U.S. Food and Drug Administration (FDA). National Drug Code Directory. Available online at: https://www.accessdata.fda.gov/scripts/cder/ndc/. Last revised 01/10/2022. Last accessed 01/10/2022.
[2] Sertraline Capsule Prescribing Information. U.S. National Library of Medicine: DailyMed. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8c8bcba9-eaeb-aa44-f9ea-b580de55a439. Last revised 10/2021. Last accessed 01/10/2022.
[3] Zoloft® (Sertraline) Prescribing Information. Pfizer. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=517. Last revised 10/2021. Last accessed 01/10/2022.

Appendix G

Vote to Prior Authorize Tyrvaya™ (Varenicline Nasal Spray) and Update the Approval Criteria for the Dry Eye Disease (DED) Medications

Oklahoma Health Care Authority
February 2022

Market News and Updates[1]

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

- **October 2021:** The FDA approved Tyrvaya™ (varenicline 0.03mg nasal spray) for the treatment of the signs and symptoms of DED. Tyrvaya™ is the first and only nasal spray approved for the treatment of DED. Tyrvaya™ is believed to bind to cholinergic receptors on the trigeminal nerve within the nasal cavity and activate the trigeminal parasympathetic pathway resulting in increased production of basal tear film as a treatment for DED.

Tyrvaya™ (Varenicline Nasal Spray) Product Summary[2,3]

Indication(s): Tyrvaya™ (varenicline nasal spray) is a cholinergic agonist indicated for the treatment of the signs and symptoms of DED.

How Supplied:

- Tyrvaya™ is available in a carton containing 2 amber glass bottles, each bottle with a nasal pump.
- Each bottle contains 4.2mL of varenicline solution and provides 1 spray in each nostril twice daily for 15 days.
- Each spray delivers 0.03mg varenicline per 0.05mL.

Dosing and Administration:

- The recommended dosing is 1 spray in each nostril twice daily (approximately 12 hours apart).
- Tyrvaya™ should be primed before initial use by pumping 7 actuations into the air away from the face. When Tyrvaya™ has not been used for >5 days, it should be re-primed with 1 spray into the air.

Mechanism of Action: The exact mechanism of action is unknown at this time. The efficacy of Tyrvaya™ in DED is believed to be the result of varenicline's activity at heteromeric sub-type(s) of the nicotinic acetylcholine (nACh) receptor where Tyrvaya™ binds and produces agonist activity. This activates the trigeminal parasympathetic pathway resulting in increased production of basal tear film as a treatment for DED.

Contraindication(s): None

Safety:

- Pregnancy: No data is available on the use of Tyrvaya™ in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.
- Lactation: No data is available on the presence of Tyrvaya™ in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, Tyrvaya™ was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.
- Pediatric Use: Safety and efficacy of Tyrvaya™ in pediatric patients have not been established.
- Geriatric Use: No overall differences in safety or effectiveness of Tyrvaya™ have been observed between elderly and younger adult patients.

Adverse Reactions: The most common adverse reaction reported in 82% of Tyrvaya™ treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site irritation (8%).

Efficacy: The efficacy of Tyrvaya™ for the treatment of DED was supported by 2 randomized, multi-center, double-masked, vehicle-controlled studies (ONSET-1 and ONSET-2). Use of artificial tears was allowed during the studies. Tear film production was measured by anesthetized Schirmer's score assessed using a Schirmer's strip (0-35mm). Of the patients treated with Tyrvaya™, a statistically significant ($P<0.01$) increase in Schirmer's score from baseline was achieved in both studies.

- The Schirmer Tear Test: This test can be performed with or without anesthesia. It evaluates tear adequacy and often aids in the diagnosis of dry eye syndrome. The Schirmer test performed with anesthesia measures basal tear secretion by eliminating the irritation that causes reflex tearing. To perform the test, the examiner places 1 end of the calibrated filter paper strip over the lateral third of the lower eyelid. After 5 minutes, the examiner removes the strips and measures the length of strip wetted by tears. With anesthesia, the interpretation is as follows: 0 to 5mm of wetting, severe dry eyes; 5 to 10mm of wetting, moderately dry eyes; 10 to 15mm of wetting, mildly dry eyes; and greater than 15mm of wetting, normal tear function.
- ONSET-1: In this study, 182 patients were randomized in a 1:1:1:1 ratio to receive 1 spray in each nostril twice daily of varenicline solution 0.006mg (N=47), varenicline solution 0.03mg (Tyrvaya™) (N=48),

varenicline solution 0.06mg (N=44), or vehicle (N=43). The average baseline Schirmer's score was 5.0mm. Of the patients treated with varenicline solution 0.03mg (Tyrvaya™), 52% achieved an increase of ≥10mm in Schirmer's score from baseline compared to 14% of the vehicle-treated patients at day 28.

- ONSET-2: In this study, 758 patients were randomized in a 1:1:1 ratio to receive 1 spray in each nostril twice daily of varenicline solution 0.03mg (Tyrvaya™) (N=260), varenicline solution 0.06mg (N=246), or vehicle (N=252). The average baseline Schirmer's score was 5.1mm. Of the patients treated with varenicline solution 0.03mg (Tyrvaya™), 47% achieved ≥10mm increase in Schirmer's score from baseline, compared 28% of vehicle-treated patients at day 28.

Cost Comparison:

Product	Cost Per Unit	Cost Per Package*
Tyrvaya™ (varenicline nasal spray)	**$70.51**	**$592.28**
Restasis® (cyclosporine 0.05% ophthalmic emulsion)⁺	$9.85	$591.00
Restasis MultiDose® (cyclosporine 0.05% ophthalmic emulsion)	$107.33	$590.21
Xiidra® (lifitegrast 5% ophthalmic solution)	$9.47	$568.20
Cequa™ (cyclosporine 0.09% ophthalmic solution)	$8.43	$252.90

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 package based on largest package size available for product listed.
⁺Restasis® single-use vials were first FDA approved in 2002 and have a significant federal rebate and thus, do not require prior authorization.
Unit = milliliter (mL) or single-use vial

Recommendations

The College of Pharmacy recommends the prior authorization of Tyrvaya™ (varenicline nasal spray) with the following criteria (shown in red):

Tyrvaya™ (Varenicline Nasal Spray) Approval Criteria:

1. An FDA approved indication for the treatment of the signs and symptoms of dry eye disease (DED) in members 18 years of age or older; and
2. Prescriber must verify that environmental factors (e.g., humidity, fans) have been addressed; and
3. Member must have trials with at least 3 over-the-counter (OTC) products for at least 3 days in duration (per product) in the last 30 days that failed to relieve signs and symptoms of DED; and
4. A patient-specific, clinically significant reason why the member cannot use Restasis® (cyclosporine 0.05% ophthalmic emulsion) single-use vials, which are available without a prior authorization, must be provided; and

5. A patient-specific, clinically significant reason why the member cannot use all available ophthalmic preparations FDA approved for the treatment of DED must be provided; and
6. A quantity limit of 8.4mL (2 bottles) per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Cequa™ (cyclosporine 0.09% ophthalmic solution) and Restasis MultiDose® (cyclosporine 0.05% ophthalmic emulsion) based on net costs (changes shown in red):

Cequa™ (Cyclosporine 0.09% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication to increase tear production in members with keratoconjunctivitis sicca (dry eye); and
2. A patient-specific, clinically significant reason why the member cannot use Restasis® (cyclosporine 0.05% ophthalmic emulsion) single-use vials, which are available without a prior authorization, must be provided; and
3. A patient-specific, clinically significant reason why the member cannot use Xiidra® (lifitegrast 5% ophthalmic solution) must be provided; and
4. A quantity limit of 60 single-use vials (1 box) per 30 days will apply.

Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Restasis® in the individual dosage formulation (single-use vials), which is available without a prior authorization, must be provided; and
2. A patient-specific, clinically significant reason why the member cannot use Xiidra® (lifitegrast 5% ophthalmic solution) must be provided.

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[1] Oyster Point Pharma. Oyster Point Pharma Announces FDA Approval of Tyrvaya™ (Varenicline Solution) Nasal Spray for the Treatment of the Signs and Symptoms of Dry Eye Disease. Available online at: https://investors.oysterpointrx.com/news-releases/news-release-details/oyster-point-pharma-announces-fda-approval-tyrvayatm-varenicline. Issued 10/18/2021. Last accessed 01/10/2022.

[2] Tyrvaya™ (Varenicline Nasal Spray) Prescribing Information. Oyster Point Pharma. Available online at: https://www.tyrvaya-pro.com/files/prescribing-information.pdf. Last revised 10/2021. Last accessed 01/10/2022.

[3] Aaron M, Solley WA, Broocker G. General Eye Examination in Primary Care Ophthalmology (Second Edition). Available online at: https://www.sciencedirect.com/topics/medicine-and-dentistry/schirmer-test. Issued 2005. Last accessed 01/10/2022.

Appendix H

Vote to Prior Authorize Byooviz™ (Ranibizumab-nuna Intravitreal Injection) and Susvimo™ (Ranibizumab Intravitreal Implant)

Oklahoma Health Care Authority
February 2022

Market News and Updates[1,2,3]

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

- **September 2021:** The FDA approved Byooviz™ (ranibizumab-nuna intravitreal injection), a biosimilar to Lucentis® (ranibizumab intravitreal injection) for the treatment of wet age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), and myopic choroidal neovascularization (mCNV). Ranibizumab is a vascular endothelial growth factor (VEGF) inhibitor that prevents vision loss in patients with retinal vascular disorders which can cause irreversible blindness or visual impairments in adults. Byooviz™ is the first ophthalmology biosimilar approved in the United States. The FDA approval was based on analytical, non-clinical, and clinical data from a Phase 3 study evaluating Byooviz™ in patients with wet AMD. The study compared the efficacy, safety, pharmacokinetics, and immunogenicity of Byooviz™ with the reference drug, Lucentis®, over 48 weeks of treatment. Data on all key endpoints from the study of Byooviz™ were comparable to Lucentis®. An agreement is in place to allow the start of commercialization of Byooviz™ in the United States in June 2022.
- **October 2021:** The FDA approved Susvimo™ (ranibizumab 100mg/mL intravitreal implant) for the treatment of patients with wet AMD who have previously responded to at least 2 anti-VEGF injections. Susvimo™, previously called Port Delivery System with ranibizumab, is the first and only FDA-approved treatment for wet AMD that offers as few as 2 treatments per year. Susvimo™ delivers ranibizumab continuously, offering patients living with wet AMD a more convenient alternative to anti-VEGF intravitreal injections needed as often as once a month. The implant is surgically inserted into the eye during a 1-time, outpatient procedure and is refilled every 6 months in an office-based setting under aseptic conditions. If necessary, supplemental intravitreal ranibizumab injections can be administered to the affected eye(s) while the Susvimo™ implant is in place.

Susvimo™ (Ranibizumab Intravitreal Implant) Product Summary[4,5,6,7,8]

Therapeutic Class: Vascular endothelial growth factor (VEGF) inhibitor

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

Boxed Warning: Endophthalmitis

- The Susvimo™ implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab. In clinical trials, 2% of patients receiving an implant experienced at least 1 episode of endophthalmitis.

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

Dosing and Administration:

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

Mechanism of Action:

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

Contraindication(s):

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

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

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

Cost Comparison

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

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Susvimo™ cost is based on 2mg (0.02mL) via implant with refills every 6 months and does not include the surgical costs for implantation.
±Lucentis® cost is based on 0.5mg once monthly.
+Eylea® cost is based on 2mg every 4 weeks for the first 3 months, followed by 2mg every 8 weeks.
≠Beovu® cost is based on 6mg monthly for 3 doses, followed by 6mg every 8 weeks.

Recommendations

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

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

1. An FDA approved indication of 1 of the following:

   a. Neovascular (wet) age-related macular degeneration (AMD); or
   b. Macular edema following retinal vein occlusion (RVO); or
   c. Myopic choroidal neovascularization (mCNV); and
2. A patient-specific, clinically significant reason why the member cannot use Lucentis® (ranibizumab intravitreal injection) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Susvimo™ (Ranibizumab Intravitreal Implant) Approval Criteria:

1. An FDA approved indication for the treatment of adults with neovascular (wet) age-related macular degeneration (AMD); and
2. Member must have previously responded to ≥2 intravitreal injections of a vascular endothelial growth factor (VEGF) inhibitor; and
3. Member must not have ocular or periocular infections or active intraocular inflammation; and
4. Susvimo™ must be prescribed and administered by an ophthalmologist or a physician experienced in vitreoretinal surgery; and
5. Prescriber must verify the member will be monitored for endophthalmitis, rhegmatogenous retinal detachment, implant dislocation, vitreous hemorrhage, conjunctival erosion, conjunctival retraction, and conjunctival blebs; and
6. A patient-specific, clinically significant reason why the member cannot use Lucentis® (ranibizumab intravitreal injection) or other VEGF inhibitor injection products (appropriate to the disease state) must be provided; and
7. Susvimo™ will have a quantity limit of 0.2mL every 180 days.

[1] U.S. Food and Drug Administration (FDA) News Release. FDA Approves First Biosimilar to Treat Macular Degeneration Disease and Other Eye Conditions. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-biosimilar-treat-macular-degeneration-disease-and-other-eye-conditions. Issued 09/17/2021. Last accessed 01/11/2022.
[2] Biogen's (BIIB) Lucentis® Biosimilar Byooviz™ Gets FDA Approval. *Nasdaq*. Available online at: https://www.nasdaq.com/articles/biogens-biib-lucentis-biosimilar-byooviz-gets-fda-approval-2021-09-21. Issued 09/21/2021. Last accessed 01/11/2022.
[3] Genentech. FDA Approves Genentech's Susvimo™, a First-of-Its-Kind Therapeutic Approach for Wet Age-Related Macular Degeneration (AMD). *Business Wire*. Available online at: https://www.businesswire.com/news/home/20211022005479/en/FDA-Approves-Genentech%E2%80%99s-Susvimo-a-First-of-Its-Kind-Therapeutic-Approach-for-Wet-Age-Related-Macular-Degeneration-AMD. Issued 10/22/2021. Last accessed 01/11/2022.
[4] Susvimo™ (Ranibizumab Injection) Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/susvimo_prescribing.pdf. Last updated 10/2021. Last accessed 01/11/2022.
[5] A Phase III Study to Evaluate the Port Delivery System with Ranibizumab Compared with Monthly Ranibizumab Injections in Participants with Wet-Related Macular Degeneration (Archway). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT03677934. Last updated 10/28/2021. Last accessed 01/11/2022.
[6] Lucentis® (Ranibizumab Injection) Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/lucentis_prescribing.pdf. Last updated 03/2018. Last accessed 01/11/2022.
[7] Eylea® (Aflibercept Injection) Prescribing Information. Regeneron Pharmaceuticals, Inc. Available online at: https://www.regeneron.com/downloads/eylea_fpi.pdf. Last updated 06/2021. Last accessed 01/11/2022.
[8] Beovu® (Brolucizumab-dbll Injection) Prescribing Information. Novartis Pharmaceuticals, Co. Available online at: https://www.novartis.us/sites/www.novartis.us/files/beovu.pdf. Last updated 06/2020. Last accessed 01/11/2022.

Appendix I

Vote to Update the Approval Criteria for the Glaucoma Medications

Oklahoma Health Care Authority
February 2022

Recommendations

The College of Pharmacy recommends the following changes to the current Glaucoma Medications Product Based Prior Authorization (PBPA) category based on net costs:

1. Moving Istalol® 0.5% (timolol maleate ophthalmic solution) from Tier-1 to the Special Prior Authorization (PA) Tier
2. Making Azopt® (brinzolamide 1% suspension) brand preferred
3. Moving Lumigan® (bimatoprost 0.01% solution) and Zioptan® (tafluprost 0.0015% solution) from Tier-2 to Tier-1
4. Moving Timoptic-XE® (timolol maleate ophthalmic gel-forming solution) and Cosopt® PF (dorzolamide/timolol 2%/0.5% preservative free solution) from the Special PA Tier to Tier-2

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
Alpha-2 Adrenergic Agonists		
brimonidine (Alphagan® 0.2%)	apraclonidine (Iopidine® 0.5%, 1%)	brimonidine (Alphagan® P 0.15%)
brimonidine (Alphagan® P 0.1%)		
brimonidine/timolol (Combigan® 0.2%/0.5%)		
brinzolamide/brimonidine (Simbrinza® 0.2%/1%)		
Beta-Blockers		
brimonidine/timolol (Combigan® 0.2%/0.5%)	betaxolol (Betoptic® 0.5%, Betoptic-S® 0.25%)	~~**dorzolamide/timolol (Cosopt® PF 2%/0.5%)**~~
carteolol (Ocupress® 1%)	**dorzolamide/timolol (Cosopt® PF 2%/0.5%)**	**timolol maleate (Istalol® 0.5%)**
dorzolamide/timolol (Cosopt® 22.3/6.8mg/mL)	**timolol maleate (Timoptic-XE® 0.25%, 0.5%)**	timolol maleate (Timoptic® in Ocudose® 0.25%, 0.5%; ~~**Timoptic-XE® 0.25%, 0.5%**~~)
levobunolol (Betagan® 0.25%, 0.5%)		
timolol maleate		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
(~~**Istalol® 0.5%,**~~ Timoptic® 0.25%, 0.5%)		
Carbonic Anhydrase Inhibitors		
acetazolamide (Diamox® 500mg caps; 125mg, 250mg tabs)+	**dorzolamide/timolol (Cosopt® PF 2%/0.5%)**	~~**dorzolamide/timolol (Cosopt® PF 2%/0.5%)**~~
brinzolamide (Azopt® 1%) – **Brand Preferred**		methazolamide (Neptazane® 25mg, 50mg tabs)+
brinzolamide/brimonidine (Simbrinza® 0.2%/1%)		
dorzolamide (Trusopt® 2%)		
dorzolamide/timolol (Cosopt® 22.3/6.8mg/mL)		
Cholinergic Agonists/Cholinesterase Inhibitors		
echothiophate iodide (Phospholine Iodide® 0.125%)	pilocarpine (Isopto® Carpine 1%, 2%, 4%)	
Prostaglandin Analogs		
bimatoprost (Lumigan® 0.01%)	bimatoprost (Lumigan® ~~**0.01%,**~~ 0.03%)	latanoprost (Xelpros™ 0.005%)
latanoprost (Xalatan® 0.005%)	~~**tafluprost (Zioptan® 0.0015%)**~~	latanoprostene bunod (Vyzulta® 0.024%)
netarsudil/latanoprost (Rocklatan®)		
tafluprost (Zioptan® 0.0015%)		
travoprost (Travatan-Z® 0.004%) – **Brand Preferred**		
Rho Kinase Inhibitors		
netarsudil (Rhopressa® 0.02%)		
netarsudil/latanoprost (Rocklatan®)		

*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).
+Indicates available oral medications; caps = capsules; PA = prior authorization; tabs = tablets
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must have documented, recent (within the last 120 days) trials with at least 3 Tier-1 medications for a minimum of 4 weeks duration each. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institutes of Health; and
6. Approvals will be for the duration of 1 year.

Glaucoma Medications Special Prior Authorization (PA) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 or Tier-2 medication must be provided; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 and Tier-2 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 and Tier-2 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institutes of Health; and
6. Approvals will be for the duration of 1 year.

Appendix J

Vote to Prior Authorize Empaveli™ (Pegcetacoplan)

Oklahoma Health Care Authority
February 2022

Market News and Updates[1]

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

- **May 2021:** The FDA approved Empaveli™ (pegcetacoplan) as the first complement protein C3 targeted therapy approved for adults with paroxysmal nocturnal hemoglobinuria (PNH). Patients with PNH have uncontrolled complement activation and destruction of red blood cells through intravascular and extravascular hemolysis. These patients will often have low levels of hemoglobin (Hb) and require blood transfusions. Empaveli™ is approved in patients with PNH who are either treatment naïve or switching from a C5 inhibitor such as Soliris® (eculizumab) or Ultomiris® (ravulizumab-cwvz). The approval of Empaveli™ was based on a head-to-head Phase 3 study, known as PEGASUS, which compared Empaveli™ to Soliris®. Empaveli™ was shown to be superior to Soliris® for the change in baseline Hb level at week 16 with an adjusted mean increase of 3.84g/dL (P<0.0001). Eighty-five percent of Empaveli™-treated patients were transfusion free over 16 weeks versus 15% of Soliris®-treated patients.

Empaveli™ (Pegcetacoplan) Product Summary[2]

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

Boxed Warning: Serious Infections Caused by Encapsulated Bacteria

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

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

Dosing and Administration:

- The recommended dosage is 1,080mg by sub-Q infusion twice weekly via a commercially available pump.
- For patients currently stable on a C5 inhibitor (Soliris® or Ultomiris®), bridging from C5 to C3 therapy should occur to reduce the risk of hemolysis from abrupt treatment discontinuation:
  - For patients switching from Soliris®, Empaveli™ should be initiated while continuing Soliris® at its current dose. After 4 weeks, Soliris® should be discontinued before continuing on monotherapy with Empaveli™.
  - For patients switching from Ultomiris®, Empaveli™ should be initiated no more than 4 weeks after the last dose of Ultomiris®.

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

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

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

Cost Comparison: PNH Therapies

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

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

Recommendations

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

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

1. An FDA approved diagnosis of PNH; and

2. Must have an established diagnosis of PNH via international classification of disease (ICD) coding in member's medical claims history; and
3. An age restriction of 18 years and older will apply; and
4. For member self-administration or caregiver administration, the prescriber must verify the member or caregiver has been trained by a health care provider on proper administration and storage of Empaveli™; and
5. Prescriber and pharmacy must be enrolled in the Empaveli™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
6. For members switching from Soliris® to Empaveli™, prescriber must verify the member will continue the current dose of Soliris® for 4 weeks before switching to Empaveli™ as monotherapy; and
7. For members switching from Ultomiris® to Empaveli™, prescriber must verify that Empaveli™ will be initiated no more than 4 weeks after the last dose of Ultomiris®.

[1] Apellis Pharmaceuticals, Inc. Apellis Announces U.S. Food and Drug Administration (FDA) Approval of Empaveli™ (Pegcetacoplan) for Adults with Paroxysmal Nocturnal Hemoglobinuria (PNH). *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2021/05/14/2230226/0/en/Apellis-Announces-U-S-Food-and-Drug-Administration-FDA-Approval-of-EMPAVELI-pegcetacoplan-for-Adults-with-Paroxysmal-Nocturnal-Hemoglobinuria-PNH.html. Issued 05/14/2021. Last Accessed 01/11/2022.

[2] Empaveli™ (Pegcetacoplan) Prescribing Information. Apellis Pharmaceuticals, Inc. Available online at: https://pi.apellis.com/files/PI_Empaveli.pdf. Last revised 05/2021. Last accessed 01/11/2022.

Appendix K

Vote to Prior Authorize Evkeeza® (Evinacumab-dgnb) and Leqvio® (Inclisiran) and Update the Approval Criteria for the Antihyperlipidemics

Oklahoma Health Care Authority
February 2022

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

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

- **February 2021:** The FDA approved Evkeeza® (evinacumab-dgnb) as add-on treatment to lipid-lowering therapies for patients 12 years of age and older with homozygous familial hypercholesterolemia (HoFH), a rare genetic condition that causes severely high cholesterol. The incidence of HoFH is approximately 1 in 250,000 individuals, and patients with this condition can develop premature cardiovascular (CV) disease early in life. Evkeeza® is an angiopoietin-like protein 3 (ANGPTL3) inhibitor which allows faster breakdown of fats that lead to high cholesterol. The safety and efficacy of Evkeeza® were assessed in a 24-week Phase 3 study, ELIPSE-HoFH, which included 65 patients diagnosed with HoFH. Patients on Evkeeza® had an average 47% decrease in low-density lipoprotein-cholesterol (LDL-C) at week 24, while patients in the placebo group had an average 2% increase in LDL-C. The most common side effects reported with evinacumab-dgnb were nasopharyngitis, influenza-like illness, dizziness, rhinorrhea, and nausea.
- **April 2021:** The FDA expanded the indication for Praluent® (alirocumab) to include adult patients with HoFH. The approval for this indication was assessed in a 12-week, double-blind, randomized, placebo-controlled study in adult patients with HoFH. In this study, 45 patients were randomized to receive Praluent® 150mg every 2 weeks, while 24 patients were randomized to receive placebo. At week 12, patients treated with Praluent® had an average LDL-C decrease of 27%, while patients on placebo had an average LDL-C increase of 9%. Patients in both arms were also taking other therapies to lower LDL-C. The most common side effects reported in this study in alirocumab-treated patients included nasopharyngitis, injection site reactions, and influenza.
- **September 2021:** The FDA expanded the indication for Repatha® (evolocumab) to include pediatric patients 10 years of age and older with heterozygous familial hypercholesterolemia (HeFH). HeFH is an inherited, genetic condition with a prevalence of 1 in 250 individuals

worldwide. These patients have high levels of LDL-C which lead to an overall increased risk of CV events. The approval for this label expansion was based on a Phase 3b study, HAUSER-RCT, which evaluated the safety and efficacy of Repatha® in pediatric patients 10 to 17 years of age. At 24 weeks, patients treated monthly with Repatha® 420mg had an average LDL-C reduction of 45% compared with a 6% reduction in patients receiving placebo. The FDA also lowered the age requirement for the use of evolocumab in pediatric patients with HoFH from 13 years of age to 10 years of age.

- **December 2021:** The FDA approved Leqvio® (inclisiran) as the first and only small interfering RNA (siRNA) therapy to reduce LDL-C via an RNA interference mechanism in patients with HeFH or atherosclerotic cardiovascular disease (ASCVD). Leqvio® works as a complement to statins and reduces LDL-C by preventing the production of the proprotein convertase subtilisin/kexin type 9 (PCSK9) protein in the liver, thus increasing hepatic uptake of LDL-C and clearing it from the blood stream. Leqvio® is dosed twice yearly via subcutaneous (sub-Q) injection by a health care professional and was shown to decrease LDL-C up to 52% at month 17 in clinical studies. The most common adverse reactions reported in clinical studies (incidence ≥3%) in patients treated with inclisiran were injection site reaction, arthralgia, urinary tract infection, diarrhea, and bronchitis.

Evkeeza® (Evinacumab-dgnb) Product Summary[6]

Indication(s): Evkeeza® is an ANGPTL3 inhibitor indicated as an adjunct to other LDL-C lowering therapies for the treatment of adult and pediatric patients 12 years of age and older with HoFH.

- Limitation(s) of Use:
  - The safety and effectiveness of evinacumab-dgnb have not been established in patients with other causes of hypercholesterolemia, including those with HeFH.
  - The effects of evinacumab-dgnb on cardiovascular morbidity and mortality have not been determined.

How Supplied: 345mg/2.3mL (150mg/mL) and 1,200mg/8mL (150mg/mL) solution in a single-dose vial (SDV)

Dosing: The recommended dose is 15mg/kg via intravenous (IV) infusion over 60 minutes every 4 weeks.

Mechanism of Action: Evinacumab-dgnb is a recombinant monoclonal antibody that binds to and inhibits ANGPTL3, which is primarily expressed in the liver. ANGPTL3 plays a role in the regulation of lipid metabolism by inhibiting lipoprotein lipase (LPL) and endothelial lipase (EL), and the

inhibition of ANGPTL3 will lead to reductions in LDL-C, HDL-C, and triglycerides.

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence ≥5%) were nasopharyngitis, influenza-like illness, dizziness, rhinorrhea, and nausea.

Cost: The Wholesale Acquisition Cost (WAC) for Evkeeza® is $37,500 for a 1,200mg/8mL vial. For a patient weighing 80kg, the annual cost would be $487,500 at the recommended dose of 15mg/kg every 4 weeks.

Cost Comparison for HoFH Therapies:

Product	Cost Per Unit	Cost Per Year*
Juxtapid® (lomitapide) 60mg capsule	$1,596.91	$581,275.24
Evkeeza® (evinacumab-dgnb) 1,200mg/8mL injection	**$4,687.50**	**$487,500.00**
Repatha® (evolocumab) 140mg/mL injection	$230.89	$6,003.14
Praluent® (alirocumab) 150mg/mL injection	$225.00	$5,850.00
rosuvastatin 40mg tablet	$0.13	$47.32
atorvastatin 80mg tablet	$0.10	$36.40

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per year based on the FDA approved maximum dose. Evkeeza® cost per year based on the recommended dosing for a patient weighing 80kg.
Unit = capsule, tablet, or mL

Leqvio® (Inclisiran) Product Summary[7]

Indication(s): Leqvio® is a siRNA directed to PCSK9 mRNA indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or ASCVD who require additional lowering of LDL-C.

- Limitation(s) of Use: The effects of inclisiran on cardiovascular morbidity and mortality have not been determined.

How Supplied: 284mg/1.5mL (189mg/mL) in a single-dose prefilled syringe

Dosing:

- The recommended dose is 284mg administered as a single sub-Q injection initially, again at 3 months, and then every 6 months thereafter
- Leqvio® should be administered by a health care professional into the abdomen, upper arm, or thigh

Mechanism of Action: Inclisiran is a double-stranded siRNA that utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for PCSK9. This increases LDL-C receptor recycling, resulting in an increase in LDL-C uptake in the liver and a decrease in LDL-C levels in circulation.

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence ≥3%) were injection site reaction, arthralgia, urinary tract infection, diarrhea, bronchitis, extremity pain, and dyspnea.

Cost: The WAC for Leqvio® is $3,250 for a 284mg/1.5mL syringe, resulting in an annual cost of $6,500 at the recommended maintenance dosing of 284mg every 6 months.

Cost Comparison for LDL-C Lowering Therapies:

Product	Cost Per Unit	Cost Per Year*
Leqvio® (inclisiran) 284mg/1.5mL injection	**$2,166.67**	**$6,500.00**
Repatha® (evolocumab) 140mg/mL injection	$230.89	$6,003.14
Praluent® (alirocumab) 150mg/mL injection	$225.00	$5,850.00
rosuvastatin 40mg tablet	$0.13	$47.32
ezetimibe 10mg tablet	$0.12	$43.68
atorvastatin 80mg tablet	$0.10	$36.40

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per year based on the FDA approved maximum dose.
Unit = mL or tablet

Recommendations

The College of Pharmacy recommends the prior authorization of Evkeeza® (evinacumab-dgnb) and Leqvio® (inclisiran) with the following criteria (shown in red):

Evkeeza® (Evinacumab-dgnb) Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following:
    a. Documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and at least 1 of the following:
        i. Documented evidence of definite HeFH in both parents; or
        ii. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; or
2. Member must be 12 years of age or older; and
3. Documented trial of high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
4. Members with statin intolerance must meet 1 of the following:
    a. Creatine kinase (CK) labs verifying rhabdomyolysis; or

b. An FDA labeled contraindication to all statins; or
c. Documented intolerance to at least 2 different statins at lower doses (dosing, dates, duration of treatment, and reason for discontinuation must be provided); or
d. Documented intolerance to at least 2 different statins at intermittent dosing (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and

5. Documented trial of a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor (e.g., Praluent®, Repatha®) at least 12 weeks in duration; and
6. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation. Female members of reproductive potential must be willing to use effective contraception while on therapy and for 5 months after discontinuation of therapy; and
8. Initial approvals will be for the duration of 6 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every 6 months thereafter for continued approval.

Leqvio® (Inclisiran) Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Heterozygous familial hypercholesterolemia (HeFH) as confirmed by 1 of the following:
      i. Documented functional mutation(s) in low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
      ii. Both of the following:
         1. Pre-treatment total cholesterol >290mg/dL or LDL-C >190mg/dL; and
         2. History of tendon xanthomas in either the member, first degree relative, or second degree relative; or
      iii. Dutch Lipid Clinic Network Criteria score of >8; or
   b. Established atherosclerotic cardiovascular disease (ASCVD); and
      i. Supporting diagnoses/conditions and dates of occurrence signifying established ASCVD; and
2. Member must be 18 years of age or older; and
3. Documented trial of all of the following for at least 12 weeks in duration each:
   a. High dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or maximally tolerated statin therapy; and
   b. Ezetimibe; and

c. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor (e.g., Praluent®, Repatha®); and

4. Members with statin intolerance must meet 1 of the following:
   a. Creatine kinase (CK) labs verifying rhabdomyolysis; or
   b. An FDA labeled contraindication to all statins; or
   c. Documented intolerance to at least 2 different statins at lower doses (dosing, dates, duration of treatment, and reason for discontinuation must be provided); or
   d. Documented intolerance to at least 2 different statins at intermittent dosing (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
5. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
6. Leqvio® must be administered by a health care professional. Approvals will not be granted for self-administration; and
   a. Prior authorization requests must indicate how Leqvio® will be administered (e.g., prescriber, pharmacist, home health care provider); and
      i. Leqvio® must be shipped to the facility where the member is scheduled to receive treatment; or
      ii. Prescriber must verify the member has been counseled on the proper storage of Leqvio®; and
7. Initial approvals will be for the duration of 6 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every 6 months thereafter for continued approval.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for PCSK9 inhibitors (changes shown in red):

Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors [Praluent® (Alirocumab) and Repatha® (Evolocumab)] Approval Criteria:

~~1. For Repatha® (evolocumab):~~
   ~~a. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following:~~
      ~~i. Documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or~~
      ~~ii. An untreated total cholesterol >500mg/dL and at least 1 of the following:~~
         ~~1. Documented evidence of definite heterozygous familial hypercholesterolemia (HeFH) in both parents; or~~

~~2. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; or~~

~~b. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or~~

~~c. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and~~

~~i. Documentation of established CVD; and~~

~~1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or~~

~~2. For Praluent® (alirocumab):~~

~~a. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or~~

~~b. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established CVD; and~~

~~i. Documentation of established CVD; and~~

~~1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; and~~

1. An FDA approved indication of 1 of the following:
    a. Heterozygous familial hypercholesterolemia (HeFH) as confirmed by 1 of the following:
        i. Documented functional mutation(s) in low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
        ii. Both of the following:
            1. Pre-treatment total cholesterol >290mg/dL or LDL-C >190mg/dL; and
            2. History of tendon xanthomas in either the member, first degree relative, or second degree relative; or
        iii. Dutch Lipid Clinic Network Criteria score of >8; or
    b. Homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following:
        i. Documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
        ii. An untreated total cholesterol >500mg/dL and at least 1 of the following:
            1. Documented evidence of definite HeFH in both parents; or
            2. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; or

c. As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and
    i. Documentation of established CVD; and
    ii. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or
d. Primary hyperlipidemia; and
    i. Member's untreated LDL-C level must be ≥190mg/dL; and
    ii. Current LDL-C level is ≥100mg/dL; and

2. For the use of Repatha® in members with HeFH or HoFH, member must be ~~13~~ 10 years of age or older ~~for the diagnosis of HoFH or must be 18 years of age or older for all other FDA-approved diagnoses or indications~~; and
3. For the use of Repatha® for FDA approved indications other than HeFH or HoFH or for the use of Praluent® for all FDA approved indications, the member must be 18 years of age or older; and
4. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
    a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
    b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment ~~with each statin medication~~; and
    ~~c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and~~
    ~~d. Tier structure rules still apply; and~~
5. Members with statin intolerance must meet 1 of the following:
    a. Creatine kinase (CK) labs verifying rhabdomyolysis; or
    b. An FDA labeled contraindication to all statins; or
    c. Documented intolerance to at least 2 different statins at lower doses (dosing, dates, duration of treatment, and reason for discontinuation must be provided); or
    d. Documented intolerance to at least 2 different statins at intermittent dosing (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
6. Member must have a recent trial of a statin with ezetimibe, or a recent trial of ezetimibe without a statin for members with documented statin intolerance, or a patient-specific, clinically significant reason why ezetimibe is not appropriate must be provided; and
7. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and

8. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
9. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent®. A quantity limit of 2 syringes or auto-injectors per 28 days will apply for Repatha® 140mg and a quantity limit of 1 auto-injector per 28 days will apply for Repatha® 420mg. Requests for the Repatha® 420mg dose will not be approved for multiple 140mg syringes or auto-injectors, but instead members should use (1) 420mg auto-injector; and
10. Initial approvals will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of the medication, and compliance will be checked at that time and every 6 months thereafter for continued approval.

Further, the College of Pharmacy recommends updating the prior authorization criteria for Nexletol® (bempedoic acid) and Nexlizet® (bempedoic acid/ezetimibe) (changes shown in red):

Nexletol® (Bempedoic Acid) and Nexlizet® (Bempedoic Acid/Ezetimibe) Approval Criteria:

1. An FDA approved indication as an adjunct to diet and maximally tolerated statin therapy for the treatment of 1 of the following:
    a. Heterozygous familial hypercholesterolemia (HeFH)~~; and~~ as confirmed by 1 of the following:
        i. Documented functional mutation(s) in low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
        ii. Both of the following:
            1. Pre-treatment total cholesterol >290mg/dL or LDL-C >190mg/dL; and
            2. History of tendon xanthomas in either the member, first degree relative, or second degree relative; or
        iii. Dutch Lipid Clinic Network Criteria score of >8; or
        ~~iv. Documentation of definite HeFH using the Simon Broome Register criteria, the Dutch Lipid Network criteria, or via genetic testing; or~~
    b. Established atherosclerotic cardiovascular disease (ASCVD); and
        i. Supporting diagnoses/conditions and dates of occurrence signifying established ASCVD; and
2. Member must be 18 years of age or older; and
3. Member must be on a stable dose of maximally tolerated statin therapy for at least 4 weeks (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and

a. LDL-cholesterol (LDL-C) levels should be included following at least 4 weeks of treatment ~~with each statin medication~~; and
b. Member must not be taking simvastatin at doses >20mg or pravastatin at doses >40mg due to drug interactions with Nexletol® and Nexlizet®; and
~~c. For statin intolerance due to myalgia, creatinine kinase (CK) labs verifying rhabdomyolysis must be provided; and~~

4. Members with statin intolerance must meet 1 of the following:
   a. Creatine kinase (CK) labs verifying rhabdomyolysis; or
   b. An FDA labeled contraindication to all statins; or
   c. Documented intolerance to at least 2 different statins at lower doses (dosing, dates, duration of treatment, and reason for discontinuation must be provided); or
   d. Documented intolerance to at least 2 different statins at intermittent dosing (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
5. Member requires additional lowering of LDL-cholesterol (LDL-C) (baseline, current, and goal LDL-C levels must be provided); and
6. A quantity limit of 30 tablets per 30 days will apply; and
7. Initial approvals will be for the duration of 3 months, after which time compliance and recent LDL-C levels to demonstrate the effectiveness of this medication will be required for continued approval. Subsequent approvals will be for the duration of 1 year.

Lastly, the College of Pharmacy recommends to remove the Kynamro® (mipomersen) prior authorization criteria based on product discontinuation and also add additional criteria for Juxtapid® (lomitapide) for members with statin intolerance (changes shown in red):

Juxtapid® (Lomitapide) ~~and Kynamro® (Mipomersen)~~ Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following criteria:
   a. A documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
   b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least 1 of the following:
      i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
      ii. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; and

2. Documented trial of high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
3. Members with statin intolerance must meet 1 of the following:
    a. Creatine kinase (CK) labs verifying rhabdomyolysis; or
    b. An FDA labeled contraindication to all statins; or
    c. Documented intolerance to at least 2 different statins at lower doses (dosing, dates, duration of treatment, and reason for discontinuation must be provided); or
    d. Documented intolerance to at least 2 different statins at intermittent dosing (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
4. Documented trial of Repatha® (evolocumab) at least 12 weeks in duration; and
5. Member requires additional lowering of LDL cholesterol (LDL-C) (baseline, current, and goal LDL-C levels must be provided); and
6. Prescriber must be certified with Juxtapid® ~~or Kynamro®~~ Risk Evaluation and Mitigation Strategy (REMS) program.

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[1] U.S. Food and Drug Administration (FDA). FDA Approves Add-On Therapy For Patients With Genetic Form Of Severely High Cholesterol. Available online at: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-add-therapy-patients-genetic-form-severely-high-cholesterol-0. Issued 02/11/2021. Last accessed 01/15/2022.

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[4] Novartis. Novartis Leqvio® (Inclisiran) Analyses Show Effective and Sustained LDL-C Reduction in Two Sub-Populations of Patients with ASCVD. Available online at: https://www.novartis.com/news/media-releases/novartis-leqvio-inclisiran-analyses-show-effective-and-sustained-ldl-c-reduction-two-sub-populations-patients-ascvd. Issued 08/30/2021. Last accessed 01/15/2022.

[5] Novartis. FDA Approves Novartis Leqvio® (Inclisiran), First-In-Class siRNA to Lower Cholesterol and Keep It Low with Two Doses a Year. Available online at: https://www.novartis.com/news/media-releases/fda-approves-novartis-leqvio-inclisiran-first-class-sirna-lower-cholesterol-and-keep-it-low-two-doses-year. Issued 12/22/2021. Last accessed 01/15/2022.

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[7] Leqvio® (Inclisiran) Prescribing Information. Novartis. Available online at: https://www.novartis.us/sites/www.novartis.us/files/leqvio.pdf. Last revised 12/2021. Last accessed 01/15/2022.

Appendix L

Fiscal Year 2021 Annual Review of Arcalyst® (Rilonacept)

Oklahoma Health Care Authority
February 2022

Current Prior Authorization Criteria

Arcalyst® (Rilonacept) Approval Criteria:

1. An FDA approved indication of cryopyrin-associated periodic syndromes (CAPS) verified by genetic testing. This includes familial cold auto-inflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS) in adults and children 12 years of age and older; and
2. Member should not be using a tumor necrosis factor blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra; and
3. Documentation that the member does not have active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus (HIV), or tuberculosis must be provided; and
4. The following dosing restrictions will apply:
    a. Dosing should not be more often than once weekly; and
    b. Approved dosing schedule for members 18 years of age and older:
        i. Initial treatment: Loading dose of 320mg delivered as (2) 2mL subcutaneous (sub-Q) injections of 160mg each given on the same day at 2 different injection sites; and
        ii. Continued treatment: (1) 160mg injection given once weekly; or
    c. Approved dosing schedule for pediatric members 12 to 17 years of age (must have member weight in kilograms):
        i. Initial treatment: Loading dose of 4.4mg/kg, up to a maximum of 320mg, delivered as 1 or 2 sub-Q injections, with a maximum single-injection volume of 2mL (given at 2 different injection sites if administered as 2 injections); and
        ii. Continued treatment: 2.2mg/kg, up to a maximum of 160mg, given once weekly; and
5. Approvals will be for the duration of 1 year.

Utilization of Arcalyst® (Rilonacept): Fiscal Year 2021

There was no SoonerCare utilization of Arcalyst® (rilonacept) during fiscal year 2021 (07/01/2020 to 06/30/2021).

Prior Authorization of Arcalyst® (Rilonacept)

There were no prior authorization requests submitted for Arcalyst® (rilonacept) during fiscal year 2021.

Market News and Updates[1,2,3,4,5,6,7,8,9,10]

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

- **December 2020:** The FDA approved Arcalyst® (rilonacept), a weekly, subcutaneously (sub-Q)-injected, recombinant fusion protein that blocks interleukin-1 alpha (IL-1α) and interleukin-1 beta (IL-1β) signaling, for the maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA) in adults and pediatric patients weighing ≥10kg. DIRA is a rare, autoinflammatory disease caused by a genetic mutation in the *IL1RN* gene, which encodes for interleukin-1 receptor antagonist (IL-1Ra) protein. In patients with DIRA, the deficiency of IL-1Ra leads to unopposed action of IL-1 signaling, resulting in life-threatening systemic inflammation with skin and bone involvement. DIRA presents at birth or within 2 months postpartum and is characterized by neonatal onset of sterile multifocal osteomyelitis, periositis, neutrophilic pustulosis, marked elevations of erythrocyte sedimentation rate and serum C-reactive protein (CRP), but fever is not present. The diagnosis is made by genetic testing for mutations involving *IL1RN*.

  Treatment of DIRA has consisted of non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), and corticosteroids, which are only partially effective. In December 2020, the FDA approved IL-1 inhibitors Kineret® (anakinra), a recombinant human IL-1Ra [Kineret® is reviewed by the Drug Utilization Review (DUR) Board within the Targeted Immunomodulator Agents medication category and was last reviewed in October 2021] and Arcalyst®, an IL-1α and IL-1β cytokine trap. Arcalyst® blocks IL-1 signaling by acting as a soluble decoy receptor that binds both IL-1α and IL-1β and prevents interaction with cell surface receptors. Arcalyst® also binds IL-1Ra.

  The approval of Arcalyst® for the maintenance of remission of DIRA was demonstrated in a 2-year, open-label study of 6 pediatric patients who previously experienced clinical benefit from daily injections of an IL-1Ra, Kineret®. The study population included patients with loss-of-function *IL1RN* mutations. Patients had a median age at baseline of 4.8 years (range 3.3 to 6.2 years), and stopped Kineret® treatment 24 hours before initiation of Arcalyst®. Remission was defined using the following criteria: diary score of <0.5 (reflecting no fever, skin rash, and bone pain), acute phase reactants (<0.5mg/dL CRP), absence of objective skin rash, and no radiological evidence of active bone lesions. Following an

Arcalyst® loading dose of 4.4mg/kg sub-Q, patients received a once-weekly maintenance dose of 2.2mg/kg (up to a maximum dose of 160mg), and were assessed for remission and possible dose escalation. During the first 3 months of Arcalyst® administration at the 2.2mg/kg dose, 5 of 6 patients exhibited recurrence of pustular rash and therefore the dose was escalated to 4.4mg/kg once weekly (up to a maximum dose of 320mg). One patient remained on the 2.2mg/kg once-weekly dose. All patients met the primary endpoint of the study, remission at 6 months and sustained the remission for the remainder of the 2-year study. No patient required steroid use during the study.

- **March 2021:** The FDA approved Arcalyst® (rilonacept) to treat recurrent pericarditis (RP) and reduce the risk of recurrence in adults and children 12 years of age and older. RP is a painful autoinflammatory cardiovascular disease that typically presents with chest pain and is often associated with changes in electrical conduction and sometimes buildup of fluid around the heart, called pericardial effusion. Patients who have additional pericarditis episodes following a symptom-free period of 4-6 weeks or longer are identified as having RP. RP symptoms have an impact on quality of life, limit physical activities, and lead to frequent emergency department visits and hospitalizations. Approximately 40,000 patients in the United States seek and receive treatment for RP each year. Of that group, approximately 14,000 patients experience a second or subsequent event (recurrence) due to persistent underlying disease or inadequate response to conventional therapies, such as NSAIDs, colchicine, and corticosteroids.

  The FDA approval of Arcalyst® in RP follows positive data from RHAPSODY, a pivotal Phase 3 trial in 86 patients with symptomatic pericarditis recurrence. Of these, 73 (85%) had a diagnosis of "idiopathic" pericarditis, and the remainder had post-cardiac injury pericarditis. The mean duration of disease was 2.4 years with a mean of 4.4 pericarditis events per year, including the qualifying pericarditis event [defined as pericarditis pain 0-10 point Numerical Rating Scale (NRS) ≥4 and CRP ≥1mg/dL]. The study consisted of a 12-week run-in period followed by a double-blind, placebo-controlled, randomized withdrawal period. The primary endpoint was time to first adjudicated pericarditis recurrence (based on pain, CRP, and clinical signs) in the event-driven withdrawal period. During the run-in period, daily NRS pain scores and CRP levels decreased and the median time to treatment response (NRS ≤2 and CRP ≤0.5mg/dL) was 5 days. All patients were required to taper off standard-of-care pericarditis medications before randomization, and median time to Arcalyst® monotherapy was 7.9 weeks during the run-in period. Of 61 patients randomized in the double-blind, placebo-controlled, randomized

withdrawal period, 23 patients (74%) in the placebo arm had a recurrence compared with 2 patients (7%) in the Arcalyst® arm who temporarily discontinued treatment for 1-3 doses. The median time-to-recurrence on Arcalyst® could not be estimated because too few events occurred and was 8.6 weeks on placebo [95% confidence interval (CI) 4.0, 11.7] with a hazard ratio (HR) of 0.04 (P<0.0001); Arcalyst® reduced the risk of recurrence by 96% with 92% of trial days being pain free or at most experiencing minimal pain, compared to 40% of trial days on placebo (P<0.0001). The 2 recurrence events in the Arcalyst® group happened in association with temporary interruptions of the trial-drug regimen, of 1 to 3 weekly doses. In the placebo group, all 23 patients who had pericarditis recurrence received bailout Arcalyst®, with resolution of the episodes. The most common adverse events were injection site reactions and upper respiratory tract infections.

Management of Acute and Recurrent Pericarditis by the American College of Cardiology published in the *Journal of the American College of Cardiology* in 2020 recommends the use of IL-1 inhibitors including Kineret® (anakinra) and Arcalyst® (rilonacept) in patients with RP who have refractory, corticosteroid-dependent disease. Other options for consideration in refractory disease include azathioprine, methotrexate, mycophenolate mofetil, and intravenous immunoglobulins. Surgical pericardiectomy is considered a last option.

Kineret®, although not FDA approved for the treatment of RP, has proven beneficial in several case studies and a randomized control trial, AIRTRIP. AIRTRIP included patients with RP resistant to colchicine and dependent on corticosteroid therapy, who received anakinra 2mg/kg per day, up to a maximum of 100mg per day, for 60 days followed by randomization to either anakinra or placebo for an additional 6 months. A statistical difference in benefit in the anakinra group compared to placebo was found without any increase in the risk of serious infections. RP occurred in 9 of 10 patients (90%; incidence rate, 2.06% of patients per year) assigned to placebo and 2 of 11 patients (18.2%; incidence rate, 0.11% of patients per year) assigned to anakinra, for an incidence rate difference of -1.95% (95% CI, -3.3% to -0.6%).

Cryopyrin-Associated Periodic Syndromes (CAPS)[11,12,13,14]

Familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disorder [NOMID, also known as chronic infantile neurologic cutaneous and articular (CINCA) syndrome] are 3 clinically overlapping, IL-1-associated, autoinflammatory disorders known collectively as the cryopyrin-associated periodic syndromes (CAPS) or cryopyrinopathies. The cryopyrinopathies are rare, with an

estimated prevalence of 1 in 360,000 according to a French study. All 3 cryopyrinopathies arise from mutations in a single gene, *NLRP3*, at chromosome 1q44, encoding a protein called cryopyrin. FCAS is the mildest form, MWS is considered moderate, and NOMID is the most severe form of inflammation. A central role for IL-1β in these disorders is confirmed by the effectiveness of therapies directed against IL-1 in preventing and alleviating symptoms and in substantially reducing levels of inflammatory markers. These therapies include anakinra, rilonacept, and canakinumab.

Arcalyst® (rilonacept) received initial FDA approval in February 2008 for the treatment of CAPS, including FCAS and MWS. In June 2009, Ilaris® (canakinumab) was FDA approved for FCAS and MWS (Ilaris® is reviewed by the DUR Board within the Targeted Immunomodulator Agents medication category and was last reviewed in October 2021). Kineret® (anakinra) received FDA approval in January 2013 for the most severe form of CAPS, NOMID. Kineret® is also supported by multiple studies for use in the less severe forms of CAPS (FCAS and MWS). In patients with FCAS, treatment with Kineret® can prevent cold-induced attacks and markedly reduce daily symptoms. Among patients with renal secondary amyloidosis due to CAPS, Kineret® has led to marked reductions in proteinuria and stabilization of serum creatinine. In MWS, Kineret® treatment has been shown to control systemic inflammation. Additionally, measurement of intrathecal inflammatory markers suggests that anakinra may be superior to Ilaris® for control of central nervous system (CNS) inflammation given its ability to penetrate the blood-brain barrier.

Arcalyst® (Rilonacept) Product Summary[1]

Therapeutic Class: IL-1 inhibitor

Indication(s):

- Treatment of cryopyrin-associated periodic syndromes (CAPS), including familial cold autoinflammatory syndrome (FCAS), and Muckle-Wells syndrome (MWS) in adults and children 12 years of age and older
- Maintenance of remission DIRA in adults and pediatric patients weighing ≥10kg
- Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children 12 years of age and older

Dosing:

- Arcalyst® (rilonacept) is a sub-Q injection available in a 220mg single-dose vial of lyophilized powder for reconstitution
- CAPS, FCAS, MWS, and RP dosing regimen:
  - Adults:
    - Loading dose: 320mg, delivered as (2) 160mg (2mL) injections
    - Maintenance dose: 160mg (2mL) injection once weekly
  - Pediatric patients 12 years to 17 years of age:
    - Loading dose: 4.4mg/kg, up to a maximum of 320mg, delivered as 1 or 2 injections (not to exceed 2mL/injection)
    - Maintenance dose: 2.2mg/kg, up to maximum of 160mg (2mL) injection, once weekly
- DIRA dosing regimen:
  - Adults and pediatrics patients weighing ≥10kg:
    - 4.4mg/kg up to a maximum of 320mg, delivered as 1 or 2 injections (2mL/injection) once weekly
    - When switching from another IL-1 blocker, discontinue the IL-1 blocker and begin Arcalyst® treatment at the time of the next dose
- Sites for sub-Q injection should be rotated (abdomen, thigh, or upper arm); injections should not be administered at sites that are bruised, red, tender, or hard
- Each Arcalyst® vial should be used for a single dose only; unused portions of Arcalyst® should be discarded

Mechanism of Action: Rilonacept is an IL-1α and IL-1β cytokine trap. Rilonacept blocks IL-1 signaling by acting as a soluble decoy receptor that binds both IL-1α and IL-1β and prevents its interaction with cell surface receptors. Rilonacept also binds IL-1Ra.

Cost: Arcalyst® 220mg vials have a Wholesale Acquisition Cost (WAC) of $5,000 per vial. The maximum cost for CAPS, FCAS, MWS, and RP is $20,000 per month and $240,000 per year. The maximum cost for DIRA is $40,000 per month and $480,000 per year. Costs based on maximum FDA recommended dosing for the diagnoses listed.

Recommendations

The College of Pharmacy recommends the following changes to the Arcalyst® (rilonacept) prior authorization criteria based on the new FDA approved indications and net costs:

Arcalyst® (Rilonacept) Approval Criteria [Cryopyrin-Associated Periodic Syndromes (CAPS) Diagnosis]:

1. An FDA approved indication of CAPS verified by genetic testing. This includes familial cold auto-inflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS) in adults and children 12 years of age and older; and
2. A patient-specific, clinically significant reason the member cannot utilize Kineret® (anakinra) or Ilaris® (canakinumab). Tier structure rules apply; and
3. The member should not be using a tumor necrosis factor blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra concomitantly with Arcalyst®;
4. Documentation that the member does not have active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus (HIV), or tuberculosis must be provided; and
5. The following dosing restrictions will apply:
    a. Dosing should not be more often than once weekly; and
    b. Approved dosing schedule for members 18 years of age and older:
        i. Initial treatment: Loading dose of 320mg delivered as (2) 2mL subcutaneous (sub-Q) injections of 160mg each given on the same day at 2 different injection sites; and
        ii. Continued treatment: (1) 160mg injection given once weekly; or
    c. Approved dosing schedule for pediatric members 12 to 17 years of age (must have member weight in kilograms):
        i. Initial treatment: Loading dose of 4.4mg/kg, up to a maximum of 320mg, delivered as 1 or 2 sub-Q injections, with a maximum single-injection volume of 2mL (given at 2 different injection sites if administered as 2 injections); and
        ii. Continued treatment: 2.2mg/kg, up to a maximum of 160mg, given once weekly; and
6. Approvals will be for the duration of 1 year.

Arcalyst® (Rilonacept) Approval Criteria [Deficiency of Interleukin-1 Receptor Antagonist (DIRA) Diagnosis]:

1. An FDA approved indication of maintenance of remission of DIRA verified by genetic testing; and
2. The member must weigh ≥10kg; and
3. The member should not be using a tumor necrosis factor blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra concomitantly with Arcalyst®; and
4. Documentation that the member does not have active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus (HIV), or tuberculosis must be provided; and

5. Arcalyst® will be used for maintenance of remission following treatment with Kineret® (anakinra); and
6. A patient-specific, clinically significant reason the member cannot continue to utilize Kineret® (anakinra) instead of switching to Arcalyst®; and
7. 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
8. The following dosing restrictions will apply:
    a. Dosing should not be more often than once weekly; and
    b. Approved dosing schedule for adults and pediatric members weighing ≥10kg is 4.4mg/kg up to a maximum of 320mg, delivered as 1 or 2 injections (2mL/injection) once weekly; and
9. Approvals will be for the duration of 1 year.

Arcalyst® (Rilonacept) Approval Criteria (Recurrent Pericarditis Diagnosis):

1. An FDA approved indication of recurrent pericarditis and reduction in risk of recurrence in members 12 years of age and older; and
2. The member has had at least 2 episodes of pericarditis; and
3. Member has failure with colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), and corticosteroids defined as symptomatic pericarditis recurrence; and
4. A patient-specific, clinically significant reason the member cannot utilize Kineret® (anakinra); and
5. The member should not be using a tumor necrosis factor blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra concomitantly with Arcalyst®; and
6. Documentation that the member does not have active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus (HIV), or tuberculosis must be provided; and
7. 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 for members 12 to 17 years of age; and
8. The following dosing restrictions will apply:
    a. Dosing should not be more often than once weekly; and
    b. Approved dosing schedule for members 18 years of age and older:
        i. Initial treatment: Loading dose of 320mg delivered as (2) 2mL subcutaneous (sub-Q) injections of 160mg each given on the same day at 2 different injection sites; and
        ii. Continued treatment: (1) 160mg injection given once weekly; or
    c. Approved dosing schedule for pediatric members 12 to 17 years of age (must have member weight in kilograms):

    i. Initial treatment: Loading dose of 4.4mg/kg, up to a maximum of 320mg, delivered as 1 or 2 sub-Q injections, with a maximum single-injection volume of 2mL (given at 2 different injection sites if administered as 2 injections); and
    ii. Continued treatment: 2.2mg/kg, up to a maximum of 160mg, given once weekly; and
9. Initial approvals will be for 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by decreased recurrence of pericarditis or improvement in signs and symptoms of recurrent pericarditis (e.g., C-reactive protein, pericarditic chest pain, pericardial effusion). Subsequent approvals will be granted for the duration of 1 year.

[1] Arcalyst® (Rilonacept) Prescribing Information. Kiniksa Pharmaceuticals. Available online at: https://www.arcalyst.com/sites/arcalyst.com/files/2021-08/PI_IFU.pdf. Last revised 05/2021. Last accessed 01/10/2022.
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Appendix M

Fiscal Year 2021 Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Erwinase® (Crisantaspase), Erwinaze® (Asparaginase *Erwinia Chrysanthemi*), Oncaspar® (Pegaspargase), Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn], and Scemblix® (Asciminib)

Oklahoma Health Care Authority
February 2022

Introduction[1,2,3,4]

Leukemia is an abnormal and autonomous proliferation of 1 or more blood-forming elements with infiltrations of the bone marrow and other organs. Leukemia is a heterogeneous group of neoplasms arising from the malignant transformation of hematopoietic cells that eventually replaces the normal marrow, leading to the signs and symptoms of leukemia. Two broad types of leukemias include acute leukemias and chronic leukemias. Acute myeloid leukemia (AML) is an aggressive disease associated with chromosomal and genetic abnormalities. Defects of certain genes have led to drug targets, such as isocitrate dehydrogenase (IDH) affecting cellular metabolism and FMS-related tyrosine kinase 3 (FLT3) affecting signaling.

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are indolent diseases, as patients may survive many years without therapy. The major difference between CLL and SLL is that in CLL a significant number of abnormal lymphocytes are found in the blood in addition to bone marrow and lymphoid tissue versus SLL, where there are few circulating abnormal lymphocytes and disease is mostly found in the lymph nodes, bone marrow, and other lymphoid tissues. CLL/SLL is primarily a disease of the elderly; the median age at diagnosis is 68 years. CLL/SLL is the most prevalent adult leukemia in western countries. In 2020, there were an estimated 21,150 new diagnoses and 4,320 deaths due to CLL. Treatment has evolved significantly over the past several decades. Immunotherapy and small molecule inhibitors targeting critical signaling pathways [e.g., Bruton's tyrosine kinase (BTK), phosphatidylinositol 3-kinase (PI3K)] have improved efficacy in therapies for CLL/SLL.

Current Prior Authorization Criteria

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease; or
2. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) for primary treatment or in relapsed/refractory disease with regional nodes.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Systemic Diagnosis]:

1. Previously untreated disease in combination with cyclophosphamide, doxorubicin, and prednisone (CHP); or
2. As a single agent in members who have received ≥1 line of therapy.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Classical Hodgkin Lymphoma (cHL) Diagnosis]:

1. Previously untreated Stage III or IV disease in combination with doxorubicin, vinblastine, and dacarbazine; or
2. Relapsed/refractory disease after failure of ≥2 multi-agent chemotherapy regimens in non-autologous stem cell transplant (SCT) candidates or after failure of autologous SCT as a single agent; or
3. Relapsed/refractory disease if not previously used in combination with multi-agent chemotherapy; or
4. Consolidation following autologous SCT in members at high-risk of relapse or progression.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade Lymphoma Diagnosis]:

1. CD30+ disease; and
2. DLBCL relapsed/refractory disease in non-autologous stem cell transplant (SCT) candidates; or
3. Members who have transformed to DLBCL from follicular lymphoma or marginal zone lymphoma and received ≥2 lines of therapy for indolent or transformed disease; and
4. As a single agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single agent as primary treatment; or
2. Relapsed/refractory disease.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. Previously untreated CD30+ disease in combination with cyclophosphamide, doxorubicin, and prednisone (CHP); or
2. As a single agent in members who have received ≥1 line of therapy.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. CD30+ disease; and
2. Member meets 1 of the following:
    a. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) in nonresponders to first-line therapy for chronic/smoldering subtype; or
    b. In combination with CHP for first-line therapy for acute or lymphoma subtype; or
    c. In combination with CHP for continued treatment in responders to first-line therapy for acute or lymphoma subtype; or
    d. As a single agent in members who have received ≥1 line of therapy.

Adcetris® (Brentuximab Vedotin) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. CD30+ disease; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used; and
3. As a single agent.

Arzerra® (Ofatumumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. For first-line treatment of CLL/SLL in combination with chlorambucil or bendamustine; or
2. Relapsed/refractory disease as a single agent or in combination with fludarabine and cyclophosphamide; or
3. Maintenance therapy as second-line extended dosing following complete or partial response to relapsed/refractory therapy (maximum 2 years).

Arzerra® (Ofatumumab) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. For previously treated disease that does not respond to primary therapy or for progressive or relapsed disease; and
2. Member is rituximab-intolerant; and
3. As a single agent or combination therapy.

Asparlas™ (Calaspargase Pegol-mknl) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. A patient-specific, clinically significant reason why the member cannot use pegaspargase must be provided; and
2. Member must be 1 month to 21 years of age.

Beleodaq® (Belinostat) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single agent for primary treatment or relapsed/refractory with multifocal lesions, or cutaneous ALCL with regional nodes.

Beleodaq® (Belinostat) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. Primary treatment in Stage IV non Sézary or visceral disease (solid organ) with or without radiation therapy for local control; or
2. Primary treatment for large cell transformation with generalized cutaneous or extracutaneous lesions with or without skin-directed therapy; or
3. As a single agent (with or without skin-directed therapy) in relapsed/refractory disease.

Beleodaq® (Belinostat) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

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

Beleodaq® (Belinostat) Approval Criteria [Adult T-Cell Leukemia/ Lymphoma Diagnosis]:

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

Beleodaq® (Belinostat) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

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

Besponsa® (Inotuzumab Ozogamicin) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have 1 of the following:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) ALL; or
    b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL who are intolerant/refractory to ≥2 tyrosine kinase inhibitors (TKIs); and
2. As a single agent only.

Blincyto® (Blinatumomab) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have 1 of the following:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) ALL; or
    b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL after failure of ≥2 tyrosine kinase inhibitors (TKIs); or
    c. Ph- ALL as consolidation in adolescent/young adults or members younger than 65 years of age without substantial comorbidity with persistent or late clearance minimal residual disease positive (MRD+) following a complete response to induction; and
2. As a single agent.

Bosulif® (Bosutinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Relapsed/refractory Ph+ ALL:
    a. As a single agent; or
    b. In combination with an induction regimen not previously given; and
2. E255K/V, F317L/VI/C, F359V/C/I, T315A, or Y253H mutations.

Bosulif® (Bosutinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Chronic, accelerated, or blast phase CML; and
2. Newly diagnosed or resistant/intolerant to other tyrosine kinase inhibitors (TKIs).

Calquence® (Acalabrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As a single agent.

Calquence® (Acalabrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As a single agent.

Copiktra® (Duvelisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Relapsed/refractory FL; and
2. Progression of disease following ≥2 lines of systemic therapy; and
3. As a single agent.

Copiktra® (Duvelisib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. Relapsed/refractory CLL or SLL; and
2. Progression of disease following ≥2 lines of systemic therapy; and
3. As a single agent.

Daurismo® (Glasdegib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly-diagnosed AML; and
2. Member meets 1 of the following:
    a. Member is 75 years of age or older; or
    b. If the member is younger than 75 years of age, must be unable to tolerate intensive induction chemotherapy; and
3. In combination with low-dose cytarabine (LDAC).

Folotyn® (Pralatrexate) Approval Criteria [Adult T-Cell Leukemia/ Lymphoma Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

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

Gazyva® (Obinutuzumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As a single agent in relapsed/refractory disease; or
2. In combination with chlorambucil, bendamustine, ibrutinib, or venetoclax for first-line therapy; and
3. When obinutuzumab is used in combination with venetoclax, maximum approval duration of obinutuzumab will be 6 treatment cycles.

Gazyva® (Obinutuzumab) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 or 2 members with Stage I (≥7cm), contiguous Stage II (≥7cm), noncontiguous Stage II, Stage III, or Stage IV members (first, second, or subsequent therapy); and

2. In combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), cyclophosphamide, vincristine, and prednisone (CVP), or bendamustine; and
3. When used for maintenance therapy, a total of 12 doses will be approved.

Gazyva® (Obinutuzumab) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy in combination with bendamustine; or
2. Maintenance therapy as second-line consolidation or extended dosing in rituximab-refractory members treated with obinutuzumab and bendamustine for a total of 12 doses.

Iclusig® (Ponatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have 1 of the following:
    a. Induction/consolidation with hyperfractionated cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride (Adriamycin®), and dexamethasone (HyperCVAD); or
    b. Maintenance therapy in combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
    c. Maintenance therapy post-hematopoietic stem cell transplantation; or
    d. Relapsed/refractory disease either as a single agent, in combination with chemotherapy not previously given, or in patients with T315I mutations.

Iclusig® (Ponatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have 1 of the following:
    a. T315I mutation; or
    b. Intolerant or resistant to ≥2 tyrosine kinase inhibitors (TKIs); or
    c. Post-hematopoietic stem cell transplantation in patients with prior accelerated or blast phase prior to transplant or who have relapsed.

Idhifa® (Enasidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML; and
    a. Member meets 1 of the following:
        i. Member is 75 years of age or older; or
        ii. If the member is younger than 75 years of age, must be unable to tolerate intensive induction chemotherapy; and
    b. As a single agent; and

    c. Isocitrate dehydrogenase-2 (IDH2*)* mutation; or
2. Relapsed/refractory AML; and
    a. IDH2 mutation; and
    b. As a single agent.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Graft-Versus-Host Disease (cGVHD) Diagnosis]:

1. Failure of 1 or more lines of therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first-line or subsequent therapy for CLL/SLL; and
2. As a single agent or in combination with bendamustine, rituximab, or obinutuzumab.

Imbruvica® (Ibrutinib) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis or Acquired Immunodeficiency Syndrome (AIDS)-Related B-Cell Lymphoma Diagnosis]:

1. Non-germinal center DLBCL; and
2. As second-line or subsequent therapy; and
3. Member is not a candidate for high-dose therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 or 2 FL; and
2. As subsequent therapy (third-line or greater) for histologic transformation to non-germinal center diffuse large B-cell lymphoma (DLBCL).

Imbruvica® (Ibrutinib) Approval Criteria [Hairy Cell Leukemia (HCL) Diagnosis]:

1. As a single agent in members with indication(s) for treatment for progression.

Imbruvica® (Ibrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. As a single agent or in combination with rituximab or lenalidomide/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Histologic Transformation of Marginal Zone Lymphoma (MZL) to Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. As third-line or greater therapy for members who have transformed to non-germinal center DLBCL.

Imbruvica® (Ibrutinib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease.

Imbruvica® (Ibrutinib) Approval Criteria [Post-Transplantation Lymphoproliferative Disorders Diagnosis]:

1. As second-line or subsequent therapy in members with partial response, persistent, or progressive disease; and
2. Non-germinal center B-cell type.

Imbruvica® (Ibrutinib) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. As first-line or subsequent therapy; and
2. As a single agent or in combination with rituximab.

Inqovi® (Decitabine/Cedazuridine) Approval Criteria [Myelodysplastic Syndromes (MDS) Diagnosis]:

1. A diagnosis of MDS (intermediate-1, intermediate-2, or high risk) in adults including previously treated and untreated, de novo, and secondary MDS with the 1 of the following subtypes:
    a. Refractory anemia; or
    b. Refractory anemia with ring sideroblasts; or
    c. Refractory anemia with excess blasts; or
    d. Chronic myelomonocytic leukemia (CMML).

Kymriah® (Tisagenlecleucel) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Members must meet all of the following:
    a. B-cell precursor ALL; and
    b. Member must be 25 years of age or younger; and
    c. Refractory or in second or later relapse:
        i. Philadelphia chromosome negative (Ph-) ALL: Must be refractory or with ≥2 relapses; or
        ii. Philadelphia chromosome positive (Ph+) ALL: Must have failed ≥2 tyrosine kinase inhibitors (TKIs); and
    d. Therapies to consider prior to tisagenlecleucel if appropriate: Clinical trial, multi-agent chemotherapy with or without hematopoietic cell transplantation (HCT), blinatumomab (category 1 recommendation), and inotuzumab (category 1 recommendation); and
2. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells, must be trained in the management of cytokine release syndrome (CRS) and neurologic toxicities, and must

comply with the Kymriah® risk evaluation and mitigation strategy (REMS) requirements.

Kymriah® (Tisagenlecleucel) Approval Criteria [Lymphoma Diagnosis]:

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

Lumoxiti® (Moxetumomab Pasudotox-tdfk) Approval Criteria [Hairy Cell Leukemia (HCL) Diagnosis]:

1. Treatment of relapsed or refractory HCL in adults; and
2. Member has received ≥2 prior systemic therapies, including treatment with a purine nucleoside analog (PNA); and
3. Creatinine clearance (CrCl) ≥30mL/min/1.73m^2; and
4. As a single agent.

Onureg® (Azacitidine) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. A diagnosis of AML; and
2. Used as maintenance therapy in members who have achieved first complete remission (CR) or complete remission with incomplete blood count recover (CRi) following intensive induction chemotherapy; and
3. Member is unable to complete intensive curative therapy.

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

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

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

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

Sprycel® (Dasatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have 1 of the following:

a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single agent; or
b. Maintenance therapy including:
    i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
    ii. Post-hematopoietic stem cell transplantation; or
c. Relapsed/refractory disease as a single agent or in combination with multi-agent chemotherapy.

Sprycel® (Dasatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have 1 of the following:
    a. Chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplantation.

Sprycel® (Dasatinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Member must have all of the following:
    a. Progressive disease and failed imatinib, sunitinib, or regorafenib; and
    b. PDGFRA D842V mutation.

Synribo® (Omacetaxine) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have 1 of the following:
    a. Primary treatment of advanced phase CML with disease progression to accelerated phase; or
    b. Post-hematopoietic stem cell transplant in members who have relapsed; or
    c. T315I mutation; or
    d. Members who are intolerant or resistant to ≥2 tyrosine kinase inhibitors (TKIs); and
2. As a single agent.

Tasigna® (Nilotinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have 1 of the following:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or

c. Relapsed/refractory disease as a single agent or in combination with multi-agent chemotherapy.

Tasigna® (Nilotinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have 1 of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Philadelphia Chromosome Positive (Ph+) CML chronic phase (CP) resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy; or
    c. Post-hematopoietic stem cell transplantation.

Tasigna® (Nilotinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Member must have progressive disease and failed imatinib, sunitinib, or regorafenib.

Tibsovo® (Ivosidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML; and
    a. Member meets 1 of the following:
        i. Member is 75 years of age or older; or
        ii. If the member is younger than 75 years of age, must be unable to tolerate intensive induction chemotherapy; and
    b. As a single agent; and
    c. Isocitrate dehydrogenase-2 (IDH2*)* mutation; or
2. Relapsed/refractory AML; and
    a. As a single agent; and
    b. IDH1 mutation.

Venclexta® (Venetoclax) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Member meets 1 of the following:
    a. Member is 75 years of age or older; or
    b. If the member is younger than 75 years of age, must be unable to tolerate intensive induction chemotherapy; and
2. As first-line therapy or in relapsed/refractory disease; and
3. In combination with azacitidine, decitabine, or low-dose cytarabine (LDAC).

Venclexta® (Venetoclax) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first-line therapy in combination with obinutuzumab for a maximum duration of 12 months; or

2. Relapsed/refractory disease in combination with rituximab or as a single agent.

Venclexta® (Venetoclax) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. As a single agent.

Xospata® (Gilteritinib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Relapsed/refractory AML; and
2. FMS-related tyrosine kinase 3 (FLT3) mutation; and
3. As a single agent.

Zelboraf® (Vemurafenib) Approval Criteria [Erdheim-Chester Disease (ECD) Diagnosis]:

1. Diagnosis of ECD; and
2. BRAF V600E or V600K mutation; and
3. As a single agent.

Zelboraf® (Vemurafenib) Approval Criteria [Hairy Cell Leukemia (HCL) Diagnosis]:

1. Disease progression following failure of purine analog therapy (i.e., pentostatin, cladribine); and
2. As a single agent.

Zelboraf® (Vemurafenib) Approval Criteria [Melanoma Diagnosis]:

1. Unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation detected by an FDA-approved test; and
    a. Not indicated for wild-type BRAF melanoma
3. As a single agent or in combination with cobimetinib; and
4. One of the following is met:
    a. First-line therapy; or
    b. Second-line therapy or subsequent therapy.

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

1. BRAF V600E or V600K mutation detected; and
    a. Not indicated for wild-type BRAF NSCLC
2. Diagnosis of refractory or metastatic disease; and
3. As a single agent.

Zydelig® (Idelalisib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. Relapsed/refractory disease; and

2. In combination with rituximab or rituximab/bendamustine; or
3. As a single agent.

Zydelig® (Idelalisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 to 2 FL; and
2. As second-line or subsequent therapy for refractory or progressive disease; and
3. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease; and
2. Refractory to both alkylator and rituximab therapy.

Utilization of Leukemia Medications: Fiscal Year 2021

The following utilization data includes medications indicated for leukemia; however, the data does not differentiate between leukemia 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
2020	48	323	$4,253,582.37	$13,168.99	$445.68	16,266	9,544
2021	51	338	$4,842,914.83	$14,328.15	$488.49	18,536	9,914
% Change	**6.30%**	**4.60%**	**13.90%**	**8.80%**	**9.60%**	**14.00%**	**3.90%**
Change	**3**	**15**	**$589,332.46**	**$1,159.16**	**$42.81**	**2,270**	**370**

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

Fiscal Year Comparison: Medical Claims

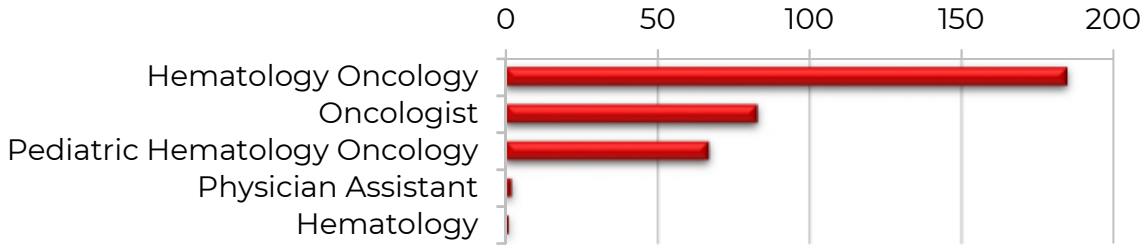
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2020	10	31	$378,691.17	$12,215.84	3.1
2021	13	48	$839,832.67	$17,496.51	3.69
% Change	**30.00%**	**54.84%**	**121.77%**	**43.23%**	**19.03%**
Change	**3**	**17**	**$461,141.50**	**$5,280.67**	**0.59**

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

Demographics of Members Utilizing Leukemia Medications: Pharmacy Claims

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

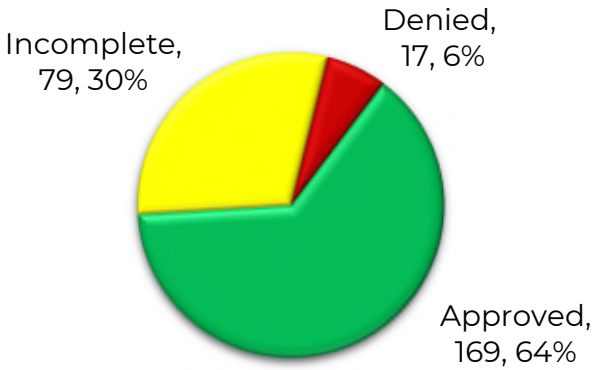
Top Prescriber Specialties of Leukemia Medications by Number of Claims: Pharmacy Claims



Prior Authorization of Leukemia Medications

There were 265 prior authorization requests submitted for leukemia medications during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



Market News and Updates[5,6,7,8,9,10,11,12]

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

- **July 2006:** The FDA approved an expanded indication for Oncaspar® (pegaspargase) for first-line treatment of pediatric and adult patients with acute lymphoblastic leukemia (ALL) as a component of a multi-agent chemotherapy regimen. Oncaspar® was originally FDA approved in 1994 as a component of a multi-agent chemotherapeutic regimen for treatment of pediatric and adult patients with ALL and hypersensitivity to asparaginase.

- **November 2011:** The FDA approved Erwinaze® (asparaginase *Erwinia chrysanthemi*) for intramuscular (IM) injection as part of a treatment regimen for ALL in patients who have had a hypersensitivity reaction to *Escherichia coli* (*E. coli*)-derived asparaginase. In 2014, the FDA approved the intravenous (IV) administration of Erwinaze® for the same indication, to give patients unable to tolerate IM injections another administration option.
- **June 2021:** The FDA approved Ayvakit™ (avapritinib) for the treatment of adult patients with advanced systemic mastocytosis, including patients with aggressive systemic mastocytosis, systemic mastocytosis with an associated hematological neoplasm, and mast cell leukemia.
- **July 2021:** The FDA approved Rylaze™ [asparaginase *Erwinia chrysanthemi* (recombinant)-rywn] as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and lymphoblastic lymphoma (LBL) in adult and pediatric patients 1 month of age or older who have developed hypersensitivity to *E. coli*-derived asparaginase.
- **August 2021:** The FDA approved Tibsovo® (ivosidenib) for the treatment of adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (*IDH1)* mutation.
- **October 2021:** The FDA approved Tecartus® (brexucabtagene autoleucel) for the treatment of adult patients with relapsed or refractory B-cell precursor ALL.
- **October 2021:** The FDA granted accelerated approval to Scemblix® (asciminib) for patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with 2 or more tyrosine kinase inhibitors (TKIs), and for the treatment of adult patients with Ph+ CML in CP with the T315I mutation.
- **December 2021:** The FDA approved Rituxan® (rituximab) in combination with chemotherapy for pediatric patients 6 months of age and older with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL), or mature B-cell acute leukemia (B-AL).

News:

- **May 2021:** In order to alleviate a critical shortage of Erwinaze® (asparaginase *Erwinia chrysanthemi*) in the United States' market, Porton Biopharma Limited (PBL) coordinated with the FDA to make available in the United States the non-FDA licensed Erwinase® (crisantaspase) 10,000 international units (IU)/vial powder for solution for injection/infusion. This does not represent a formal FDA approval of Erwinase® in the United States. Like the FDA approved Erwinaze®, Erwinase® is an L-asparaginase enzyme derived from the bacterium *Erwinia chrysanthemi* and is indicated for the treatment of ALL.

Erwinase® was first licensed in the United Kingdom in 1985 and is supplied to many countries worldwide.

Guideline Update(s):

- The National Comprehensive Cancer Network (NCCN) guidelines recommend combination therapy with asparaginase-based regimens as preferred induction therapy in patients with extranodal NK/T-cell lymphoma with nasal involvement.

Product Summaries[13,6,14,15]

Erwinaze® (Asparaginase *Erwinia Chrysanthemi*)

- **Therapeutic Class:** Asparagine specific enzyme
- **Indication(s):** As a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL who have developed hypersensitivity to *E. coli*-derived asparaginase
- **How Supplied:** 10,000 IU of lyophilized powder per single-dose vial (SDV)
- **Dose:**
  - To substitute for a dose of pegaspargase: 25,000 IU/m^2 administered IM or IV 3 times a week for 6 doses
  - To substitute for a dose of native *E. coli* asparaginase: 25,000 IU/m^2 administered IM or IV for each scheduled dose of native *E. coli* asparaginase
- **Cost:** The Wholesale Acquisition Cost (WAC) is $4,030.84 per SDV, resulting in a cost of $20,154.20 per dose for an adult with a body surface area (BSA) of 1.7m^2.

Oncaspar® (Pegaspargase):

- **Therapeutic Class:** Asparagine specific enzyme
- **Indication(s):** As a component of a multi-agent chemotherapeutic regimen for the treatment adult and pediatric patients for the following:
  - First-line treatment of ALL
  - ALL and hypersensitivity to asparaginase
- **How Supplied:** 3,750 IU/5mL (750 IU/mL) solution in a SDV
- **Dose:**
  - 21 years of age and younger: 2,500 IU/m^2
  - Older than 21 years of age: 2,000 IU/m^2
  - Oncaspar® should be administered IM or IV no more frequently than every 14 days
- **Cost:** The WAC is $4,448.49 per mL, resulting in a cost per dose of $44,484.90 for an adult with a BSA of 1.7m^2.

Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn]:

- **Therapeutic Class:** Asparagine specific enzyme
- **Indication(s):** As a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL in adult and pediatric patients 1 month of age or older who have developed hypersensitivity to *E. coli*-derived asparaginase
- **How Supplied:** 10mg/0.5mL solution in a SDV
- **Dose:** When replacing a long-acting asparaginase product, the recommended dosage is 25mg/m^2 administered IM every 48 hours.
- **Cost:** The WAC is $8,780.00 per mL, resulting in a cost per dose of $21,950.00 for an adult with a BSA of 1.7m^2.

Scemblix® (Asciminib):

- **Therapeutic Class:** TKI
- **Indication(s):**
  - Ph+ CML in CP, previously treated with 2 or more TKIs
  - Ph+ CML in CP with the T315I mutation
- **How Supplied:** 20mg and 40mg oral tablets
- **Dose:**
  - Ph+ CML in CP: 80mg once daily or 40mg twice daily
  - Ph+ CML in CP with the T315I mutation: 200mg twice daily
- **Cost:** The WAC is $298.33 per tablet for the 20mg and 40mg strengths, resulting in monthly cost of $89,499.00 based on the recommended dosing for Ph+ CML in CP with the T315I mutation.

Recommendations

The College of Pharmacy recommends the prior authorization of Erwinase® (crisantaspase), Erwinaze® (asparaginase *Erwinia chrysanthemi*), Rylaze™ [asparaginase *Erwinia chrysanthemi* (recombinant)-rywn], and Scemblix® (asciminib) with the following criteria (shown in red):

Erwinase® (Crisantaspase), Erwinaze® (Asparaginase *Erwinia Chrysanthemi*), and Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn] Approval Criteria [Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma Diagnosis]:

1. Diagnosis of ALL or lymphoblastic lymphoma; and
2. Used as a component of multi-agent chemotherapy; and
3. Member has a documented hypersensitivity to *Escherichia coli*-derived asparaginase.

Scemblix® (Asciminib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Diagnosis of Philadelphia chromosome-positive (Ph+) CML in chronic phase; and
    a. Previously treated with ≥2 tyrosine kinase inhibitors (TKIs); or
2. Frontline or subsequent therapy in members with the T315I mutation.

Additionally, College of Pharmacy recommends the prior authorization of Oncaspar® (pegaspargase) with criteria similar to Asparlas™ (calaspargase pegol-mknl) and updating the Asparlas™ criteria based on NCCN guideline recommendations and product availability with the following criteria (changes and updates shown in red):

Asparlas™ (Calaspargase Pegol-mknl) and Oncaspar® (Pegaspargase) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

~~1. A patient-specific, clinically significant reason why the member cannot use pegaspargase must be provided; and~~
~~2. Member must be 1 month to 21 years of age.~~
3. Diagnosis of ALL; and
4. Used as first line therapy; or
5. May be used to treat members with a hypersensitivity to native forms of L-asparaginase; or
6. Used as systemic central nervous system (CNS)-directed therapy; or
7. Used in relapsed/refractory disease ; and
    a. Philadelphia chromosome negative (Ph-); or
    b. Philadelphia chromosome positive (Ph+); and
        i. Refractory to tyrosine kinase inhibitor (TKI) therapy or used in conjunction with a TKI (if not previously used).

Asparlas™ (Calaspargase Pegol-mknl) and Oncaspar® (Pegaspargase) Approval Criteria [Extranodal NK/T-Cell Lymphoma Diagnosis]:

1. Diagnosis of NK/T-Cell lymphoma; and
2. Member has nasal disease; and
    a. Used as induction therapy; or
    b. Used as additional therapy in members with a positive biopsy following a partial or no response to induction therapy.

Finally, the College of Pharmacy recommends updating the prior authorization criteria for Ayvakit™ (avapritinib), Tecartus® (brexucabtagene autoleucel), and Tibsovo® (ivosidenib) based on recent FDA approvals (changes shown in red):

Ayvakit™ (Avapritinib) Approval Criteria [Systemic Mastocytosis Diagnosis]:

1. Diagnosis of advanced systemic mastocytosis, including members with aggressive systemic mastocytosis, systemic mastocytosis with an associated hematologic neoplasm, and mast cell leukemia; and
2. Platelet count ≥50 x 10^9/L.

Tecartus® (Brexucabtagene Autoleucel) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

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

Tibsovo® (Ivosidenib) Approval Criteria [Cholangiocarcinoma Diagnosis]:

1. Diagnosis of locally advanced or metastatic cholangiocarcinoma; and
2. An isocitrate dehydrogenase-1 (*IDH1*) mutation; and
3. Member has received prior treatment for this diagnosis.

Utilization Details of Leukemia Medications: Fiscal Year 2021

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
DASATINIB PRODUCTS					
SPRYCEL TAB 100MG	113	14	$1,616,176.14	8.07	$14,302.44
SPRYCEL TAB 20MG	18	2	$99,336.04	9	$5,518.67
SPRYCEL TAB 140MG	10	1	$147,770.54	10	$14,777.05
SUBTOTAL	**141**	**17**	**$1,863,282.72**	**8.29**	**$13,214.77**
IBRUTINIB PRODUCTS					
IMBRUVICA TAB 420MG	37	6	$497,320.59	6.17	$13,441.10
IMBRUVICA CAP 140MG	17	2	$247,622.38	8.5	$14,566.02
IMBRUVICA TAB 280MG	9	2	$118,708.57	4.5	$13,189.84
SUBTOTAL	**63**	**10**	**$863,651.54**	**6.3**	**$13,708.75**
NILOTINIB PRODUCTS					
TASIGNA CAP 150MG	43	4	$654,769.56	10.75	$15,227.20
TASIGNA CAP 200MG	19	2	$287,994.13	9.5	$15,157.59
SUBTOTAL	**62**	**6**	**$942,763.69**	**10.33**	**$15,205.87**
ENASIDENIB PRODUCTS					
IDHIFA TAB 100MG	14	2	$384,600.49	7	$27,471.46
SUBTOTAL	**14**	**2**	**$384,600.49**	**7**	**$27,471.46**
PONATINIB PRODUCTS					
ICLUSIG TAB 45MG	11	1	$185,611.51	11	$16,873.77

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ICLUSIG TAB 15MG	1	1	$33,133.41	1	$33,133.41
SUBTOTAL	**12**	**2**	**$218,744.92**	**6**	**$18,228.74**
BOSUTINIB PRODUCTS					
BOSULIF TAB 400MG	9	1	$145,077.40	9	$16,119.71
BOSULIF TAB 100MG	2	1	$23,532.22	2	$11,766.11
BOSULIF TAB 500MG	1	1	$16,468.00	1	$16,468.00
SUBTOTAL	**12**	**3**	**$185,077.62**	**4**	**$15,423.14**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	10	3	$64,117.86	3.33	$6,411.79
SUBTOTAL	**10**	**3**	**$64,117.86**	**3.33**	**$6,411.79**
VENETOCLAX PRODUCTS					
VENCLEXTA TAB 100MG	7	6	$63,371.22	1.17	$9,053.03
VENCLEXTA TAB STARTER PACK	2	2	$5,454.17	1	$2,727.09
SUBTOTAL	**9**	**8**	**$68,825.39**	**1.13**	**$7,647.27**
ACALABRUTINIB PRODUCTS					
CALQUENCE CAP 100MG	8	2	$112,571.28	4	$14,071.41
SUBTOTAL	**8**	**2**	**$112,571.28**	**4**	**$14,071.41**
GILTERITINIB PRODUCTS					
XOSPATA TAB 40MG	4	1	$94,545.64	4	$23,636.41
SUBTOTAL	**4**	**1**	**$94,545.64**	**4**	**$23,636.41**
IDELALISIB PRODUCTS					
ZYDELIG TAB 150MG	2	1	$23,564.16	2	$11,782.08
SUBTOTAL	**2**	**1**	**$23,564.16**	**2**	**$11,782.08**
AZACITIDINE PRODUCTS					
ONUREG TAB 300MG	1	1	$21,169.52	1	$21,169.52
SUBTOTAL	**1**	**1**	**$21,169.52**	**1**	**$21,169.52**
TOTAL	**338**	**51***	**$4,842,914.83**	**6.63**	**$14,328.15**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS⁺	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
BRENTUXIMAB VEDOTIN J9042	24	6	$551,482.28	4	$22,978.43
OBINUTUZUMAB J9301	8	2	$44,647.00	4	$5,580.88
BLINATUMOMAB J9039	8	2	$40,333.13	4	$5,041.64
ASPARAGINASE J9019	7	2	$161,288.60	3.5	$23,041.23
INOTUZUMAB OZOGAMICIN J9229	1	1	$42,081.66	1	$42,081.66
TOTAL	**48**	**13**	**$839,832.67**	**3.69**	**$17,496.51**

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

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[2] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. *CA Cancer J Clin* 2018; 68:7-30.
[3] National Comprehensive Cancer Network (NCCN) Guidelines. CLL/SLL V 1.2022. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Last accessed 01/12/2022.
[4] Hallek M. Chronic Lymphocytic Leukemia: 2015 Update on Diagnosis, Risk Stratification, and Treatment. *Am J Hematol* 2015; 90:446-460.
[5] Dinndorf PA, Gootenberg J, Cohen MH, et al. FDA Drug Approval Summary: Pegaspargase (Oncaspar®) for the First-Line Treatment of Children with Acute Lymphoblastic Leukemia (ALL). *Oncologist* 2007; 12(8):991-998.
[6] Oncaspar® (Pegaspargase) Prescribing Information. Servier Pharmaceuticals. Available online at: https://www.oncaspar.com/resource/1636640946000/oncaspar_files/prescribing_information.pdf. Last revised 11/2021. Last accessed 01/12/2022.
[7] Traynor K. FDA Approves Erwinaze® for Treatment of Leukemia. *ASHP*. Available online at: https://www.ashp.org/news/2011/11/18/fda_approves_erwinaze_for_treatment_of_leukemia?loginreturnUrl=SSOCheckOnly. Issued 11/18/2011. Last accessed 01/10/2022.
[8] Jazz Pharmaceuticals. Jazz Pharmaceuticals Receives FDA Approval For Intravenous Administration Of Erwinaze® (Asparaginase *Erwinia Chrysanthemi*). *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/jazz-pharmaceuticals-receives-fda-approval-for-intravenous-administration-of-erwinaze-asparaginase-erwinia-chrysanthemi-300012792.html. Issued 12/19/2014. Last accessed 01/10/2022.
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[10] Porton Biopharma. Temporary Importation of Erwinase® (Crisantaspase) Injection, Powder, Lyophilized, for Solution to Address a Drug Shortage in the United States (U.S.). Available online at: https://www.fda.gov/media/149614/download#:~:text=In%20order%20to%20alleviate%20a,the%20non%2DFDA%20licensed%20Erwinase%20. Issued 05/25/2021. Last accessed 01/10/2022.
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[13] Erwinaze® (Asparaginase *Erwinia Chrysanthemi*) Prescribing Information. Jazz Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125359s088lbl.pdf. Last revised 03/2016. Last accessed 01/05/2022.
[14] Rylaze™ [Asparaginase *Erwinia Chrysanthemi* (Recombinant)-rywn] Prescribing Information. Jazz Pharmaceuticals. Available online at: https://pp.jazzpharma.com/pi/rylaze.en.USPI.pdf. Last revised 06/2021. Last accessed 01/05/2022.
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Appendix N

Fiscal Year 2021 Annual Review of Azedra® (Iobenguane I-131)

Oklahoma Health Care Authority
February 2022

Introduction[1]

Pheochromocytoma refers to the adrenal tumor, and paraganglioma (PPGL) refers to its extra-adrenal counterpart. This is a rare neuroendocrine tumor and can be present anywhere along the sympathetic chain. While most are benign, about 10% are malignant and can be difficult to diagnose; unfortunately, diagnosis is made with presence of local invasion or metastatic disease. Metastatic disease frequently invades the bones, lymph nodes, liver, lungs, and brain. Patients may have symptoms of catecholamine excess due to some being catecholamine secreting, and patients can present with hypertension, episodic headache, sweating, tremor, and forceful palpitations. Local therapy includes surgical resection, radiation therapy, nonsurgical ablative therapy, radionuclide therapy, peptide receptor radioligand therapy, octreotide, systemic chemotherapy, and iobenguane I-131.

Approximately 60% of pheochromocytoma or PPGL take up meta-iodobenzylguanidine (MIBG) as determined by iobenguane I-123 diagnostic scintigraphy. For patients with MIBG-positive tumors with unresectable, symptomatic, progressive disease that have no options for locoregional treatment, iobenguane I-131 therapy may be more appropriate than systemic chemotherapy.

Current Prior Authorization Criteria

Azedra® (Iobenguane I-131) Approval Criteria [Pheochromocytoma or Paraganglioma (PPGL) Diagnosis]:

1. Adult and pediatric members 12 years of age and older; and
2. Iobenguane scan positive; and
3. Unresectable, locally advanced or metastatic pheochromocytoma or PPGL requiring systemic anticancer therapy.

Utilization of Azedra® (Iobenguane I-131): Fiscal Year 2021

There was no SoonerCare utilization of Azedra® (iobenguane I-131), including pharmacy and medical claims, during fiscal year 2021 (07/01/2020 to 06/30/2021).

Prior Authorization of Azedra® (Iobenguane I-131)

There were no prior authorization requests submitted for Azedra® (iobenguane I-131) during fiscal year 2021.

Market News and Updates[2]

Anticipated Patent Expiration(s):

- Azedra® (iobenguane I-131 intravenous solution): July 2025

Recommendations

The College of Pharmacy does not recommend any changes to the current Azedra® (iobenguane I-131) prior authorization criteria at this time.

[1] Kantorovich V, Pacak K. Pheochromocytoma and Paraganglioma. *Prog Brain Res* 2010; 182:343-73.
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Appendix O

Fiscal Year 2021 Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Elepsia™ XR [Levetiracetam Extended-Release (ER) Tablet] and Eprontia™ (Topiramate Oral Solution)

Oklahoma Health Care Authority
February 2022

Current Prior Authorization Criteria

1. Anticonvulsants are included in the mandatory generic plan.
    a. All brand name anticonvulsants (with a generic equivalent) will require prior authorization.
        i. Brand name medications (with a generic equivalent) will be approved for all members who are currently stable on these medications and have a seizure diagnosis.
2. Prior authorization will be required for certain non-standard dosage forms of medications when the drug is available in standard dosage forms.
    a. Members 12 years of age and older must have a documented medical reason demonstrating the need for non-standard dosage forms.
    b. Criteria for approval of extended-release formulations:
        i. Previously stabilized on the short-acting formulation; and
        ii. Dosing is not more than once daily; and
        iii. A reason why the short-acting formulation is not adequate must be provided; and
        iv. Dose packs will not be approved if standard dosage forms are available.
3. Quantity limit restrictions will be placed on lower strength tablets and capsules. The highest strengths will continue to have no quantity restrictions unless a maximum dose is specified for a particular medication.

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

1. An FDA approved diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and
3. Member must have failed therapy with at least 3 other medications commonly used for seizures; and

4. Afinitor® 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. Verification from the prescriber that female members 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.

Aptiom® (Eslicarbazepine) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Member must not currently be taking oxcarbazepine (concurrent use is contraindicated); and
3. A patient-specific, clinically significant reason why the member cannot use oxcarbazepine must be provided; and
4. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (200mg and 400mg) and 60 tablets per 30 days on the higher strength tablets (600mg and 800mg).

Banzel® (Rufinamide) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome (LGS); and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other medications commonly used for seizures; and
4. Members currently stable on Banzel® (rufinamide) and who have a seizure diagnosis will be grandfathered.

Briviact® (Brivaracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and

2. Initial prescription must be prescribed by, or in consultation with, a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants; and
4. Members currently stable on Briviact® and who have a seizure diagnosis will be grandfathered; and
5. For Briviact® oral solution, an age restriction of 12 years and younger will apply. Members older than 12 years of age will require a patient-specific, clinically significant reason why the member cannot take the oral tablet formulation; and
6. Approval length for Briviact® intravenous (IV) will be for a maximum of 7 days of therapy. Further approval may be granted if prescriber documents an ongoing need for Briviact® IV therapy over Briviact® oral formulations.

Diacomit® (Stiripentol) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Dravet syndrome in members 2 years of age and older; and
2. Initial prescription must be written by, or in consultation with, a neurologist; and
3. Member must have failed or be inadequately controlled with clobazam and valproate; and
4. Member must take clobazam and valproate concomitantly with Diacomit® or a reason why concomitant clobazam and valproate are not appropriate for the member must be provided; and
5. Members currently stable on Diacomit® and who have a seizure diagnosis will be grandfathered; and
6. 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
7. For Diacomit® powder for oral suspension, an age restriction of 12 years and younger will apply. Members older than 12 years of age will require a patient-specific, clinically significant reason why the member cannot take the oral capsule formulation; and
8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/ effectiveness of the medication.

Epidiolex® (Cannabidiol Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Lennox-Gastaut syndrome (LGS); or
    b. Dravet syndrome; or
    c. Tuberous sclerosis complex (TSC)-associated seizures; and

2. Member must be 1 year of age or older; and
3. Initial prescription must be written by, or in consultation with, a neurologist; and
4. For a diagnosis of Dravet syndrome, the member must have failed therapy or be inadequately controlled with at least 1 anticonvulsant; or
5. For a diagnosis of LGS or TSC-associated seizures, the member must have failed therapy or be inadequately controlled with at least 3 other anticonvulsants; and
6. Members currently stable on Epidiolex® and who have a seizure diagnosis will be grandfathered; and
7. 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
8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Felbatol® (Felbamate) Approval Criteria:

1. Initial prescription must be written by a neurologist; and
2. Member must have failed therapy with at least 3 other medications commonly used for seizures.

Fintepla® (Fenfluramine) Approval Criteria:

1. An FDA approved indication for the treatment of seizures associated with Dravet syndrome; and
2. Member must be 2 years of age or older; and
3. Initial prescription must be written by, or in consultation with, a neurologist; and
4. Member must not be taking monoamine oxidase inhibitors (MAOIs) within 14 days of administration of Fintepla®, and
5. Prescriber must verify the member's blood pressure will be monitored; and
6. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Fintepla® therapy and throughout treatment; and
7. Member must have failed or be inadequately controlled with at least 2 other anticonvulsants; and
8. Pharmacy and prescriber must be certified in the Fintepla® Risk Evaluation and Mitigation Strategy (REMS) program; and
9. Member must be enrolled in the Fintepla® REMS program; and
10. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and

11. Prescriber must verify that dose titration and maximum maintenance dose will be followed according to package labeling based on member weight and concomitant medications; and
12. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication; and
13. A quantity limit of 360mL per 30 days will apply.

Oxtellar XR® [Oxcarbazepine Extended-Release (ER)] Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation must be provided; and
2. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (150mg and 300mg).

Qudexy® XR [Topiramate Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Treatment of partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
    b. Adjunctive therapy in seizures associated with Lennox-Gastaut syndrome (LGS); or
    c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate), must be provided; and
3. A quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (150mg and 200mg).

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of refractory complex seizures in adults and pediatric members 2 years of age or older, or infantile spasms in children 1 month to 2 years of age; and
2. Authorization of generic vigabatrin (in place of brand Sabril®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
3. Members with refractory complex seizures must have failed therapy with at least 3 other anticonvulsants; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the Sabril® Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy.

Spritam® (Levetiracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures, myoclonic seizures, or primary generalized tonic-clonic (PGTC) seizures; and

2. A patient-specific, clinically significant reason why the member cannot use generic formulations of levetiracetam must be provided; and
3. A quantity limit of 60 tablets per 30 days will apply.

Sympazan® (Clobazam Oral Film) Approval Criteria:

1. An FDA approved indication of adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in members 2 years of age and older; and
2. Previous failure of at least 2 non-benzodiazepine anticonvulsants; and
3. Previous failure of clonazepam; and
4. A patient-specific, clinically significant reason why the member cannot use clobazam oral tablets or clobazam oral suspension must be provided; and
5. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Trokendi XR® [Topiramate Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Treatment of partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
   b. Adjunctive therapy in seizures associated with Lennox-Gastaut syndrome (LGS); or
   c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate), must be provided; and
3. A patient-specific, clinically significant reason why the member cannot use Qudexy® XR (topiramate ER) must be provided; and
4. Members currently stable on Trokendi XR® (topiramate ER) and who have a seizure diagnosis will be grandfathered; and
5. A quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (200mg).

Xcopri® (Cenobamate) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants.

Utilization of Anticonvulsants: Fiscal Year 2021

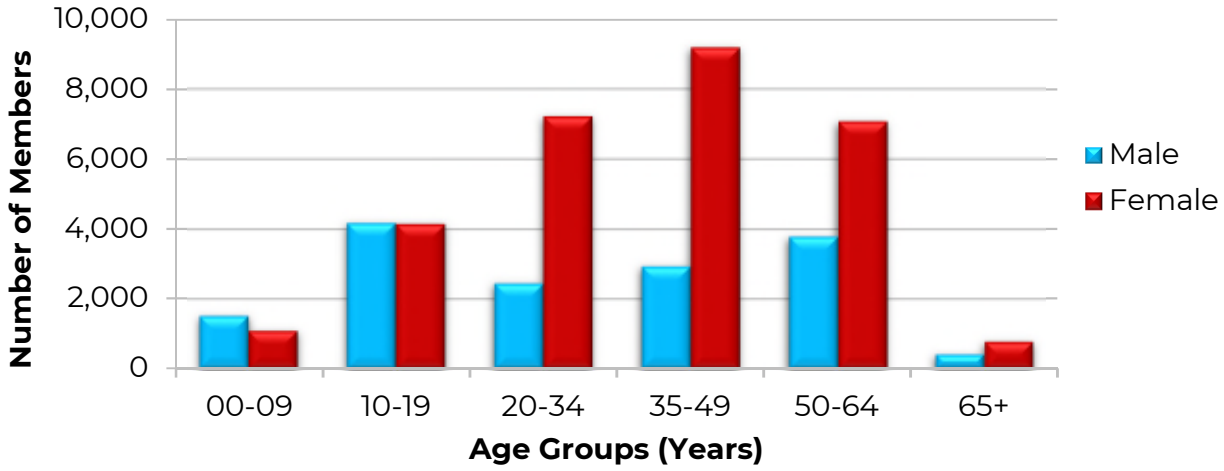
The following utilization data includes anticonvulsants used for all diagnoses and does not differentiate between seizure diagnoses and other diagnoses, for which use may be appropriate.

Comparison of Fiscal Years

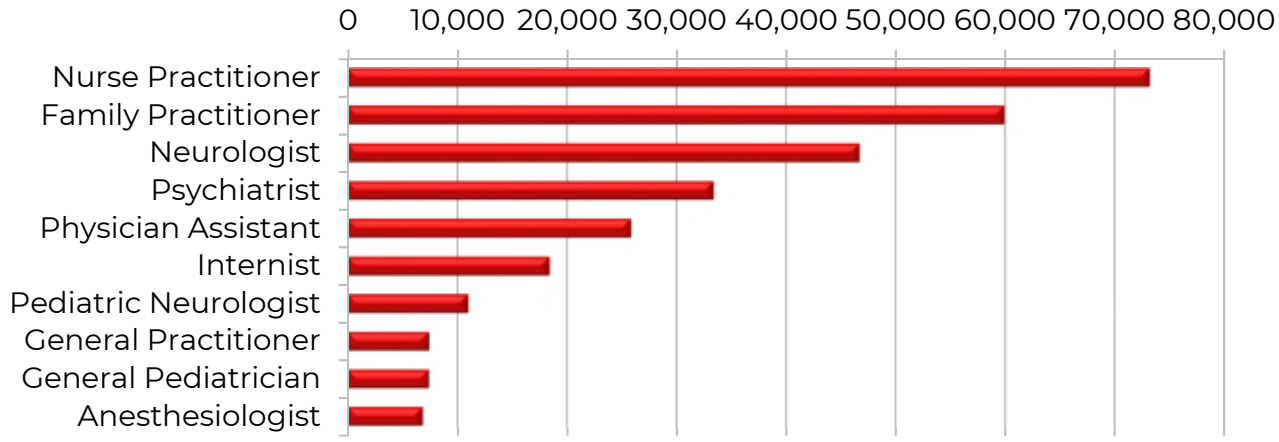
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	42,227	315,099	$28,219,439.06	$89.56	$2.86	31,712,778	9,880,748
2021	44,750	317,442	$28,176,473.33	$88.76	$2.64	33,696,697	10,667,714
% Change	**6.0%**	**0.7%**	**-0.2%**	**-0.9%**	**-7.7%**	**6.3%**	**8.0%**
Change	**2,523**	**2,343**	**-$42,965.73**	**-$0.80**	**-$0.22**	**1,983,919**	**786,966**

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

Demographics of Members Utilizing Anticonvulsants



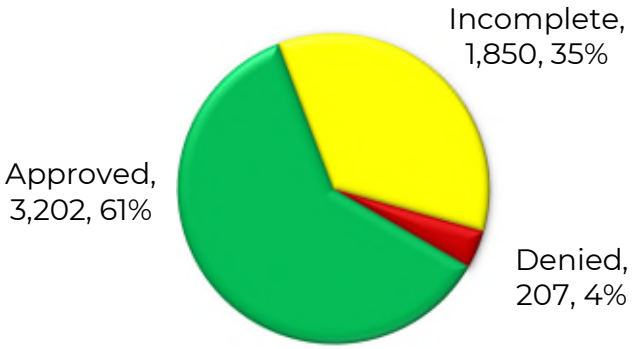
Top Prescriber Specialties of Anticonvulsants by Number of Claims



Prior Authorization of Anticonvulsants

There were 5,259 prior authorization requests submitted for anticonvulsants during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Vimpat® [lacosamide tablets, oral solution, intravenous (IV) solution]: March 2022
- Banzel® (rufinamide tablets, oral suspension): May 2023
- Sympazan® (clobazam oral films): April 2024
- Diacomit® (stiripentol capsules, oral suspension): August 2025*
  *Diacomit® does not have any unexpired patents; however, it does currently have exclusivity through August 2025.
- Fycompa® (perampanel tablets, oral suspension): July 2026
- Oxtellar XR® [oxcarbazepine extended-release (ER) tablets]: April 2027
- Elepsia™ XR (levetiracetam ER tablets): October 2027
- Nayzilam® (midazolam nasal spray): January 2028
- Trokendi XR® (topiramate ER capsules): April 2028
- Valtoco® (diazepam nasal spray): March 2029
- Briviact® (brivaracetam tablets, oral solution, IV solution): April 2030
- Aptiom® (eslicarbazepine tablets): August 2032
- Qudexy® XR (topiramate ER capsules): March 2033
- Spritam® (levetiracetam tablets for oral suspension): March 2034
- Epidiolex® (cannabidiol oral solution): June 2035
- Fintepla® (fenfluramine oral solution): October 2039

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

- **September 2020:** In 2018, the FDA approved Elepsia™ XR (levetiracetam ER) as adjunctive therapy for the treatment of partial-

onset seizures in patients 12 years of age and older. Elepsia™ XR contains the same active ingredient as Keppra® XR, but is available in higher strength tablets (1,000mg and 1,500mg). Elepsia™ XR was formulated to decrease the pill burden in patients taking higher doses of Keppra® XR since this medication is only available in 500mg and 750mg strength tablets. In September 2020, Sun Pharma announced an exclusive license agreement with Tripoint Therapeutics to commercialize Elepsia™ XR tablets in the United States.

- **November 2021:** The FDA approved Eprontia™ (topiramate oral solution) as the first and only liquid formulation of topiramate indicated for the treatment of partial-onset or primary generalized tonic-clonic seizures, adjunctive therapy in seizures associated with Lennox-Gastaut syndrome (LGS), and prophylaxis of migraine headaches.
- **August 2021:** The FDA approved an expanded indication for Briviact® CV tablets, oral solution, and injection to treat partial-onset seizures in patients as young as 1 month of age. The availability of both an injectable and oral formulation will now allow these young patients to have continuity of treatment when transitioning from hospital to home. The most common adverse reactions reported in the adult Briviact® studies were somnolence and sedation, dizziness, fatigue, and nausea and vomiting. In the pediatric Briviact® studies, the safety profile for pediatric patients were found to be similar to that of adults.

Elepsia™ XR (Levetiracetam ER) Product Summary[6]

Indication(s): Elepsia™ XR is indicated as adjunctive therapy for the treatment of partial-onset seizures in patients 12 years of age and older.

How Supplied: 1,000mg and 1,500mg oral ER tablets

Dosing: The initial recommended dose is 1,000mg once daily and may be increased by 1,000mg every 2 weeks to a maximum dose of 3,000mg once daily; tablets should not be split or cut.

Contraindication(s):

- Known hypersensitivity to levetiracetam

Adverse Reactions: The most common adverse reactions reported in clinical studies (incidence ≥5%) were somnolence and irritability.

Efficacy: The efficacy of Elepsia™ XR is based upon bioavailability studies comparing levetiracetam extended-release tablets (Keppra® XR) to Elepsia™ XR extended-release tablets and prior clinical studies using immediate-release and extended-release levetiracetam tablets.

Cost Comparison:

Product	Cost Per Unit	Cost Per Month*
Elepsia™ XR (levetiracetam ER) 1,500mg tablet	**$33.08**	**$1,984.80**
Elepsia™ XR (levetiracetam ER) 1,000mg tablet	**$26.42**	**$2,377.80**
levetiracetam ER 750mg tablet	$0.57	$68.40
levetiracetam ER 500mg tablet	$0.26	$46.80

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per month based on the FDA approved maximum daily dose of 3,000mg/day.
ER = extended-release

Eprontia™ (Topiramate Oral Solution) Product Summary[7]

Indication(s): Eprontia™ (topiramate oral solution) is indicated for the treatment of partial-onset or primary generalized tonic-clonic seizures, adjunctive therapy in seizures associated with LGS, and prophylaxis of migraine headaches.

How Supplied: 25mg/mL oral solution

Dosing: The initial, titration, and recommended maintenance doses vary by indication and age group and can be found in the Eprontia™ *Prescribing Information*.

Contraindication(s): None

Adverse Reactions:

- The most common adverse reactions reported in the epilepsy clinical studies (incidence ≥10%) were paresthesia, anorexia, weight loss, disorders related to speech problems, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, and fever.
- The most common adverse reactions reported in the migraine clinical studies (incidence ≥5%) were paresthesia, anorexia, weight loss, difficulty with memory, taste perversion, diarrhea, hypoesthesia, nausea, abdominal pain, and upper respiratory tract infection.

Efficacy: The safety and efficacy of Eprontia™ are based on the relative bioavailability of Eprontia™ compared topiramate sprinkle capsules (Topamax®) in healthy subjects. Topiramate sprinkle capsules have comparable bioavailability to topiramate tablets.

Cost Comparison:

Product	Cost Per Unit	Cost Per Month*
Eprontia™ (topiramate) 25mg/mL oral solution	**$1.41**	**$676.80**
topiramate 25mg sprinkle capsule	$0.67	$321.60
topiramate 200mg tablet	$0.12	$7.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per month based on the FDA approved maximum daily dose of 400mg/day.

Recommendations

The College of Pharmacy recommends the prior authorization of Elepsia™ XR (levetiracetam ER tablet) and Eprontia™ (topiramate oral solution) with the following criteria:

Elepsia™ XR [Levetiracetam Extended-Release (ER) Tablet] Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use generic formulations of levetiracetam ER must be provided; and
3. A quantity limit of 60 tablets per 30 days will apply.

Eprontia™ (Topiramate Oral Solution) Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
   b. Adjunctive therapy in seizures associated with Lennox-Gastaut syndrome (LGS); or
   c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use topiramate tablets and sprinkle capsules must be provided; and
3. An age restriction of 11 years of age and younger will apply. Members older than 11 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed; and
4. A quantity limit of 473mL per 29 days will apply.

Utilization Details of Anticonvulsants: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
GABAPENTIN PRODUCTS					
GABAPENTIN CAP 300MG	33,660	9,843	$476,616.43	$14.16	3.42
GABAPENTIN TAB 600MG	21,341	4,437	$382,293.92	$17.91	4.81
GABAPENTIN TAB 800MG	17,285	2,932	$385,793.20	$22.32	5.9
GABAPENTIN CAP 100MG	11,213	4,258	$137,673.86	$12.28	2.63

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
GABAPENTIN CAP 400MG	6,091	1,483	$85,505.68	$14.04	4.11
GABAPENTIN SOL 250MG/5ML	1,328	235	$63,998.32	$48.19	5.65
NEURONTIN CAP 300MG	9	1	$4,718.74	$524.30	9
GABAPENTIN SOL 300MG/6ML	4	1	$365.60	$91.40	4
SUBTOTAL	**90,931**	**23,190**	**$1,536,965.75**	**$16.90**	**3.92**
LEVETIRACETAM PRODUCTS					
LEVETIRACETAM SOL 100MG/ML	11,149	1,630	$227,173.90	$20.38	6.84
LEVETIRACETAM TAB 500MG	9,189	2,072	$160,670.07	$17.49	4.43
LEVETIRACETAM TAB 1,000MG	6,362	1,016	$156,423.48	$24.59	6.26
LEVETIRACETAM TAB 750MG	4,192	794	$99,507.95	$23.74	5.28
LEVETIRACETAM TAB 250MG	1,596	350	$24,505.01	$15.35	4.56
LEVETIRACETAM TAB 500MG ER	527	114	$16,604.74	$31.51	4.62
LEVETIRACETAM TAB 750MG ER	375	67	$18,876.56	$50.34	5.6
KEPPRA XR TAB 500MG	60	8	$55,358.47	$922.64	7.5
KEPPRA TAB 1,000MG	58	6	$73,706.47	$1,270.80	9.67
KEPPRA XR TAB 750MG	54	7	$57,513.09	$1,065.06	7.71
LEVETIRACETAM INJ 500MG/5ML	51	1	$3,056.71	$59.94	51
KEPPRA TAB 750MG	37	4	$45,318.96	$1,224.84	9.25
KEPPRA TAB 500MG	33	3	$12,002.65	$363.72	11
KEPPRA SOL 100MG/ML	18	3	$11,103.89	$616.88	6
KEPPRA TAB 250MG	3	2	$2,333.98	$777.99	1.5
ROWEEPRA TAB 500MG	1	1	$17.79	$17.79	1
SUBTOTAL	**33,705**	**6,078**	**$964,173.72**	**$28.61**	**5.55**
LAMOTRIGINE PRODUCTS					
LAMOTRIGINE TAB 100MG	10,393	2,382	$126,701.45	$12.19	4.36
LAMOTRIGINE TAB 25MG	8,469	2,966	$101,344.38	$11.97	2.86
LAMOTRIGINE TAB 200MG	6,995	1,207	$94,417.39	$13.50	5.8
LAMOTRIGINE TAB 150MG	3,760	820	$48,071.78	$12.79	4.59
LAMOTRIGINE CHW 25MG	207	35	$ 8,739.55	$42.22	5.91
LAMOTRIGINE TAB 200MG ER	169	30	$15,744.49	$93.16	5.63
LAMOTRIGINE TAB 300MG ER	124	20	$23,113.85	$186.40	6.2
LAMOTRIGINE CHW 5MG	119	30	$3,786.18	$31.82	3.97
LAMICTAL TAB 200MG	81	10	$100,684.72	$1,243.02	8.1
LAMOTRIGINE TAB 50MG ODT	78	15	$24,781.65	$317.71	5.2
LAMOTRIGINE TAB 50MG ER	76	17	$5,273.55	$69.39	4.47
LAMICTAL TAB 150MG	75	7	$94,218.05	$1,256.24	10.71
LAMOTRIGINE TAB 100MG ER	74	17	$5,524.32	$74.65	4.35
LAMOTRIGINE TAB 25MG ODT	69	8	$53,742.55	$778.88	8.63
LAMOTRIGINE TAB 100MG	62	10	$15,767.75	$254.32	6.2
LAMOTRIGINE TAB 250MG ER	52	10	$15,122.21	$290.81	5.2
LAMICTAL TAB 100MG	48	5	$56,274.51	$1,172.39	9.6

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
LAMICTAL XR TAB 200MG	37	6	$70,399.27	$1,902.68	6.17
LAMOTRIGINE TAB 200MG	35	4	$11,286.11	$322.46	8.75
LAMICTAL CHW 25MG	12	1	$96,010.21	$8,000.85	12
SUBVENITE TAB 100MG	8	5	$85.38	$10.67	1.6
LAMOTRIGINE TAB 25MG ER	6	3	$555.05	$92.51	2
LAMOTRIGINE TAB 100MG ODT	5	2	$1,804.89	$360.98	2.5
SUBVENITE TAB 200MG	4	3	$56.37	$14.09	1.33
SUBVENITE TAB 25MG	2	2	$26.02	$13.01	1
LAMICTAL XR TAB 250MG	2	1	$10,346.66	$5,173.33	2
LAMICTAL TAB 25MG ODT	1	1	$316.31	$316.31	1
SUBVENITE TAB 150MG	1	1	$14.78	$14.78	1
LAMICTAL XR KIT	1	1	$589.85	$589.85	1
SUBTOTAL	**30,965**	**7,619**	**$984,799.28**	**$31.80**	**4.06**
DIVALPROEX, VALPROATE, AND VALPROIC ACID PRODUCTS					
DIVALPROEX TAB 500MG DR	7,079	1,367	$142,530.87	$20.13	5.18
DIVALPROEX TAB 500MG ER	6,360	1,216	$166,497.34	$26.18	5.23
DIVALPROEX TAB 250MG DR	4,916	1,118	$70,909.80	$14.42	4.4
DIVALPROEX TAB 250MG ER	3,229	714	$70,645.85	$21.88	4.52
VALPROIC ACID SOL 250MG/5ML	2,264	306	$45,681.63	$20.18	7.4
DIVALPROEX CAP 125MG	1,697	263	$113,652.67	$66.97	6.45
DIVALPROEX TAB 125MG DR	1,419	343	$20,466.84	$14.42	4.14
VALPROIC ACID CAP 250MG	750	146	$22,162.62	$29.55	5.14
DEPAKOTE SPR CAP 125MG	100	12	$40,428.70	$404.29	8.33
DEPAKOTE ER TAB 250MG	47	4	$9,776.34	$208.01	11.75
DEPAKOTE ER TAB 500MG	45	5	$33,384.49	$741.88	9
DEPAKOTE TAB 500MG DR	39	4	$23,908.72	$613.04	9.75
DEPAKOTE TAB 250MG DR	31	3	$7,261.37	$234.24	10.33
DEPAKOTE TAB 125MG DR	2	1	$120.30	$60.15	2
SUBTOTAL	**27,978**	**5,502**	**$767,427.54**	**$27.43**	**5.09**
OXCARBAZEPINE PRODUCTS					
OXCARBAZEPINE TAB 300MG	9,840	2,041	$189,507.93	$19.26	4.82
OXCARBAZEPINE TAB 600MG	7,797	1,247	$251,467.00	$32.25	6.25
OXCARBAZEPINE TAB 150MG	6,434	1,604	$110,208.24	$17.13	4.01
OXCARBAZEPINE SUS 300MG/5ML	3,412	531	$527,613.26	$154.63	6.43
TRILEPTAL SUS 300MG/5ML	234	46	$151,132.37	$645.86	5.09
OXTELLAR XR TAB 600MG	146	24	$215,088.72	$1,473.21	6.08
OXTELLAR XR TAB 300MG	49	9	$16,339.30	$333.46	5.44
TRILEPTAL TAB 600MG	28	4	$52,484.78	$1,874.46	7
OXTELLAR XR TAB 150MG	22	4	$4,872.43	$221.47	5.5
SUBTOTAL	**27,962**	**5,510**	**$1,518,714.03**	**$54.31**	**5.07**
TOPIRAMATE PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TOPIRAMATE TAB 50MG	8,664	2,588	$111,030.84	$12.82	3.35
TOPIRAMATE TAB 25MG	8,447	3,126	$100,289.49	$11.87	2.7
TOPIRAMATE TAB 100MG	6,909	1,517	$96,826.59	$14.01	4.55
TOPIRAMATE TAB 200MG	2,628	471	$39,962.13	$15.21	5.58
TOPIRAMATE CAP 25MG	380	74	$22,584.06	$59.43	5.14
TOPIRAMATE CAP 15MG	296	77	$15,078.66	$50.94	3.84
TROKENDI XR CAP 200MG	135	22	$196,465.17	$1,455.30	6.14
TROKENDI XR CAP 100MG	94	19	$98,325.76	$1,046.02	4.95
TOPIRAMATE CAP ER 100MG	38	5	$19,865.75	$522.78	7.6
TOPAMAX TAB 200MG	35	3	$67,683.69	$1,933.82	11.67
TROKENDI XR CAP 50MG	33	10	$15,941.10	$483.06	3.3
TOPIRAMATE CAP ER 200MG	28	4	$17,658.46	$630.66	7
TOPAMAX TAB 100MG	16	3	$28,407.14	$1,775.45	5.33
TOPAMAX TAB 50MG	13	1	$9,513.72	$731.82	13
TROKENDI XR CAP 25MG	11	5	$4,591.45	$417.40	2.2
TOPIRAMATE CAP ER 150MG	11	2	$7,116.56	$646.96	5.5
TOPIRAMATE CAP ER 50MG	9	3	$5,138.57	$570.95	3
TOPAMAX SPR CAP 25MG	6	1	$40,200.20	$6,700.03	6
QUDEXY XR CAP 100MG/24HR	5	2	$3,154.37	$630.87	2.5
TOPIRAMATE CAP ER 25MG	4	2	$846.65	$211.66	2
QUDEXY XR CAP 50MG/24HR	2	2	$1,287.36	$643.68	1
SUBTOTAL	**27,764**	**7,937**	**$901,967.72**	**$32.49**	**3.50**
CLONAZEPAM PRODUCTS					
CLONAZEPAM TAB 1MG	11,663	2,102	$128,032.18	$10.98	5.55
CLONAZEPAM TAB 0.5MG	10,498	2,454	$107,635.71	$10.25	4.28
CLONAZEPAM TAB 2MG	2,733	453	$30,103.21	$11.01	6.03
CLONAZEPAM ODT TAB 0.25MG	1,153	380	$40,940.36	$35.51	3.03
CLONAZEPAM ODT TAB 0.5MG	628	219	$23,126.49	$36.83	2.87
CLONAZEPAM ODT TAB 0.125MG	612	216	$21,741.40	$35.53	2.83
CLONAZEPAM ODT TAB 1MG	341	125	$12,808.19	$37.56	2.73
CLONAZEPAM ODT TAB 2MG	61	21	$1,795.18	$29.43	2.9
KLONOPIN TAB 2MG	2	1	$498.86	$249.43	2
SUBTOTAL	**27,691**	**5,971**	**$366,681.58**	**$13.24**	**4.64**
PREGABALIN PRODUCTS					
PREGABALIN CAP 150MG	3,682	770	$58,484.53	$15.88	4.78
PREGABALIN CAP 75MG	2,934	1,026	$43,938.25	$14.98	2.86
PREGABALIN CAP 100MG	2,531	657	$40,013.99	$15.81	3.85
PREGABALIN CAP 50MG	1,514	618	$22,981.09	$15.18	2.45
PREGABALIN CAP 200MG	1,377	232	$22,300.04	$16.19	5.94
PREGABALIN CAP 300MG	987	170	$15,816.98	$16.03	5.81
PREGABALIN CAP 25MG	305	166	$4,502.92	$14.76	1.84

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
PREGABALIN CAP 225MG	197	50	$3,006.02	$15.26	3.94
LYRICA CAP 150MG	192	46	$120,431.38	$627.25	4.17
LYRICA CAP 200MG	141	24	$86,120.79	$610.79	5.88
LYRICA CAP 300MG	91	21	$51,809.15	$569.33	4.33
LYRICA CAP 100MG	83	33	$49,622.15	$597.86	2.52
LYRICA CAP 75MG	73	32	$43,751.74	$599.34	2.28
LYRICA CAP 50MG	40	11	$23,482.04	$587.05	3.64
LYRICA CAP 225MG	21	3	$12,163.57	$579.22	7
PREGABALIN SOL 20MG/ML	12	1	$730.56	$60.88	12
LYRICA CAP 25MG	3	3	$1,292.58	$430.86	1
SUBTOTAL	**14,183**	**3,863**	**$600,447.78**	**$42.34**	**3.67**
LACOSAMIDE PRODUCTS					
VIMPAT TAB 200MG	2,382	300	$2,253,180.70	$945.92	7.94
VIMPAT SOL 10MG/ML	1,380	181	$1,232,741.63	$893.29	7.62
VIMPAT TAB 100MG	1,247	251	$1,084,214.81	$869.46	4.97
VIMPAT TAB 150MG	1,166	181	$1,045,554.14	$896.70	6.44
VIMPAT TAB 50MG	711	149	$374,451.85	$526.66	4.77
SUBTOTAL	**6,886**	**1,062**	**$5,990,143.13**	**$869.90**	**6.48**
CARBAMAZEPINE PRODUCTS					
CARBAMAZEPINE TAB 200MG	2,611	521	$84,755.36	$32.46	5.01
CARBAMAZEPINE CHW 100MG	479	89	$18,966.68	$39.60	5.38
CARBAMAZEPINE TAB 400MG ER	426	80	$71,972.75	$168.95	5.33
CARBAMAZEPINE CAP 300MG ER	325	61	$44,269.97	$136.22	5.33
CARBAMAZEPINE TAB 200MG ER	275	61	$25,771.73	$93.72	4.51
CARBAMAZEPINE TAB 100MG ER	204	58	$11,130.24	$54.56	3.52
CARBAMAZEPINE CAP 200MG ER	188	44	$25,234.20	$134.22	4.27
CARBAMAZEPINE SUS 100MG/5ML	185	21	$15,811.57	$85.47	8.81
CARBAMAZEPINE CAP 100MG ER	93	36	$9,201.84	$98.94	2.58
EPITOL TAB 200MG	51	30	$1,897.06	$37.20	1.7
CARBATROL CAP 200MG	50	5	$9,585.28	$191.71	10
TEGRETOL TAB 200MG	46	6	$24,089.49	$523.68	7.67
TEGRETOL SUS 100MG/5ML	43	5	$18,223.31	$423.80	8.6
TEGRETOL-XR TAB 400MG	41	5	$19,167.35	$467.50	8.2
TEGRETOL-XR TAB 200MG	33	3	$13,057.12	$395.67	11
CARBATROL CAP 300MG	14	2	$3,567.87	$254.85	7
CARBATROL CAP 100MG	1	1	$224.15	$224.15	1
SUBTOTAL	**5,065**	**1,028**	**$396,925.97**	**$78.37**	**4.93**
ZONISAMIDE PRODUCTS					
ZONISAMIDE CAP 100MG	2,994	448	$60,342.18	$20.15	6.68
ZONISAMIDE CAP 50MG	691	135	$10,176.32	$14.73	5.12
ZONISAMIDE CAP 25MG	432	99	$6,882.50	$15.93	4.36

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
ZONEGRAN CAP 100MG	6	1	$6,312.24	$1,052.04	6
SUBTOTAL	**4,123**	**683**	**$83,713.24**	**$20.30**	**6.04**
CLOBAZAM PRODUCTS					
CLOBAZAM SUS 2.5MG/ML	1,589	207	$234,871.63	$147.81	7.68
CLOBAZAM TAB 10MG	1,279	183	$41,337.65	$32.32	6.99
CLOBAZAM TAB 20MG	1,091	123	$65,637.17	$60.16	8.87
ONFI TAB 20MG	86	12	$327,423.56	$3,807.25	7.17
ONFI SUS 2.5MG/ML	37	5	$129,841.71	$3,509.24	7.4
ONFI TAB 10MG	28	4	$30,461.56	$1,087.91	7
SUBTOTAL	**4,110**	**534**	**$829,573.28**	**$201.84**	**7.70**
PHENYTOIN AND FOSPHENYTOIN PRODUCTS					
PHENYTOIN EX CAP 100MG	2,565	435	$80,080.18	$ 31.22	5.9
DILANTIN CAP 100MG	214	31	$44,155.99	$206.34	6.9
PHENYTOIN SUS 125MG/5ML	202	27	$5,277.77	$26.13	7.48
PHENYTOIN CHW 50MG	149	21	$5,995.00	$40.23	7.1
PHENYTOIN EX CAP 200MG	111	29	$8,944.04	$80.58	3.83
DILANTIN CAP 30MG	81	14	$14,164.67	$174.87	5.79
PHENYTOIN EX CAP 300MG	63	18	$3,823.71	$60.69	3.5
DILANTIN CHW 50MG	23	4	$2,689.34	$116.93	5.75
FOSPHENYTOIN INJ 100MG/2ML	15	2	$1,779.15	$118.61	7.5
PHENYTEK CAP 200MG	11	1	$984.94	$89.54	11
DILANTIN SUS 125MG/5ML	5	1	$2,060.50	$412.10	5
CEREBYX INJ 100MG/2ML	2	1	$856.29	$428.15	2
SUBTOTAL	**3,441**	**584**	**$170,811.58**	**$49.64**	**5.89**
PHENOBARBITAL PRODUCTS					
PHENOBARBITAL ELX 20MG/5ML	434	99	$23,021.30	$53.04	4.38
PHENOBARBITAL TAB 64.8MG	419	48	$14,478.94	$34.56	8.73
PHENOBARBITAL TAB 32.4MG	369	53	$12,616.86	$34.19	6.96
PHENOBARBITAL SOL 20MG/5ML	295	73	$15,306.63	$51.89	4.04
PHENOBARBITAL TAB 30MG	147	22	$2,897.96	$ 19.71	6.68
PHENOBARBITAL TAB 97.2MG	145	18	$6,079.96	$41.93	8.06
PHENOBARBITAL TAB 60MG	108	14	$2,631.34	$24.36	7.71
PHENOBARBITAL TAB 16.2MG	90	13	$2,239.82	$24.89	6.92
PHENOBARBITAL TAB 15MG	27	4	$229.43	$8.50	6.75
PHENOBARBITAL TAB 100MG	20	2	$357.22	$17.86	10
SUBTOTAL	**2,054**	**346**	**$79,859.46**	**$38.88**	**5.94**
DIAZEPAM PRODUCTS					
DIAZEPAM GEL 10MG	1,186	706	$471,566.19	$397.61	1.68
DIAZEPAM GEL 20MG	341	140	$157,786.78	$462.72	2.44
VALTOCO SPR 10MG	181	126	$130,922.08	$723.33	1.44
DIASTAT ACDL GEL 5-10MG	88	72	$39,581.82	$449.79	1.22

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
DIAZEPAM GEL 2.5MG	83	68	$28,308.45	$341.07	1.22
VALTOCO SPR 15MG	65	47	$67,942.79	$1,045.27	1.38
VALTOCO SPR 5MG	42	23	$31,522.13	$750.53	1.83
VALTOCO SPR 20MG	26	15	$28,008.66	$1,077.26	1.73
DIASTAT ACDL GEL 12.5-20MG	26	25	$13,434.51	$516.71	1.04
DIASTAT PED GEL 2.5MG	6	6	$2,191.05	$365.18	1
SUBTOTAL	**2,044**	**1,228**	**$971,264.46**	**$475.18**	**1.66**
CANNABIDIOL PRODUCTS					
EPIDIOLEX SOL 100MG/ML	1,604	195	$3,369,786.66	$2,100.86	8.23
SUBTOTAL	**1,604**	**195**	**$3,369,786.66**	**$2,100.86**	**8.23**
ETHOSUXIMIDE PRODUCTS					
ETHOSUXIMIDE CAP 250MG	928	137	$68,393.71	$73.70	6.77
ETHOSUXIMIDE SOL 250MG/5ML	499	80	$26,245.09	$52.60	6.24
SUBTOTAL	**1,427**	**217**	**$94,638.80**	**$66.32**	**6.58**
BRIVARACETAM PRODUCTS					
BRIVIACT TAB 100MG	545	76	$624,340.28	$1,145.58	7.17
BRIVIACT TAB 50MG	331	64	$373,313.97	$1,127.84	5.17
BRIVIACT SOL 10MG/ML	152	21	$163,225.51	$1,073.85	7.24
BRIVIACT TAB 75MG	45	11	$55,339.93	$1,229.78	4.09
BRIVIACT TAB 25MG	35	8	$53,043.20	$1,515.52	4.38
BRIVIACT TAB 10MG	3	1	$3,572.28	$1,190.76	3
SUBTOTAL	**1,111**	**181**	**$1,272,835.17**	**$1,145.67**	**6.14**
PRIMIDONE PRODUCTS					
PRIMIDONE TAB 50MG	639	132	$10,984.64	$17.19	4.84
PRIMIDONE TAB 250MG	207	32	$4,497.53	$21.73	6.47
MYSOLINE TAB 250MG	19	2	$88,110.40	$4,637.39	9.5
SUBTOTAL	**865**	**166**	**$103,592.57**	**$119.76**	**5.21**
ACETAZOLAMIDE PRODUCTS					
ACETAZOLAMIDE TAB 250MG	397	119	$22,050.96	$55.54	3.34
ACETAZOLAMIDE CAP 500MG ER	291	103	$12,120.27	$41.65	2.83
ACETAZOLAMIDE TAB 125MG	58	21	$3,200.67	$55.18	2.76
SUBTOTAL	**746**	**243**	**$37,371.90**	**$50.10**	**3.07**
PERAMPANEL PRODUCTS					
FYCOMPA SUS 0.5MG/ML	153	27	$149,158.89	$974.89	5.67
FYCOMPA TAB 8MG	111	17	$88,963.71	$801.47	6.53
FYCOMPA TAB 4MG	87	20	$80,423.89	$ 924.41	4.35
FYCOMPA TAB 6MG	73	16	$85,355.66	$1,169.26	4.56
FYCOMPA TAB 10MG	65	10	$72,217.89	$1,111.04	6.5
FYCOMPA TAB 12MG	61	7	$62,783.29	$1,029.23	8.71
FYCOMPA TAB 2MG	49	11	$25,067.93	$511.59	4.45
SUBTOTAL	**599**	**108**	**$563,971.26**	**$941.52**	**5.55**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
RUFINAMIDE PRODUCTS					
BANZEL TAB 400MG	288	35	$1,085,422.66	$3,768.83	8.23
BANZEL SUS 40MG/ML	160	26	$313,608.87	$1,960.06	6.15
RUFINAMIDE SUS 40MG/ML	80	17	$178,894.74	$2,236.18	4.71
BANZEL TAB 200MG	47	9	$41,441.20	$881.73	5.22
RUFINAMIDE TAB 400MG	4	4	$6,695.14	$1,673.79	1
SUBTOTAL	**579**	**91**	**$1,626,062.61**	**$2,808.40**	**6.36**
FELBAMATE PRODUCTS					
FELBAMATE TAB 600MG	174	21	$31,038.56	$178.38	8.29
FELBAMATE SUS 600MG/5ML	153	13	$64,781.10	$423.41	11.77
FELBAMATE TAB 400MG	45	6	$4,538.14	$100.85	7.5
FELBATOL TAB 600MG	23	2	$43,548.83	$1,893.43	11.5
FELBATOL TAB 400MG	16	2	$28,481.85	$1,780.12	8
SUBTOTAL	**411**	**44**	**$172,388.48**	**$419.44**	**9.34**
MIDAZOLAM PRODUCTS					
NAYZILAM SPR 5MG	405	235	$308,122.21	$760.80	1.72
SUBTOTAL	**405**	**235**	**$308,122.21**	**$760.80**	**1.72**
VIGABATRIN PRODUCTS					
SABRIL POW 500MG	161	21	$3,484,457.56	$21,642.59	7.67
VIGADRONE POW 500MG	28	3	$116,648.64	$4,166.02	9.33
VIGABATRIN PAK 500MG	20	4	$54,838.87	$2,741.94	5
SABRIL TAB 500MG	10	1	$277,991.28	$27,799.13	10
VIGABATRIN TAB 500MG	4	1	$14,772.08	$3,693.02	4
SUBTOTAL	**223**	**30**	**$3,948,708.43**	**$17,707.21**	**7.43**
CENOBAMATE PRODUCTS					
XCOPRI TAB 200MG	62	18	$59,584.41	$961.04	3.44
XCOPRI TAB 150MG	35	16	$49,516.77	$1,414.76	2.19
XCOPRI PAK 12.5-25MG	30	22	$2,932.41	$97.75	1.36
XCOPRI PAK 50-200MG	28	9	$27,292.62	$974.74	3.11
XCOPRI TAB 100MG	25	14	$23,682.81	$947.31	1.79
XCOPRI TAB 50MG	15	8	$15,363.95	$1,024.26	1.88
XCOPRI PAK 50-100MG	10	10	$9,003.93	$900.39	1
XCOPRI PAK 100-150MG	5	4	$5,189.70	$1,037.94	1.25
XCOPRI PAK 150-200MG	3	1	$6,198.18	$2,066.06	3
SUBTOTAL	**213**	**102**	**$198,764.78**	**$933.17**	**2.09**
ESLICARBAZAPINE PRODUCTS					
APTIOM TAB 600MG	95	14	$142,367.28	$1,498.60	6.79
APTIOM TAB 800MG	76	9	$96,186.52	$1,265.61	8.44
APTIOM TAB 200MG	8	2	$10,067.46	$1,258.43	4
APTIOM TAB 400MG	8	3	$8,010.20	$1,001.28	2.67
SUBTOTAL	**187**	**28**	**$256,631.46**	**$1,372.36**	**6.68**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TIAGABINE PRODUCTS					
TIAGABINE TAB 4MG	56	7	$20,713.78	$369.89	8
TIAGABINE TAB 2MG	25	4	$5,813.05	$232.52	6.25
TIAGABINE TAB 12MG	14	2	$2,110.40	$150.74	7
TIAGABINE TAB 16MG	7	1	$1,402.31	$200.33	7
SUBTOTAL	**102**	**14**	**$30,039.54**	**$294.51**	**7.29**
METHSUXIMIDE PRODUCTS					
CELONTIN CAP 300MG	36	3	$8,644.32	$240.12	12
SUBTOTAL	**36**	**3**	**$8,644.32**	**$240.12**	**12**
FENFLURAMINE PRODUCTS					
FINTEPLA SOL 2.2MG/ML	30	4	$15,423.80	$514.13	7.5
SUBTOTAL	**30**	**4**	**$15,423.80**	**$514.13**	**7.5**
STIRIPENTOL PRODUCTS					
DIACOMIT CAP 250MG	2	2	$6,022.82	$3,011.41	1
SUBTOTAL	**2**	**2**	**$6,022.82**	**$3,011.41**	**1**
TOTAL	**317,442**	**44,750***	**$28,176,473.33**	**$88.76**	**7.09**

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
ACDL = AcuDial; CAP = capsule; CHW = chewable; DR = delayed-release; ELX = elixir; ER = extended-release; EX = extended; HR = hour; INJ = injection; ODT = orally disintegrating tablet; PAK = pack; PED = pediatric; POW = powder; SOL = solution; SPR = spray or sprinkle; SUS = suspension; TAB = tablet; XR = extended-release

The utilization details above include anticonvulsants used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate.
The above utilization data does not include Afinitor® (everolimus) for the diagnosis of TSC-associated partial-onset seizures; utilization data for everolimus is included in the annual review of oncology medications.

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[7] Eprontia™ (Topiramate Oral Solution) Prescribing Information. Azurity Pharmaceuticals, Inc. Available online at: https://eprontia.com/wp-content/uploads/2021/11/65628-00603_EPRONTIA-PI-REV-01.pdf. Last revised 11/2021. Last accessed 01/11/2022.

Appendix P

Fiscal Year 2021 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Qulipta™ (Atogepant) and Trudhesa™ (Dihydroergotamine Nasal Spray)

Oklahoma Health Care Authority
February 2022

Current Prior Authorization Criteria

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan tablet (Relpax®) – **Brand Preferred**	naratriptan tablet (Amerge®)	almotriptan tablet (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan tablet, ODT (Maxalt®, Maxalt MLT®)	zolmitriptan tablet, ODT, nasal spray (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan tablet (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan tablet (Imitrex®)			eletriptan tablet (generic Relpax®)
sumatriptan/ naproxen tablet (Treximet®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan tablet (Reyvow®)
			rimegepant ODT (Nurtec® ODT)
			sumatriptan injection (Imitrex®)
			sumatriptan injection (Zembrace® SymTouch®)
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan nasal spray (Tosymra®)
			ubrogepant tablet (Ubrelvy®)

*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).
ODT = orally disintegrating tablet; PA = prior authorization

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response or a patient-specific, clinically significant reason why a Tier-1 product is not appropriate for the member must be provided; or
2. Documented adverse effect(s) to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response or a patient-specific, clinically significant reason why a lower tiered product is not appropriate for the member must be provided; or
2. Documented adverse effect(s) to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days; and
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

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

1. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
2. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications and dihydroergotamine injection (D.H.E. 45®).
3. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
4. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent CYP3A4 inhibitor, women who are or may become pregnant, peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, sepsis, hypersensitivity to any of the components); and
    b. A quantity limit of 20 tablets per 28 days will apply.
5. Use of Reyvow® (lasmiditan) or Ubrelvy® (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications and Nurtec® ODT (rimegepant); and

    a. Reyvow® and Ubrelvy® will not be approved for concurrent use with a prophylactic calcitonin gene-related peptide (CGRP) inhibitor.
6. Use of Nurtec® ODT (rimegepant) requires failed therapy with at least 2* triptan medications or a patient-specific, clinically significant reason why a triptan is not appropriate for the member must be provided; and
    a. Nurtec® ODT will not be approved for concurrent use with a prophylactic CGRP inhibitor.

   (*The manufacturer of Nurtec® ODT has currently provided a supplemental rebate to require a trial with 2 triptan medications and to be the preferred CGRP product for acute treatment over Reyvow® and Ubrelvy®; however, Nurtec® ODT will follow the same criteria as Reyvow® and Ubrelvy® if the manufacturer chooses not to participate in supplemental rebates.)
7. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation and lower-tiered triptan medications.
8. Use of Zembrace® SymTouch® (sumatriptan injection) or Tosymra® (sumatriptan nasal spray) will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) and lower-tiered triptan medications.

Aimovig® (Erenumab-aooe) and Vyepti® (Eptinezumab-jjmr) Approval Criteria:

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:
    a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
    b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months; and
        i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and
4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:

    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 3 agents with different mechanisms of action. Trials must be at least 8 weeks in duration (or documented adverse effects) within the last 365 days. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and
8. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Aimovig®, Vyepti®) recommended as treatment (not necessarily prescribed by a neurologist); and
9. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
10. Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
11. For Aimovig®, prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and

13. For Vyepti®, prescriber must verify the medication will be prepared and administered according the Vyepti® *Prescribing Information*; and
14. A patient-specific, clinically significant reason why member cannot use Ajovy® (fremanezumab-vfrm) or Emgality® (galcanezumab-gnlm) must be provided; and
15. For consideration of Vyepti® at the maximum recommended dosing (300mg every 3 months), a patient-specific, clinically significant reason why other available CGRP inhibitors for migraine prophylaxis are not appropriate for the member must be provided; and
16. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
17. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig®, a quantity limit of 1 syringe or autoinjector per 30 days will apply; and
    b. For Vyepti®, a quantity limit of 3 vials per 90 days will apply.

Ajovy® (Fremanezumab-vfrm) and Emgality® (Galcanezumab-gnlm) Approval Criteria [Migraine Diagnosis]:

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:
    a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
    b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months; and
        i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and
4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and

6. The member has failed medical migraine preventive therapy with at least 2¥ agents with different mechanisms of action. Trials must be at least 8 weeks in duration (or documented adverse effects) within the last 365 days. [¥The manufacturers of Ajovy® and Emgality® have currently provided a supplemental rebate to be the preferred calcitonin gene-related peptide (CGRP) inhibitor(s) and require a trial with 2 other migraine preventative therapies; however, Ajovy® and Emgality® will follow the original criteria and require trials with 3 other migraine preventative therapies if the manufacturers choose not to participate in supplemental rebates.] This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and
8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Ajovy®, Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and
10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative CGRP inhibitor; and
11. Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and

12. Prescriber must verify member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
14. Quantity limits will apply based on FDA-approved dosing:
    a. For Ajovy® prefilled syringe and autoinjector, a quantity limit of 1 syringe or 1 autoinjector per 30 days will apply. Requests for quarterly dosing (675mg every 3 months) will be approved for a quantity limit override upon meeting Ajovy® approval criteria; and
    b. For Emgality®, a quantity limit of 1 syringe or pen per 30 days will apply. Requests for an initial loading dose (240mg administered as 2 consecutive 120mg injections) will be approved for a quantity limit override upon meeting Emgality® approval criteria.

Emgality® (Galcanezumab-gnlm) Approval Criteria [Episodic Cluster Headache Diagnosis]:

1. An FDA approved indication for the treatment of episodic cluster headache in adults; and
2. Member must be 18 years of age or older; and
3. Member has a diagnosis of episodic cluster headache as defined by the International Headache Society (IHS) International Classification of Headache Disorders (ICHD) guideline and meets the following criteria:
    a. Member has a history of episodic cluster headache with at least 2 cluster periods lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥1 month; and
4. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and

5. Member has failed prophylactic therapy with at least 1 other medication (e.g., verapamil, select anticonvulsants, corticosteroids); and
6. Member must have been evaluated within the last 6 months by a neurologist for cluster headaches and the requested medication (e.g., Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and
7. Member will not use Emgality® concurrently with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
8. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
9. Initial approvals will be for the duration of 3 months. Continuation approvals will be granted until the end of the cluster period if the prescriber documents that the member is responding well to treatment as indicated by a reduction in cluster headache attack frequency; and
10. A quantity limit of (3) 100mg/mL syringes per 30 days will apply.

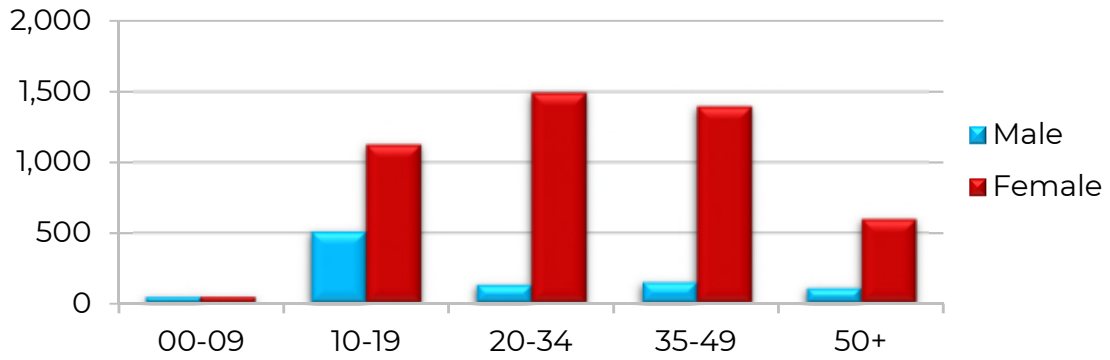
Utilization of Anti-Migraine Medications: Fiscal Year 2021

Comparison of Fiscal Years

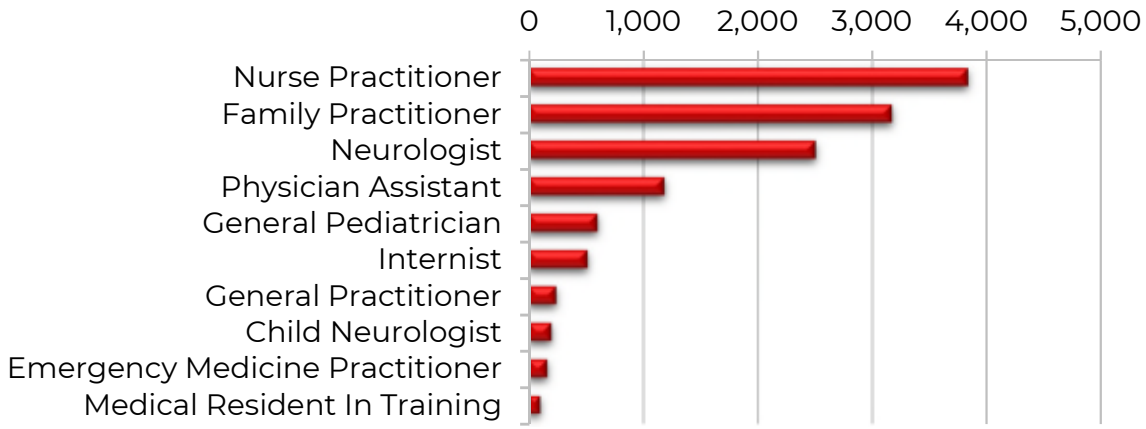
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	4,951	11,633	$768,531.74	$66.06	$3.71	120,394	207,189
2021	5,561	13,200	$1,189,809.38	$90.14	$4.73	134,924	251,405
% Change	**12.30%**	**13.50%**	**54.80%**	**36.50%**	**27.50%**	**12.10%**	**21.30%**
Change	**610**	**1,567**	**$421,277.64**	**$24.08**	**$1.02**	**14,530**	**44,216**

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

Demographics of Members Utilizing Anti-Migraine Medications



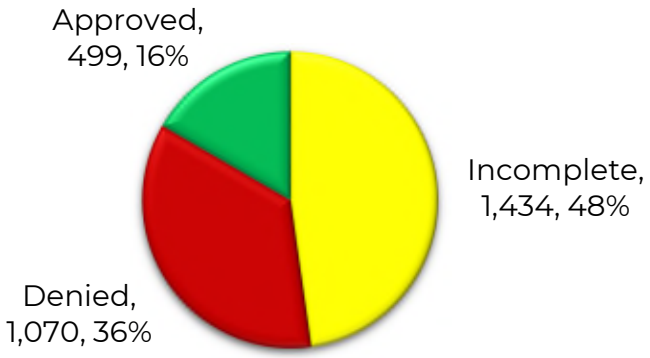
Top Prescriber Specialties of Anti-Migraine Medications by Number of Claims



Prior Authorization of Anti-Migraine Medications

There were 3,003 prior authorization requests submitted for anti-migraine medications during fiscal year 2021. Computer edits are in place to detect lower tiered medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



Market News and Updates[1,2,3,4,5,6,7,8,9,10]

Anticipated Patent Expiration(s):

- Tosymra® (sumatriptan nasal spray): July 2031
- Onzetra® Xsail® (sumatriptan nasal powder): October 2034
- Qulipta™ (atogepant tablet): January 2035
- Ubrelvy® (ubrogepant tablet): January 2035
- Zembrace® SymTouch® [sumatriptan subcutaneous (sub-Q) injection]: January 2036

- Reyvow® (lasmiditan tablet): December 2037
- Trudhesa™ (dihydroergotamine nasal spray): January 2039
- Nurtec® ODT [rimegepant orally disintegrating tablet (ODT)]: March 2039

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

- **May 2021:** The FDA approved Nurtec® ODT (rimegepant) for the preventive treatment of episodic migraine (e.g., those who experience <15 headache days per month) in adults. The approved product label was also expanded to include the use of Nurtec® ODT for up to 18 doses/month, allowing for both acute and preventive therapy in the same patient. This new approval makes Nurtec® ODT the first oral calcitonin gene-related peptide (CGRP) receptor antagonist approved for the preventive treatment of migraine, and the only migraine medication approved as a dual therapy for both acute and preventive treatment. Nurtec® ODT can be taken up to once daily as needed (up to 18 doses/month) to stop migraine attacks or taken every other day to help prevent migraine. The FDA approval of Nurtec® ODT is based on a double-blind, randomized, placebo-controlled Phase 3 clinical trial with an open label extension. Primary study endpoint results demonstrated that Nurtec® ODT was superior to placebo, decreasing monthly migraine days by 4.3 days/month after 3 months of treatment. The preventive effects of Nurtec® ODT were seen as early as the first week of therapy. Further, a key secondary endpoint result showed that approximately half of Nurtec® ODT-treated patients had a 50% or greater reduction in the number of moderate-to-severe migraine days per month. In the pivotal trial for the preventive treatment of migraine, Nurtec® ODT was generally well tolerated, with the most common side effects being nausea (2.7% vs. 0.8% in placebo) and stomach pain/indigestion (2.4% vs. 0.8% in placebo).
- **September 2021:** The FDA approved Trudhesa™ [dihydroergotamine mesylate nasal spray] for the acute treatment of migraine with or without aura in adults. Trudhesa™ uses Impel's proprietary Precision Olfactory Delivery (POD®) technology which allows quick absorption of dihydroergotamine into the bloodstream through the vascular-rich upper nasal space, bypassing the gastrointestinal (GI) tract and potential absorption issues.
- **September 2021:** The FDA approved Qulipta™ (atogepant) for the preventive treatment of episodic migraine in adults. Qulipta™ is the first and only CGRP receptor antagonist specifically developed for the preventive treatment of migraine.

News:

- **October 2021:** A systematic review and network meta-analysis comparing triptans to 5-hydroxytryptamine$_{1F}$ receptor agonists (i.e., ditans) and CGRP receptor antagonists (i.e., gepants) in reducing pain and adverse effects (AEs) for acute management of migraines was published in *JAMA Network*. This review included 4 randomized clinical trials with a total of 46,442 patients. The primary outcome was the odds ratio (OR) for freedom from pain at 2 hours after the dose, and the secondary outcomes were ORs for pain relief at 2 hours after the dose and any AEs. Most of the included treatments were associated with reduced pain at 2 hours compared with placebo. Most triptans were associated with higher ORs for pain freedom at 2 hours compared with lasmiditan, rimegepant, and ubrogepant. Also, most triptans were associated with higher ORs for pain relief at 2 hours compared with lasmiditan, rimegepant, and ubrogepant. The comparisons between lasmiditan, rimegepant, and ubrogepant were not statistically significant for both pain freedom and pain relief at 2 hours. Lasmiditan was associated with the highest risk of any AEs, and certain triptans (rizatriptan, sumatriptan, and zolmitriptan) were also associated with a higher risk of any AEs than the CGRP receptor antagonists. However, most of the AEs were mild-to-moderate (e.g., dizziness, nausea, fatigue) and were considered tolerable. This study showed eletriptan 40mg was associated with the best therapeutic efficacy in pain freedom at 2 hours. Eletriptan is a 5-HT$_{1B/1D/1F}$–selective receptor agonist with a higher affinity for receptors than other triptans. This study also found rimegepant and ubrogepant were associated with lower ORs for pain freedom or pain relief compared with certain triptans at 2 hours after the dose. Some investigators noted a late benefit, in the 3-hour to 8-hour post-dose period, for ubrogepant and rimegepant because of their relatively long half-lives but this was not included in this study. Some study limitations include focusing only on short-term headache responses and AEs after a single dose during the double-blinded period. As such, the findings of this study should be interpreted with caution. Most studies presented results based on a single migraine attack, and information about the consistency of the medications' effectiveness when used for repeated attacks within a longer period is unknown.
- **November 2021:** A real-world study of Ajovy® (fremanezumab-vfrm) evaluated 6-month outcomes of patients with either episodic or chronic migraines who had comorbid depression, anxiety, or hypertension (HTN). The researchers gathered data from 2014 to 2019, and included 172 patients in the comorbid depression subgroup, 180 patients in the comorbid anxiety subgroup, and 142 patients with comorbid HTN. All patients were at least 18 years of age with a

diagnosis of migraine. Those who were treated with any other CGRP pathway-targeted therapy prior to the study were excluded. Among the 172 patients with baseline comorbid depression, there was a 12.2% reduction in the proportion using an antidepressant after starting Ajovy® (68.6% at baseline vs. 56.4%, P=0.0025). A significant proportion of patients with comorbid anxiety also were able to stop using anxiolytics within the 6 months of starting treatment with Ajovy® (55% vs. 47.2%, P=0.04). However, patients with migraine and comorbid HTN did not experience a greater benefit from Ajovy® treatment. Among this group of 142 patients, there were no significant change in mean systolic blood pressure (BP, 127.32mmHg vs. 126.98mmHg) or mean diastolic BP (78.43mmHg vs. 77.84 mmHg) during the 6-month follow-up.

- **December 2021:** In a post hoc secondary analysis of 4 randomized clinical trials, Aimovig® (erenumab-aooe) was associated with reduced migraine frequency and fewer days of using acute migraine-specific medication in patients with and without aura. No differences were observed in safety profiles of patients with and without history of aura. A recent FDA analysis of postmarketing case reports suggested Aimovig® was linked to elevated BP that required treatment and, in some cases, hospitalization. In 2021, a warning about new-onset or worsening of pre-existing HTN was added to the Aimovig® *Prescribing Information*. In the pooled trial analysis, safety profiles were similar across treatment groups regardless of aura history over 12 weeks. AEs did not increase over time. Cardiovascular, cerebrovascular, and HTN AE rates were low and similar among subgroups. In the open-label treatment phase, HTN-related AEs occurred in 2.2% of migraine patients with aura and 2.3% of patients without aura.

Pipeline:

- **STS101:** Satsuma Pharmaceuticals announced an update to the development plan for STS101 (dihydroergotamine nasal powder), an investigational acute treatment for migraine. The updated STS101 development plan includes a new Phase 3 efficacy trial, which the company anticipates initiating in mid-2021, with topline results expected in the second half of 2022. The new Phase 3 trial takes into account findings from the EMERGE pivotal study in which STS101 showed numerical differences in favor of STS101 5.2mg and 3.9mg versus placebo but did not achieve statistical significance versus placebo on the co-primary endpoints of freedom from pain and most bothersome symptom at 2 hours post-administration. In addition, the company evaluated dose strengths ≥5.2mg by conducting a Phase 1 trial evaluating the pharmacokinetics, safety, and tolerability of STS101 5.2mg and 2 higher dose strengths. Based on results from this Phase 1 trial and other data, including preliminary results to date from the

ongoing Phase 3 ASCEND long-term, open-label safety trial of STS101 5.2mg, Satsuma is initiating its SUMMIT Phase 3 efficacy trial with the 5.2mg dosage strength of STS101.

- **Zavegepant:** Topline results were announced from a Phase 3 trial evaluating intranasal zavegepant, an investigational CGRP receptor antagonist, for the acute treatment of migraine in adults. The randomized, double-blind, placebo-controlled trial evaluated the efficacy and safety of zavegepant in adults with at least a 1-year history of migraine (with or without aura) and migraine attacks lasting, on average, 4 to 72 hours if untreated. Patients were randomly assigned to receive a single dose of zavegepant 10mg intranasal spray (N=623) or placebo (N=646) as needed. Results showed treatment with zavegepant was statistically superior to placebo on the co-primary endpoints of pain freedom (24% vs. 15%; P<0.0001) and freedom from most bothersome symptom (40% vs. 31%; P<0.0012) at 2 hours. At 15 minutes post dose, pain relief was achieved by 16% of the zavegepant group vs. 8% of the placebo group (P<0.0015). Patients treated with zavegepant demonstrated return to normal function as early as 30 minutes after dosing (P<0.006). The most common AE reported with zavegepant was abnormal taste. Biohaven Pharmaceutical Holding Company expects to file a New Drug Application for zavegepant with the FDA in the first quarter of 2022.

Qulipta™ (Atogepant) Product Summary[11]

Indication(s): Qulipta™ (atogepant) is a CGRP receptor antagonist indicated for the preventive treatment of episodic migraine in adults.

How Supplied: Qulipta™ is supplied as an oral tablet available in 3 strengths: 10mg, 30mg, and 60mg.

Dosing and Administration:

- The recommended dosing is (1) 10, 30, or 60mg tablet daily with or without food.
- The following dose modifications apply for concomitant use of specific drugs or for patients with renal impairment:
  - Strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin): 10mg daily
  - Strong and moderate CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin): 30mg or 60mg daily
  - OATP inhibitors (e.g., cyclosporine): 10mg or 30mg daily
  - Severe renal impairment/end-stage renal disease (ESRD) [creatinine clearance (CrCl) <30mL/min]: 10mg daily

Contraindication(s): None

Safety:

- Pregnancy: There are no adequate data on the developmental risk associated with the use of atogepant in pregnant women. In animal studies, oral administration of atogepant during the period of organogenesis or throughout pregnancy and lactation resulted in adverse developmental effects (i.e., decreased body weight, increased incidence of fetal structural variations) at exposures greater than those used clinically.
- Lactation: There are no data on the presence of atogepant in human milk, the effects of atogepant on the breastfed infant, or the effects of atogepant on milk production. In lactating rats, oral dosing with atogepant resulted in levels of atogepant in milk approximately 2-fold higher than that in maternal plasma.
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
- Geriatric Use: Population pharmacokinetic modeling suggests no clinically significant pharmacokinetic differences between elderly and younger subjects. Clinical studies of atogepant did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.
- Renal Impairment: The renal route of elimination plays a minor role in the clearance of atogepant. In patients with severe renal impairment (CrCl 15-29mL/min), and in patients with ESRD (CrCl <15mL/min) the recommended dosage of atogepant is 10mg once daily. For patients with ESRD undergoing intermittent dialysis, atogepant should preferably be taken after dialysis. No dose adjustment is recommended for patients with mild or moderate renal impairment.
- Hepatic Impairment: Dose adjustment of atogepant is not recommended for patients with mild or moderate hepatic impairment. Use of atogepant should be avoided in patients with severe hepatic impairment.

Adverse Reactions: The most common adverse reactions in the clinical studies (incidence ≥4% and more frequently than placebo) were nausea, constipation, and fatigue.

Efficacy: The efficacy of Qulipta™ for the preventive treatment of episodic migraine in adults was demonstrated in 2 randomized, multicenter, double-blind, placebo-controlled studies (study 1 and study 2). The studies enrolled patients with at least a 1-year history of migraine with or without aura. In both studies, patients were allowed to use acute headache treatments [i.e., triptans, ergotamine derivatives, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids] as needed. The use of a concomitant

medication that acts on the CGRP pathway was not permitted for either acute or preventive treatment of migraine.

- **Study 1:** This study included 910 patients who were randomized 1:1:1:1 to receive atogepant 10mg (N=222), atogepant 30mg (N=230), atogepant 60mg (N=235), or placebo (N=223), once daily for 12 weeks.
  - Primary Endpoint: Change from baseline in mean monthly migraine days (MMD) across the 12-week treatment period
    - The mean migraine frequency at baseline was approximately 8 migraine days per month and was similar across treatment groups.
  - Results: The mean number of migraine days per month at baseline ranged from 7.5 to 7.9 in the 4 groups. The changes from baseline across 12 weeks were −3.7 days with atogepant 10mg, −3.9 days with atogepant 30mg, −4.2 days with atogepant 60mg, and −2.5 days with placebo. The mean differences from placebo in the change from baseline were −1.2 days with atogepant 10mg, −1.4 days with atogepant 30mg, and −1.7 days with atogepant 60mg. Across 12 weeks of treatment, all the atogepant-treated patients had a statistically significant decrease from baseline of MMD ($P<0.001$) compared to placebo.
- **Study 2:** This study included 652 patients who were randomized 1:2:2:2 to receive atogepant 10mg (N=94), atogepant 30mg (N=185), atogepant 60mg (N=187), or placebo (N=186), once daily for 12 weeks.
  - Primary Endpoint: Change from baseline in MMD across the 12-week treatment period
    - The mean migraine frequency at baseline was approximately 8 migraine days per month.
  - Results: The mean number of migraine days per month at baseline ranged from 7.6 to 7.8 in the 4 groups. The changes from baseline across 12 weeks were −4 days with atogepant 10mg, −3.8 days with atogepant 30mg, −3.6 days with atogepant 60mg, and −2.8 days with placebo. The mean differences from placebo in the change from baseline were −1.1 days with atogepant 10mg, −0.9 days with atogepant 30mg, and −0.7 days with atogepant 60mg. There was a statistically significantly greater reduction in mean MMD across the 12-week treatment period in all 3 atogepant treatment groups, compared with placebo.

Cost Comparison:

Medication	Cost Per Dose	Cost Per 30 Days*
Qulipta™ (atogepant tablet) all strengths	**$33.03**	**$990.90**
Nurtec® ODT 75mg (rimegepant ODT)	$106.98	$1,604.70
Emgality® 120mg (galcanezumab-gnlm auto-injection pen)	$607.58	$607.58

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 FDA recommended dosing (does not include loading dose for Emgality®).
ODT = orally disintegrating tablet

Trudhesa™ (Dihydroergotamine Nasal Spray) Product Summary[1,2]

Indication(s): Trudhesa™ is an ergotamine derivative indicated for the acute treatment of migraine with or without aura in adults.

- Limitation(s) of Use: Trudhesa™ is not indicated for the preventive treatment of migraine or for the management of hemiplegic or basilar migraine.

Boxed Warning: Peripheral Ischemia Following Coadministration with Potent CYP3A4 Inhibitors

- Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with strong CYP3A4 inhibitors (e.g., ritonavir, clarithromycin, ketoconazole)
- Concomitant use of Trudhesa™ with strong CYP3A4 inhibitors is contraindicated

How Supplied: Trudhesa™ is supplied as a nasal spray that delivers 0.725mg per spray and is available in a package containing 4 single-dose units.

- Each single-dose unit contains 1 amber glass vial with 4mg dihydroergotamine mesylate in a 1mL solution and 1 nasal spray device.

Dosing and Administration:

- Prior to initiation of treatment with Trudhesa™, a cardiovascular evaluation is recommended.
- The recommended dose of Trudhesa™ is 1.45mg (administered as 1 metered spray of 0.725mg into each nostril).
- The dose may be repeated, if needed, a minimum of 1 hour after the first dose. No more than 2 doses should be used within a 24-hour period or no more than 3 doses within 7 days.
- Trudhesa™ should be assembled and primed (i.e., pumped 4 times) before use and used immediately after priming.
- Each single-dose unit should be discarded after 1 dose (0.725mg into each nostril) is administered.
- After a Trudhesa™ vial has been opened, it must be thrown away after 8 hours.

Contraindication(s):

- Concomitant use of strong CYP3A4 inhibitors
- Ischemic heart disease or coronary artery vasospasm
- Uncontrolled HTN, peripheral arterial diseases, sepsis, following vascular surgery, or severe hepatic or renal impairment
- Hypersensitivity to ergot alkaloids
- Concomitant use of other 5-HT_1 agonists (e.g., sumatriptan) or ergotamine containing or ergot-type medications within 24 hours
- Concomitant use of peripheral and central vasoconstrictors

Adverse Reactions: The most common adverse reactions with Trudhesa™ (incidence ≥1% and more frequently than placebo) were rhinitis, nausea, altered sense of taste, application site reactions, dizziness, vomiting, somnolence, pharyngitis, and diarrhea.

Efficacy: The efficacy of Trudhesa™ is based on the relative bioavailability of Trudhesa™ nasal spray compared to Migranal® (dihydroergotamine mesylate nasal spray) in healthy patients. Trudhesa™ met the predefined statistical criteria for comparative bioavailability with Migranal®.

Cost Comparison:

Medication	Cost Per Day*	Cost Per 30 Days+
Trudhesa™ (dihydroergotamine 4mg/mL nasal spray)	**$212.50**	**$2,550.00**
dihydroergotamine 1mg/mL injection (generic D.H.E. 45®)	$232.14	$1,857.12
dihydroergotamine 4mg/mL nasal spray (generic Migranal®)	$143.52	$1,148.16

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 day based on FDA recommended dosing for each product in a 24 hour period.
+Cost per 30 days based on maximum FDA recommended dosing per 7 days.

Recommendations

The College of Pharmacy recommends the prior authorization of Qulipta™ (atogepant) with criteria similar to Aimovig® (erenumab-aooe) and Vyepti® (eptinezumab-jjmr) and the addition of Nurtec® ODT (rimegepant) to the current criteria for Aimovig® and Vyepti® based on the recent FDA approval for the preventive treatment of episodic migraine (changes noted in red):

Aimovig® (Erenumab-aooe), Nurtec® ODT (Rimegepant)*, Qulipta™ (Atogepant)*, and Vyepti® (Eptinezumab-jjmr) Approval Criteria:

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:
    a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
    b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months (*Nurtec® ODT and Qulipta™ are only FDA approved for the preventive treatment of episodic migraines.); and
        i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and
4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:

   a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
   b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
   a. Hormone replacement therapy or hormone-based contraceptives; and
   b. Chronic insomnia; and
   c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 3 agents with different mechanisms of action. Trials must be at least 8 weeks in duration (or documented adverse effects) within the last 365 days. This includes, but is not limited to:
   a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
   b. Select anticonvulsant therapy; or
   c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
   a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
   b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
   c. Opioids (≥10 days/month for >3 months); and
   d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
   e. Ergotamine-containing medications (≥10 days/month for >3 months); and
   f. Triptans (≥10 days/month for >3 months); and
8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Aimovig®, Nurtec® ODT, Qulipta™, Vyepti®) recommended as treatment (not necessarily prescribed by a neurologist); and

10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. For Aimovig®, prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. For Vyepti®, prescriber must verify the medication will be prepared and administered according the Vyepti® *Prescribing Information*; and
14. A patient-specific, clinically significant reason why member cannot use Ajovy® (fremanezumab-vfrm) or Emgality® (galcanezumab-gnlm) must be provided (members currently taking Nurtec® ODT for acute migraine treatment are not exempt from this criteria requirement); and
15. For consideration of Vyepti® at the maximum recommended dosing (300mg every 3 months), a patient-specific, clinically significant reason why other available CGRP inhibitors for migraine prophylaxis are not appropriate for the member must be provided; and
16. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
17. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig®, a quantity limit of 1 syringe or autoinjector per 30 days will apply; and
    b. For Nurtec® ODT, a quantity limit of 15 tablets per 30 days will apply; and
    c. For Qulipta™, a quantity limit of 30 tablets per 30 days will apply; and
    d. For Vyepti®, a quantity limit of 3 vials per 90 days will apply.

Additionally, the College of Pharmacy recommends the placement of Trudhesa™ (dihydroergotamine nasal spray) into the Special Prior Authorization (PA) Tier of the Anti-migraine Product Base Prior Authorization (PBPA) category and updating the D.H.E. 45® (dihydroergotamine injection) and Migranal® (dihydroergotamine nasal spray) criteria based on net cost with the following criteria (changes noted in red in the following criteria and Tier chart):

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of brand D.H.E. 45® (dihydroergotamine injection) or brand Migranal® (dihydroergotamine nasal spray) will require a patient-specific, clinically significant reason why the member cannot use lower-

tiered triptan medications. Brand formulation is preferred for D.H.E. 45® and Migranal®; use of the generic formulations will require a patient-specific, clinically significant reason why the member cannot use the brand formulation and lower-tiered triptan medications.

~~2. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications and dihydroergotamine injection (D.H.E. 45®).~~

3. Use of Trudhesa™ (dihydroergotamine nasal spray) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of D.H.E. 45®, Migranal®, and lower-tiered triptan medications.
4. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
5. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent CYP3A4 inhibitor, women who are or may become pregnant, peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, sepsis, hypersensitivity to any of the components); and
    b. A quantity limit of 20 tablets per 28 days will apply.
6. Use of Reyvow® (lasmiditan) or Ubrelvy® (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications and Nurtec® ODT (rimegepant); and
    a. Reyvow® and Ubrelvy® will not be approved for concurrent use with a prophylactic calcitonin gene-related peptide (CGRP) inhibitor.
7. Nurtec® ODT (rimegepant) Approval Criteria [Migraine Diagnosis (Acute Treatment)]+:
    a. Member must have failed therapy with at least 2* triptan medications or a patient-specific, clinically significant reason why a triptan is not appropriate for the member must be provided; and
    b. Nurtec® ODT will not be approved for concurrent use with a prophylactic CGRP inhibitor.

*The manufacturer of Nurtec® ODT has currently provided a supplemental rebate to require a trial with 2 triptan medications and to be the preferred CGRP product for acute treatment over Reyvow® and Ubrelvy®; however, Nurtec® ODT will follow the same criteria as Reyvow® and Ubrelvy® if the manufacturer chooses not to participate in supplemental rebates.

†Nurtec® ODT approval criteria for the preventive treatment of episodic migraines can be found with the Aimovig®, Qulipta™, and Vyepti® approval criteria.

8. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation and lower-tiered triptan medications.
9. Use of Zembrace® SymTouch® (sumatriptan injection) or Tosymra® (sumatriptan nasal spray) will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) and lower-tiered triptan medications.

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan tablet (Relpax®) – **Brand Preferred**	naratriptan tablet (Amerge®)	almotriptan tablet (Axert®)	dihydroergotamine injection (D.H.E. 45®) – **Brand Preferred**
rizatriptan tablet, ODT (Maxalt®, Maxalt MLT®)	zolmitriptan tablet, ODT, nasal spray (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan tablet (Frova®)	dihydroergotamine nasal spray (Migranal®) – **Brand Preferred**
sumatriptan tablet (Imitrex®)			**dihydroergotamine nasal spray (Trudhesa™)**
sumatriptan/ naproxen tablet (Treximet®)			eletriptan tablet (generic Relpax®)
			ergotamine sublingual tablet (Ergomar®)
			lasmiditan tablet (Reyvow®)
			rimegepant ODT (Nurtec™ ODT)
			sumatriptan injection (Imitrex®)
			sumatriptan injection (Zembrace® SymTouch®)
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
			sumatriptan nasal spray (Tosymra®)
			ubrogepant tablet (Ubrelvy®)

*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).
ODT = orally disintegrating tablet; PA = prior authorization

Utilization Details of Anti-Migraine Medications: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-1 MEDICATIONS						
SUMATRIPTAN PRODUCTS						
SUMATRIPTAN TAB 50MG	3,079	1,665	$48,409.84	$15.72	1.85	4.07%
SUMATRIPTAN TAB 100MG	2,926	1,209	$46,636.47	$15.94	2.42	3.92%
SUMATRIPTAN TAB 25MG	1,942	1,150	$35,453.24	$18.26	1.69	2.98%
SUBTOTAL	**7,947**	**4,024**	**$130,499.55**	**$16.42**	**1.97**	**10.97%**
RIZATRIPTAN PRODUCTS						
RIZATRIPTAN TAB 10MG	1,619	717	$25,558.43	$15.79	2.26	2.15%
RIZATRIPTAN ODT 10MG	1,046	480	$22,752.82	$21.75	2.18	1.91%
RIZATRIPTAN TAB 5MG	535	298	$8,987.81	$16.80	1.8	0.76%
RIZATRIPTAN ODT 5MG	329	193	$5,636.53	$17.13	1.7	0.47%
SUBTOTAL	**3,529**	**1,688**	**$62,935.59**	**$17.83**	**2.09**	**5.29%**
ELETRIPTAN PRODUCTS						
RELPAX TAB 40MG	167	76	$97,317.60	$582.74	2.2	8.18%
RELPAX TAB 20MG	70	35	$38,348.84	$547.84	2	3.22%
SUBTOTAL	**237**	**111**	**$135,666.44**	**$572.43**	**2.14**	**11.40%**
SUMATRIPTAN/NAPROXEN COMBINATION PRODUCTS						
SUMAT-NAPROX TAB 85-500MG	54	29	$13,538.08	$250.71	1.86	1.14%
SUBTOTAL	**54**	**29**	**$13,538.08**	**$250.71**	**1.86**	**1.14%**
TIER-1 SUBTOTAL	**11,767**	**5,417***	**$342,639.66**	**$29.12**	**2.17**	**28.80%**
TIER-2 MEDICATIONS						
ZOLMITRIPTAN PRODUCTS						
ZOLMITRIPTAN TAB 5MG	44	11	$888.78	$20.20	4	0.07%
ZOMIG SPR 5MG	16	4	$8,726.40	$545.40	4	0.73%
ZOLMITRIPTAN ODT 2.5MG	12	3	$382.41	$31.87	4	0.03%
ZOMIG SPR 2.5MG	11	4	$6,216.55	$565.14	2.75	0.52%
ZOLMITRIPTAN TAB 2.5MG	9	1	$148.48	$16.50	9	0.01%
ZOLMITRIPTAN ODT 5MG	3	2	$84.02	$28.01	1.5	0.01%
ZOLMITRIPTAN SPR 5MG	3	2	$1,580.92	$526.97	1.5	0.13%
ZOLMITRIPTAN SPR 2.5MG	2	1	$1,059.28	$529.64	2	0.09%
SUBTOTAL	**100**	**28**	**$19,086.84**	**$190.87**	**3.57**	**1.59%**
NARATRIPTAN PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
NARATRIPTAN TAB 2.5MG	19	7	$506.95	$26.68	2.71	0.04%
NARATRIPTAN TAB 1MG	3	2	$109.47	$36.49	1.5	0.01%
SUBTOTAL	**22**	**9**	**$616.42**	**$28.02**	**2.44**	**0.05%**
TIER-2 SUBTOTAL	**122**	**34***	**$19,703.26**	**$161.50**	**3.59**	**1.64%**
TIER-3 MEDICATIONS						
ALMOTRIPTAN PRODUCTS						
ALMOTRIPTAN TAB 12.5MG	8	1	$1,616.54	$1,616.54	8	0.14%
ALMOTRIPTAN TAB 6.25MG	1	1	$403.41	$403.41	1	0.03%
SUBTOTAL	**9**	**2**	**$2,019.95**	**$224.44**	**4.5**	**0.17%**
TIER-3 SUBTOTAL	**9**	**2***	**$2,019.95**	**$224.44**	**4.5**	**0.17%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
SUMATRIPTAN PRODUCTS						
SUMATRIPTAN INJ 6MG/0.5ML	15	3	$4,360.23	$290.68	5	0.37%
SUMATRIPTAN SPR 20MG/ACT	7	2	$3,283.05	$469.01	3.5	0.28%
SUBTOTAL	**22**	**5**	**$7,643.28**	**$347.42**	**4.4**	**0.65%**
UBROGEPANT PRODUCTS						
UBRELVY TAB 100MG	6	2	$5,095.30	$849.22	3	0.43%
UBRELVY TAB 50MG	2	1	$1,644.14	$822.07	2	0.14%
SUBTOTAL	**8**	**3**	**$6,739.44**	**$842.43**	**2.67**	**0.57%**
LASMIDITAN PRODUCTS						
REYVOW TAB 100MG	2	1	$668.52	$334.26	2	0.06%
SUBTOTAL	**2**	**1**	**$668.52**	**$334.26**	**2**	**0.06%**
ELETRIPTAN PRODUCTS						
ELETRIPTAN TAB 20MG	1	1	$33.15	$33.15	1	0.00%
SUBTOTAL	**1**	**1**	**$33.15**	**$33.15**	**1**	**0.00%**
SPECIAL PA SUBTOTAL	**33**	**10***	**$15,084.39**	**$457.10**	**3.3**	**1.28%**
CALCITONIN GENE-RELATED PEPTIDE (CGRP) PRODUCTS						
GALCANEZUMAB PRODUCTS						
EMGALITY INJ 120MG/ML	856	166	$522,933.30	$610.90	5.16	43.95%
EMGALITY SYR 120MG/ML	85	18	$52,071.51	$612.61	4.72	4.38%
EMGALITY SYR 100MG/ML	2	1	$2,926.44	$1,463.22	2	0.25%
SUBTOTAL	**943**	**185**	**$577,931.25**	**$612.86**	**5.1**	**48.58%**
RIMEGEPANT PRODUCTS						
NURTEC ODT 75MG	124	48	$108,302.57	$873.41	2.58	9.10%
SUBTOTAL	**124**	**48**	**$108,302.57**	**$873.41**	**2.58**	**9.10%**
ERENUMAB PRODUCTS						
AIMOVIG INJ 140MG/ML	80	14	$50,714.03	$633.93	5.71	4.26%
AIMOVIG INJ 70MG/ML	44	9	$25,614.68	$582.15	4.89	2.15%
SUBTOTAL	**124**	**23**	**$76,328.71**	**$615.55**	**5.39**	**6.41%**
FREMANEZUMAB PRODUCTS						
AJOVY INJ 225MG/1.5ML	53	17	$32,434.44	$611.97	3.12	2.73%
AJOVY SYR 225MG/1.5ML	25	7	$15,365.15	$614.61	3.57	1.29%
SUBTOTAL	**78**	**24**	**$47,799.59**	**$612.82**	**3.25**	**4.02%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CGRP SUBTOTAL	**1,269**	**261***	**$810,362.12**	**$638.58**	**4.86**	**68.11%**
TOTAL	**13,200**	**5,561***	**$1,189,809.38**	**$90.14**	**2.37**	**100.00%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
ACT = actuation; INJ = injection; NAPROX = naproxen; ODT = orally disintegrating tablet; SPR = nasal spray; SUMAT = sumatriptan; SYR = prefilled syringe; TAB = tablet
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 01/2022. Last accessed 01/13/2022.
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Appendix Q

Fiscal Year 2021 Annual Review of Topical Acne and Rosacea Products and 30-Day Notice to Prior Authorize Winlevi® (Clascoterone 1% Cream)

Oklahoma Health Care Authority
February 2022

Current Prior Authorization Criteria

Aczone® (Dapsone Gel) Approval Criteria:

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

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

1. An FDA approved indication of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris; and
2. Member must be 9 years of age or older; and
3. Amzeeq® will not be covered for members older than 20 years of age; and
4. A patient-specific, clinically significant reason why the member cannot use erythromycin 2% topical solution, clindamycin 1% topical solution, benzoyl peroxide, brand name Tazorac®, oral isotretinoin medications, and other generically available preferred oral or topical antibiotic products must be provided; and
5. A quantity limit of 30 grams per 30 days will apply.

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

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

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

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

MetroGel® (Metronidazole 1% Gel) Approval Criteria:

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

Noritate® (Metronidazole 1% Cream) Approval Criteria:

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

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. For the diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and
    b. Tazorac® 0.1% cream, Tazorac® 0.05% gel, Tazorac® 0.1% gel, and tazarotene 0.1% cream will not require prior authorization for members 20 years of age or younger; and
4. A quantity limit of 100 grams per 30 days will apply.

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

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

Utilization of Topical Acne and Rosacea Products: Fiscal Year 2021

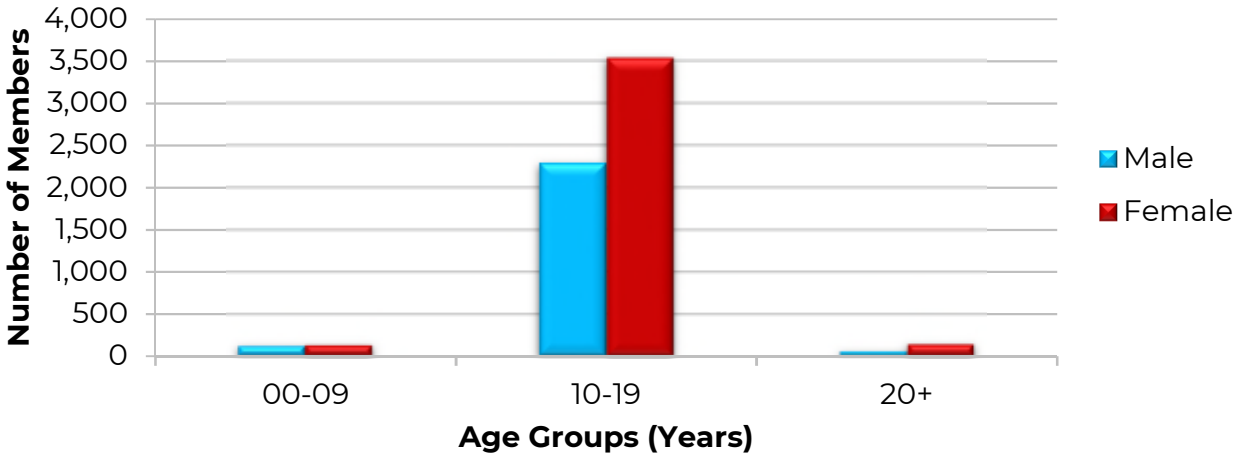
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	5,719	11,873	$1,864,751.14	$157.06	$6.10	597,228	305,534
2021	6,250	12,538	$1,430,218.03	$114.07	$4.40	642,348	325,335
% Change	**9.30%**	**5.60%**	**-23.30%**	**-27.40%**	**-27.90%**	**7.60%**	**6.50%**
Change	**531**	**665**	**-$434,533.11**	**-$42.99**	**-$1.70**	**45,120**	**19,801**

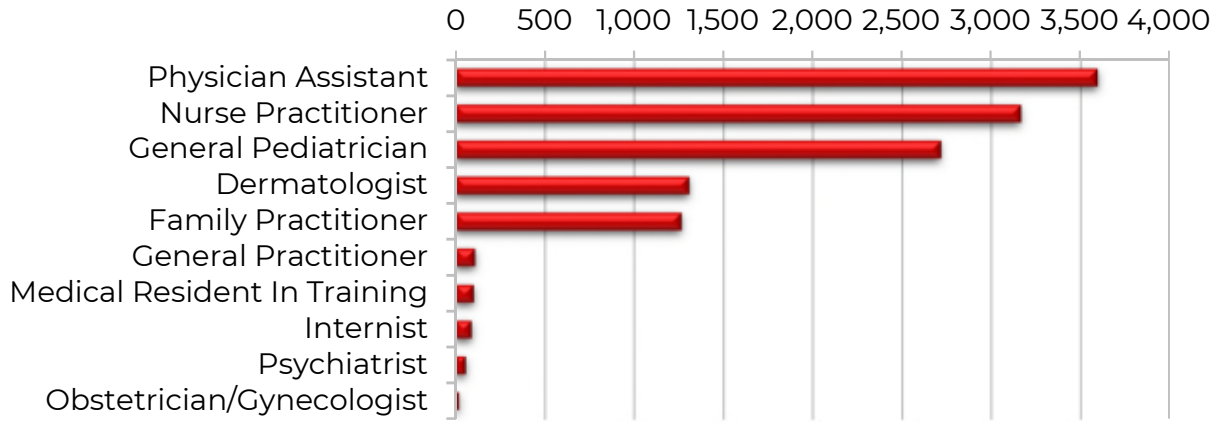
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020; Fiscal Year 2021 = 07/01/2020 to 06/30/2021

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

Demographics of Members Utilizing Topical Acne and Rosacea Products



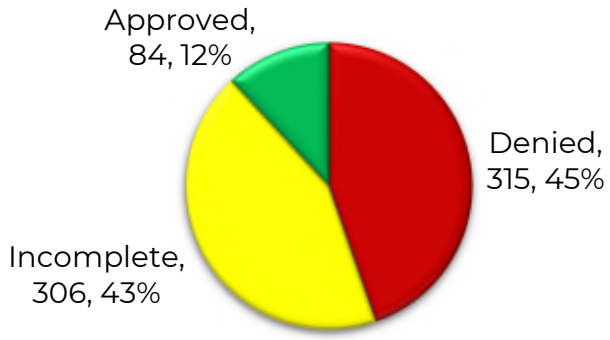
Top Prescriber Specialties of Topical Acne and Rosacea Products by Number of Claims



Prior Authorization of Topical Acne and Rosacea Products

There were 705 prior authorization requests submitted for topical acne and rosacea products during fiscal year 2021. The following chart shows the status of the submitted petitions for fiscal year 2021.

Status of Petitions



Market News and Updates[1,2]

Anticipated Patent Expiration(s):

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

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

- **August 2020:** The FDA approved Winlevi® (clascoterone 1% cream), an androgen receptor inhibitor, for the topical treatment of acne vulgaris in patients 12 years of age and older. Winlevi® is the first product with a novel mechanism of action to be FDA approved for acne in nearly 40 years.

Winlevi® (Clascoterone 1% Cream) Product Summary[3,4,5]

Indication: Winlevi® (clascoterone 1% cream) is an androgen receptor inhibitor indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

How Supplied: 1% topical cream (containing 10mg clascoterone per gram) in a 60g tube

Dosing and Administration:

- A thin, uniform layer of cream should be applied to clean and dry skin twice daily to the affected area in the morning and evening.

- Patients should avoid accidental transfer of the cream into the eyes, mouth, or other mucous membranes, and should rinse those areas thoroughly with water if contact occurs.

Contraindication(s): None

Safety:

- Local Skin Reactions: Winlevi® may induce local irritation, including erythema, pruritus, and scaling/dryness. Concomitant use with other potentially irritating topical products should be limited. Winlevi® should not be applied to cuts, abrasions, eczematous, or sunburned skin.
- Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression: HPA axis suppression was observed in clinical studies of Winlevi®, and may occur during or after treatment. In patients experiencing HPA axis suppression, HPA axis function returned to normal 4 weeks after stopping treatment. Conditions which augment systemic absorption include use over large surface areas, prolonged use, and use of occlusive dressings. If HPA axis suppression develops, an attempt should be made to withdraw the drug. Pediatric patients may be more susceptible to systemic toxicity.

Efficacy: The efficacy and safety of clascoterone 1% cream for the topical treatment of acne vulgaris were assessed in 2 identical Phase 3 randomized, double-blind, vehicle-controlled studies (study 1 and study 2). A total of 1,440 patients 9 years of age or older with facial acne were enrolled in the studies. Of those patients enrolled, 1,421 (98.7%) were 12 years of age or older. Patients were randomized 1:1 to receive clascoterone 1% cream or vehicle cream twice daily for 12 weeks.

- Key Inclusion Criteria: Patients were eligible for inclusion if they had moderate-to-severe facial acne vulgaris with 30-75 inflammatory lesions and 30-100 non-inflammatory lesions. Patients were required to have been on a consistent skin care regimen for at least 1 month prior to enrollment and had to agree to continue the same skin care regimen throughout the study period.
- Key Exclusion Criteria: Patients were excluded if they had >2 facial nodules, had use of topical anti-acne preparations (e.g., over-the-counter acne cleansers or treatments, retinoids, light treatments), or use of systemic anti-acne medications (e.g., corticosteroids, antibiotics, spironolactone, retinoids) within a specified period of time, depending on the type of medication, prior to study initiation.
- Primary Endpoint: The 3 co-primary efficacy endpoints included:
    - The proportion of patients achieving treatment success, defined as an Investigator's Global Assessment (IGA) score of 0 (clear skin) or 1 (almost clear skin) and ≥2-point improvement from baseline at week 12

- The absolute change and percent change from baseline in non-inflammatory lesion count at week 12
- The absolute change and percent change from baseline in inflammatory lesion count at week 12

- Results: In both studies, all 3 co-primary efficacy endpoints were met at week 12. Treatment success was achieved in 18.8% and 20.9% of patients receiving clascoterone and 8.7% and 6.6% of patients receiving vehicle in study 1 and study 2, respectively. The mean percent reduction in non-inflammatory lesions was 32.6% and 29.6% in patients receiving clascoterone and 21.8% and 15.7% in patients receiving vehicle in study 1 and study 2, respectively. The mean percent reduction in inflammatory lesions was 44.6% and 47.1% in patients receiving clascoterone and 36.3% and 29.7% in patients receiving vehicle in study 1 and study 2, respectively.

Cost Comparison:

Product	Cost Per Unit*	Cost Per Package⁺
Winlevi® (clascoterone) 1% topical cream	**$9.17**	**$550.20**
Amzeeq® (minocycline) 4% topical foam	$15.51	$465.30
dapsone 5% topical gel (generic)	$2.85	$171.00
tazarotene 0.1% cream (generic)	$2.81	$168.60
erythromycin 2% topical solution (generic)	$0.43	$25.80
clindamycin 1% topical solution (generic)	$0.20	$12.00

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Unit = 1 gram or 1mL
⁺Cost per package based on 60g for Winlevi®, dapsone, and tazarotene; 30g for Amzeeq®; and 60mL for erythromycin 2% solution and clindamycin 1% solution.

Recommendations

The College of Pharmacy recommends the prior authorization of Winlevi® (clascoterone 1% cream) with the following criteria:

Winlevi® (Clascoterone 1% Cream) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. Member must be 12 to 20 years of age; and
3. A patient-specific, clinically significant reason why the member cannot use erythromycin 2% topical solution, clindamycin 1% topical solution, benzoyl peroxide, preferred tazarotene formulations, oral isotretinoin medications, and other generically available preferred oral or topical antibiotic products must be provided; and
4. A quantity limit of 60 grams per 30 days will apply.

Utilization Details of Topical Acne and Rosacea Products: Fiscal Year 2021

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CLINDAMYCIN PRODUCTS						
CLINDAMYCIN GEL 1%	4,925	2,784	$238,167.89	$48.36	1.77	16.65%
CLINDAMYCIN SOL 1%	2,168	1,223	$48,044.50	$22.16	1.77	3.36%
CLINDAMYCIN LOT 10MG/ML	1,125	662	$90,107.14	$80.10	1.7	6.30%
CLINDAMYCIN SWAB 1%	880	351	$27,305.27	$31.03	2.51	1.91%
CLINDAMYCIN LOT 1%	871	564	$72,842.39	$83.63	1.54	5.09%
CLINDACIN-P SWAB 1%	9	7	$325.80	$36.20	1.29	0.02%
CLINDACIN ETZ SWAB 1%	4	3	$131.88	$32.97	1.33	0.01%
CLINDAGEL GEL 1%	1	1	$1,788.67	$1,788.67	1	0.13%
SUBTOTAL	**9,983**	**5,595**	**$478,713.54**	**$47.95**	**1.78**	**33.47%**
TAZAROTENE PRODUCTS						
TAZORAC GEL 0.05%	925	635	$525,696.18	$568.32	1.46	36.76%
TAZAROTENE CRE 0.1%	679	534	$104,975.54	$154.60	1.27	7.34%
TAZORAC GEL 0.1%	261	196	$143,517.15	$549.87	1.33	10.03%
TAZORAC CRE 0.05%	202	166	$115,551.02	$572.03	1.22	8.08%
TAZORAC CRE 0.1%	48	42	$25,374.76	$528.64	1.14	1.77%
SUBTOTAL	**2,115**	**1,573**	**$915,114.65**	**$432.68**	**1.34**	**63.98%**
ERYTHROMYCIN PRODUCTS						
ERYTHROMYCIN SOL 2%	260	159	$10,235.11	$39.37	1.64	0.72%
SUBTOTAL	**260**	**159**	**$10,235.11**	**$39.37**	**1.64**	**0.72%**
METRONIDAZOLE PRODUCTS						
METRONIDAZOLE CRE 0.75%	81	65	$4,614.31	$56.97	1.25	0.32%
METRONIDAZOLE GEL 0.75%	44	37	$2,001.09	$45.48	1.19	0.14%
METRONIDAZOLE LOT 0.75%	6	4	$495.56	$82.59	1.5	0.03%
SUBTOTAL	**131**	**106**	**$7,110.96**	**$54.28**	**1.24**	**0.50%**
DAPSONE PRODUCTS						
DAPSONE GEL 5%	16	13	$5,028.84	$314.30	1.23	0.35%
DAPSONE GEL 7.5%	9	8	$4,553.02	$505.89	1.13	0.32%
ACZONE GEL 7.5%	1	1	$672.13	$672.13	1	0.05%
ACZONE GEL 5%	1	1	$880.09	$880.09	1	0.06%
SUBTOTAL	**27**	**23**	**$11,134.08**	**$412.37**	**1.17**	**0.78%**
MINOCYCLINE PRODUCTS						
AMZEEQ AER 4%	16	14	$7,260.88	$453.81	1.14	0.51%
SUBTOTAL	**16**	**14**	**$7,260.88**	**$453.81**	**1.14**	**0.51%**
SULFACETAMIDE PRODUCTS						
SULFACETAMIDE LOT 10%	6	5	$648.81	$108.14	1.2	0.05%
SUBTOTAL	**6**	**5**	**$648.81**	**$108.14**	**1.2**	**0.05%**
TOTAL	**12,538**	**6,250***	**$1,430,218.03**	**$114.07**	**2.01**	**100%**

Costs do not reflect rebated prices or net costs.
*Total number of unduplicated utilizing members.
AER = aerosol foam; CRE = cream; ETZ = pledgets; LOT = lotion; SOL = solution
Fiscal Year 2021 = 07/01/2020 to 06/30/2021

[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 12/2021. Last accessed 12/30/2021.

[2] Cassiopea. Cassiopea Receives FDA Approval for Winlevi® (Clascoterone Cream 1%), First-in-Class Topical Acne Treatment Targeting the Androgen Receptor. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/cassiopea-receives-fda-approval-for-winlevi-clascoterone-cream-1-first-in-class-topical-acne-treatment-targeting-the-androgen-receptor-301119454.html. Issued 08/07/2020. Last accessed 12/30/2021.

[3] Winlevi® (Clascoterone) Prescribing Information. Sun Pharmaceutical Industries, Inc. Available online at: https://www.winlevi-hcp.com/pdf/winlevi-prescribing-information.pdf. Last revised 09/2021. Last accessed 12/30/2021.

[4] Hebert A, Thiboutot D, Stein Gold L, et al. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials. *JAMA Dermatol* 2020; 156(6):621-630.

[5] U.S. FDA. Drugs@FDA. Drug Approval Package: Winlevi®: Multi-Discipline Review. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/213433Orig1s000MultidisciplineR.pdf. Last accessed 01/05/2022.

Appendix R

30-Day Notice to Prior Authorize Dojolvi® (Triheptanoin)

Oklahoma Health Care Authority
February 2022

Introduction[1,2,3,4]

Long-chain fatty acid oxidation disorders (LC-FAODs) are a group of rare, autosomal recessive metabolic disorders caused by mutations in genes coding for enzymes and proteins involved in the transport and metabolism of long-chain fatty acids in the mitochondria. In patients with a specific LC-FAOD, there may be reduced or loss of function of a specific enzyme or protein, which can result in tissue accumulation of fatty acids or their metabolites or metabolic decompensation due to the depletion of tricarboxylic acid cycle intermediates.

During periods of fasting, decreased carbohydrate intake, or increased energy demand, the body's stores of glycogen may be diminished or depleted. During these times, approximately 80% of the energy needs of the heart, skeletal muscle, and liver are met by the oxidation of fatty acids. In patients with LC-FAODs, the ability to generate energy from long-chain fatty acids is compromised or absent. Patients can experience acute metabolic crises during times of increased energy demand, which may lead to hypoglycemia, rhabdomyolysis, or cardiomyopathy. In some patients, these events can occur suddenly and unpredictably and may be life-threatening, requiring emergency medical care.

Several types of LC-FAODs have been identified, each affecting a different enzyme or protein. The most common LC-FAOD is very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, with an incidence of approximately 1 in 85,000 births. Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency and trifunctional protein (TFP) deficiency occur in approximately 1 in 250,000 to 1 in 750,000 births. Carnitine-acylcarnitine translocase (CACT) deficiency, carnitine palmitoyltransferase I (CPT I) deficiency, and carnitine palmitoyltransferase II (CPT II) deficiency are the rarest forms, occurring in approximately 1 in 750,000 to 1 in 2,000,000 births. In Oklahoma, these LC-FAODs are included in routine newborn screening, and subsequent molecular genetic testing can confirm the diagnosis and the specific gene affected.

The management of LC-FAODs involves dietary restrictions to minimize reliance on long-chain fatty acid metabolism, with a goal of preventing metabolic crises. In symptomatic patients with a LC-FAOD, dietary intake of long-chain fatty acids should be limited and should be substituted by

medium-chain triglycerides (MCTs). MCTs containing ≤8 carbon atoms can freely enter the mitochondria, bypassing the carnitine shuttle and beta-oxidation pathway required for the metabolism of long-chain fatty acids. MCTs therefore provide a source of calories and fatty acids that can be utilized by patients with LC-FAODs. MCTs occur naturally in some products such as coconut oil, palm kernel oil, and some dairy products, however the percentage of MCTs in these products is low compared to the 100% MCT oil products which are available over-the-counter (OTC).

In June 2020, the U.S. Food and Drug Administration (FDA) approved Dojolvi® (triheptanoin) as the first FDA approved product for the treatment of patients with molecularly confirmed LC-FAODs.

Dojolvi® (Triheptanoin) Product Summary[5,6,7]

Indication(s): Dojolvi® (triheptanoin) is an MCT indicated as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed LC-FAODs.

How Supplied: Oral liquid containing 100% triheptanoin in a 500mL bottle

Dosing and Administration:

- The patient's metabolic requirements should be assessed and the patient's total prescribed daily caloric intake (DCI) should be determined before calculating the Dojolvi® dose.
- The caloric value of Dojolvi® is 8.3kcal/mL.
- The recommended target daily dosage of Dojolvi® is up to 35% of DCI divided into ≥4 daily doses.
- Patients Not Currently Taking an MCT Product:
  - Dojolvi® should be initiated at a total daily dosage of approximately 10% of DCI divided into ≥4 daily doses.
  - The dose should be increased to the recommended target daily dosage over a period of 2 to 3 weeks.
- Patients Switching from Another MCT Product:
  - The other MCT product should be discontinued prior to the first dose of Dojolvi®.
  - Dojolvi® should be initiated at the last tolerated daily dosage of MCT divided into ≥4 daily doses.
  - The dose should be increased by approximately 5% of DCI every 2 to 3 days until the target daily dosage is achieved.
- Dojolvi® should be mixed with semi-solid food or liquids and administered at mealtimes or with snacks orally or enterally via a silicone or polyurethane feeding tube. Dojolvi® should not be administered alone to avoid gastrointestinal (GI) upset.

- For patients experiencing GI adverse reactions, dosage reduction should be considered until the GI symptoms resolve. If a patient is unable to achieve the target daily dosage of 35% of DCI, the patient should be maintained at the maximum tolerated dosage.

Mechanism of Action: Triheptanoin is an MCT consisting of 3 odd-chain 7-carbon length fatty acids (heptanoate) that provide a source of calories and fatty acids to bypass the LC-FAOD enzyme deficiencies for energy production and replacement.

Contraindication(s): None

Safety:

- Feeding Tube Dysfunction: In clinical studies of Dojolvi®, feeding tube dysfunction was reported in patients receiving triheptanoin. Feeding tube performance and functionality can degrade over time depending on usage and environmental conditions. The contribution of Dojolvi® cannot be ruled out. Dojolvi® is not compatible with certain plastics. Dojolvi® should not be administered in feeding tubes manufactured of polyvinyl chloride (PVC), and feeding tubes should be regularly monitored to ensure proper functioning and integrity.
- Intestinal Malabsorption in Patients with Pancreatic Insufficiency: Pancreatic enzymes hydrolyze triheptanoin and release heptanoate as medium-chain fatty acids in the small intestine. Low or absent pancreatic enzymes may result in reduced absorption of heptanoate, leading to insufficient supplementation of medium-chain fatty acids. Administration of Dojolvi® should be avoided in patients with pancreatic insufficiency.
- Drug Interactions: Pancreatic lipase inhibitors (e.g., orlistat) may reduce exposure to the triheptanoin metabolite, heptanoate, and reduce the clinical effect of triheptanoin. Coadministration of Dojolvi® with pancreatic lipase inhibitors should be avoided.
- Pregnancy: There are no human data available on the use of triheptanoin in pregnant women to evaluate the drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
- Lactation: There are no data available on the presence of triheptanoin or its metabolites in human or animal milk, the effects on the breastfed child, or the effects on milk production.

Adverse Reactions: The most common adverse reactions reported in clinical studies of triheptanoin were GI-related, including abdominal pain (60%), diarrhea (44%), vomiting (44%), and nausea (14%).

Efficacy: The efficacy of triheptanoin for the treatment of LC-FAODs was assessed in a 4-month Phase 3, double-blind, randomized study which compared triheptanoin, a 7-carbon chain fatty acid, to trioctanoin, an 8-carbon chain fatty acid. A total of 32 adult and pediatric patients with a confirmed LC-FAOD diagnosis were enrolled, with a median age of 12 years (range: 7 to 64 years of age). Patients were randomized 1:1 to receive a target of 20% of DCI with either triheptanoin or trioctanoin for 4 months.

- Inclusion Criteria: All patients had a molecularly confirmed LC-FAOD diagnosis and history of at least 1 significant episode of rhabdomyolysis.
- Exclusion Criteria: Patients were excluded if they had anemia (hemoglobin <10g/dL), had peripheral neuropathy limiting the ability to walk, were pregnant, were breastfeeding, or had a history of myocardial infarction.
- Primary Endpoint: The primary efficacy endpoints were changes from baseline in total energy expenditure (TEE), cardiac function assessed by echocardiogram (ECHO) [including left ventricular ejection fraction (LVEF) and left ventricular wall mass (LVWM)], exercise tolerance [including maximum heart rate (HR) during moderate intensity exercise], and phosphocreatine recovery following acute exercise.
- Results: After 4 months of treatment, there were no statistically significant differences in TEE or phosphocreatine recovery following acute exercise between the triheptanoin and trioctanoin groups. Additionally, there were no significant differences between the 2 groups in musculoskeletal symptoms (including the incidence of rhabdomyolysis) or blood glucose concentrations. ECHO data was only available for 21 of 32 patients (65.6%), and ECHO results were uninterpretable in 4 patients due to technical difficulties. Among patients with interpretable ECHO results, LVEF was on average 7.5% greater in the triheptanoin group relative to the trioctanoin group (P=0.046). LVWM decreased 8% from baseline in the triheptanoin group and increased 15% from baseline in the trioctanoin group; the difference between the 2 groups at month 4 was statistically significant (P=0.041). At month 4, maximum HR during moderate intensity exercise was on average 6.98 beats per minute lower in the triheptanoin group relative to the trioctanoin group (P=0.040). These observed differences in LVEF, LVWM, and HR, while statistically significant, occurred within the normal range and within the test/retest variability normally observed in repeated ECHOs. Based on these data, the FDA determined no clinically meaningful differences were observed between the 2 treatment groups. After 4 months of treatment, both groups had similar mean changes from baseline in LVEF and LVWM, and similar maximal HR during moderate intensity exercise.

Cost Comparison:

Product	Cost Per mL	Cost Per Package[+]
Dojolvi® (triheptanoin) oral liquid, 8.3kcal/mL	**$9.75**	**$4,875.00**
MCT Oil® (medium-chain triglycerides) oral oil, 7.7kcal/mL	$0.06	$56.76

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 package based on 500mL for Dojolvi® and 946mL for MCT Oil®.

Recommendations

The College of Pharmacy recommends the prior authorization of Dojolvi® (triheptanoin) with the following criteria:

Dojolvi® (Triheptanoin) Approval Criteria:

1. An FDA approved diagnosis of molecularly confirmed long-chain fatty acid oxidation disorder (LC-FAOD); and
2. Molecular testing confirms 1 of the following types of LC-FAOD:
   a. Carnitine-acylcarnitine translocase (CACT) deficiency; or
   b. Carnitine palmitoyltransferase I (CPT I) deficiency; or
   c. Carnitine palmitoyltransferase II (CPT II) deficiency; or
   d. Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency; or
   e. Trifunctional protein (TFP) deficiency; or
   f. Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency; and
3. Prescriber must verify member has a history of at least 1 significant or recurrent manifestation of LC-FAOD (e.g., cardiomyopathy, rhabdomyolysis, hypoglycemia); and
4. Member must have tried and failed dietary management with an alternate medium chain triglyceride (MCT) product (e.g., MCT oil) or a patient-specific, clinically significant reason why dietary management with an alternate MCT product is not appropriate for the member must be provided; and
5. Dojolvi® will not be approved for concomitant use with another MCT product (other MCT products must be discontinued prior to the first dose of Dojolvi®); and
6. Member must not be taking a pancreatic lipase inhibitor concomitantly with Dojolvi®; and
7. Prescriber must verify the member does not have pancreatic insufficiency; and
8. Prescriber must verify that member or member's caregiver has been counseled on the proper storage, preparation, and administration of Dojolvi®, including specific considerations for use in a feeding tube, if applicable; and

9. Dojolvi® must be prescribed by a geneticist or other specialist with expertise in the treatment of LC-FAOD; and
10. Prescriber must verify the member is under the care of a clinical specialist knowledgeable in appropriate disease-related dietary management based on member's specific LC-FAOD and current nutritional recommendations; and
11. The member's daily caloric intake (DCI) must be provided (in kcal) on the prior authorization request to verify appropriate dosing based on package labeling; and
12. Initial approvals will be for the duration of 3 months. After 3 months of treatment, compliance will be required and the prescriber must verify the member has had a positive response to and is tolerating treatment with Dojolvi®. Additionally, for members who switched from another MCT product due to adverse effects, the prescriber must verify the member has experienced fewer adverse effects with Dojolvi®; and
13. Quantity limits according to package labeling will apply, with the maximum approvable dosing regimen based on a target daily dosage of Dojolvi® up to 35% of the member's total DCI.

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Appendix S

Fiscal Year 2021 Annual Review of Zokinvy® (Lonafarnib)

Oklahoma Health Care Authority
February 2022

Current Prior Authorization Criteria

Zokinvy® (Lonafarnib) Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. To reduce the risk of mortality in Hutchinson-Gilford Progeria Syndrome (HGPS); or
   b. Treatment of processing-deficient Progeroid Laminopathies (PL) with either:
      i. Heterozygous *LMNA* mutation with progerin-like protein accumulation; or
      ii. Homozygous or compound heterozygous *ZMPSTE24* mutations; and
2. Member must have confirmatory mutational analysis showing mutation in the *LMNA* gene; and
3. Zokinvy® will not be approved for other progeroid syndromes or processing-proficient PL (based upon its mechanism of action, Zokinvy® would not be effective in these populations); and
4. Member must be 1 year of age or older; and
5. Member must have a body surface area (BSA) ≥0.39m^2; and
6. Member must have clinical signs of progeria (e.g., characteristic facial features, growth deficiency, atherosclerosis); and
7. Zokinvy® must be prescribed by, or in consultation with, a specialist with expertise in treating HGPS or PL (or an advanced care practitioner with a supervising physician who is a specialist in treating HGPS or PL); and
8. Member must not be taking any of the following medications: strong/moderate CYP3A inhibitors, CYP2C9 inhibitors, midazolam, lovastatin, simvastatin, atorvastatin, or loperamide if younger than 2 years of age; and
9. Prior to and during treatment, the potential for drug interactions should be considered, concomitant medications reviewed, and members should be monitored for adverse reactions; and
10. Member should have ophthalmological evaluations performed at regular intervals and at the onset of any new visual changes; and
11. Prescriber must verify the member will be monitored for changes in electrolytes, complete blood counts, renal function, and liver enzymes; and

12. Member's recent BSA must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to the package labeling; and
13. The maximum approvable dose of Zokinvy® is 300mg/m^2 per day; and
14. Initial approvals will be for 6 months. After 6 months of utilization, compliance and information regarding efficacy, such as a positive response to treatment including no new or worsening heart failure and no stroke incidence, will be required for continued approval. Subsequent approvals will be for 12 months and compliance and documentation of a positive response to Zokinvy® therapy will be required on each continuation request.

Utilization of Zokinvy® (Lonafarnib): Fiscal Year 2021

There was no SoonerCare utilization of Zokinvy® (lonafarnib) during fiscal year 2021 (07/01/2020 to 06/30/2021).

Prior Authorization of Zokinvy® (Lonafarnib)

There were no prior authorization requests submitted for Zokinvy® (lonafarnib) during fiscal year 2021.

Market News and Updates[12,3,4,5,6,7]

Anticipated Patent Expiration(s):

- Zokinvy® (lonafarnib): July 2024

Pipeline:

- **Lonafarnib/Everolimus:** A Phase 1/2 dose-escalation trial of everolimus in combination with lonafarnib in HGPS and PL is currently being conducted. It is hypothesized that while lonafarnib inhibits the progerin formation, everolimus may help clear progerin from cells. Phase 1, to determine the safe and appropriate dosage of everolimus, began in April 2016 and was successfully completed in June 2017. Phase 2, which is testing the effectiveness of the 2-drug combination, began in July 2017. Sixty children from 27 countries were enrolled. The estimated study completion date is December 2023. The primary outcomes in the Phase 2 portion are the annual increase in weight gain and change in pulse wave velocity [(PWV), a measure of cardiac health] in a 24-month timeframe. Everolimus is a form of the drug rapamycin; however, everolimus can be more easily given to children with progeria because it requires fewer blood draws to measure drug levels. While lonafarnib may block the toxic progerin from developing, rapamycin appears to allow cells to more rapidly clear out progerin, targeting 2 different mechanisms of action.
- **Ribonucleic Acid (RNA) Therapies:**

- **SRP-2001:** The results of a preclinical study investigating the efficacy of RNA targeting *in vitro* in HGPS cell lines and then *in vivo* using a transgenic mouse model that expresses the human *LMNA* gene harboring the classic G608G mutation was published in *Nature Medicine* in March 2021. The study showed that treating progeria mice with intravenous delivery of SRP-2001 reduced the harmful progerin messenger RNA (mRNA) and protein expression in the aorta as well as in other tissues. At study completion, the aortic wall remained stronger with significant reduction of progerin transcripts in the aorta, a critical target tissue in HGPS, and the mice demonstrated an increased survival of 61.6%.
- **LB143:** A study using combined *in vitro* and *in vivo* screening approach to identify optimized, therapeutically useful antisense oligonucleotides (ASOs) targeting *LMNA* pre-mRNA in HGPS was published in March 2021 in *Nature Medicine*. The results showed a 90-95% reduction of the toxic progerin-producing RNA in different tissues after treatment with LB143. The progerin protein reduction was most effective in the liver, with additional improvements in the heart and aorta. These results identify a novel therapeutic agent for HGPS and provide insight into the HGPS disease mechanism.

Recommendations

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

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Appendix T

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: January 31, 2022

Coronavirus (COVID-19) Update: FDA Takes Key Action by Approving Second COVID-19 Vaccine

The FDA approved a second COVID-19 vaccine. The vaccine has been known as the Moderna COVID-19 Vaccine; the approved vaccine will be marketed as Spikevax™ for the prevention of COVID-19 in individuals 18 years of age and older.

Spikevax™ has the same formulation as the emergency use authorization (EUA) Moderna COVID-19 Vaccine and is administered as a primary series of 2 doses, 1 month apart. Spikevax™ can be used interchangeably with the EUA Moderna COVID-19 Vaccine to provide the COVID-19 vaccination series. Moderna COVID-19 Vaccine remains available under EUA as a 2-dose primary series for individuals 18 years of age and older, as a third primary series dose for immunocompromised individuals 18 years of age and older, and as a single booster dose for individuals 18 years of age and older at least 5 months after completing a primary series of the vaccine. It is also authorized for use as a heterologous (or "mix and match") single booster dose for individuals 18 years of age and older following completion of primary vaccination with a different available COVID-19 vaccine.

FDA Evaluation of Effectiveness Data for Approval for Individuals 18 Years of Age and Older

The Spikevax™ biologics license application (BLA) builds upon the data and information that supported the EUA, such as preclinical and clinical data, as well as details of the manufacturing process and the sites where the vaccine is made. The FDA evaluates and conducts its own analyses of the data to determine whether the safety and effectiveness of the vaccine has been demonstrated and meets the standard for approval, and whether the manufacturing and facility information assure vaccine quality and consistency.

The approval of Spikevax™ is based on the FDA's evaluation and analysis of follow-up safety and effectiveness data from the ongoing randomized, placebo-controlled, blinded clinical trial that supported the December 2020 EUA for the Moderna COVID-19 Vaccine and information from post EUA experience to further inform safety and effectiveness.

The updated analyses to determine effectiveness of Spikevax™ included 14,287 vaccine recipients and 14,164 placebo recipients 18 years of age and older who did not have evidence of SARS-CoV-2 infection prior to receiving the first dose. The data used for the analyses were accrued before the Omicron variant emerged. These data demonstrated that Spikevax™ was 93% effective in preventing COVID-19, with 55 cases of COVID-19 occurring in the vaccine group and 744 COVID-19 cases in the placebo group. The vaccine was also 98% effective in preventing severe disease.

FDA Evaluation of Safety Data for Approval for Individuals 18 Years of Age and Older

The FDA's safety analysis of Spikevax™ included approximately 15,184 vaccine recipients and 15,162 placebo recipients 18 years of age and older, more than half of these participants were followed for safety outcomes for at least 4 months after the second

dose. Approximately 7,500 participants originally assigned to receive Spikevax™ in the blinded phase of the clinical trial completed safety follow-up for at least 6 months after the second dose.

The most commonly reported side effects by clinical trial participants were pain, redness and swelling at the injection site, fatigue, headache, muscle or joint pain, chills, nausea/vomiting, swollen lymph nodes under the arm and fever.

Additionally, the FDA conducted a rigorous evaluation of the post-authorization safety surveillance data pertaining to myocarditis and pericarditis following vaccination with the Moderna COVID-19 Vaccine and has determined that the data demonstrate increased risks particularly within 7 days following the second dose, with the observed risk highest in males 18 through 24 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. However, some individuals required intensive care support. Information is not yet available about potential long-term health outcomes. The Spikevax™ *Prescribing Information* includes a warning about these risks.

The FDA conducted its own benefit-risk assessment using modeling to predict how many symptomatic COVID-19 cases, hospitalizations, intensive care unit (ICU) admissions and deaths from COVID-19 the vaccine in individuals 18 years of age and older would prevent versus the number of potential myocarditis/pericarditis cases, hospitalizations, ICU admissions and deaths that might be associated with the vaccine. FDA has determined that the benefits of the vaccine outweigh the risk of myocarditis and pericarditis in individuals 18 years of age and older.

The FDA is requiring the company to conduct postmarketing studies to further assess the risks of myocarditis and pericarditis following vaccination with Spikevax™. These studies will include an evaluation of long-term outcomes among individuals who develop myocarditis following vaccination with Spikevax™. In addition, although not an FDA requirement, the company has committed to conducting additional post-marketing safety studies, including conducting a pregnancy registry study to evaluate pregnancy and infant outcomes after receipt of Spikevax™ during pregnancy.

FDA NEWS RELEASE

For Immediate Release: January 24, 2022

Coronavirus (COVID-19) Update: FDA Limits Use of Certain Monoclonal Antibodies to Treat COVID-19 Due to the Omicron Variant

The FDA has used the best available science as the virus has evolved to make informed decisions with the health and safety of the American public in mind. Ensuring that healthcare providers on the frontlines have the best tools available to treat patients is a top priority for the FDA.

In light of the most recent information and data available, the FDA revised the authorizations for 2 monoclonal antibody treatments – bamlanivimab and etesevimab (administered together) and REGEN-COV® (casirivimab and imdevimab) – to limit their use to only when the patient is likely to have been infected with or exposed to a variant that is susceptible to these treatments.

Because data show these treatments are highly unlikely to be active against the omicron variant, which is circulating at a very high frequency throughout the United States, these treatments are not authorized for use in any U.S. states, territories, and jurisdictions at this time. In the future, if patients in certain geographic regions are likely to be infected or exposed to a variant that is susceptible to these treatments, then use of these treatments may be authorized in these regions.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses, like SARS-CoV-2. And like other infectious organisms, SARS-CoV-2 can mutate over time, resulting in certain treatments not working against certain variants such as omicron. This is the case with these 2 treatments for which changes are being made.

Based on Centers for Disease Control and Prevention (CDC) data, the omicron variant of SARS-CoV-2 is estimated to account for more than 99% of cases in the U.S. as of January 15, 2022. Therefore, it's highly unlikely that COVID-19 patients seeking care in the U.S. at this time are infected with a variant other than omicron, and these treatments are not authorized to be used at this time. This avoids exposing patients to side effects, such as injection site reactions or allergic reactions, which can be potentially serious, from specific treatment agents that are not expected to provide benefit to patients who have been infected with or exposed to the omicron variant.

The National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel, an independent panel of national experts, recently recommended against the use of bamlanivimab and etesevimab (administered together) and REGEN-COV® (casirivimab and imdevimab) because of markedly reduced activity against the omicron variant and because real-time testing to identify rare, non-omicron variants is not routinely available.

Importantly, there are several other therapies – Paxlovid™, sotrovimab, Veklury® (remdesivir), and molnupiravir – that are expected to work against the omicron variant, and that are authorized or approved to treat patients with mild-to-moderate COVID-19 who are at high risk for progression to severe disease, including hospitalization or death. Healthcare providers should consult the NIH panel's COVID-19 treatment guidelines and assess whether these treatments are right for their patients.

While it's critical that we have ways to treat those who contract COVID-19, the authorized treatments are not a substitute for vaccination in individuals for whom COVID-19 vaccination and a booster dose are recommended. Data has clearly demonstrated that the available, safe and effective vaccines can lower the risk of developing COVID-19 and experiencing the potential associated serious disease progression, including hospitalization and death.

The FDA is committed to continuing to review emerging data on all COVID-19 therapies related to the potential impact of variants and revise the authorizations further as appropriate to ensure healthcare providers have an effective arsenal of treatments for patients.

FDA NEWS RELEASE

For Immediate Release: January 21, 2022

FDA Takes Actions to Expand Use of Treatment for Outpatients with Mild-to-Moderate COVID-19

The FDA took action to expand the use of the antiviral drug Veklury® (remdesivir) to certain non-hospitalized adults and pediatric patients for the treatment of mild-to-moderate COVID-19 disease. This provides another treatment option to reduce the risk of hospitalization in high-risk patients. Previously, the use of Veklury® was limited to patients requiring hospitalization.

Veklury® is not a substitute for vaccination in individuals for whom COVID-19 vaccination and a booster dose are recommended. The FDA has approved 1 vaccine and authorized others to prevent COVID-19 and the serious clinical outcomes associated with COVID-19, including hospitalization and death. The FDA urges the public to get vaccinated and receive a booster if eligible.

The FDA has expanded the approved indication for Veklury® to include its use in adults and pediatric patients (12 years of age and older who weigh at least 40kg) with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

The FDA also revised the EUA for Veklury® to additionally authorize the drug for treatment of pediatric patients weighing 3.5kg to <40kg or pediatric patients less than 12 years of age weighing at least 3.5kg, with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization of death.

Based on the FDA's actions, these high-risk non-hospitalized patients may receive Veklury® via intravenous (IV) infusion for a total of 3 days for the treatment of mild-to-moderate COVID-19 disease.

The approval of Veklury® for use in non-hospitalized patients is supported by a randomized, placebo-controlled clinical trial that included 562 non-hospitalized patients with mild-to-moderate COVID-19 who were at high risk for progression to severe COVID-19, including hospitalization or death. The main outcome measured in the trial was whether a patient was hospitalized for any COVID-19 related reason or died from any reason within 28 days of treatment. Overall, 2 of 279 patients who received Veklury® (0.7%) required COVID-19 related hospitalization compared to 15 of 283 patients who received a placebo (5.3%). There were no deaths in either group.

Pediatric patients for whom Veklury® is authorized will receive doses adjusted for their body weight in order to achieve comparable exposures to adults and pediatric patients receiving the approved dose. Given the similar course of COVID-19 disease, the authorization of Veklury® in certain pediatric patients is based on extrapolation of efficacy from adequate and well-controlled studies in adults.

Important details about using Veklury® to treat COVID-19 for its approved use is available in the *Prescribing Information*. Possible side effects include increased levels of liver enzymes, allergic reactions, changes in blood pressure and heart rate, low blood oxygen level, fever, shortness of breath, wheezing, swelling (e.g., lips, around eyes, under the skin), rash, nausea, sweating or shivering. Similar safety information about using Veklury® to treat COVID-19 in certain non-hospitalized pediatric patients under the EUA is available in the fact sheets for health care providers and parents/caregivers.

FDA NEWS RELEASE

For Immediate Release: January 7, 2022

Coronavirus (COVID-19) Update: FDA Shortens Interval for Booster Dose of Moderna COVID-19 Vaccine to 5 Months

The FDA amended the emergency use authorization (EUA) for the Moderna COVID-19 vaccine to shorten the time between the completion of a primary series of the vaccine and a booster dose to at least 5 months for individuals 18 years of age and older.

The most commonly reported side effects by individuals who received a booster dose of the Moderna COVID-19 vaccine after completion of a 2-dose primary series were pain, redness and swelling at the injection site, as well as fatigue, headache, muscle or joint pain, and chills. The fact sheets for recipients and caregivers and for health care providers include information about the potential side effects, as well as the risks of myocarditis and pericarditis.

FDA NEWS RELEASE

For Immediate Release: December 23, 2021

Coronavirus (COVID-19) Update: FDA Authorizes Additional Oral Antiviral for Treatment of COVID-19 in Certain Adults

The FDA issued an EUA for Merck's molnupiravir for the treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by the FDA are not accessible or clinically appropriate. Molnupiravir is available by prescription only and should be initiated as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.

Molnupiravir is not authorized for use in patients younger than 18 years of age since it may affect bone and cartilage growth. It is not authorized for the pre-exposure or post-exposure prevention of COVID-19 or for initiation of treatment in patients hospitalized due to COVID-19 because the benefit of treatment has not been observed in patients when treatment started after hospitalization due to COVID-19.

Molnupiravir is not a substitute for vaccination in individuals for whom COVID-19 vaccination and a booster dose are recommended. The FDA has approved 1 vaccine and authorized others to prevent COVID-19 and serious clinical outcomes associated with a COVID-19 infection, including hospitalization and death. The FDA urges the public to get vaccinated and receive a booster if eligible.

Molnupiravir works by introducing errors into the SARS-CoV-2 virus' genetic code, which prevents the virus from further replicating. Molnupiravir is administered as (4) 200mg capsules taken orally every 12 hours for 5 days, for a total of 40 capsules. Molnupiravir is not authorized for use for longer than 5 consecutive days.

The primary data supporting this EUA for molnupiravir are from MOVe-OUT, a randomized, double-blind, placebo-controlled clinical trial studying molnupiravir for the treatment of non-hospitalized patients with mild-to-moderate COVID-19 at high risk for progression to severe COVID-19 and/or hospitalization. Patients were adults 18 years of age and older with a pre-specified chronic medical condition or at increased risk of SARS-CoV-2 infection for other reasons who had not received a COVID-19 vaccine. The main outcome measured in the trial was the percentage of patients who were hospitalized or died due to any cause during 29 days of follow-up. Of the 709 patients who received molnupiravir, 6.8% were hospitalized or died within this time period compared to 9.7% of the 699 people who received a placebo. Of the patients who received molnupiravir, 1 died during the follow-up period compared to 9 people who received placebo. Side effects observed in the trial included diarrhea, nausea, and dizziness. The safety and effectiveness of molnupiravir for the treatment of COVID-19 continue to be evaluated.

Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals. Therefore, molnupiravir is not recommended for use during pregnancy. Molnupiravir is only authorized to be prescribed to a pregnant individual after the prescribing health care provider has determined that the benefits of being treated with molnupiravir would outweigh the risks for that individual patient and after the prescribing health care provider has communicated the known and potential benefits and the potential risks of using molnupiravir during pregnancy to the pregnant individual. Females of childbearing potential are advised to use a reliable method of birth control correctly and consistently during treatment with molnupiravir and for 4 days after the final dose. Males of reproductive potential who are sexually active with females of childbearing potential are advised to use a reliable method

of birth control correctly and consistently during treatment with molnupiravir and for at least 3 months after the final dose. Questions and concerns about reliable birth control methods that are appropriate for use during treatment with molnupiravir, as well as how molnupiravir may affect sperm cells, should be directed at one's health care provider.

FDA NEWS RELEASE

For Immediate Release: December 22, 2021

Coronavirus (COVID-19) Update: FDA Authorizes First Oral Antiviral for Treatment of COVID-19

The FDA issued an EUA for Pfizer's Paxlovid™ (nirmatrelvir tablets/ritonavir tablets, co-packaged for oral use) for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40kg) with positive results of direct SARS-CoV-2 testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. Paxlovid™ is available by prescription only and should be initiated as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.

Paxlovid™ is not authorized for the pre-exposure or post-exposure prevention of COVID-19 or for initiation of treatment in those requiring hospitalization due to severe or critical COVID-19. Paxlovid™ is not a substitute for vaccination in individuals for whom COVID-19 vaccination and a booster dose are recommended.

Paxlovid™ consists of nirmatrelvir, which inhibits a SARS-CoV-2 protein to stop the virus from replicating, and ritonavir, which slows down nirmatrelvir's breakdown to help it remain in the body for a longer period at higher concentrations. Paxlovid™ is administered as 3 tablets (2 tablets of nirmatrelvir and 1 tablet of ritonavir) taken together orally twice daily for 5 days, for a total of 30 tablets. Paxlovid™ is not authorized for use for longer than 5 consecutive days.

Based on the FDA's review of the totality of the scientific evidence available, the FDA has determined that it is reasonable to believe that Paxlovid™ may be effective for the treatment of mild-to-moderate COVID-19 in authorized patients. The FDA has also determined that the known and potential benefits of Paxlovid™, when used consistent with the terms and conditions of the authorization, outweigh the known and potential risks of the product. There are no adequate, approved, and available alternatives to Paxlovid™ for the treatment of COVID-19.

The primary data supporting this EUA for Paxlovid™ are from EPIC-HR, a randomized, double-blind, placebo-controlled clinical trial studying Paxlovid™ for the treatment of non-hospitalized symptomatic adults with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Patients were adults 18 years of age and older with a pre-specified risk factor for progression to severe disease or were 60 years of age and older regardless of pre-specified chronic medical conditions. All patients had not received a COVID-19 vaccine and had not been previously infected with COVID-19. The main outcome measured in the trial was the proportion of patients who were hospitalized due to COVID-19 or died due to any cause during 28 days of follow-up. Paxlovid™ significantly reduced the proportion of patients with COVID-19 related hospitalization or death from any cause by 88% compared to placebo among patients treated within 5 days of symptom onset and who did not receive COVID-19 therapeutic monoclonal antibody treatment. In this analysis, 1,039 patients had received Paxlovid™, and 1,046 patients had received placebo and among these patients, 0.8% who received Paxlovid™ were hospitalized or died during 28 days of follow-up compared to 6% of the patients who

received placebo. The safety and effectiveness of Paxlovid™ for the treatment of COVID-19 continue to be evaluated.

Possible side effects of Paxlovid™ include impaired sense of taste, diarrhea, high blood pressure, and muscle aches. Using Paxlovid™ at the same time as certain other drugs may result in potentially significant drug interactions. Using Paxlovid™ in patients with uncontrolled or undiagnosed HIV-1 infection may lead to HIV-1 drug resistance. Ritonavir may cause liver damage, so caution should be exercised when giving Paxlovid™ to patients with preexisting liver diseases, liver enzyme abnormalities, or liver inflammation.

Because Paxlovid™ works, in part, by inhibiting the CYP3A enzyme, Paxlovid™ is contraindicated with certain drugs that are highly dependent on CYP3A for metabolism and for which elevated concentrations of certain drugs are associated with serious and/or life-threatening reactions. Paxlovid™ is also contraindicated with drugs that, conversely, strongly induce CYP3A, leading to the faster breakdown of nirmatrelvir or ritonavir, as reduced concentrations of nirmatrelvir or ritonavir may be associated with potentially losing virologic response and developing viral resistance. Paxlovid™ cannot be started immediately after discontinuing such medications because the effects of those medications remain after discontinuation.

Paxlovid™ is not recommended in patients with severe kidney or severe liver impairment. In patients with moderate renal impairment, a reduced Paxlovid™ dose is needed.

FDA NEWS RELEASE

For Immediate Release: December 20, 2021

FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention

The FDA approved Apretude (cabotegravir extended-release injectable suspension) for use in at-risk adults and adolescents weighing at least 35kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV. Apretude is given first as 2 initiation injections administered 1 month apart, and then every 2 months thereafter. Patients can either start their treatment with Apretude or take oral cabotegravir (Vocabria) for 4 weeks to assess how well they tolerate the drug.

According to the CDC, notable gains have been made in increasing PrEP use for HIV prevention in the United States and preliminary data show that in 2020, about 25% of the 1.2 million people for whom PrEP is recommended were prescribed it, compared to only about 3% in 2015. However, there remains significant room for improvement. PrEP requires high levels of adherence to be effective and certain high-risk individuals and groups, such as young men who have sex with men, are less likely to adhere to daily medication. Other interpersonal factors, such as substance use disorders, depression, poverty, and efforts to conceal medication also can impact adherence. It is hoped that the availability of a long-acting injectable PrEP option will increase PrEP uptake and adherence in these groups.

The safety and efficacy of Apretude to reduce the risk of acquiring HIV were evaluated in 2 randomized, double-blind trials that compared Apretude to Truvada®, a once daily oral medication for HIV PrEP. Trial 1 included HIV-uninfected men and transgender women who have sex with men and have high-risk behavior for HIV infection. Trial 2 included uninfected cisgender women at risk of acquiring HIV.

Participants who took Apretude started the trial with cabotegravir (oral, 30mg tablet) and a placebo daily for up to 5 weeks, followed by Apretude 600mg injection at months 1 and 2, then every 2 months thereafter and a daily placebo tablet.

Participants who took Truvada® started the trial taking oral Truvada® and placebo daily for up to 5 weeks, followed by oral Truvada® daily and placebo intramuscular injection at months 1 and 2 and every 2 months thereafter.

In Trial 1, 4,566 cisgender men and transgender women who have sex with men received either Apretude or Truvada®. The trial measured the rate of HIV infections among trial participants taking daily cabotegravir followed by Apretude injections every 2 months compared to daily oral Truvada®. The trial showed participants who took Apretude had 69% less risk of getting infected with HIV when compared to participants who took Truvada®.

In Trial 2, 3,224 cisgender women received either Apretude or Truvada®. The trial measured the rate of HIV infections in participants who took oral cabotegravir and injections of Apretude compared to those who took Truvada® orally. The trial showed participants who took Apretude had 90% less risk of getting infected with HIV when compared to participants who took Truvada®.

Side effects occurring more frequently in participants who received Apretude compared to participants who received Truvada® in either trial include injection site reactions, headache, pyrexia, fatigue, back pain, myalgia, and rash.

Apretude includes a *Boxed Warning* to not use the drug unless a negative HIV test is confirmed. It must only be prescribed to individuals confirmed to be HIV-negative immediately prior to starting the drug and before each injection to reduce the risk of developing drug resistance. Drug-resistant HIV variants have been identified in people with undiagnosed HIV when they use Apretude for HIV PrEP. Individuals who become infected with HIV while receiving Apretude for PrEP must transition to a complete HIV treatment regimen. The drug labeling also includes warnings and precautions regarding hypersensitivity reactions, hepatotoxicity, and depressive disorders.

FDA NEWS RELEASE

For Immediate Release: December 17, 2021

FDA Approves New Treatment for Myasthenia Gravis

The FDA approved Vyvgart™ (efgartigimod) for the treatment of generalized myasthenia gravis (gMG) in adults who test positive for the anti-acetylcholine receptor (AChR) antibody.

Myasthenia gravis is a chronic autoimmune, neuromuscular disease that causes weakness in the skeletal muscles that worsens after periods of activity and improves after periods of rest. Myasthenia gravis affects voluntary muscles, especially those that are responsible for controlling the eyes, face, mouth, throat, and limbs. In myasthenia gravis, the immune system produces AChR antibodies that interfere with communication between nerves and muscles, resulting in weakness. Severe attacks of weakness can cause breathing and swallowing problems that can be life-threatening.

Vyvgart™ is the first approval of a new class of medication. It is an antibody fragment that binds to the neonatal Fc receptor (FcRn), preventing FcRn from recycling immunoglobulin G (IgG) back into the blood. The medication causes a reduction in overall levels of IgG, including the abnormal AChR antibodies that are present in myasthenia gravis.

The safety and efficacy of Vyvgart™ were evaluated in a 26-week clinical study of 167 patients with myasthenia gravis who were randomized to receive either Vyvgart™ or placebo. The study showed that more patients with myasthenia gravis with antibodies responded to treatment during the first cycle of Vyvgart™ (68%) compared to those who received placebo (30%) on a measure that assesses the impact of myasthenia gravis on

daily function. More patients receiving Vyvgart™ also demonstrated response on a measure of muscle weakness compared to placebo.

The most common side effects associated with the use of Vyvgart™ include respiratory tract infections, headache, and urinary tract infections. As Vyvgart™ causes a reduction in IgG levels, the risk of infections may increase. Hypersensitivity reactions such as eyelid swelling, shortness of breath, and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy. Patients using Vyvgart™ should monitor for signs and symptoms of infections during treatment. Health care professionals should administer appropriate treatment and consider delaying administration of Vyvgart™ to patients with an active infection until the infection is resolved.

Current Drug Shortages Index (as of January 12, 2021):

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

Acetazolamide Injection	***Currently in Shortage***
Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Amphetamine Oral Suspension, Extended Release	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azacitidine for Injection	***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***
Bumetanide Injection	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection	***Currently in Shortage***
Bupivacaine Hydrochloride Injection	***Currently in Shortage***
Calcium Disodium Versenate Injection	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Ceftazidime and Avibactam (Avycaz®) for Injection, 2gm/0.5gms	***Currently in Shortage***
Ceftolozane and Tazobactam (Zerbaxa®) Injection	***Currently in Shortage***
Chlordiazepoxide Hydrochloride Capsules	***Currently in Shortage***
Chloroprocaine Hydrochloride Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cortisone Acetate Tablets	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***

Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Cytarabine Injection	***Currently in Shortage***
Dacarbazine Injection	***Currently in Shortage***
Desmopressin Acetate Nasal Spray	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Digoxin Injection	***Currently in Shortage***
Diltiazem Hydrochloride Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace®) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection	***Currently in Shortage***
Epinephrine Injection, 0.1mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Fentanyl Citrate (Sublimaze®) Injection	***Currently in Shortage***
Floxuridine for Injection	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive®) Tablets	***Currently in Shortage***
Gentamicin Sulfate Injection	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydrocortisone Tablets	***Currently in Shortage***
Hydromorphone Hydrochloride Injection	***Currently in Shortage***
Hydroxocobalamin Injection	***Currently in Shortage***
Hydroxypropyl (Lacrisert®) Cellulose Ophthalmic Insert	***Currently in Shortage***
Imipenem and Cilastatin for Injection	***Currently in Shortage***
Isoniazid Injection	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) Injection with Epinephrine	***Currently in Shortage***
Lipid Injection	***Currently in Shortage***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***

Mannitol Injection	***Currently in Shortage***
Mepivacaine Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylprednisolone Acetate Injection	***Currently in Shortage***
Midazolam Injection	***Currently in Shortage***
Misoprostol Tablets	***Currently in Shortage***
Morphine Sulfate Injection	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Paclitaxel Injection (protein-bound particles)	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara®) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection	***Currently in Shortage***
Potassium Acetate Injection	***Currently in Shortage***
Potassium Chloride Concentrate Injection	***Currently in Shortage***
Promethazine (Phenergan®) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Protamine Sulfate Injection	***Currently in Shortage***
Rifampin Capsules	***Currently in Shortage***
Rifampin Injection	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac®) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection	***Currently in Shortage***
Sodium Bicarbonate Injection	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***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***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc 99m Sulfur Colloid Injection	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Teprotumumab-trbw	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Tocilizumab Injection	***Currently in Shortage***
Triamcinolone Acetonide Injectable Suspension	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable suspension	***Currently in Shortage***

Trimethobenzamide Hydrochloride Capsules	***Currently in Shortage***
Valproate Sodium Injection	***Currently in Shortage***
Varenicline Tartrate (Chantix®) Tablets	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***
Vitamin A Palmitate (Aquasol A®) Injection	***Currently in Shortage***