OKLAHOMA
Health Care Authority

Drug Utilization Review Board

OHCA Webinar
Wednesday,
February 17, 2021
4:00pm

OHCA Webinar

Please register for the meeting at:
https://zoom.us/j/96869909152?pwd=Q0JOeXZ2VndaQ0RDVzJOemo4UjEwdz09
After registering, you will receive a confirmation email
containing information about joining the webinar.

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 17, 2021

DATE: February 11, 2021

NOTE: In response to COVID-19, the February 2021 DUR Board meeting will be held via OHCA webinar at 4:00pm. Please register for the meeting using the following website address: https://zoom.us/j/96869909152?pwd=Q0JOeXZ2VndaQ0RDVzJOemo4UjEwdz09 After registering, you will receive a confirmation email containing information about joining the webinar.

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

Narrow Therapeutic Index (NTI) Drug List – Appendix B

Update on Medication Coverage Authorization Unit/Montelukast in Allergic Rhinitis Safety Mailing Update – Appendix C

Action Item – Approval of November 2020 DUR Recommendations – Appendix D

Action Item – Approval of December 2020 DUR Recommendations – Appendix E

Action Item – Vote to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe) – Appendix F

Action Item – Vote to Prior Authorize Imcivree™ (Setmelanotide) – Appendix G

Action Item – Vote to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) – Appendix H

Action Item – Vote to Prior Authorize Durysta™ (Bimatoprost Implant) – Appendix I

Action Item – Annual Review of Crysvita® (Burosumab) – Appendix J

Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Inqovi® (Decitabine/Cedzuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx) – Appendix K

Annual Review of Azedra® (Iobenguane) – Appendix L

Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Fintepla® (Fenfluramine) – Appendix M

Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr) – Appendix N

Annual Review of Systemic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System) – Appendix O

30-Day Notice to Prior Authorize Oxlumo® (Lumasiran) – Appendix P

Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Teriparatide – Appendix Q

30-Day Notice to Prior Authorize Zokinvy® (Lonafarnib) – Appendix R

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – February 17, 2021 @ 4:00pm

Oklahoma Health Care Authority (OHCA) Webinar
Please register for the meeting at:
https://zoom.us/j/96869909152?pwd=Q0JOeXZ2VndaQ0RDVzJOemo4UjEwdz09
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AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Wilcox

DUR Board Members:	**Telephone Conference Participants**
Dr. Stephen Anderson –	participating via Zoom teleconference
Dr. Jennifer de los Angeles –	participating via Zoom teleconference
Ms. Jennifer Boyett –	participating via Zoom teleconference
Dr. Markita Broyles –	participating via Zoom teleconference
Dr. Theresa Garton –	participating via Zoom teleconference
Dr. Megan Hanner –	participating via Zoom teleconference
Dr. Lynn Mitchell –	participating via Zoom teleconference
Dr. John Muchmore –	participating via Zoom teleconference
Dr. Lee Muñoz –	participating via Zoom teleconference
Dr. James Osborne –	participating via Zoom teleconference

Public Access to Meeting via Zoom:

Please register for the meeting at:
https://zoom.us/j/96869909152?pwd=Q0JOeXZ2VndaQ0RDVzJOemo4UjEwdz09

Or join by phone:
Dial: +1-213-338-8477 or +1-253-215-8782
Webinar ID: 968 6990 9152
Passcode: 64434335

Public Comment for Meeting:

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing by visiting www.okhca.org/DUR and completing the Speaker Registration Form. Completed Speaker Registration forms should be submitted to *DURPublicComment@okhca.org*. Forms must be received after the DUR Board agenda has been posted and no later than 24 hours before the meeting.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

3. Action Items – Approval of DUR Board Meeting Minutes – See Appendix A

A. **Action Item –** November 4, 2020 DUR Minutes – Vote
B. November 4, 2020 DUR Recommendations Memorandum
C. **Action Item –** December 9, 2020 DUR Minutes – Vote
D. December 9, 2020 DUR Recommendations Memorandum
E. January 13, 2021 DUR Recommendations Memorandum

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

4. Narrow Therapeutic Index (NTI) Drug List – See Appendix B

A. Introduction
B. SoonerCare NTI Drug List

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

5. Update on Medication Coverage Authorization Unit/Montelukast in Allergic Rhinitis Safety Mailing Update – See Appendix C

A. Pharmacy Helpdesk Activity for January 2021
B. Medication Coverage Activity for January 2021
C. Montelukast in Allergic Rhinitis Safety Mailing Update

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

6. Action Items – Approval of November 2020 DUR Recommendations – See Appendix D

A. **Action Item –** Vote to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate), Asmanex® HFA (Mometasone Furoate) 50mcg, and Dulera® (Mometasone/Formoterol) 50mcg/5mcg and to Update the Approval Criteria for Nucala® (Mepolizumab)
    i. New U.S. Food and Drug Administration (FDA) Approval(s)
    ii. New FDA Expanded Indication(s) and/or Formulation(s)
    iii. College of Pharmacy Recommendations
B. **Action Item –** Vote to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)
    i. U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
    ii. Product Summaries
    iii. College of Pharmacy Recommendations
C. **Action Item –** Vote to Prior Authorize Lenvima® (Lenvatinib)
    i. Lenvima® (Lenvatinib) Product Summary
    ii. College of Pharmacy Recommendations

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

7. Action Items – Approval of December 2020 DUR Recommendations – See Appendix E

A. **Action Item –** Vote to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon) and to Update the Approval Criteria for Soliris® (Eculizumab)
    i. New U.S. Food and Drug Administration (FDA) Approval(s)
    ii. College of Pharmacy Recommendations
B. **Action Item –** Vote to Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), and Hulio® (Adalimumab-fkjp) and to Update the Targeted Immunomodulator Agents Tier-2 Approval Criteria and the Approval Criteria for Entyvio® (Vedolizumab), Benlysta® (Belimumab), and Ilaris® (Canakinumab)

i. Introduction
ii. College of Pharmacy Recommendations

C. **Action Item –** Vote to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule]
   i. New U.S. Food and Drug Administration (FDA) Approval(s)
   ii. College of Pharmacy Recommendations
D. **Action Item –** Vote to Prior Authorize Pizensy™ (Lactitol)
   i. Introduction
   ii. College of Pharmacy Recommendations
E. **Action Item –** Vote to Update the Approval Criteria for Spravato® (Esketamine)
   i. New U.S. Food and Drug Administration (FDA) Approval(s)
   ii. College of Pharmacy Recommendations
F. **Action Item –** Vote to Update the Approval Criteria for Bavencio® (Avelumab), Braftovi® (Encorafenib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), and Yervoy® (Ipilimumab)
   i. U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
   ii. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe) – See Appendix F

A. New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
B. Product Summaries
C. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Imcivree™ (Setmelanotide) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) – See Appendix H

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Durysta™ (Bimatoprost Implant) – See Appendix I

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. College of Pharmacy Recommendations

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

12. Action Item – Annual Review of Crysvita® (Burosumab-twza) – See Appendix J

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

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

13. Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Inqovi® (Decitabine/Cedzuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Leukemia Medications
D. Prior Authorization of Leukemia Medications
E. Market News and Updates
F. Product Summaries
G. College of Pharmacy Recommendations
H. Utilization Details of Leukemia Medications

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

14. Annual Review of Azedra® (Iobenguane I-131) – See Appendix L

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Azedra® (Iobenguane I-131)
D. Prior Authorization of Azedra® (Iobenguane I-131)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

15. Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Fintepla® (Fenfluramine) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Anticonvulsants
C. Prior Authorization of Anticonvulsants
D. Market News and Updates
E. Fintepla® (Fenfluramine) Product Summary
F. Cost Comparison: Anticonvulsant Therapies for DS
G. College of Pharmacy Recommendations
H. Utilization Details of Anticonvulsants

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

16. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Migraine Medications

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

17. Annual Review of Systemic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of NSAIDs
C. Prior Authorization of NSAIDs
D. Market News and Updates
E. Product Summaries

F. College of Pharmacy Recommendations
G. Utilization Details of NSAIDs

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

18. 30-Day Notice to Prior Authorize Oxlumo™ (Lumasiran) – See Appendix P

A. Introduction
B. Oxlumo™ (Lumasiran) Product Summary
C. College of Pharmacy Recommendations

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

19. Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Teriparatide – See Appendix Q

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

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

20. 30-Day Notice to Prior Authorize Zokinvy™ (Lonafarnib) – See Appendix R

A. Introduction
B. Market News and Updates
C. Zokinvy™ (Lonafarnib) Product Summary
D. College of Pharmacy Recommendations

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

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

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

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

A. Multiple Sclerosis Medications
B. Hereditary Angioedema (HAE) Medications
C. Granulocyte Colony-Stimulating Factors (G-CSFs)
D. Hemophilia Medications

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

23. Adjournment

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

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING NOVEMBER 4, 2020

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; DUR Manager	x	
Rebekah Bargewell; Administrative Assistant		x
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Andrew Craig; Database Analyst		x
Lisa Daniel, Pharm.D.; Pharmacy Resident	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Mark Fuelling; Client Support Analyst		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Katrina Harris, Pharm.D.; Clinical Pharmacist		x
Robert Klatt, Pharm.D.; Clinical Pharmacist	x	
Amy Miller; Operations Coordinator		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Karen O'Neill, Pharm.D.; Clinical Pharmacist		x
Wynn Phung, Pharm.D.; Clinical Pharmacist		x
Leslie Robinson, D.Ph.; Pharmacy PA Coordinator		x
Vickie Sams, CPhT.; Quality/Training Coordinator	x	
Grant H. Skrepnek, Ph.D.; Associate Professor	x	
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Devin Wilcox, D.Ph.; Pharmacy Director	x	
Justin Wilson, Pharm.D.; Clinical Pharmacist	x	
PA Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		x
Emily Borders, Pharm.D., BCOP	x	
Sarah Schmidt, Pharm.D., BCPS, BCOP		x
Graduate Students: Matthew Dickson, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): N/A		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		x
Ellen Buettner, Chief of Staff		x
Kevin Corbett, C.P.A.; Chief Executive Officer		x
Terry Cothran, D.Ph.; Pharmacy Director	x	
Susan Eads, J.D.; Director of Litigation	x	
Stacey Hale; Drug Rebate Manager		x
Michael Herndon, D.O.; Chief Medical Officer		x
Paula Root, M.D.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Michelle Tahah, Pharm.D.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Senior Medical Director		x
Kerri Wade; Pharmacy Operations Manager	x	

OTHERS PRESENT:	
Bob Atkins, Biogen	Frances Bauman, Novo Nordisk
Jomy Joseph, Sanofi-Genzyme	Tom Telly, Ascendis Pharmaceuticals
David Prather, Novo Nordisk	Denise Capo, Karyopharm Therapeutics
Dennis Liu, Sanofi-Genzyme	Melanie Curlett, Takeda
Travis Cooper, Chiasma Pharmaceuticals	Antrice Kay, Horizon Therapeutics
Cheryl Gay, Genentech	Brent Hildebrand, Gilead
Kevin Duhrkopf, Sanofi-Genzyme	Bobby White, Eisai
Curt Griffith, Horizon Therapeutics	Roxann Dominquez, AbbVie
Mark Kaiser, Otsuka	Ronald Cain, Pfizer
Robert Greely, Biogen	Nima Nabavi, Amgen
Gina Heinen, Novo Nordisk	Doug Wood, ViiV Health Care
Bart Vleugels, ODOT	James Beal, Karyopharm Therapeutics
Rick Andrews, Chiasma Pharmaceuticals	Gloria Ross, OMES
Sieana Mackiewicz, ODOT	

PRESENT FOR PUBLIC COMMENT:	
Brent Hildebrand	Gilead

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

1A: ROLL CALL

Dr. Muchmore called the meeting to order. Roll call by Dr. Wilcox established the presence of a quorum.

ACTION: NONE REQUIRED

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

2A: AGENDA ITEM NO. 8 BRENT HILDEBRAND

ACTION: NONE REQUIRED

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

3A: OCTOBER 14, 2020 DUR MINUTES – VOTE

3B: OCTOBER 14, 2020 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

Dr. Hanner moved to approve; seconded by Dr. Boyett

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: 2021 DUR BOARD MEETING DATES
4A: 2021 DUR BOARD MEETING DATES
Materials included in agenda packet; presented by Dr. Adams
Dr. Muñoz moved to approve; seconded by Dr. Mitchell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS
5A: PHARMACY HELPDESK ACTIVITY FOR OCTOBER 2020
5B: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2020
5C: U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS
Materials included in agenda packet; presented by Dr. Chandler, Dr. Ha
ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE EVRYSDI™ (RISDIPLAM)
6A: INTRODUCTION
6B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Garton moved to approve; seconded by Dr. Hanner
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE TRIKAFTA® (ELEXACAFTOR/TEZACAFTOR/IVACAFTOR AND IVACAFTOR)
7A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE EPCLUSA® (SOFOSBUVIR/VELPATASVIR) 200MG/50MG TABLET
8A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND LABEL UPDATE(S)
8B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Ford
Dr. Garton moved to approve; seconded by Dr. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE CYSTADROPS® (CYSTEAMINE 0.37% OPHTHALMIC SOLUTION) AND CYSTARAN™ (CYSTEAMINE 0.44% OPHTHALMIC SOLUTION)
9A: INTRODUCTION
9B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Dr. Muñoz moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE MYCAPSSA® (OCTREOTIDE)
10A: INTRODUCTION
10B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE ZEJULA® (NIRAPARIB)
11A: MARKET NEWS AND UPDATES
11B: ZEJULA® (NIRAPARIB) PRODUCT SUMMARY
11C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF MULTIPLE MYELOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BLENREP (BELANTAMAB MAFODOTIN-BLMF), DARZALEX® (DARATUMUMAB), DARZALEX FASPRO™ (DARATUMUMAB/HYALURONIDASE-FIHJ), EMPLICITI® (ELOTUZUMAB), HEMADY™ (DEXAMETHASONE 20MG TABLET), NINLARO® (IXAZOMIB), SARCLISA® (ISATUXIMAB-IRFC), AND XPOVIO® (SELINEXOR)
12A: INTRODUCTION
12B: UTILIZATION OF MULTIPLE MYELOMA MEDICATIONS
12C: PRIOR AUTHORIZATION OF MULTIPLE MYELOMA MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: PRODUCT SUMMARIES
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
12G: UTILIZATION DETAILS OF MULTIPLE MYELOMA MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE LENVIMA® (LENVATINIB)
13A: INTRODUCTION
13B: LENVIMA® (LENVATINIB) PRODUCT SUMMARY
13C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AIRDUO® DIGIHALER® (FLUTICASONE PROPIONATE/SALMETEROL), ARMONAIR® DIGIHALER® (FLUTICASONE PROPIONATE), AND BREZTRI AEROSPHERE™ (BUDESONIDE/GLYCOPYRROLATE/ FORMOTEROL FUMARATE)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: AIRDUO® DIGIHALER® (FLUTICASONE PROPIONATE/SALMETEROL) PRODUCT SUMMARY
14F: ARMONAIR® DIGIHALER® (FLUTICASONE PROPIONATE) PRODUCT SUMMARY

14G: BREZTRI AEROSPHERE™ (BUDESONIDE/GLYCOPYRROLATE/ FORMOTEROL) PRODUCT SUMMARY
14H: COLLEGE OF PHARMACY RECOMMENDATIONS
14I: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14J: UTILIZATION DETAILS OF INHALED CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ATOPIC DERMATITIS (AD) MEDICATIONS
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF AD MEDICATIONS
15C: PRIOR AUTHORIZATION OF AD MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF AD MEDICATIONS
Materials included in agenda packet; presented by Dr. Wilson
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

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

AGENDA ITEM NO. 17: ANNUAL REVIEW OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17D: PRIOR AUTHORIZATION OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17E: MARKET NEWS AND UPDATES
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF TEPEZZA® (TEPROTUMUMAB-TRBW)
Materials included in agenda packet; Non-presentation/Questions only
ACTION: NONE REQUIRED

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

<u>AGENDA ITEM NO. 19:</u> **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

19A: NONDISCRIMINATION IN HEALTH CARE COVERAGE ACT

- **i. DISCUSSION OF THE NONDISCRIMINATION IN HEALTH CARE COVERAGE ACT, WHICH BECAME EFFECTIVE ON NOVEMBER 1, 2020 (63 OKLA. STAT. §§2560-2565), AND THE DUR BOARD'S COMPLIANCE THEREWITH.**

19B: UPCOMING PRODUCT AND CLASS REVIEWS*

- **i. TARGETED IMMUNOMODULATOR AGENTS**
- **ii. ANTIDEPRESSANTS**
- **iii. ULCERATIVE COLITIS (UC) AND CROHN'S DISEASE MEDICATIONS**
- **iv. THROMBOCYTOPENIA MEDICATIONS**

**Future business subject to change.*

Materials included in agenda packet; presented by Susan Eads, Dr. Adams

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 20:</u> **ADJOURNMENT**

The meeting was adjourned at 5:37pm.

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

Memorandum

Date: November 5, 2020

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

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

Subject: DUR Board Recommendations from Meeting of November 4, 2020

Recommendation 1: 2021 DUR Meeting Dates

MOTION CARRIED by unanimous approval.

January 13, 2021
February 10, 2021
March 10, 2021
April 14, 2021
May 12, 2021
June 9, 2021
July 14, 2021
August 11, 2021
September 8, 2021
October 13, 2021
November 10, 2021
December 8, 2021

Recommendation 2: U.S. Food and Drug Administration (FDA) Safety Alerts

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Evrysdi™ (Risdiplam)

MOTION CARRIED by unanimous approval.

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

Evrysdi™ (Risdiplam) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in members 2 months of age and older; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Evrysdi™ must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Prescriber must agree to monitor member's liver function prior to initiating Evrysdi™ and periodically while receiving Evrysdi™ treatment; and
6. Pharmacy must confirm Evrysdi™ will be constituted to an oral solution by a pharmacist prior to dispensing and must confirm Evrysdi™ will be shipped via cold chain supply to adhere to the storage and handling requirements in the Evrysdi™ *Prescribing Information*; and
7. Prescriber must confirm the member or caregiver has been counseled on the proper storage of Evrysdi™ and has been instructed on how to prepare the prescribed daily dose of Evrysdi™ prior to administration of the first dose; and
8. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
9. Female members of reproductive potential must be willing to use effective contraception during treatment with Evrysdi™ and for at least 1 month after the last dose; and
10. Prescriber must verify male members of reproductive potential have been counseled on the potential effects on fertility and the potential of compromised male fertility is acceptable; and
11. Member will not be approved for concomitant treatment with Spinraza® (nusinersen); and
12. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
13. A baseline assessment must be provided using a functionally appropriate exam [e.g., Children's Hospital of Philadelphia Infant Test of

Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale Expanded (HFMSE), Hammersmith Infant Neurological Exam (HINE), Upper Limb Module (ULM) Test]; and
14. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is compliant with Evrysdi™ and responding to the medication as demonstrated by clinically significant improvement or maintenance of function from pre-treatment baseline status using the same exam as performed at baseline assessment; and
15. Member's recent weight must be provided to ensure accurate dosing in accordance with Evrysdi™ *Prescribing Information*; and
16. A quantity limit of 240mL per 36 days will apply.

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

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
   a. Type 1; or
   b. Type 2; or
   c. Type 3 with symptoms; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
6. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam); and
7. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing must be conducted at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
8. Spinraza® must be administered in a health care facility by a specialist experienced in performing lumbar punctures; and
   a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
9. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
   a. Hammersmith Infant Neurological Exam (HINE); or

   b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
   c. Upper Limb Module (ULM) Test; or
   d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically-significant improvement or maintenance of function from pretreatment baseline status using the same exam as performed at baseline assessment:
   a. HINE; or
   b. CHOP-INTEND; or
   c. ULM Test; or
   d. HFMSE; and
11. Approval quantity will be based on Spinraza® *Prescribing Information* and FDA approved dosing regimen(s).
   a. Only (1) 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

Zolgensma® (Onasemnogene Abeparvovec-xioi) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in pediatric members younger than 2 years of age; and
2. Member must have reached full-term gestational age prior to Zolgensma® infusion; and
3. Molecular genetic testing to confirm bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene; and
4. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
5. Zolgensma® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
6. Member must have baseline anti-AAV9 antibody titers ≤1:50; and
7. Prescriber must agree to monitor liver function tests, platelet counts, and troponin-I at baseline and as directed by the Zolgensma® *Prescribing Information*; and
8. Prescriber must agree to administer systemic corticosteroids starting 1 day prior to the Zolgensma® infusion and continuing as recommended in the Zolgensma® *Prescribing Information* based on member's liver function; and
9. Zolgensma® must be shipped to the facility where the member is scheduled to receive treatment and must adhere to the storage and handling requirements in the Zolgensma® *Prescribing Information*; and
10. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam) or Spinraza® (nusinersen) following Zolgensma® infusion

(current authorizations for risdiplam or nusinersen will be discontinued upon Zolgensma® approval); and
11. Member's recent weight must be provided to ensure accurate dosing in accordance with Zolgensma® *Prescribing Information*; and
12. Only 1 Zolgensma® infusion will be approved per member per lifetime.

Recommendation 4: Vote to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor)

MOTION CARRIED by unanimous approval.

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

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

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify that member has been counseled on proper administration of Trikafta® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify that the member does not have severe hepatic impairment; and
9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and
10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and

11. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
12. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events than with a previous CFTR therapy must be provided for members who switched from Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor).

Kalydeco® (Ivacaftor) Approval Criteria:

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

Recommendation 5: Vote to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet

MOTION CARRIED by unanimous approval.

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

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

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

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

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

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

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

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

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

8. For members 6 years of age or older who request the oral pellet formulation of Harvoni®, a patient-specific, clinically significant reason to support use of the oral pellet formulation in place of the tablet formulation must be provided; and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
18. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and

21. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.
****The brand formulation of Harvoni® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

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

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

8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
10. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
13. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
~~14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine twice daily equivalent, omeprazole doses >20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses >40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and
17. If member is using antacids, they must agree to separate antacid and Vosevi® administration by 4 hours; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and

21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 6: Vote to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

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

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

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

Recommendation 7: Vote to Prior Authorize Mycapssa® (Octreotide)

MOTION CARRIED by unanimous approval.

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

Mycapssa® (Octreotide) Approval Criteria:

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

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

Recommendation 8: Vote to Prior Authorize Zejula® (Niraparib)

MOTION CARRIED by unanimous approval.

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

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

1. **Single-Agent Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of recurrent or refractory disease; and
    b. Previous treatment with ≥3 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
    c. Diagnosis is associated with homologous recombination deficiency (HRD) positive status defined by either:
        i. A deleterious or suspected deleterious BRCA mutation; or
        ii. Genomic instability and progression >6 months after response to last platinum-based chemotherapy; and
    d. Used as a single-agent; or
2. **Treatment of Advanced Recurrent/Refractory Disease in Combination with Bevacizumab:**
    a. Used in combination with bevacizumab for platinum-sensitive persistent disease or recurrence; and
    b. Meets 1 of the following:
        i. As immediate treatment for serially rising CA-125 in members who previously received chemotherapy, or
        ii. Evidence of radiographic and/or clinical relapse in members with previous complete remission and relapse ≥6 months after completing prior chemotherapy; or
3. **Maintenance Treatment of Advanced Disease:**
    a. Diagnosis of advanced or recurrent disease; and
    b. Disease must be in a complete or partial response to platinum chemotherapy; and
    c. Used as a single-agent.

Additionally, the College of Pharmacy recommends updating the current Mekinist® (trametinib) prior authorization criteria based on NCCN

Compendium approval (changes noted in red in the following approval criteria; only criteria with changes are listed):

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

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

Recommendation 9: Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Lenvima® (Lenvatinib)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Atopic Dermatitis (AD) Medications

MOTION CARRIED by unanimous approval.

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

Eucrisa® (Crisaborole Ointment) Approval Criteria:

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

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

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

6. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Recommendation 13: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Tepezza® (Teprotumumab-trbw)

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 16: Future Business

NO ACTION REQUIRED.

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING DECEMBER 9, 2020

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; DUR Manager	x	
Rebekah Bargewell; Administrative Assistant		x
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Andrew Craig; Database Analyst		x
Lisa Daniel, Pharm.D.; Pharmacy Resident	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Mark Fuelling; Client Support Analyst		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Katrina Harris, Pharm.D.; Clinical Pharmacist		x
Robert Klatt, Pharm.D.; Clinical Pharmacist		x
Amy Miller; Operations Coordinator		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Karen O'Neill, Pharm.D.; Clinical Pharmacist		x
Wynn Phung, Pharm.D.; Clinical Pharmacist		x
Leslie Robinson, D.Ph.; Pharmacy PA Coordinator		x
Vickie Sams, CPhT.; Quality/Training Coordinator	x	
Grant H. Skrepnek, Ph.D.; Associate Professor	x	
Regan Smith, Pharm.D.; Clinical Pharmacist	x	
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Devin Wilcox, D.Ph.; Pharmacy Director	x	
Justin Wilson, Pharm.D.; Clinical Pharmacist	x	
PA Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		x
Emily Borders, Pharm.D., BCOP	x	
Sarah Schmidt, Pharm.D., BCPS, BCOP		x
Graduate Students: Matthew Dickson, Pharm.D.	x	
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): Alicia O'Halloran	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		x
Ellen Buettner, Chief of Staff		x
Kevin Corbett, C.P.A.; Chief Executive Officer		x
Terry Cothran, D.Ph.; Pharmacy Director	x	
Susan Eads, J.D.; Director of Litigation	x	
Michael Herndon, D.O.; Chief Medical Officer		x
Paula Root, M.D.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Michelle Tahah, Pharm.D.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Senior Medical Director		x
Kerri Wade; Pharmacy Operations Manager	x	

OTHERS PRESENT:	
Adrian Nanez, Takeda	Joe Garcia, AbbVie
Aaron Shaw, Boehringer-Ingelheim	Brent Hildebrand, Gilead
Jomy Joseph, Sanofi	Robert Greely, Biogen
Gwendolyn Caldwell, PhRmA	Burl Beasley, OMES
Joe Payne, Viela Bio	Ronald Cain, Pfizer
Tara McKinley, Otsuka	Marc Parker, Sunovion
Evie Knisely, Novartis	China Izatt, Takeda
Tim Grogan, OK Hemophilia Foundation	Matthew Wright, Artia Solutions
Bob Atkins, Biogen	Maureen Mealy, Viela Bio
William Eicholzer, Alexion	Francisco Alvarado, Johnson & Johnson
Jim Chapman, AbbVie	Brent Parker, Merck
Melanie Curlett, Takeda	Jeff Knappen, Spark Therapeutics
Nima Nabavi, Amgen	Donald Nopper, Apellis
Gina Heinen, Novo Nordisk	Kelli Amick, Alexion
Michael Nicholson, Takeda	Mark Kaiser, Otsuka
Deron Grothe, Teva Pharmaceuticals	Kathy Gornatti, Greenwich Biosciences

PRESENT FOR PUBLIC COMMENT:	
N/A	

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

1A: ROLL CALL

Dr. Muchmore called the meeting to order. Roll call by Dr. Wilcox did not establish the presence of a quorum.

ACTION: NONE REQUIRED

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

ACTION: NONE REQUIRED

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

3A: NOVEMBER 4, 2020 DUR MINUTES

3B: NOVEMBER 4, 2020 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Muchmore

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

AGENDA ITEM NO. 4: **MAINTENANCE DRUG LIST**

4A: INTRODUCTION

4B: SOONERCARE MAINTENANCE DRUG LIST

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/PEDIATRIC ANTIPSYCHOTIC MONITORING PROGRAM UPDATE**

5A: PHARMACY HELPDESK ACTIVITY FOR NOVEMBER 2020

5B: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2020

5C: PEDIATRIC ANTIPSYCHOTIC MONITORING PROGRAM UPDATE

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE AIRDUO® DIGIHALER® (FLUTICASONE PROPIONATE/SALMETEROL), ARMONAIR® DIGIHALER® (FLUTICASONE PROPIONATE), AND BREZTRI AEROSPHERE™ (BUDESONIDE/GLYCOPYRROLATE/FORMOTEROL FUMARATE)**

6A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)

6B: NEW FDA EXPANDED INDICATION(S) AND/OR FORMULATION(S)

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE BLENREP (BELANTAMAB MAFODOTIN-BLMF), DARZALEX® (DARATUMUMAB), DARZALEX FASPRO™ (DARATUMUMAB/HYALURONIDASE-FIHJ), EMPLICITI® (ELOTUZUMAB), HEMADY™ (DEXAMETHASONE 20MG TABLET), NINLARO® (IXAZOMIB), SARCLISA® (ISATUXIMAB-IRFC), AND XPOVIO® (SELINEXOR)**

7A: U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND INDICATION(S)

7B: PRODUCT SUMMARIES

7C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE LENVIMA® (LENVATINIB)**

8A: LENVIMA® (LENVATINIB) PRODUCT SUMMARY

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

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
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

AGENDA ITEM NO. 10: ANNUAL REVIEW OF ANTIDEPRESSANTS
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF ANTIDEPRESSANTS
10C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS
10D: MARKET NEWS AND UPDATES
10E: COLLEGE OF PHARMACY RECOMMENDATIONS
10F: UTILIZATION DETAILS OF ANTIDEPRESSANTS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

AGENDA ITEM NO. 11: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ABRILADA™ (ADALIMUMAB-AFZB), AVSOLA™ (INFLIXIMAB-AXXQ), AND HULIO® (ADALIMUMAB-FKJP)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS
11C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
11F: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF SOLIRIS® (ECULIZUMAB) AND ULTOMIRIS® (RAVULIZUMAB-CWVZ) AND 30-DAY NOTICE TO PRIOR AUTHORIZE ENSPRYNG™ (SATRALIZUMAB-MWGE) AND UPLIZNA™ (INEBILIZUMAB-CDON)
12A: INTRODUCTION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF SOLIRIS® (ECULIZUMAB) AND ULTOMIRIS® (RAVULIZUMAB-CWVZ)
12D: PRIOR AUTHORIZATION OF SOLIRIS® (ECULIZUMAB) AND ULTOMIRIS® (RAVULIZUMAB-CWVZ)
12E: MARKET NEWS AND UPDATES
12F: ENSPRYNG™ (SATRALIZUMAB-MWGE) PRODUCT SUMMARY
12G: UPLIZNA™ (INEBILIZUMAB-CDON) PRODUCT SUMMARY
12H: COLLEGE OF PHARMACY RECOMMENDATIONS
12I: UTILIZATION DETAILS OF SOLIRIS® (ECULIZUMAB) AND ULTOMIRIS® (RAVULIZUMAB-CWVZ)
Materials included in agenda packet; presented by Dr. Ha
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF ULCERATIVE COLITIS (UC) AND CROHN'S DISEASE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ORTIKOS™ [BUDESONIDE EXTENDED-RELEASE (ER) CAPSULE]
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF UC AND CROHN'S DISEASE MEDICATIONS
13C: PRIOR AUTHORIZATION OF UC AND CROHN'S DISEASE MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: ORTIKOS™ (BUDESONIDE ER CAPSULE) PRODUCT SUMMARY

13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF UC AND CROHN'S DISEASE MEDICATIONS
Materials included in agenda packet; presented by Dr. Wilson
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PIZENSY™ (LACTITOL)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
14C: PRIOR AUTHORIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: PIZENSY™ (LACTITOL) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF CONSTIPATION MEDICATIONS
14H: UTILIZATION DETAILS OF DIARRHEA MEDICATIONS
Materials included in agenda packet; presented by Dr. Daniel
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF THROMBOCYTOPENIA MEDICATIONS
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF THROMBOCYTOPENIA MEDICATIONS
15C: PRIOR AUTHORIZATION OF THROMBOCYTOPENIA MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF THROMBOCYTOPENIA MEDICATIONS
Materials included in agenda packet; Non-presentation/Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (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 MEETING SCHEDULED FOR JANUARY 2021. JANUARY 2021 WILL BE A PACKET ONLY MEETING.
17A: ANTIVIRAL MEDICATIONS
17B: GLAUCOMA MEDICATIONS
17C: GONADOTROPIN-RELEASING HORMONE (GNRH) MEDICATIONS
17D: HYPERLIPIDEMIA MEDICATIONS
*Future product and class reviews subject to change.
Materials included in agenda packet; Non-presentation/Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ADJOURNMENT
The meeting was adjourned at 5:30pm.

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

Memorandum

Date: December 11, 2020

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

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

Subject: DUR Board Recommendations from Meeting of December 9, 2020

Recommendation 1: Maintenance Drug List

NO ACTION REQUIRED.

Recommendation 2: Pediatric Antipsychotic Monitoring Program Update

NO ACTION REQUIRED.

Recommendation 3: Prior Authorization of AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

VOTE ITEM AT FEBRUARY MEETING

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

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

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why the member requires AirDuo® Digihaler® over AirDuo RespiClick® and all preferred Tier-1 inhaled corticosteroid and long-acting beta2-agonist (ICS/LABA) products (Advair®, Dulera®, and Symbicort®) must be provided; and
4. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member must be provided; and
5. Member must have used an ICS for at least 1 month immediately prior; and
6. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
7. A clinical situation warranting initiation with combination therapy due to severity of asthma; and
8. The prescriber agrees to closely monitor member adherence; and
9. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
10. The member's phone camera must be functional and able to scan the inhaler QR code and register the AirDuo® Digihaler® inhaler; and
11. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

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

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) or other preferred monotherapy inhaled corticosteroid (ICS) is not appropriate for the member must be provided; and
4. The prescriber agrees to closely monitor member adherence; and
5. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
6. The member's phone camera must be functional and able to scan the inhaler QR code and register the ArmonAir® Digihaler® inhaler; and

7. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

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

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

1. An FDA approved diagnosis ~~of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in patients with a history of exacerbations~~; and
2. Member must be 18 years of age or older; and
3. A 4-week trial of at least 1 long-acting beta2 agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
4. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA must be provided.

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

1. An FDA approved diagnosis of hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause; and
2. Member must be 12 years of age or older; and
3. Member must have a past history of at least 2 confirmed HES flares [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of cytotoxic or immunosuppressive therapy, or hospitalization] within the past 12 months; and
4. Member must have a baseline blood eosinophil count of 1,000 cells/mcL or higher in the last 4 weeks prior to initiating Nucala®; and
5. Diagnosis of FIP1L1-PDGFRα kinase-positive HES will not be approved; and
6. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥10mg/day) for a minimum of 4 weeks duration or member is unable to tolerate corticosteroid therapy due to significant side effects from glucocorticoid therapy; and

7. Nucala® must be prescribed by a hematologist or a specialist with expertise in treatment of HES (or an advanced care practitioner with a supervising physician who is a hematologist or a specialist with expertise in treatment of HES); and
8. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
9. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
10. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by fewer HES flares from baseline or a decrease in daily OCS dosing from baseline.

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

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

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

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

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

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

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

Recommendation 4: Prior Authorization of Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

VOTE ITEM AT FEBRUARY MEETING

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

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

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

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

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

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
    a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
    b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
    c. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or
    d. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or
    e. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or
    f. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or
    g. As a single-agent in members who have received ≥3 prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.

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

1. Diagnosis of multiple myeloma; and
2. Used in 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 and dexamethasone in members who have received at least 1 prior therapy; or
    d. As a single-agent in members who have received ≥3 prior therapies, including a proteasome inhibitor (PI) and an immunomodulatory agent, or in members who are double refractory to a PI and an immunomodulatory agent.

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

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

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

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

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

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

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

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

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

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

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

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

Recommendation 5: Prior Authorization of Lenvima® (Lenvatinib)

VOTE ITEM AT FEBRUARY MEETING

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

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

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

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

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

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

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

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

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

Recommendation 6: Annual Review of Skin Cancer Medications

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Antidepressants

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), and Hulio® (Adalimumab-fkjp)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz) and 30-Day Notice to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Ulcerative Colitis (UC) and Crohn's Disease Medications and 30-Day Notice to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule]

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Pizensy™ (Lactitol)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Thrombocytopenia Medications

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 14: Future Business

No live DUR meeting is scheduled for January 2021. January 2021 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 15, 2021

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

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

Subject: DUR Board Recommendations from Packet Meeting of January 13, 2021

Recommendation 1: SoonerCare Opioid Initiative Update

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Gonadotropin Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix)

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Hyperlipidemia Medications and 30-Day Notice to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Durysta™ (Bimatoprost Implant)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Antiviral Medications

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Korlym® (Mifepristone)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Turalio® (Pexidartinib)

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 9: 30-Day Notice to Prior Authorize Imcivree™ (Setmelanotide)

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

Narrow Therapeutic Index (NTI) Drug List

Oklahoma Health Care Authority
February 2021

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.

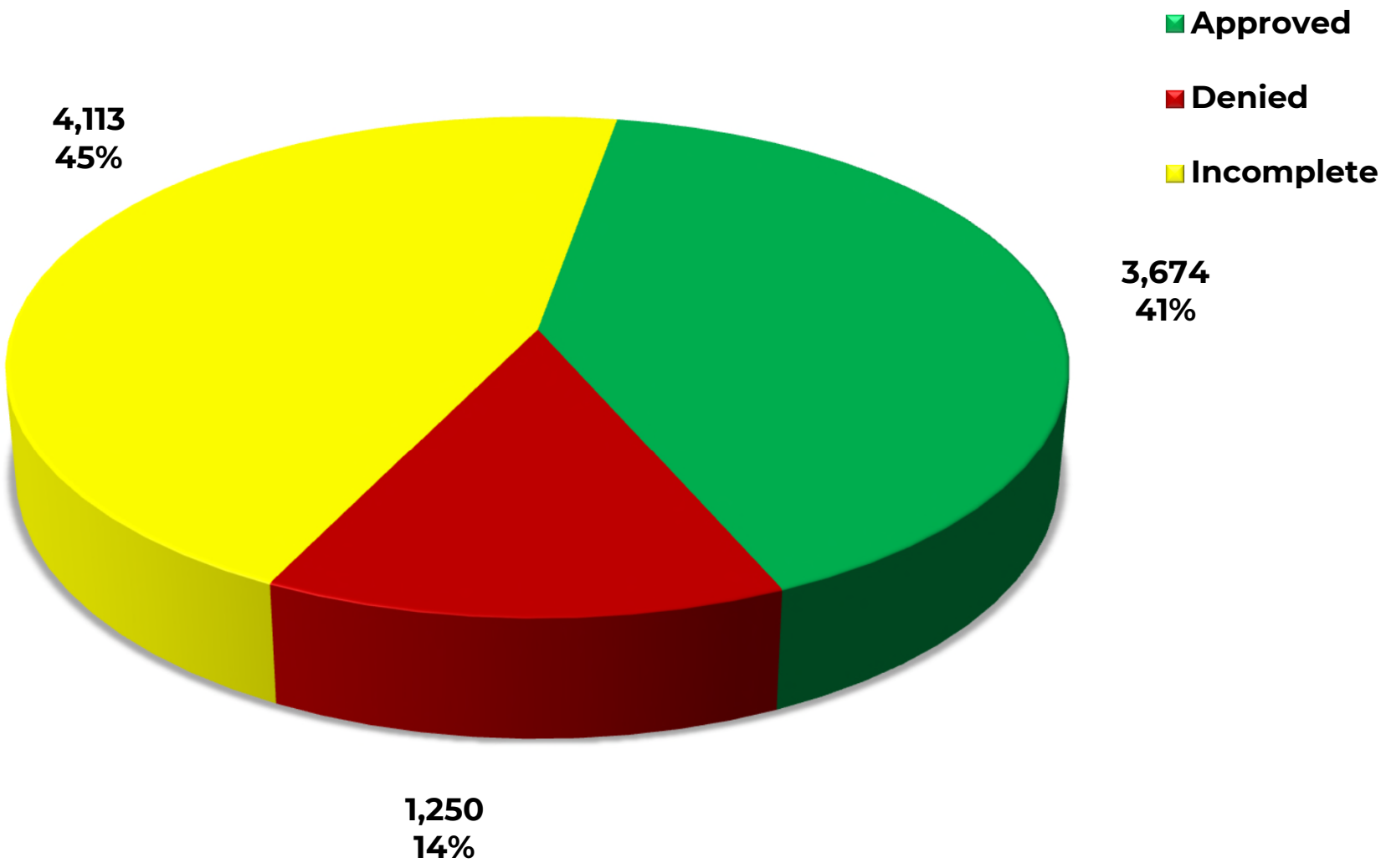
SoonerCare NTI Drug List

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

[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 01/21/2021.
[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 01/21/2021.
[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 01/21/2021.

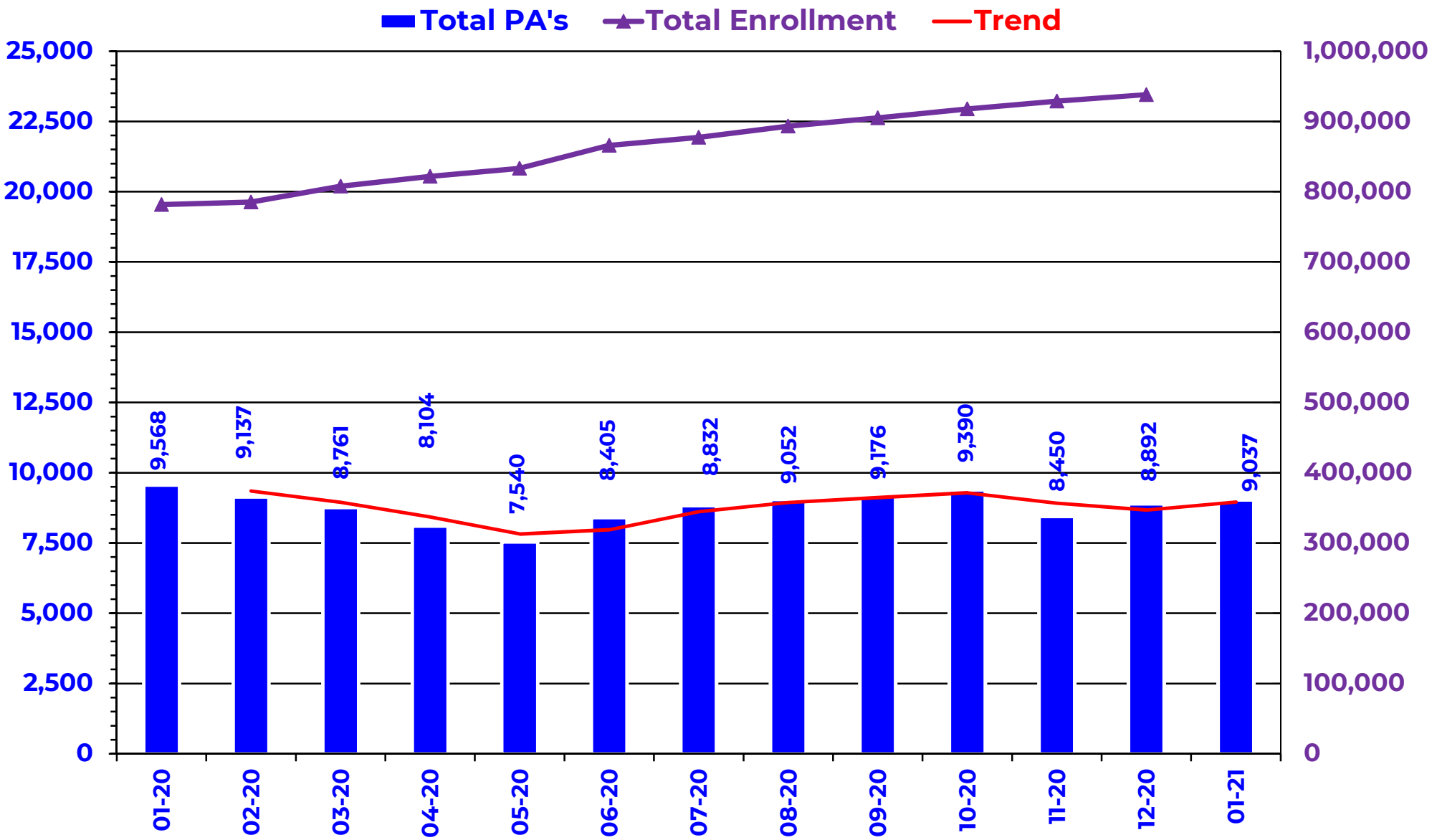
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY 2021



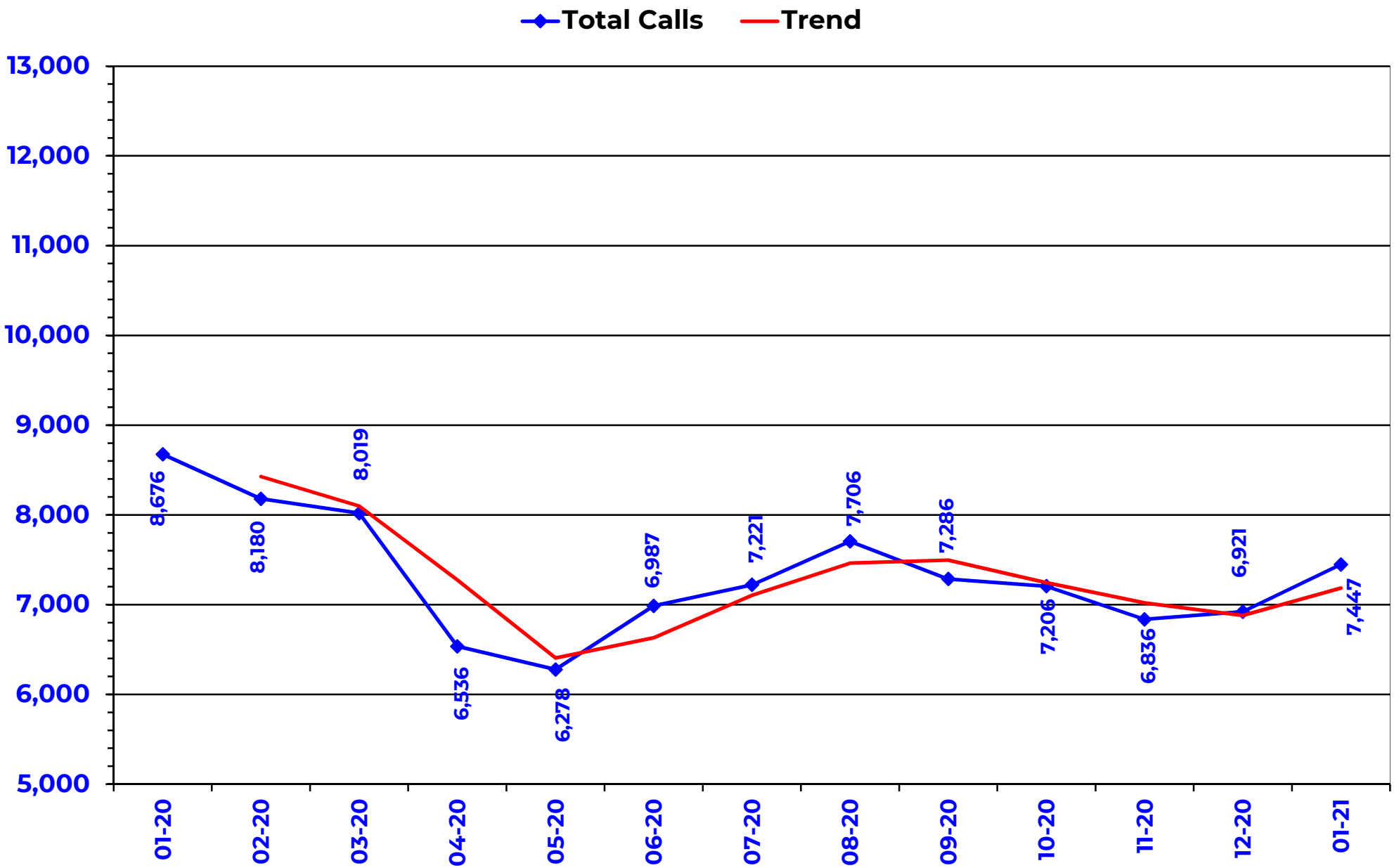
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2020 – JANUARY 2021



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: JANUARY 2020 – JANUARY 2021



Prior Authorization Activity

1/1/2021 Through 1/31/2021

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	81	9	10	62	359
Analgesic - NonNarcotic	20	1	7	12	358
Analgesic, Narcotic	386	132	39	215	156
Angiotensin Receptor Antagonist	16	3	3	10	360
Antiasthma	47	16	13	18	228
Antibiotic	56	25	3	28	108
Anticonvulsant	173	71	12	90	304
Antidepressant	189	35	31	123	322
Antidiabetic	344	123	41	180	355
Antigout	13	5	2	6	359
Antihemophilic Factor	10	5	0	5	358
Antihistamine	43	16	8	19	306
Antimigraine	236	36	70	130	210
Antineoplastic	91	60	2	29	149
Antiulcers	64	8	11	45	137
Anxiolytic	32	1	4	27	357
Atypical Antipsychotics	310	123	33	154	347
Biologics	192	85	29	78	276
Bladder Control	49	10	21	18	358
Blood Thinners	339	175	25	139	331
Botox	58	25	23	10	316
Buprenorphine Medications	210	21	11	178	85
Cardiovascular	84	37	5	42	301
Chronic Obstructive Pulmonary	195	26	52	117	358
Constipation/Diarrhea	167	16	64	87	255
Contraceptive	31	12	7	12	334
Dermatological	303	89	63	151	147
Diabetic Supplies	774	425	70	279	226
Endocrine & Metabolic Drugs	83	42	7	34	204
Erythropoietin Stimulating	14	8	1	5	104
Fibromyalgia	1	0	0	1	0
Fish Oils	24	4	5	15	359
Gastrointestinal Agents	110	19	32	59	189
Genitourinary Agents	12	1	4	7	357
Glaucoma	25	8	2	15	97
Growth Hormones	124	74	20	30	154
Hematopoietic Agents	13	3	3	7	84
Hepatitis C	138	73	17	48	9

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Insomnia	46	2	8	36	174
Insulin	142	33	19	90	358
Miscellaneous Antibiotics	18	2	3	13	20
Multiple Sclerosis	46	12	11	23	217
Muscle Relaxant	54	8	17	29	130
Nasal Allergy	78	10	23	45	173
Neurological Agents	91	15	38	38	195
Neuromuscular Agents	14	6	5	3	295
NSAIDs	36	1	8	27	79
Ocular Allergy	13	0	3	10	0
Ophthalmic	15	1	7	7	358
Ophthalmic Anti-infectives	15	6	1	8	16
Osteoporosis	13	7	4	2	358
Other*	335	76	71	188	235
Otic Antibiotic	22	0	3	19	0
Pediculicide	22	4	0	18	8
Prenatal Vitamins	12	0	0	12	0
Respiratory Agents	28	17	2	9	235
Statins	23	2	8	13	84
Stimulant	791	297	69	425	346
Synagis	113	63	8	42	76
Testosterone	66	16	18	32	306
Topical Antifungal	32	2	11	19	11
Topical Corticosteroids	77	1	56	20	83
Vitamin	72	15	36	21	242
Pharmacotherapy	68	58	1	9	257
Emergency PAs	0	0	0	0	
Total	7,315	2,476	1,182	3,657	

Overrides					
Brand	29	14	2	13	280
Compound	7	5	0	2	149
Diabetic Supplies	9	7	0	2	112
Dosage Change	293	265	0	28	12
High Dose	4	3	0	1	144
Lost/Broken Rx	70	64	2	4	16
MAT Override	296	204	3	89	67
NDC vs Age	278	155	29	94	237
NDC vs Sex	6	4	1	1	82
Nursing Home Issue	31	29	0	2	14
Opioid MME Limit	90	40	4	46	110
Other*	61	58	0	3	14

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Prescriber Temp Unlock	1	1	0	0	360
Quantity vs. Days Supply	453	283	25	145	223
STBS/STBSM	16	7	1	8	74
Step Therapy Exception	2	1	0	1	358
Stolen	13	12	0	1	13
Third Brand Request	34	23	0	11	13
Overrides Total	**1,722**	**1,198**	**68**	**456**	
Total Regular PAs + Overrides	**9,037**	**3,674**	**1,250**	**4,113**	

Denial Reasons	
Unable to verify required trials.	3,294
Does not meet established criteria.	1,280
Lack required information to process request.	775
Other PA Activity	
Duplicate Requests	806
Letters	16,790
No Process	4
Changes to existing PAs	750
Helpdesk Initiated Prior Authorizations	717
PAs Missing Information	4

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

Montelukast in Allergic Rhinitis Safety Mailing Update

Oklahoma Health Care Authority
February 2021

Introduction[1]

In March 2020, the U.S Food and Drug Administration (FDA) issued a Drug Safety Communication about serious mental health side effects with montelukast and advised restricting use for allergic rhinitis (AR). The *Prescribing Information* for montelukast already included warnings about mental health side effects; however, many providers and patients may not be aware of this risk. Mental health side effects that have been reported to the FDA Adverse Event Reporting System (FAERS) database include agitation, bad or vivid dreams, depression, hallucinations, irritability, restlessness, and suicidal thoughts and actions.

Due to the wide availability of other safe and effective allergy medications, the FDA decided to strengthen the warnings for montelukast. The FDA is requiring a *Boxed Warning* in the *Prescribing Information* for montelukast (Singulair®) to describe the serious mental health side effects and to limit its use to treat AR in patients who are not effectively treated or who cannot tolerate other allergy medications. The FDA is also requiring a new patient *Medication Guide* to educate patients about these risks.

SoonerCare Action

The Oklahoma Health Care Authority (OHCA) is engaged in an effort to ensure the quality of care for SoonerCare members initiating and continuing treatment with montelukast (Singulair®) for AR. The goal is to minimize the risk of serious mental health side effects associated with montelukast by limiting its use for AR.

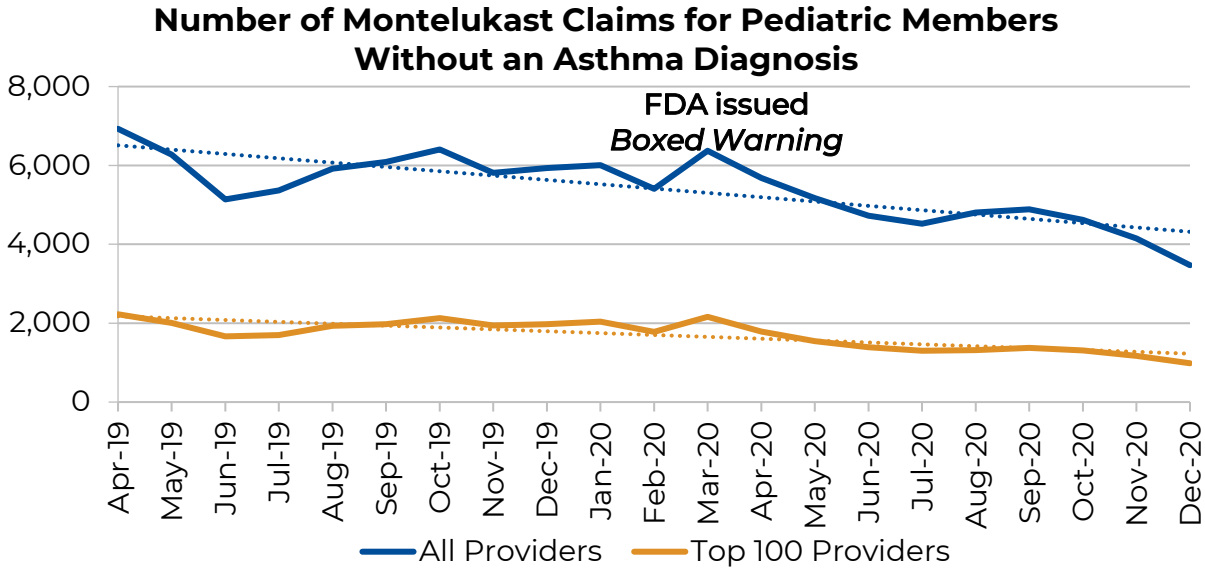
In June 2020, the College of Pharmacy provided a targeted mailing to SoonerCare providers to inform them of the montelukast safety update from the FDA, along with recommendations on alternative medications for the treatment of AR and counseling about potential mental health side effects. Also included in the mailing was a list of the provider's pediatric members who received at least 1 claim for montelukast and who did not have an asthma diagnosis.

Additionally, based on the new *Boxed Warning,* the College of Pharmacy recommended an update to the prior authorization criteria for the allergen

immunotherapies to remove the montelukast trial requirement. This requirement was removed for Grastek®, Oralair®, Ragwitek®, and Odactra®.

SoonerCare Update

From April 2019 to December 2020, there were 113,685 montelukast claims for 28,300 unique pediatric members without an asthma diagnosis from 3,002 unique providers. Targeted mailings were sent to the top 100 providers based of the total number of unique members utilizing montelukast without an asthma diagnosis; the targeted mailing included 7,978 unique pediatric members. The following chart shows a comparison in the total number of claims between all providers and the top 100 providers that received the mailings.



The number of claims for montelukast has significantly decreased in both groups since the FDA issued the *Boxed Warning* in March 2020. For the top 100 providers, there was a 55% decrease in the number of montelukast claims when comparing claims from March 2020 and December 2020 (2,165 claims vs. 984 claims).

The College of Pharmacy will continue to monitor montelukast utilization in members who do not have a diagnosis of asthma and will provide additional educational mailings to providers as appropriate. Further, the College of Pharmacy will continue to work with OHCA to improve the quality of care for SoonerCare members.

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[1] U.S. Food and Drug Administration (FDA). FDA Requires Boxed Warning About Serious Mental Health Side Effects for Asthma and Allergy Drug Montelukast (Singulair); Advises Restricting Use For Allergic Rhinitis. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-boxed-warning-about-serious-mental-health-side-effects-asthma-and-allergy-drug. Issued 03/04/2020. Last accessed 01/08/2021.

Appendix D

Vote to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

Oklahoma Health Care Authority
February 2021

New U.S. Food and Drug Administration (FDA) Approval(s)[1,2,3,4,5,6]

- **AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder)**, a combination therapy digital inhaler with built-in sensors that connects to a companion mobile application (app) to provide information on inhaler use to patients with asthma, was FDA approved in July 2019. AirDuo® Digihaler® is indicated for the treatment of asthma in patients 12 years of age and older. AirDuo® Digihaler® is not indicated for the relief of acute bronchospasm. AirDuo® Digihaler® contains a built-in electronic module which detects, records, and stores data on inhaler events for transmission to a mobile app. Use of the mobile app is not required for administration of medication to the patient. The starting dosage is based on prior asthma therapy and disease severity. The recommended dose is 1 inhalation of AirDuo® Digihaler® 55/14mcg, 113/14mcg, or 232/14mcg twice daily. The approval of AirDuo® Digihaler® is based on the review of the supplemental New Drug Application (sNDA) submitted by Teva to the FDA, and efficacy was based primarily on the dose-ranging trials and the confirmatory trials for AirDuo RespiClick®. AirDuo® Digihaler® was approved in a low, medium, and high dose (55/14mcg, 113/14mcg, and 232/14mcg). As a fixed dose combination asthma therapy containing an inhaled corticosteroid (ICS) and a long-acting beta$_2$ agonist (LABA), AirDuo® Digihaler® contains the same active ingredients as Advair Diskus®, which is also approved in low, medium, and high doses: 100/50mcg, 250/50mcg, and 500/50mcg. The annual estimated cost for AirDuo® Digihaler® is $5,388.00.
- **ArmonAir® Digihaler® (fluticasone propionate inhalation powder)**, an ICS delivered via Teva's Digihaler® device (*refer to AirDuo® Digihaler® above for additional information on the Digihaler® device*) was FDA approved in February 2020. ArmonAir® Digihaler® is indicated for the maintenance treatment of asthma in patients 12 years of age and older. ArmonAir® Digihaler® is not indicated for the relief of acute bronchospasm. The starting dose of ArmonAir® Digihaler® is based on prior asthma therapy and disease severity. The recommended treatment of asthma in patients 12 years of age and older is 1 inhalation

of ArmonAir® Digihaler® 55mcg, 113mcg, or 232mcg twice daily. ArmonAir® Digihaler® should not be used with a spacer or volume holding chamber. The approval of ArmonAir® Digihaler® is based on the review of the sNDA submitted by Teva to the FDA, and efficacy was based primarily on the dose-ranging trials and the confirmatory trials for ArmonAir™ RespiClick®. ArmonAir® Digihaler® was approved in a low, medium, and high dose (55mcg, 113mcg, and 232mcg). The annual estimated cost of ArmonAir® Digihaler® is $3,588.00.

- **Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol)** was FDA approved in July 2020 for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Breztri Aerosphere™ is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Breztri Aerosphere™ is supplied as an inhalation aerosol pressurized metered dose inhaler (MDI) containing 160mcg budesonide/9mcg glycopyrrolate/4.8mcg formoterol fumarate per actuation. The recommended dosage of Breztri Aerosphere™ for the maintenance treatment of COPD is 2 inhalations twice daily. The FDA approval was based on positive results from the Phase 3 ETHOS trial in which Breztri Aerosphere™, a triple-combination therapy, showed a statistically significant reduction in the rate of moderate or severe exacerbations compared with dual-combination therapies glycopyrrolate/formoterol fumarate and PT009 (budesonide/formoterol fumarate). The approval was also supported by efficacy and safety data from the Phase 3 KRONOS trial. Results from the Phase 3 ETHOS trial were published in *The New England Journal of Medicine* in June 2020 and results from the Phase 3 KRONOS trial were published in *The Lancet Respiratory Medicine* in September 2018. In both trials, the safety and tolerability of Breztri Aerosphere™ were consistent with the profiles of the dual comparators. The estimated annual cost of Breztri Aerosphere™ is $7,084.80.

New FDA Expanded Indication(s) and/or Formulation(s)[7,8,9,10,11,12,13,14]

- **Dulera® (mometasone/formoterol inhalation aerosol)** was approved by the FDA in August 2019 for a new strength, 50mcg/5mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on findings from a trial evaluating the efficacy of Dulera® 50mcg/5mcg in pediatric patients 5 years of age to younger than 12 years of age compared with mometasone furoate MDI 50mcg. Patients included in the trial were adequately controlled on an ICS/LABA for at least 4 weeks and had no symptoms of asthma worsening during a 2-week run-in on mometasone furoate MDI 50mcg. Results showed that patients on Dulera® 50mcg/5mcg had a statistically significant change from baseline to week 12 in 60-minute

morning post-dose percent predicted forced expiratory volume per 1 second ($ppFEV_1$) compared with mometasone furoate MDI 50mcg [primary end point: 5.21; 95% confidence interval (CI): 3.22, 7.20]. With regard to safety, patients in this age group demonstrated safety results similar to those seen in patients 12 years of age and older. Dulera® was previously FDA approved for patients 12 years of age and older and is also available as 100mcg/5mcg and 200mcg/5mcg strengths.

- **Asmanex® HFA (mometasone furoate)** was FDA approved in August 2019 for a new strength, 50mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on data from a 12-week, double-blind, placebo-controlled study in 583 patients 5 years of age to younger than 12 years of age with persistent asthma (mean baseline FEV_1: 79% of predicted) who had been using a low-to-medium dose of an ICS with or without a LABA for at least 12 weeks prior to study entry. After an approximate 2-week run-in period, patients were randomized to receive Asmanex® HFA 50mcg, 2 other doses of Asmanex® HFA, Asmanex® dry-powder inhaler (DPI), or placebo. Results showed that after 12 weeks of treatment, Asmanex® HFA 50mcg was statistically superior to placebo as measured by improvement from baseline in morning pre-dose $ppFEV_1$ at the end of the dosing interval (primary end point: 6.29%; 95% CI: 3.05, 9.53). The safety profile and overall effectiveness in this age group were consistent with that observed in patients 12 years of age and older who also received Asmanex® HFA. Asmanex® HFA was previously FDA approved for patients 12 years of age and older and is also available as 100mcg and 200mcg strengths.
- **Nucala® (mepolizumab)** was FDA approved in September 2020 for adults and children 12 years of age and older with hypereosinophilic syndrome (HES) for 6 months or longer without another identifiable non-blood related cause of the disease. The new indication for Nucala® is the first FDA approval for HES patients in nearly 14 years. HES is a heterogeneous group of rare disorders associated with persistent eosinophilia with evidence of organ damage. HES is defined as an absolute eosinophil count (AEC) >1,500cells/mcL in the peripheral blood on 2 examinations separated in time by at least 1 month and/or pathologic confirmation of tissue hypereosinophilia (HE). Symptoms of HES include skin rashes, itching, asthma, difficulty breathing, abdominal pain, vomiting, diarrhea, arthritis, muscle inflammation, congestive heart failure, deep venous thrombosis (DVT), and anemia. Nucala® was evaluated in a randomized, double-blind, multicenter, placebo-controlled trial in 108 patients with HES. Patients entering the trial had experienced at least 2 HES flares within the past 12 months and had a blood eosinophil count of ≥1,000cells/mcL during screening. In the trial, patients were randomly assigned to receive Nucala® or

placebo by injection every 4 weeks. The trial compared the proportion of patients who experienced a HES flare during the 32-week treatment period. An HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils on at least 2 occasions. The trial compared the proportion of patients with at least 1 flare over a 32-week treatment period, as well as the time to the first flare. Fewer patients in the Nucala® treatment group (28%) had HES flares compared to patients in the placebo group (56%), with a 50% relative reduction. In addition, the time to the first HES flare was later, on average, for patients treated with Nucala® vs. placebo. Nucala® is also FDA approved for patients 6 years of age and older with severe asthma with an eosinophilic phenotype and for adult patients with eosinophilic granulomatosis with polyangiitis (EGPA), a rare autoimmune condition that causes blood vessel inflammation.

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

Recommendations

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

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

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why the member requires AirDuo® Digihaler® over AirDuo RespiClick® and all preferred Tier-1 inhaled corticosteroid and long-acting beta$_2$-agonist (ICS/LABA) products (Advair®, Dulera®, and Symbicort®) must be provided; and
4. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member must be provided; and
5. Member must have used an ICS for at least 1 month immediately prior; and

6. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
7. A clinical situation warranting initiation with combination therapy due to severity of asthma; and
8. The prescriber agrees to closely monitor member adherence; and
9. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
10. The member's phone camera must be functional and able to scan the inhaler QR code and register the AirDuo® Digihaler® inhaler; and
11. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

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

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

Additionally, the College of Pharmacy recommends the prior authorization of Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) and recommends updating the current approval criteria for Trelegy Ellipta

(fluticasone furoate/umeclidinium/vilanterol) and Nucala® (mepolizumab) based on the newly FDA approved indications, with the following criteria (new criteria and changes are shown in red):

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

1. An FDA approved diagnosis ~~of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in patients with a history of exacerbations~~; and
2. Member must be 18 years of age or older; and
3. A 4-week trial of at least 1 long-acting $beta_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
4. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of an ICS/LABA combination product with a LAMA must be provided.

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

1. An FDA approved diagnosis of hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause; and
2. Member must be 12 years of age or older; and
3. Member must have a past history of at least 2 confirmed HES flares [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of cytotoxic or immunosuppressive therapy, or hospitalization] within the past 12 months; and
4. Member must have a baseline blood eosinophil count of ≥1,000 cells/mcL in the last 4 weeks prior to initiating Nucala®; and
5. A diagnosis of FIP1L1-PDGFRα kinase-positive HES will not be approved; and
6. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥10mg/day) for a minimum of 4 weeks duration or member is unable to tolerate corticosteroid therapy due to significant side effects from corticosteroid therapy; and
7. Nucala® must be prescribed by a hematologist or a specialist with expertise in treatment of HES (or an advanced care practitioner with a supervising physician who is a hematologist or a specialist with expertise in treatment of HES); and
8. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or

9. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
10. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by fewer HES flares from baseline or by a decrease in daily OCS dosing from baseline.

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

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

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

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

1. An FDA approved diagnosis of asthma; and
2. Member must be ~~4 years of age or older~~ at the age indicated for the requested product:

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

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

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

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Vote to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

Oklahoma Health Care Authority
February 2021

Introduction[1,2,3,4]

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

- **November 2015:** The FDA approved Ninlaro® (ixazomib) for use in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.
- **November 2015:** The FDA approved Empliciti® (elotuzumab) for use in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received 1 to 3 prior therapies.
- **June 2019:** The FDA approved Darzalex® (daratumumab) for intravenous (IV) use in combination with lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).
- **July 2019:** The FDA granted accelerated approval to Xpovio® (selinexor) for use in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received ≥4 prior therapies and whose disease is refractory to ≥2 proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-cluster of differentiation 38/cyclic adenosine diphosphate ribose hydrolase (anti-CD38) monoclonal antibody.
- **September 2019:** The FDA approved Darzalex® (daratumumab) for the treatment of adult patients with multiple myeloma for use in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT.
- **October 2019:** The FDA approved Hemady™ (dexamethasone 20mg tablet) for use in combination with other anti-myeloma therapies for the treatment of adult patients with multiple myeloma.

- **March 2020:** The FDA approved Sarclisa® (isatuximab-irfc) for use in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI.
- **May 2020:** The FDA approved Darzalex Faspro™ (daratumumab/hyaluronidase-fihj) for the treatment of adult patients with newly diagnosed RRMM. This new product allows for subcutaneous (sub-Q) dosing of daratumumab.
- **June 2020:** The FDA granted accelerated approval to Xpovio® (selinexor) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy.
- **August 2020:** The FDA approved Blenrep (belantamab mafodotin-blmf) for the treatment of adult patients with RRMM who have received ≥4 prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an immunomodulatory agent.
- **August 2020:** The FDA approved Kyprolis® (carfilzomib) and Darzalex® (daratumumab) in combination with dexamethasone for the treatment of adult patients with RRMM who have received 1 to 3 prior therapies.
- **December 2020:** The FDA approved Xpovio® (selinexor) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.
- **January 2021:** The FDA granted accelerated approval to Darzalex Faspro™ (daratumumab/hyaluronidase-fihj) in combination with bortezomib, cyclophosphamide, and dexamethasone for newly diagnosed light chain amyloidosis.

Guideline Update(s): The latest revisions to the National Comprehensive Cancer Network (NCCN) Guidelines for the treatment of multiple myeloma indicate that the daratumumab IV and sub-Q formulations can be used interchangeably. The dosing and administration instructions differ but where daratumumab is recommended, either product can be selected. Additionally, the guidelines included an updated indication for daratumumab to include the treatment of light chain amyloidosis in the first-line and refractory/relapsed settings. The final revision allows for the combination of daratumumab, bortezomib, cyclophosphamide, and dexamethasone to be considered as an alternative to other regimens in previously treated myeloma patients.

Product Summaries[5,6,7,8,9,10,11]

Blenrep (Belantamab Mafodotin-blmf):

- **Therapeutic Class:** B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate

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

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

Darzalex® (Daratumumab):

- **Therapeutic Class:** CD38-directed cytolytic antibody
- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
  - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
  - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
  - In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT
  - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
  - In combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior therapies
  - In combination with pomalidomide and dexamethasone in patients who have received ≥2 prior therapies including lenalidomide and a PI

    - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- **How Supplied:** 100mg/5mL and 400mg/20mL solution in SDVs
- **Dose:** 16mg/kg (based on actual body weight) administered via IV infusion; dosing schedule varies based on regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $111.14 per milliliter (mL), resulting in a cost of $555.70 per 100mg/5mL SDV and $2,222.80 per 400mg/20mL SDV; cost will vary due to weight-based dosing and dosing regimen

Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj):

- **Therapeutic Class:** Combination of a CD38-directed cytolytic antibody (daratumumab) and an endoglycosidase (hyaluronidase)
- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
    - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
    - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
    - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
    - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
    - In combination with bortezomib, cyclophosphamide, and dexamethasone in newly diagnosed light chain amyloidosis (this indication is approved under accelerated approval based on response rate; continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial)
- **How Supplied:** 1,800mg daratumumab/30,000 units hyaluronidase/15mL (120mg/2,000 units/mL) solution in SDVs
- **Dose:** 1,800mg/30,000 units via sub-Q injection over 3 to 5 minutes; dosing schedule varies based on indication and regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $504.93 per mL, resulting in a cost of $7,573.95 per SDV; cost will vary based on dosing regimen

Empliciti® (Elotuzumab):

- **Therapeutic Class:** Signaling lymphocytic activation molecule family member 7 (SLAMF7)-directed immunostimulatory antibody

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

Hemady™ (Dexamethasone 20mg Tablet):

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

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

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

Ninlaro® (Ixazomib):

- **Therapeutic Class:** Proteasome inhibitor (PI)
- **Indication(s):** For use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least 1 prior therapy
- **How Supplied:** 2.3mg, 3mg, and 4mg oral capsules
- **Dose:** 4mg once a week on days 1, 8, and 15 of a 28-day treatment cycle; alternative strengths available for dose reductions/modifications if needed

- **Cost:** The WAC is $3,491.67 per capsule for all available strengths, resulting in a cost of $10,475.01 per 28 days based on the recommended dosing of 4mg on days 1, 8, and 15 of a 28-day cycle

Sarclisa® (Isatuximab-irfc):

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

Xpovio® (Selinexor):

- **Therapeutic Class:** Nuclear export inhibitor
- **Indication(s):**
  - For use in combination with dexamethasone for the treatment of adult patients with RRMM who have received ≥4 prior therapies and whose disease is refractory to ≥2 PIs, ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody
  - For use in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy
  - For the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy
- **How Supplied:** 20mg oral tablets packaged in 7 dose presentations (allowing for dose reduction based on adverse effects and diagnosis being treated); each dosing option is available in a 28-day supply carton containing 4 weekly blister packs
- **Dose:**
  - Multiple Myeloma:
    - In combination with dexamethasone for RRMM: 80mg [(4) 20mg tablets] in combination with 20mg dexamethasone taken on days 1 and 3 of each week
    - In combination with bortezomib and dexamethasone for multiple myeloma: 100mg once weekly on day 1 of each week in combination with bortezomib 1.3mg/m^2 once weekly on

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

Recommendations

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

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

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

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

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

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

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
    a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
    b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
    c. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or

d. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or
e. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or
f. In combination with cyclophosphamide, bortezomib, and dexamethasone in members who have received at least 1 prior therapy; or
g. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or
h. As a single-agent in members who have received ≥3 prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.

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

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

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

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

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

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

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

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

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

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Used in 1 of the following settings:
    a. In combination with dexamethasone in members who have received ≥4 prior therapies including refractory disease to ≥2 proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody; or
    b. Used in combination with bortezomib and dexamethasone in members who have failed at least 1 prior therapy.

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

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

[1] U.S. Food and Drug Administration (FDA). Drugs@FDA: FDA Approved Drugs. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Last accessed 01/22/2021.
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[4] National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 4.2021.* Fort Washington (PA): National Comprehensive Cancer Network; 2021. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Last accessed 02/01/2021.
[5] Darzalex® Prescribing Information. Janssen Biotech, Inc. Available online at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Last revised 08/2020. Last accessed 01/29/2021.
[6] Darzalex Faspro™ Prescribing Information. Janssen Biotech, Inc. Available online at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX+Faspro-pi.pdf. Last revised 01/2021. Last accessed 01/29/2021.
[7] Empliciti® Prescribing Information. Bristol-Myers Squibb Company. Available online at: https://packageinserts.bms.com/pi/pi_empliciti.pdf. Last revised 10/2019. Last accessed 01/22/2021.
[8] Hemady™ Prescribing Information. Dexcel Pharma Technologies. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211379s000lbl.pdf. Last revised 10/2019. Last accessed 01/22/2021.
[9] Ninlaro® Prescribing Information. Millennium Pharmaceuticals, Inc. Available online at: https://www.ninlaro.com/prescribing-information.pdf. Last revised 02/2020. Last accessed 01/22/2021.
[10] Sarclisa® Prescribing Information. Sanofi-Aventis. Available online at: http://products.sanofi.us/Sarclisa/sarclisa.pdf. Last revised 03/2020. Last accessed 01/22/2021.
[11] Xpovio® Prescribing Information. Karyopharm Therapeutics, Inc. Available online at: https://www.karyopharm.com/wp-content/uploads/2019/07/NDA-212306-SN-0071-Prescribing-Information-01July2019.pdf. Last revised 12/2020. Last accessed 01/22/2021.

Vote to Prior Authorize Lenvima® (Lenvatinib)

Oklahoma Health Care Authority
February 2021

Lenvima® (Lenvatinib) Product Summary[1]

Lenvima® (Lenvatinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)
  - In combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (RCC) following 1 prior anti-angiogenic therapy
  - First-line treatment of patients with unresectable hepatocellular carcinoma (HCC)
  - In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), with disease progression following prior systemic therapy, and who are not candidates for curative surgery or radiation
- **How Supplied:** 4mg and 10mg oral capsules supplied in cartons of (6) 5-day blister cards as follows:
  - 24mg/day: (10) 10mg capsules and (5) 4mg capsules per card
  - 20mg/day: (10) 10mg capsules per card
  - 18mg/day: (5) 10mg capsules and (10) 4mg capsules per card
  - 14mg/day: (5) 10mg capsules and (5) 4mg capsules per card
  - 12mg/day: (15) 4mg capsules per card
  - 10mg/day: (5) 10mg capsules per card
  - 8mg/day: (10) 4mg capsules per card
  - 4mg/day: (5) 4mg capsules per card
- **Dose:**
  - DTC: 24mg once daily
  - RCC: 18mg once daily with everolimus 5mg once daily
  - HCC: Based on actual body weight:
    - 8mg once daily for patients <60kg
    - 12mg once daily for patients ≥60kg
  - Endometrial carcinoma: 20mg once daily with pembrolizumab 200mg via intravenous (IV) infusion every 3 weeks

- **Cost:** The Wholesale Acquisition Cost (WAC) ranges from $211.34 to $634.03 per capsule, resulting in an approximate cost of $19,000.00 per 30-day supply dose pack

Recommendations

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

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

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

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

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

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

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

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

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

[1] Lenvima® Prescribing Information. Eisai, Inc. Available online at: http://www.lenvima.com/pdfs/prescribing-information.pdf. Last revised 12/2020. Last accessed 01/11/2021.

Appendix E

Vote to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna® (Inebilizumab-cdon)

Oklahoma Health Care Authority
February 2021

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

- **June 2020:** The FDA approved Uplizna® (inebilizumab-cdon), the first and only B-cell depleter approved for anti-aquaporin-4 (AQP4) seropositive neuromyelitis optica spectrum disorder (NMOSD). The safety and efficacy of inebilizumab were evaluated in a Phase 2/3, randomized (3:1), double-blind, placebo-controlled trial, known as the N-Momentum trial. In this trial, 89% of patients in the AQP4 seropositive treatment arm remained relapse-free during the 6 month period post treatment, compared to 58% in the placebo group.
- **August 2020:** The FDA approved Enspryng™ (satralizumab-mwge), the first and only self-administered treatment for AQP4 seropositive NMOSD. The safety and efficacy of satralizumab was demonstrated in (2) Phase 3 clinical trials, known as the SAkuraStar and SAkuraSky trials. In the SAkuraStar monotherapy trial, 76.5% of satralizumab patients in the AQP4 seropositive treatment arm were relapse-free at 96 weeks, compared to 41.1% in the placebo group. In the SAkuraSky trial, the safety and efficacy of satralizumab used concurrently with baseline immunosuppressant treatment (IST) were evaluated. In the AQP4 seropositive treatment arm, 91.1% of the patients taking satralizumab plus IST were relapse-free at 96 weeks, compared to 56.8% in the placebo plus IST group.

Product Summaries[3,4]

Enspryng™ (Satralizumab-mwge):

- **Therapeutic Class:** Interleukin-6 (IL-6) receptor antagonist
- **Indication(s):** Treatment of NMOSD in adult patients who are AQP4 antibody positive
- **How Supplied:** 120mg/mL single-dose prefilled syringe (PFS) with a needle safety device
- **Dose:** The recommended loading dose of Enspryng™ is 120mg subcutaneously (sub-Q) at weeks 0, 2, and 4, followed by a maintenance dosage of 120mg every 4 weeks
- **Cost:** Wholesale Acquisition Cost (WAC) of $14,615.39 per PFS

Uplizna® (Inebilizumab-cdon):

- **Therapeutic Class:** CD19-directed cytolytic antibody
- **Indication(s):** Treatment of NMOSD in adult patients who are AQP4 antibody positive
- **How Supplied:** A carton containing (3) 100mg/10mL single-dose vials (SDVs) for intravenous (IV) infusion
- **Dose:** The recommended initial dosing of Uplizna® is 300mg via IV infusion, followed by a second 300mg dose 2 weeks later; subsequent doses (starting 6 months from the first infusion) are 300mg via IV infusion every 6 months
- **Cost:** WAC of $43,666.70 per SDV

Cost Comparison: NMOSD Therapies

Medication	Cost for First Year	Cost per Year for Maintenance
Enspryng™ (satralizumab-mwge)	**$219,230.85**	**$190,000.07**
Uplizna® (inebilizumab-cdon)	**$393,000.30**	**$262,000.20**
Soliris® (eculizumab)	$704,473.20	$678,381.60

Cost of therapy calculated based on WAC.
Costs do not reflect rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Enspryng™ (satralizumab-mwge) and Uplizna® (inebilizumab-cdon) with the following criteria (items shown in red are changes from what was presented at the December 2020 DUR Board meeting):

Enspryng™ (Satralizumab-mwge) Approval Criteria:

1. An FDA approved indication of neuromyelitis optica spectrum disorder (NMOSD) in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have experienced at least 1 acute NMOSD attack in the prior 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤6.5; and
5. Prescriber must verify hepatitis B virus (HBV) and tuberculosis (TB) screening are negative before the first dose; and
6. Approvals will not be granted for members with active HBV infection or active or untreated latent TB; and
7. Prescriber must verify liver function tests have been assessed prior to initiation of treatment with Enspryng™ and levels are acceptable to prescriber; and

8. Prescriber must agree to counsel the member to monitor for clinically significant active infection(s) prior to each dose (for active infections, the dose should be delayed until the infection resolves); and
9. Prescriber must agree to monitor neutrophil counts 4 to 8 weeks after initiation of therapy and thereafter as clinically appropriate; and
10. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
11. Member and/or caregiver must be trained by a health care professional on subcutaneous administration and storage of Enspryng™; and
12. A quantity limit override for the loading dose will be approved upon meeting the Enspryng™ approval criteria. A quantity limit of 1 syringe per 28 days will apply for the maintenance dose, according to the package labeling; and
13. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Uplizna® (Inebilizumab-cdon) Approval Criteria:

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

11. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of treatment; and
12. Female members of reproductive potential must use contraception while receiving Uplizna® and for 6 months after the last infusion; and
13. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
~~14. A patient-specific, clinically significant reason why the member cannot use Enspryng™ must be provided; and~~
14. A quantity limit override for the loading dose will be approved upon meeting the Uplizna® approval criteria. A quantity limit of 30mL per 180 days will apply for the maintenance dose; and
15. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Soliris® (eculizumab) approval criteria for NMOSD, including the removal of criteria number 5 following discussion at the December 2020 DUR Board meeting:

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

~~1. An FDA approved diagnosis of NMOSD; and~~
~~2. Member is anti-aquaporin-4 (AQP4) antibody positive; and~~
~~3. Member must be 18 years of age or older.~~
1. An FDA approved indication of NMOSD in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have a history of at least 2 NMOSD attacks in last 12 months or 3 attacks in the last 24 months, with at least 1 attack in the past 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤7; and
~~5. A patient-specific, clinically significant reason why the member cannot use Enspryng™ or Uplizna® must be provided; and~~
6. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

[1] Viela Bio. Viela Bio Announces U.S. FDA Approval of Uplizna® (Inebilizumab-cdon) for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD). *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/06/11/2047190/0/en/Viela-Bio-Announces-U-S-FDA-Approval-of-UPLIZNA-inebilizumab-cdon-for-the-Treatment-of-Neuromyelitis-Optica-Spectrum-Disorder-NMOSD.html. Issued 06/11/2020. Last Accessed: 01/04/2021.

[2] Genentech, Inc. FDA Approves Genentech's Enspryng™ for Neuromyelitis Optica Spectrum Disorder. Available online at: https://www.gene.com/media/press-releases/14873/2020-08-14/fda-approves-genentechs-enspryng-for-neu. Issued 08/14/2020. Last Accessed 01/04/2021.

[3] Enspryng™ (Satralizumab-mwge) Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/enspryng_prescribing.pdf. Last revised 08/2020. Last accessed 01/04/2021.

[4] Uplizna® (Inebilizumab-cdon) Prescribing Information. Viela Bio. Available online at: https://www.uplizna.com/Uplizna_Prescribing_Information.pdf. Last revised 06/20/2020. Last accessed 01/04/2021.

Vote to Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), and Hulio® (Adalimumab-fkjp)

Oklahoma Health Care Authority
February 2021

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

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

- **Abrilada™ (Adalimumab-afzb):** In November 2019, the FDA approved Abrilada™ (adalimumab-afzb), the fifth biosimilar to Humira® (adalimumab), for the treatment of patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), and plaque psoriasis (PsO). The FDA approval was based on the review of a comprehensive data package, which demonstrated biosimilarity of Abrilada™ to the reference product. This includes results from the REFLECTIONS B538-02 clinical comparative study, which evaluated the efficacy, safety, and immunogenicity of Abrilada™. No clinically meaningful differences in efficacy, safety, or immunogenicity were found compared to the reference product, each used in combination with methotrexate in patients with moderate-to-severe RA. Pfizer is working to make Abrilada™ available in the United States based on the terms of an agreement with AbbVie and plans to launch Abrilada™ in 2023.
- **Avsola™ (Infliximab-axxq):** In December 2019, the FDA approved Avsola™ (infliximab-axxq) for all approved indications of the reference product, Remicade® (infliximab), which includes moderate-to-severe RA, moderate-to-severe CD in the adult and pediatric population, moderate-to-severe UC in the adult and pediatric population, chronic severe PsO, PsA, and AS. Avsola™, an anti-tumor necrosis factor alpha (anti-TNF) monoclonal antibody, was proven to be highly similar to Remicade® with no clinically meaningful differences based on a totality of evidence which included comparative analytical, nonclinical, and clinical data. The data package was composed of results from a pharmacokinetic (PK) similarity study conducted in healthy subjects, and a comparative clinical study conducted in patients with moderate-to-severe RA. The randomized, double-blind comparative clinical study evaluated the efficacy and safety of Avsola™ compared to Remicade® in patients with moderate-to-severe RA. There were 558 patients enrolled

and randomized (1:1) to receive either Avsola™ or Remicade® at a dose of 3mg/kg administered as an intravenous (IV) infusion on day 1, at weeks 2 and 6, and every 8 weeks thereafter. The primary endpoint was the response difference (RD) of 20% improvement in American College of Rheumatology (ACR) core set measurements at week 22. The study also incorporated the evaluation of a single transition in 119 subjects from Remicade® to Avsola™ at week 22, which demonstrated similar safety and immunogenicity in patients who were previously on Remicade®.

- **Ilaris® (Canakinumab):** In June 2020, the FDA approved Ilaris® (canakinumab) injection for the treatment of active Still's disease, including adult-onset Still's disease (AOSD). Ilaris® was previously FDA approved for systemic JIA (SJIA) in patients 2 years of age and older. AOSD is a rare and serious autoinflammatory disease of unknown origin. Characteristics of AOSD have considerable overlap with SJIA, and include fever, arthritis, rash, and elevated markers for inflammation. The overlapping features of AOSD and SJIA suggest this is a disease continuum, rather than 2 separate diseases. The role of IL-1, a type of cytokine important in regulating the body's immune system, is well-established in AOSD and SJIA. Ilaris® works by blocking the effects of IL-1 and suppressing inflammation in patients with this autoinflammatory disorder. The safety and efficacy of Ilaris® for the treatment of patients with AOSD were established using comparable PK exposure and extrapolation of established efficacy of canakinumab in patients with SJIA, as well as the safety of canakinumab in patients with AOSD and other diseases. The efficacy and safety data in AOSD were generally consistent with the results of a pooled analysis of SJIA patients. Ilaris® was granted Priority Review designation.
- **Hulio® (Adalimumab-fkjp):** In July 2020, the FDA approved Hulio® (adalimumab-fkjp), a biosimilar of Humira® (adalimumab), to treat chronic inflammatory disorders including RA, JIA, PsA, AS, CD, UC, and PsO. However, Hulio® will not be available in the United States until July 2023 due to a patent agreement with AbbVie, the company that markets Humira®. Hulio® will be available as both pre-filled syringes and auto-injectors. The FDA's decision was based on positive results from the ARABESC Phase 3 clinical study in patients with RA. Results showed no clinically meaningful differences compared to Humira® in terms of safety, efficacy, and immunogenicity.
- **Benlysta® (Belimumab):** In December 2020, the FDA approved Benlysta® (belimumab) for the treatment of adult patients with active lupus nephritis (LN) who are receiving standard therapy. LN is serious inflammation of the kidneys caused by systemic lupus erythematosus (SLE), the most common form of lupus, which can lead to end-stage kidney disease, requiring dialysis or a kidney transplant. The approval

extends the current indication in the United States to include both SLE and LN for both the IV and subcutaneous formulations. The FDA approval for adults with active LN is based on the BLISS-LN Phase 3, 104-week, randomized, double-blind, placebo-controlled study evaluating IV Benlysta® 10mg/kg plus standard therapy (mycophenolate mofetil for induction and maintenance, or cyclophosphamide for induction followed by azathioprine for maintenance, plus steroids) compared to placebo plus standard therapy in adult patients with active LN. The BLISS-LN study is the largest and longest Phase 3 study conducted in active LN, involving 448 adult patients. The study met its primary endpoint demonstrating that a statistically significantly greater number of patients achieved Primary Efficacy Renal Response (PERR) at 2 years when treated with Benlysta® plus standard therapy compared to placebo plus standard therapy in adults with active LN [43% vs. 32%; Odds Ratio (95% Confidence Interval) 1.55 (1.04, 2.32); P=0.0311). PERR was defined as a response at week 100 confirmed by a repeat measurement at week 104 of the following parameters: urinary protein:creatinine ratio (uPCR) ≤0.7g/g and estimated glomerular filtration rate (eGFR) ≥60mL/min/1.73m^2 or no decrease in eGFR of >20% from pre-flare value. Statistical significance compared to placebo across major secondary endpoints was achieved, including complete renal response (uPCR <0.5g/g; eGRF was not >10% below the pre-flare value or ≥90 mL/min/1.73m^2 and was not a treatment failure), PERR at week 52, and time to renal-related event or death (events defined as the first event experienced among the following: death, progression to end stage renal disease, doubling of serum creatinine from baseline, renal worsening, or renal-related treatment failure). The safety results are consistent with the known safety profile of Benlysta®.

News:

- **April 2018:** The American College of Gastroenterology (ACG) Clinical Guideline of the Management of Crohn's Disease in Adults was most recently published in 2018 in the *American Journal of Gastroenterology*. An important update from this treatment guideline was that the use of oral mesalamine has not consistently been demonstrated to be effective compared with placebo for induction of remission and achieving mucosal healing in patients with active CD and should not be used to treat patients with active CD (*strong recommendation, moderate level of evidence*).
- **January 2020:** A new guideline from the American Gastroenterological Association (AGA) on the management of moderate-to-severe UC was published in *Gastroenterology*, the official journal of the AGA Institute. The guideline focused on immunomodulators, biologics, and small

molecules to induce and maintain remission for patients with moderate-to-severe UC and to decrease the risk of colectomy. Some important guideline recommendations according to the AGA are as follows:

- In adult outpatients with moderate-to-severe UC, AGA recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab over no treatment (*strong recommendation; moderate quality evidence*).
- In adult outpatients with moderate-to-severe UC who are new to biologics, AGA suggests using infliximab or vedolizumab rather than adalimumab for induction of remission (*conditional recommendation; moderate quality evidence*).
    - AGA Comment: Patients, particularly those with less severe disease, who place higher value on the convenience of self-administered subcutaneous injection and lower value on the relative efficacy of medications, may reasonably choose adalimumab as an alternative.
- In adult outpatients with moderate-to-severe UC who have been exposed to infliximab, particularly those who were not responsive, AGA suggests using ustekinumab or tofacitinib, rather than vedolizumab or adalimumab, for induction of remission (*conditional recommendation; low quality evidence*).
    - AGA Comment: Patients, particularly those with less severe disease who place higher value on the potential safety of medications and lower value on the relative efficacy of medications, may reasonably choose vedolizumab as an alternative.
- In adult outpatients with moderate-to-severe UC, AGA suggests early use of biologics with or without immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates (5-ASA) (*conditional recommendation; very low quality evidence*).
    - AGA Comment: Patients, particularly those with less severe disease, who place higher value on the safety of 5-ASA therapy and lower value on the efficacy of biologic agents, may reasonably choose gradual step therapy with 5-ASA therapy.
- In hospitalized adult patients with acute, severe UC refractory to IV corticosteroids, AGA suggests using infliximab or cyclosporine (*conditional recommendation; low quality evidence*).

Recommendations

The College of Pharmacy recommends the removal of the trial requirement of a mesalamine product for a diagnosis of CD or UC for the Tier-2 Targeted

Immunomodulator Agents and Entyvio® (vedolizumab) approval criteria to be consistent with current guideline recommendations (changes noted in red):

Targeted Immunomodulator Agents Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least 1 Tier-1 medication in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. ~~For a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) authorization of a Tier-2 product requires history of failure of a mesalamine product (does not have to be within the last 90 days) and a trial of 1 Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or~~
4. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Entyvio® (Vedolizumab) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of moderate-to-severely active Crohn's disease (CD) or moderate-to-severely active ulcerative colitis (UC); and
3. ~~History of failure of a mesalamine medication (does not have to be within the last 90 days) and a trial of 1 Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; and~~
4. A minimum of a 4 week trial of a Tier-2 tumor necrosis factor (TNF) blocker indicated for the treatment of CD or UC that did not yield adequate relief of symptoms or resulted in intolerable adverse effects. Current Tier-2 medications include the following:
   a. UC: Humira® (adalimumab); or
   b. CD: Humira® (adalimumab); or
5. Prior stabilization on the medication documented within the last 100 days; and
6. A quantity limit of 300mg every 8 weeks will apply. Approvals will be granted for titration quantities required for initial dosing; and
7. Initial approvals will be for the duration of 14 weeks as Entyvio® should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Benlysta® (belimumab) to add hydroxychloroquine and chloroquine as acceptable trials based on the standard of care for the treatment of SLE and to reflect the new FDA approved indication of LN. The following criteria will apply (changes and additions noted in red):

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical only benefit while the subcutaneous (sub-Q) formulation will be covered as a pharmacy only benefit; and
2. An FDA approved indication of 1 of the following:
   a. The treatment of members 5 years of age and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) already receiving standard therapy; or
   b. The treatment of members 18 years of age and older with active lupus nephritis who are receiving standard therapy; and
3. Documented inadequate response to at least 2 of the following medications appropriate to member's specific disease state:
   a. High-dose oral corticosteroids; or
   b. Methotrexate; or
   c. Azathioprine; or
   d. Mycophenolate; or
   e. Cyclophosphamide; or
   f. Hydroxychloroquine/chloroquine; and
4. Member must not have ~~severe active lupus nephritis or~~ severe active central nervous system lupus; and
5. Benlysta® will not be approved for combination use with biologic therapies ~~or IV cyclophosphamide~~; and
6. Benlysta® will not be approved for combination use with IV cyclophosphamide (exception for induction treatment with IV cyclophosphamide for members with a diagnosis of lupus nephritis).

The College of Pharmacy also recommends updating the prior authorization criteria for Ilaris® (canakinumab) based on the new FDA approved indication for the treatment of AOSD. The following criteria will apply (changes and additions noted in red):

Ilaris® (Canakinumab) Approval Criteria [Active Systemic Juvenile Idiopathic Arthritis (SJIA) or Adult-Onset Still's Disease (AOSD) Diagnosis]:

1. An FDA approved indication of SJIA or AOSD; and
2. The member should not be using a tumor necrosis factor (TNF) blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra; and
3. Ilaris® should not be initiated in members with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
4. Dosing should not be more often than once every 4 weeks; and
   a. Weight-based dosing in members 2 years of age and older (the member's recent weight must be provided):

   i. Body weight ≥7.5kg: 4mg/kg subcutaneous injection every 4 weeks (maximum 300mg/dose); and
5. Recent trials of 1 Tier-1 medication and all appropriate Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
6. Prior stabilization on the Tier-3 medication documented within the last 100 days; and
7. Approvals will be for the duration of 1 year.

Lastly, the College of Pharmacy recommends the placement of Abrilada™ (adalimumab-afzb), Avsola™ (infliximab-axxq), and Hulio® (adalimumab-fkjp) into Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply (changes and additions noted in red):

Targeted Immunomodulator Agents Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of 1 Tier-1 medication and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA approved indication not covered by Tier-2 medications.

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

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Humira® (adalimumab) must be provided.

Avsola™ (Infliximab-axxq), Inflectra™ (Infliximab-dyyb), and Renflexis™ (Infliximab-abda) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Remicade® (infliximab) must be provided.

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®, Orencia® ClickJect™)≠
azathioprine	etanercept (Enbrel®)	**adalimumab-afzb (Abrilada™)±**
hydroxychloroquine		adalimumab-atto (Amjevita™)±
leflunomide		adalimumab-adbm (Cyltezo™)±

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

DMARDs = disease modifying anti-rheumatic drugs; NSAIDs = nonsteroidal anti-inflammatory drugs
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC) or State Maximum Allowable Costs (SMAC) if NADAC unavailable. Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.
±Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.
†Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) and noninfectious intermediate and posterior uveitis and panuveitis.
ß Unique criteria applies for a diagnosis of Behçet's disease (BD).
¥Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), Familial Mediterranean Fever (FMF), Systemic Juvenile Idiopathic Arthritis (SJIA), or Adult-Onset Still's Disease (AOSD).
~Unique criteria applies for a diagnosis of pemphigus vulgaris (PV). Unique criteria applies for a diagnosis of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

ΩFor Cosentyx® (secukinumab), only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).
ᵀUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome (CRS).
≠Orencia® ClickJect™ requires a patient-specific, clinically significant reason why the member cannot use the typical pre-filled syringe formulation.
** Unique criteria applies to this medication for approval.

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Vote to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule]

Oklahoma Health Care Authority
February 2021

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

Ortikos™ (budesonide ER capsule) was FDA approved in June 2019 for the treatment of mild-to-moderate active Crohn's disease (CD) involving the ileum and/or the ascending colon in patients 8 years of age and older and for maintenance of clinical remission of mild-to-moderate CD involving the ileum and/or the ascending colon for up to 3 months in adults. In July 2020, Ferring Pharmaceuticals announced the launch of Ortikos™ in the United States. Ortikos™ contains a controlled ileal-release anti-inflammatory corticosteroid and is available as 6mg and 9mg ER capsules. The recommended dose for mild-to-moderate active CD is 9mg once daily for up to 8 weeks in adults and 9mg once daily for up to 8 weeks, followed by 6mg once daily for up to 2 weeks in pediatric patients 8 to 17 years of age weighing >25kg. The recommended dose for maintenance of clinical remission of mild-to-moderate CD is 6mg once daily for up to 3 months in adults and should be tapered to cessation. Continued treatment for >3 months has not been shown to provide substantial clinical benefit. Ortikos™ is not approved for maintenance of mild-to-moderate CD in pediatric patients. The FDA approval of Ortikos™ was based primarily on previous clinical studies of another oral budesonide product, Entocort® EC [budesonide delayed release (DR) capsule]. A bioequivalence study was conducted to demonstrate bioequivalence of Ortikos™ 9mg to (3) Entocort® EC 3mg capsules. The study evaluated pharmacokinetic parameters in 48 healthy adult patients and showed systemic exposure was comparable between Ortikos™ 9mg capsule and (3) Entocort® EC 3mg capsules, meeting the FDA's bioequivalence criteria.

Cost Comparison:

Product	Cost Per Capsule	Cost Per 30 Days*
Ortikos™ (budesonide ER) 6mg or 9mg capsule	**$40.00**	**$1,200.00**
budesonide DR 3mg capsule	$0.96	$86.40

DR = delayed-release; ER = extended-release
Costs do not reflect rebated prices or net costs.
Costs based on Wholesale Acquisition Costs (WAC) for Ortikos™ and State Maximum Allowable Cost (SMAC) for budesonide DR.
*Cost per 30 days based on 1 capsule daily for Ortikos™ and 3 capsules daily for budesonide DR.

Recommendations

The College of Pharmacy recommends the prior authorization of Ortikos™ (budesonide ER capsule) with the following criteria:

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

1. An FDA approved indication of 1 of the following:
    a. For the treatment of mild-to-moderate active Crohn's disease (CD) involving the ileum and/or the ascending colon, in members 8 years of age or older; or
    b. For the maintenance of clinical remission of mild-to-moderate CD involving the ileum and/or the ascending colon for up to 3 months duration in adult members; and
2. Member must have previous failure of Entocort® EC (budesonide controlled ileal-release enteric coated capsules) within the last 3 months at recommended dosing and a reason for trial failure with Entocort® EC must be provided; or
3. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use other oral corticosteroids, including Entocort® EC, that are available without prior authorization must be provided; and
4. Dosing regimen and duration of therapy must be in accordance with the Ortikos™ *Prescribing Information*; and
5. Approval length will be based on the manufacturer maximum recommended duration of therapy; and
6. A quantity limit of 30 capsules per 30 days will apply.

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[1] Ferring Pharmaceuticals, Inc. Ortikos™ (Budesonide), the First and Only Once-Daily Dose for Treatment of Mild to Moderate Crohn's Disease, Now Available in the U.S. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20200729005225/en/ORTIKOS%E2%84%A2-budesonide-Once-Daily-Dose-Treatment-Mild-Moderate. Issued 07/29/2020. Last accessed 01/21/2021.
[2] Ortikos™ (Budesonide Extended-Release Capsules) Prescribing Information. Ferring Pharmaceuticals, Inc. Available online at: http://www.ferringusa.com/wp-content/uploads/2020/07/Ortikos-PI_6794-02.pdf. Last revised 10/2019. Last accessed 01/21/2021.
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Vote to Prior Authorize Pizensy™ (Lactitol)

Oklahoma Health Care Authority
February 2021

Introduction[1]

In February 2020, the U.S. Food and Drug Administration (FDA) approved Pizensy™ (lactitol oral solution) for the once-daily treatment of chronic idiopathic constipation (CIC) in adults. Pizensy™ is a simple monosaccharide sugar alcohol that exerts an osmotic effect, causing the influx of water into the small intestine leading to laxative effects. Pizensy™ is the only FDA approved product in which the patient can self-titrate, based on their own results, for stool consistency. Pizensy™ is supplied in 280 and 560 gram multi-dose bottles which are equipped with a measuring cap marked to contain 10 grams of powder when filled to the top of the white section within the cap. Pizensy™ is also supplied in unit-dose packets that contain 10 grams of lactitol each. The recommended adult dosage is 20 grams orally once daily, preferably with meals. The dose should be reduced to 10 grams once daily for persistent loose stools. Cost information is not yet available for Pizensy™.

Recommendations

The College of Pharmacy recommends the prior authorization of Pizensy™ (lactitol) with the following criteria:

Pizensy™ (Lactitol) Approval Criteria:

1. An FDA approved indication for the treatment of chronic idiopathic constipation (CIC) in members 18 years of age or older; and
2. Member must not have a known contraindication to Pizensy™ (i.e., suspected gastrointestinal obstruction, galactosemia); and
3. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and

6. A patient-specific, clinically significant reason why the member cannot use Linzess® (linaclotide), Amitiza® (lubiprostone), or Trulance® (plecanatide) must be provided; and
7. Use of the unit-dose packets will require a patient-specific, clinically significant reason why the member cannot use the multi-dose bottle; and
8. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
9. A quantity limit of 560 grams per 28 days will apply.

[1] Pizensy™ (Lactitol) Prescribing Information. Sebela Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211281s000lbl.pdf. Last revised 02/2020. Last accessed 01/22/2021.

Vote to Update the Prior Authorization Criteria for Spravato® (Esketamine Nasal Spray)

Oklahoma Health Care Authority
February 2021

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

- **July 2020:** The FDA approved a supplemental New Drug Application (sNDA) for Spravato® (esketamine nasal spray), in conjunction with an oral antidepressant, to treat depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior. The sNDA approval was based on 2 identical Phase 3 clinical studies in which Spravato® (84mg twice weekly) plus comprehensive standard of care (SOC) demonstrated a statistically significant, rapid reduction of depressive symptoms within 24 hours, with some patients responding as early as 4 hours. The primary efficacy measure was the change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at 24 hours after the first dose. MADRS is a tool used to assess severity of depressive symptoms. Spravato® plus comprehensive SOC demonstrated statistical superiority with a 15.9 and 16 point decrease on the MADRS in the 2 studies at 24 hours after the first dose of study medication (P=0.006 in both studies). Comparatively, in the placebo plus comprehensive SOC group, there was a decrease of 12 and 12.2 points in the 2 studies. The comprehensive SOC included initial hospitalization and a newly initiated or optimized oral antidepressant. The recommended dosage of Spravato® for the treatment of depressive symptoms in adults with MDD with acute suicidal ideation or behavior is 84mg twice weekly for 4 weeks in conjunction with an oral antidepressant. The dosage may be reduced to 56mg twice weekly based on tolerability. After 4 weeks of treatment with Spravato®, evidence of therapeutic benefit should be evaluated to determine need for continued treatment. The use of Spravato®, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior. Due to the risks of serious adverse outcomes resulting from sedation, dissociation, abuse, and misuse, Spravato® is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Spravato® REMS program. The Wholesale Acquisition Cost (WAC) for Spravato® is $309.46 per 28mg nasal spray device, resulting in a cost of $7,427.04 per 28 days at the recommended dose of 84mg twice weekly for patients with MDD with acute suicidal ideation or behavior.

Recommendations

The College of Pharmacy recommends updating the Spravato® (esketamine nasal spray) criteria based on the new FDA approved indication with the following criteria (new criteria and changes are shown in red):

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

1. An FDA approved indication of depressive symptoms in adults with MDD with acute suicidal ideation or behavior; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
5. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
6. Member must not have any contraindications to therapy [i.e., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
7. Member must not have severe hepatic impairment (Child Pugh C); and
8. Prescriber must verify that female members are not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
9. Prescriber must verify female member is not breastfeeding; and
10. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
11. Member must be enrolled in the Spravato® REMS program; and
12. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
13. For initial approval, the number of doses the member received while hospitalized, if applicable, and the dates of these doses must be provided to allow authorization of the appropriate quantity for the initial 4 weeks of treatment; and
14. For continued authorization, prescriber must verify member demonstrated an adequate response during the initial 4 weeks of treatment, verify member is using Spravato® in combination with an oral antidepressant, and provide patient-specific, clinically significant information to support continued use of Spravato®; and
15. A quantity limit of 8 kits per 28 days will apply.

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

1. An FDA approved indication of treatment-resistant depression in adults; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Member must have had an inadequate response to at least 2 different antidepressants from different classes at least 4 weeks in duration each and titrated to recommended dosing during the current depressive episode, unless contraindicated or clinically significant adverse effects; and
5. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
6. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
7. Member must not have any contraindications to therapy [e.g., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
8. Member must not have severe hepatic impairment (Child Pugh C); and
9. Prescriber must verify that female members are not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
10. Prescriber must verify female member is not breastfeeding; and
11. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
12. Member must be enrolled in the Spravato® REMS program; and
13. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
14. Initial approvals will be for the duration of the induction phase. For continued authorization, prescriber must verify member demonstrated an adequate response during the induction phase and verify member is using Spravato® in combination with an oral antidepressant; and
15. A quantity limit of 4 kits per 28 days will apply for maintenance dosing. ~~A quantity limit override will be approved for induction of therapy upon meeting Spravato® approval criteria.~~

[1] Janssen Pharmaceutical Companies. Janssen Announces U.S. FDA Approval of Spravato® (Esketamine) CIII Nasal Spray to Treat Depressive Symptoms in Adults with Major Depressive Disorder with Acute Suicidal Ideation or Behavior. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/janssen-announces-us-fda-approval-of-spravato-esketamine-ciii-nasal-spray-to-treat-depressive-symptoms-in-adults-with-major-depressive-disorder-with-acute-suicidal-ideation-or-behavior-301104437.html. Issued 08/03/2020. Last accessed 01/21/2021.

[2] Fu DJ, Ionescu DF, Li X, et al. Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients who have Active Suicidal Ideation with Intent: Double-Blind, Randomized Study (ASPIRE I). *J Clin Psychiatry* 2020; 81(3): 19m13191. doi: 10.4088/JCP.19m13191.

[3] Ionescu DF, Fu DJ, Qiu X, et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients with Major Depressive Disorder who have Active Suicide Ideation with Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II). *Int J Neuropsychopharmacol* 2020. doi: 10.1093/ijnp/pyaa068.

[4] Spravato® Prescribing Information. Janssen Pharmaceutical Companies. Available online at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SPRAVATO-pi.pdf. Last revised 07/2020. Last accessed 01/21/2021.

Vote to Update the Prior Authorization Criteria for Bavencio® (Avelumab), Braftovi® (Encorafenib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), and Yervoy® (Ipilimumab)

Oklahoma Health Care Authority
February 2021

U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)[1]

- **March 2020:** The FDA granted accelerated approval to the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.
- **April 2020:** The FDA approved Braftovi® (encorafenib) in combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer (mCRC) with a *BRAF* V600E mutation.
- **May 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) as first-line treatment for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express programmed death ligand 1 (PD-L1) ≥1% with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
- **May 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) and 2 cycles of platinum-doublet chemotherapy as first-line treatment for patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations.
- **June 2020:** The FDA approved Opdivo® (nivolumab) for the treatment of patients with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.
- **June 2020:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.
- **June 2020:** The FDA approved Keytruda® (pembrolizumab) for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.

- **June 2020:** The FDA approved Keytruda® (pembrolizumab) for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).
- **June 2020:** The FDA approved Bavencio® (avelumab) for maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy.
- **October 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) as first-line treatment for adult patients with unresectable malignant pleural mesothelioma.
- **October 2020:** The FDA extended the approval of Keytruda® (pembrolizumab) for adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) and for pediatric patients with refractory cHL or cHL that has relapsed after ≥2 therapies.
- **November 2020:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) in combination with chemotherapy for the treatment of patients with locally recurrent, unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 with a combined positive score (CPS) ≥10.

Recommendations

The College of Pharmacy recommends to update the prior authorization criteria for Bavencio® (avelumab), Braftovi® (encorafenib), Keytruda® (pembrolizumab), Opdivo® (nivolumab), and Yervoy® (ipilimumab) to reflect the new FDA approved indications; changes and new criteria noted in red (only criteria with updates are listed):

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

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

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

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

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

1. Diagnosis of locally recurrent unresectable or metastatic triple-negative breast cancer; and
2. Tumors express programmed death ligand 1 (PD-L1) with a combined positive score (CPS) ≥10.

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

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

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

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

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

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

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

1. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e., Opdivo® (nivolumab)]; and
2. ~~Member must have 1 of the following: a.~~ MSI-H or dMMR solid tumors that have progressed following prior treatment with no satisfactory alternative treatment options~~; or~~
    ~~b. MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.~~

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

1. Diagnosis of unresectable or metastatic TMB-H [≥10 mutations/megabase (mut/Mb)] solid tumors; and

2. Used following disease progression after prior treatment; and
3. No satisfactory alternative treatment options.

Opdivo® (Nivolumab) Approval Criteria [Esophageal Squamous Cell Carcinoma (ESCC) Diagnosis]:

1. Diagnosis of unresectable, advanced, recurrent, or metastatic disease; and
2. Used following prior fluoropyrimidine- and platinum-based chemotherapy.

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

~~1. Relapsed or progressive disease; and~~
~~2. The patient has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and~~
~~3. Member must have been previously treated with sorafenib.~~

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

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

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

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

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

i. Adenocarcinoma; or
ii. Squamous cell; or
iii. Large cell; and

b. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
c. The patient has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
d. As a single-agent; and
e. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

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

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

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

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

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

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

[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 12/2020. Last accessed 12/17/2020.

Appendix F

Vote to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe)

Oklahoma Health Care Authority
February 2021

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

- **November 2019:** The FDA's Endocrinologic and Metabolic Drugs Advisory Committee unanimously recommended the approval of Vascepa® (icosapent ethyl) to reduce cardiovascular (CV) events as an adjunct to statin therapy in patients with elevated triglycerides levels. This new indication was based on the results from the REDUCE-IT trial, which showed a 25% relative risk reduction in major CV events with Vascepa® when compared to placebo in patients with triglycerides >135mg/dL and who had established cardiovascular disease (CVD) (secondary prevention), or who were high-risk primary prevention patients with diabetes mellitus (DM) and 1 additional risk factor. There was a disagreement between the committee members on which population for whom to approve this indication. All committee members voted in favor of the approval for patients with established CV events for secondary prevention. The disagreement was over whether it should be indicated for the high-risk primary prevention population, including those patients with DM. In the patients with established CVD for secondary prevention, there was a 35% relative risk reduction in major CV events when compared to 16% for the high-risk primary prevention patients. Several committee members voiced concerns about approval for the high-risk primary prevention population because they only comprised 30% of the trial population.
- **December 2019:** The FDA approved a new indication for Vascepa® as an adjunctive therapy to reduce the risk of CV events in adults with a triglyceride level ≥150mg/dL on a maximally tolerated statin therapy. Patients must have either established CVD or DM with 2 or more additional risk factors for CVD. The safety and efficacy of this new indication were assessed in the REDUCE-IT trial, which included 8,179 patients who were either 45 years of age and older with established CVD or 50 years of age and older with DM and additional risk factors for CVD. Patients who received Vascepa® were significantly less likely to experience a CV event when compared to placebo. In this trial, Vascepa® was associated with an increased risk of atrial fibrillation, atrial flutter, and bleeding events.
- **February 2020:** The FDA approved Nexletol® (bempedoic acid), an oral, once-daily, non-statin, low-density lipoprotein cholesterol (LDL-C)

lowering medication indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with established atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of LDL-C. Nexletol® is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL-C by inhibiting the production of cholesterol in the liver. The approval of Nexletol® was supported by multiple Phase 3 trials including over 3,000 patients. Nexletol® provided an average of 18% placebo-corrected LDL-C lowering when used with moderate or high intensity statins.

- **February 2020:** The FDA approved Nexlizet™ (bempedoic acid/ ezetimibe), an oral, once-daily, non-statin LDL-C lowering medication as adjunct therapy to diet and maximally tolerated statin therapy for adult patients with ASCVD or HeFH who require additional LDL-C lowering. Nexlizet™ has the same mechanism of action as Nexletol®, but also has an additional ingredient, ezetimibe, that inhibits cholesterol absorption in the intestines. The approval of Nexlizet™ is supported by a Phase 3 fixed combination drug product (FCDP) LDL-C lowering trial in which enrolled patients on maximally tolerated statins had a mean difference in LDL-C reduction of 38% when compared to placebo.

Product Summaries[5,6]

Nexletol® (Bempedoic Acid):

- **Therapeutic Class:** ACL inhibitor
- **Indication(s):** Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C
- **How Supplied:** 180mg oral tablet
- **Dose:** 180mg once daily with or without food
- **Cost:** National average drug acquisition cost (NADAC) of $10.53 per tablet

Nexlizet™ (Bempedoic Acid/Ezetimibe):

- **Therapeutic Class:** ACL inhibitor and cholesterol absorption inhibitor
- **Indication(s):** Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C
- **How Supplied:** An oral tablet containing 180mg bempedoic acid and 10mg ezetimibe
- **Dose:** 1 tablet (180mg bempedoic acid/10mg ezetimibe) once daily with or without food
- **Cost:** NADAC of $10.55 per tablet

Cost Comparison: LDL-C Lowering Therapies as an Adjunct to Statins

Medication	Cost Per Unit*	Cost of Therapy for 4 weeks†
Nexletol® (bempedoic acid) 180mg tablet	**$10.53**	**$294.84**
Nexlizet™ (bempedoic acid/ezetimibe) 180mg/10mg tablet	**$10.55**	**$295.40**
ezetimibe 10mg tablet	$0.14	$3.92
Praluent® (alirocumab) 150mg/mL injection	$216.98	$433.96
Repatha® (evolocumab) 420mg/3.5mL injection	$134.26	$469.91

Cost of therapy calculated based on National Average Drug Acquisition Cost (NADAC).
Costs do not reflect rebated prices or net costs.
*Unit = tablet or mL
†Cost of therapy for 4 weeks based on maximum FDA recommended dosing for each product.

Recommendations

The College of Pharmacy recommends the prior authorization of Nexletol® (bempedoic acid) and Nexlizet™ (bempedoic acid/ezetimibe) with the following criteria (items shown in red are changes from what was included in the January 2021 DUR Board packet):

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
        i. 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, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
4. Member requires additional lowering of LDL-cholesterol (LDL-C) (baseline, current, and goal LDL-C levels must be provided); and

5. A quantity limit of 30 tablets per 30 days will apply; and
6. 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.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current omega-3 fatty acids approval criteria based on the new FDA approved indication for Vascepa® (icosapent ethyl):

Omega-3 Fatty Acids Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Severe hypertriglyceridemia; and
        i. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL) and controlled diabetes mellitus [fasting glucose <150mg/dL at the time of triglycerides measurement and hemoglobin A1c (HgA1c) <7.5%]; and
        ii. Previous failure with fibric acid medications; and
        iii. Use of Vascepa® or Epanova® requires a previous failure of or a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®), which is available without prior authorization; or
    b. For the use of Vascepa® as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride levels; and
        i. 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
        ii. Laboratory documentation of fasting triglycerides ≥150mg/dL; and
        iii. Member must have 1 of the following:
            1. Established cardiovascular disease (CVD); or
            2. Diabetes mellitus and ≥2 additional risk factors for CVD; and
2. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

[1] Hughes S. FDA Panel Recommends High-Dose EPA for CV Event Reduction. *Medscape*. Available online at: https://www.medscape.com/viewarticle/921374#vp_1. Issued 11/14/2019. Last accessed 01/13/2021.
[2] U.S. Food and Drug Administration (FDA). FDA Approves Use of Drug to Reduce Risk of Cardiovascular Events in Certain Adult Patient Groups. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-use-drug-reduce-risk-cardiovascular-events-certain-adult-patient-groups. Issued 12/13/2019. Last accessed 01/13/2021.
[3] Esperion Therapeutics. Esperion Announces FDA Approval of Nexletol® (Bempedoic Acid) Tablet, an Oral, Once-Daily, Non-Statin LDL-Cholesterol Lowering Medicine. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/02/21/1988825/0/en/Esperion-Announces-FDA-Approval-of-NEXLETOL-bempedoic-acid-Tablet-an-Oral-Once-Daily-Non-Statin-LDL-Cholesterol-Lowering-Medicine.html. Issued 02/21/2020. Last accessed 01/13/2021.
[4] Esperion Therapeutics. Esperion Announces FDA Approval of the Nexlizet™ (Bempedoic Acid and Ezetimibe) Tablet, an Oral, Once-Daily, Non-Statin LDL-Cholesterol Lowering Medicine. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/02/26/1991460/0/en/Esperion-Announces-FDA-Approval-of-the-NEXLIZET-bempedoic-acid-and-ezetimibe-Tablet-an-Oral-Once-Daily-Non-Statin-LDL-Cholesterol-Lowering-Medicine.html. Issued 02/26/2020. Last accessed 01/13/2021.
[5] Nexletol® (Bempedoic Acid) Prescribing Information. Esperion Therapeutics, Inc. Available online at: https://pi.esperion.com/nexletol/nexletol-pi.pdf. Last revised 02/2020. Last accessed 01/13/2021.
[6] Nexlizet™ (Bempedoic Acid/Ezetimibe) Prescribing Information. Esperion Therapeutics, Inc. Available online at: https://pi.esperion.com/nexlizet/nexlizet-pi.pdf. Last revised 02/2020. Last accessed 01/13/2021.

Appendix G

Vote to Prior Authorize Imcivree™ (Setmelanotide)

Oklahoma Health Care Authority
February 2021

Introduction[1]

Imcivree™ (setmelanotide) was approved by the U.S. Food and Drug Administration (FDA) in November 2020 for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Imcivree™ is supplied as a 10mg/mL solution in a 1mL multiple-dose vial (MDV) and is administered subcutaneously (sub-Q) in the abdomen, thigh, or arm. Prior to initiation of Imcivree™, patients or caregivers should be trained on proper sub-Q injection technique. The recommended dosing of Imcivree™ varies based on patient age and tolerance. For adults and pediatric patients 12 years of age and older, the starting dose is 2mg sub-Q once daily for 2 weeks. The dose may be increased to 3mg once daily if the 2mg dose is tolerated and additional weight loss is desired. For pediatric patients 6 years to younger than 12 years of age, the starting dose is 1mg sub-Q once daily for 2 weeks. The dose may be increased to 2mg once daily if the 1mg dose is tolerated. The dose may further be increased to 3mg once daily if the 2mg dose is tolerated and additional weight loss is desired. The most common adverse reactions, occurring in ≥20% of patients treated with setmelanotide in the 52-week open-label clinical study, were injection site reaction, skin hyper-pigmentation, nausea, headache, diarrhea, abdominal pain, back pain, fatigue, vomiting, depression, upper respiratory tract infection, and spontaneous penile erection.

The safety and efficacy of setmelanotide for chronic weight management in 21 patients with obesity due to POMC, PCSK1, and LEPR deficiency were evaluated in 2 identically designed, 1-year, open-label studies, each with an 8-week, double-blind withdrawal period. In both studies, adult patients had a BMI of ≥30kg/m^2 and pediatric patients had a weight ≥95th percentile using growth chart assessments. The primary endpoint was the proportion of patients with ≥10% weight loss compared with baseline at approximately 1 year. Study 1 included patients 6 years of age and older with obesity and genetically confirmed or suspected POMC (N=9) or PCSK1 (N=1) deficiency. In this study, 8 of the 10 patients achieved ≥10% weight loss compared to baseline at 1 year (P<0.0001 compared with historical data). Study 2 included

11 patients, 6 years of age and older, with obesity and genetically confirmed or suspected LEPR deficiency. In this study, 5 of the 11 patients achieved ≥10% weight loss compared to baseline at 1 year (P=0.0001 compared with historical data).

The Wholesale Acquisition Cost (WAC) of Imcivree™ is $3,300.00 per mL, resulting in a cost of $29,700.00 per 30 days at the maximum FDA recommended dose of 3mg once daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Imcivree™ (setmelanotide) with the following criteria:

Imcivree™ (Setmelanotide) Approval Criteria:

1. An FDA approved indication of chronic weight management in adult and pediatric members 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency; and
2. Molecular genetic testing to confirm variants in the *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance; and
3. Requests for Imcivree™ for obesity due to suspected POMC-, PCSK1-, or LEPR-deficiency with *POMC, PCSK1, or LEPR* variants classified as benign or likely benign, obesity associated with other genetic syndromes, or general obesity will not be approved; and
4. Member's baseline weight and body mass index (BMI) must be provided; and
5. Baseline BMI must be ≥30kg/m^2 for adults or ≥95th percentile on BMI-for-age growth chart assessment for children; 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 Imcivree™ therapy and throughout treatment; and
7. Prescriber must verify member has been counseled on potential sexual adverse reactions and when to seek emergency medical care; and
8. Prescriber must verify member does not have moderate, severe, or end stage renal disease [estimated glomerular filtration rate (eGFR) <60mL/min/1.73m^2]; and
9. Prescriber must verify female member is not pregnant or breastfeeding; and
10. Prescriber must confirm member or caregiver has been trained on the proper storage and administration of Imcivree™ prior to the first dose; and
11. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member's current

weight or BMI and member has achieved weight loss of ≥5% of baseline body weight or ≥5% of BMI; and

12. A quantity limit of 9mL per 30 days will apply.

[1] Imcivree™ Prescribing Information. Rhythm Pharmaceuticals, Inc. Available online at: https://www.rhythmtx.com/IMCIVREE/prescribing-information.pdf. Last revised 11/2020. Last accessed 01/11/2021.

Appendix H

Vote to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix)

Oklahoma Health Care Authority
February 2021

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

Fensolvi® (leuprolide acetate) was approved by the FDA in May 2020 for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). Fensolvi® is an injectable polymeric matrix formulation of leuprolide acetate, a gonadotropin-releasing hormone (GnRH) receptor agonist, which forms a solid drug delivery depot when administered subcutaneously (sub-Q) and is designed to release the medication at a controlled rate over a 6-month period. Fensolvi® is supplied as a kit containing a syringe with 45mg lyophilized leuprolide acetate and a separate syringe prefilled with diluent for reconstitution. The recommended dose is 45mg once every 6 months and should be administered by a health care professional. Treatment should be discontinued at the appropriate age of onset of puberty. The FDA approval of Fensolvi® was based on data from an uncontrolled, open-label, single-arm study which included 64 children 4 to 9 years of age (62 females and 2 males) with CPP who were all naïve to GnRH agonist treatment. The primary endpoint was suppression of peak stimulated luteinizing hormone (LH) concentrations to <4IU/L by month 6 and was achieved in 87% of pediatric patients with CPP. Additionally, at month 6, estradiol and testosterone levels were suppressed in 97% and 100% of patients, respectively. Treatment with Fensolvi® also stopped or reversed progression of clinical signs of puberty and resulted in reductions in growth velocity and bone age.

Fensolvi® may cause fetal harm based on findings from animal studies and the drug's mechanism of action and is contraindicated in pregnancy. Pregnancy should be excluded prior to initiating treatment in women of reproductive potential. Non-hormonal methods of contraception should be used during treatment. During the early phase of therapy, Fensolvi® may cause gonadotropins and sex steroid levels to rise above baseline due to the initial stimulatory effect of leuprolide acetate, and may lead to increased signs and symptoms of puberty during the first weeks of treatment and after subsequent doses. Additionally, patients taking GnRH agonists have reported psychiatric events such as emotional lability, crying, irritability, impatience, anger, and aggression. Convulsions have also been reported with the use of GnRH agonists, in patients with and without a history of convulsions and in

patients taking medications such as bupropion and selective serotonin reuptake inhibitors (SSRIs).

Cost Comparison:

Product	Cost Per Unit*	Cost Per Year+
Fensolvi® (leuprolide) 45mg	**$22,578.00**	**$45,156.00**
Lupron Depot-Ped® (leuprolide) 15mg 1-month kit	$3,359.51	$40,314.12
Lupron Depot-Ped® (leuprolide) 30mg 3-month kit	$10,078.56	$40,314.24
Supprelin® LA (histrelin) 50mg	$30,441.90	$30,441.90
Triptodur® (triptorelin) 22.5mg	$17,230.25	$34,460.50

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), Specialty Pharmaceutical Allowable Cost (SPAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.
*Cost per unit based on each package.
+Cost per year based on 1 injection every 6 months for Fensolvi® and Triptodur®, 1 injection monthly for Lupron Depot-Ped® 1-month kit, 1 injection every 3 months for Lupron Depot-Ped® 3-month kit, and 1 implantation yearly for Supprelin® LA.

Oriahnn™ (elagolix/estradiol/norethindrone and elagolix) was approved by the FDA in May 2020 for the management of heavy menstrual bleeding associated with uterine leiomyomas, also known as fibroids, in premenopausal women. Oriahnn™ is a combination of elagolix (a GnRH receptor antagonist), estradiol (an estrogen), and norethindrone (a progestin) and is available in an oral capsule formulation. Oriahnn™ is the first non-surgical, oral medication approved by the FDA for this indication. Use of Oriahnn™ should be limited to 24 months due to the risk of continued bone loss, which may not be reversible. Oriahnn™ is supplied as 2 capsules: 1 capsule to be taken in the morning (containing elagolix 300mg/estradiol 1mg/norethindrone 0.5mg) and 1 capsule to be taken in the evening (containing elagolix 300mg). Each morning and evening dose should be taken at approximately the same time each day, with or without food. The FDA approval of Oriahnn™ was based on data from 2 identical randomized, double-blind, placebo-controlled studies, including a total of 790 premenopausal women with heavy menstrual bleeding. Patients were randomized to receive Oriahnn™ or placebo for 6 months. Both studies demonstrated a statistically significant decrease in menstrual blood loss from baseline to the final month.

Due to the estrogen and progestin components, Oriahnn™ has a *Boxed Warning* regarding thromboembolic disorders and vascular events and 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 and women with uncontrolled hypertension (HTN). Oriahnn™ is also contraindicated in pregnancy, known osteoporosis, current or history of breast cancer or other

hormonally-sensitive malignancies, known liver impairment or disease, undiagnosed abnormal uterine bleeding, known hypersensitivity to ingredients in Oriahnn™, and with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations (e.g., cyclosporine, gemfibrozil).

Cost Comparison:

Product	Cost Per Unit*	Cost Per Year+
Oriahnn™ (elagolix/estradiol/norethindrone and elagolix) 300mg/1mg/0.5mg capsule	**$16.20**	**$11,796.07**
norgestimate/ethinyl estradiol 0.25mg/0.035mg tablet	$0.21	$74.65
Lupron Depot® (leuprolide) 3.75mg 1-month kit	$1,351.37	$16,216.45
Lupron Depot® (leuprolide) 11.25mg 3-month kit	$4,034.48	$16,137.93

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), Specialty Pharmaceutical Allowable Cost (SPAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.
*Cost per unit based on each capsule for Oriahnn™, each tablet for norgestimate/ethinyl estradiol, and each package for Lupron Depot®.
+Cost per year based on 1 capsule twice daily for Oriahnn™, 1 tablet daily for 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 moving Supprelin® LA (histrelin) and Synarel® (nafarelin) to Tier-1 of the GnRH Medications Product Based Prior Authorization (PBPA) category based on net costs and recommends the placement of Fensolvi® (leuprolide) into Tier-3 of the GnRH Medications PBPA category with the following criteria (additions and changes shown in red in the criteria and Tier chart):

~~**Supprelin® LA (Histrelin), Synarel® (Nafarelin), and** **Fensolvi® (Leuprolide)**~~
Approval Criteria:

1. An FDA approved diagnosis of central precocious puberty confirmed by submitting the following:
    a. Documentation of onset of symptoms prior to 8 years of age in females and 9 years of age in males; and
    b. Documentation that bone age is advanced 1 year beyond the chronological age; and
    c. Lab assessment:
        i. Documentation of abnormal basal gonadotropin levels; or
        ii. Documentation of pubertal response to a gonadotropin-releasing hormone analog stimulation test; and

2. Approvals may be granted with documentation of failed trials of all lower tiered products or an FDA approved indication not covered by a lower tiered product; or
3. A patient-specific, clinically significant reason why the member cannot use all available lower tiered products must be provided for approval consideration.

Gonadotropin-Releasing Hormone (GnRH) Medications		
Tier-1	**Tier-2**	**Tier-3**
histrelin (Supprelin® LA)	~~**histrelin (Supprelin® LA)**~~	~~**nafarelin (Synarel®)**~~
leuprolide (Lupron Depot®)		**leuprolide (Fensolvi®)**
leuprolide (Lupron Depot-Ped®)		
nafarelin (Synarel®)		
triptorelin (Triptodur®)		

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Additionally, the College of Pharmacy recommends the prior authorization of Oriahnn™ (elagolix/estradiol/norethindrone and elagolix) with the following criteria:

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 Oriahnn™ 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 with Oriahnn™ 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; and
    f. Current or history of breast cancer or other hormonally-sensitive malignancies; and
    g. Known hypersensitivity to ingredients in Oriahnn™; and
    h. Concomitant use with an organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and

4. Oriahnn™ 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. A quantity limit of 56 capsules per 28 days will apply; and
8. Lifetime approval duration will be limited to a maximum of 24 months.

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[1] Tolmar Pharmaceuticals, Inc. FDA Approves Fensolvi® (Leuprolide Acetate) for Injectable Suspension for Pediatric Patients with Central Precocious Puberty. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-fensolvi-leuprolide-acetate-for-injectable-suspension-for-pediatric-patients-with-central-precocious-puberty-301051621.html. Issued 05/04/2020. Last accessed 12/11/2020.

[2] Fensolvi® (Leuprolide Acetate) Prescribing Information. Tolmar, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213150s000lbl.pdf. Last revised 05/2020. Last accessed 12/11/2020.

[3] AbbVie. FDA Approves the First Oral Medication for the Management of Heavy Menstrual Bleeding Due to Uterine Fibroids in Pre-Menopausal Women. Available online at: https://news.abbvie.com/news/press-releases/fda-approves-first-oral-medication-for-management-heavy-menstrual-bleeding-due-to-uterine-fibroids-in-pre-menopausal-women.htm. Issued 05/29/2020. Last accessed 12/11/2020.

[4] Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) Prescribing Information. AbbVie, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213388s000lbl.pdf. Last revised 05/2020. Last accessed 12/11/2020.

[5] Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for Heavy Menstrual Bleeding in Women with Uterine Fibroids. *N Engl J Med* 2020; 382(4):328-340.

Appendix I

Vote to Prior Authorize Durysta™ (Bimatoprost Implant)

Oklahoma Health Care Authority
February 2021

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

- **Durysta™ (Bimatoprost Implant):** In March 2020, the FDA approved Durysta™ (bimatoprost implant) 10mcg as the first intracameral, ophthalmic drug delivery system with a biodegradable, sustained-release prostaglandin analog implant indicated to reduce intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT). Due to possible corneal endothelial cell loss, administration of Durysta™ should be limited to a single implant per eye without retreatment. Durysta™ is preloaded into a single-use applicator to facilitate the administration of the biodegradable implant directly into the anterior chamber of the eye. The FDA approval is based on results from (2) 20-month (including an 8-month extended follow up) Phase 3 ARTEMIS studies evaluating 1,122 patients on the efficacy and safety of Durysta™ versus twice daily topical timolol ophthalmic drops, an FDA accepted comparator for registrational clinical studies, in patients with OAG or OHT. In the 2 Phase 3 ARTEMIS studies, Durysta™ reduced IOP by approximately 30% from baseline over the 12-week primary efficacy period, meeting the predefined criteria for non-inferiority to the study comparator. The Wholesale Acquisition Cost (WAC) of each Durysta™ 10mcg implant is $1,950.00.

Recommendations

The College of Pharmacy recommends the prior authorization of Durysta™ (bimatoprost implant) with the following criteria:

Durysta™ (Bimatoprost Implant) Approval Criteria:

1. An FDA approved indication to reduce intraocular pressure (IOP) in members with open-angle glaucoma (OAG) or ocular hypertension (OHT); and
2. Member must be 18 years of age or older; and
3. Durysta™ must be prescribed by, or in consultation with, an ophthalmologist; and
4. A patient-specific, clinically significant reason why the member requires Durysta™ and cannot utilize ophthalmic preparations, such as solution or suspension, to treat OAG or OHT must be provided; and

5. The affected eye(s) has not received prior treatment with Durysta™; and
6. The member has no contraindications to Durysta™; and
7. A quantity limit of (1) Durysta™ 10mcg implant per eye per lifetime will apply.

[1] Allergan. Allergan Receives FDA Approval for Durysta™ (Bimatoprost Implant) the First and Only Intracameral Biodegradable Sustained-Release Implant to Lower Intraocular Pressure in Open-Angle Glaucoma or Ocular Hypertension Patients. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/allergan-receives-fda-approval-for-durysta-bimatoprost-implant-the-first-and-only-intracameral-biodegradable-sustained-release-implant-to-lower-intraocular-pressure-in-open-angle-glaucoma-or-ocular-hypertension-patients-301017349.html. Issued 03/05/2020. Last accessed 01/12/2021.

[2] Durysta™ Prescribing Information. Allergan. Available online at: https://media.allergan.com/products/durysta_pi.pdf. Last revised 11/2020. Last accessed 01/12/2021.

Appendix J

Fiscal Year 2020 Annual Review of Crysvita® (Burosumab-twza)

Oklahoma Health Care Authority
February 2021

Introduction[1,2,3]

X-linked hypophosphatemia (XLH) is an inherited, X-linked disorder caused by mutations in the *PHEX* (phosphate-regulating endopeptidase on the X chromosome) gene. Mutations in *PHEX* result in increased concentrations of fibroblast growth factor 23 (FGF23), a protein produced by osteocytes in bones that regulates serum phosphate levels. Excess FGF23 inhibits renal sodium/phosphate cotransporters resulting in inhibition of phosphate reabsorption and causing subsequent hypophosphatemia. Chronic hypophosphatemia leads to poor bone mineralization and fractures. XLH is inherited in an X-linked dominant pattern; therefore, both males and females can develop XLH. While the majority of cases are inherited, de novo mutations in *PHEX* can occur in a person with no family history of the disease. It is estimated that XLH occurs in approximately 1 in 20,000 live births. In children, XLH causes rickets that leads to lower-extremity deformity, delayed growth, and decreased height. Adults with XLH have an increased risk of fractures.

Tumor-induced osteomalacia (TIO) is a rare disease caused by typically benign, slow-growing tumors that produce excess levels of FGF23, which is involved in phosphate reabsorption. Patients with TIO can experience symptoms including severe hypophosphatemia, osteomalacia, muscle weakness, fatigue, bone pain, and fractures. There are an estimated 500 to 1,000 people in the United States with TIO, and approximately half of all cases are believed to be inoperable. In patients for whom the tumor or lesion is inoperable, the current treatment consists of oral phosphate and/or active vitamin D replacement. Efficacy of this management is often limited, and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis and hyperparathyroidism.

Current Prior Authorization Criteria

Crysvita® (Burosumab-twza) Approval Criteria:

1. An FDA approved indication for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric members 1 year of age and older. Diagnosis of XLH must be confirmed by 1 of the following:
   a. Genetic testing; or

   b. Elevated serum fibroblast growth factor 23 (FGF23) level; and
2. Member's serum phosphorus level must be below the normal range for member age; and
3. Member must not have any contraindications to taking Crysvita® including the following:
   a. Concomitant use with oral phosphate and active vitamin D analogs; and
   b. Serum phosphorus within or above the normal range for member age; and
   c. Severe renal impairment or end-stage renal disease; and
4. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
   a. Crysvita® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
   b. Crysvita® must be shipped via cold chain supply to the member's home and administered by a home health care provider if the member's caregiver has been trained on the proper storage of Crysvita®; and
5. Member must have clinical signs and symptoms of XLH (symptoms beyond hypophosphatemia alone); and
6. Every 2 week dosing will not be approved for members 18 years of age or older; and
7. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment, and thereafter as appropriate; and
8. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and
9. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; 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.

Utilization of Crysvita® (Burosumab-twza): Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	4	21	$313,027.63	$14,906.08	$532.36	46	588
2020	7	67	$914,663.59	$13,651.70	$487.56	159	1,876
%	**75.00%**	**219.00%**	**192.20%**	**-8.40%**	**-8.40%**	**245.70%**	**219.00%**
Change	**3**	**46**	**$601,635.96**	**-$1,254.38**	**-$44.80**	**113**	**1,288**

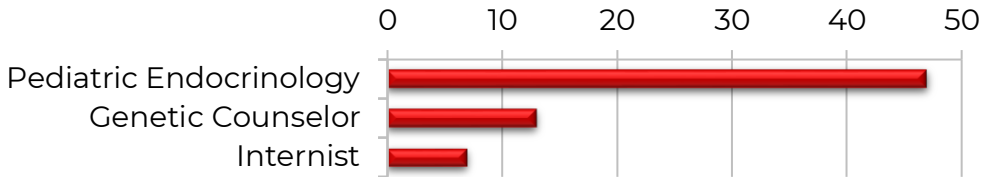
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

- There were no SoonerCare paid medical claims for Crysvita® (burosumab-twza) during fiscal year 2020.

Demographics of Members Utilizing Crysvita® (Burosumab-twza)

- Due to the limited number of members utilizing Crysvita® (burosumab-twza), detailed demographic information could not be provided.

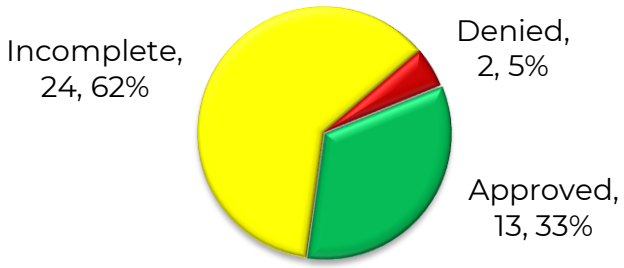
Top Prescriber Specialties of Crysvita® (Burosumab-twza) by Number of Claims



Prior Authorization of Crysvita® (Burosumab-twza)

There were 39 prior authorization requests submitted for Crysvita® (burosumab-twza) for 7 unique members during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[2,3]

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

- **September 2019:** The FDA approved a label expansion for Crysvita® (burosumab-twza) to include new clinical data demonstrating superiority of treatment with Crysvita® versus oral phosphate and active vitamin D (conventional therapy) in pediatric patients with XLH, and improvement in stiffness and maintenance of efficacy of Crysvita® in adult patients with longer-term treatment. The indication has also been expanded to include infants as young as 6 months of age. Crysvita® is an antibody that binds to and inhibits the biological activity of FGF23, restoring renal phosphate reabsorption and increasing the serum concentration of 1,25-dihydroxy vitamin D. It was first approved in the United States in April 2018 for the treatment of XLH in adult and pediatric patients 1 year of age and older. For the pediatric XLH population, the FDA label update is based on 64-week efficacy and safety data from the randomized active-controlled Phase 3 study of Crysvita® compared with oral phosphate and active vitamin D in 61 children with XLH. The results showed that Crysvita® was superior to conventional therapy for all key efficacy endpoints, showing a meaningful improvement in rickets severity, lower limb deformity and growth. The 64-week safety profile was similar to that observed at 40 weeks and in other Crysvita® pediatric XLH studies. For the adult XLH population, the label update incorporates results from the open-label treatment period of the Phase 3 study in 134 adult patients with XLH through week 48, demonstrating that serum phosphorus levels were maintained with no evidence of loss of effect. The updated label also includes results demonstrating the continued healing of fractures and pseudofractures at week 48 and improvement in the patient-reported outcome of stiffness at week 24. The safety profile is consistent with what has been previously observed in this study, with no new adverse reactions identified during the extended treatment period.
- **June 2020:** The FDA approved Crysvita® (burosumab-twza) for the treatment of FGF23-related hypophosphatemia in TIO associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older. TIO is a rare disease caused by typically benign, slow-growing tumors that produce excess levels of FGF23, which is involved in phosphate reabsorption. The FDA approval of Crysvita® for TIO was based on data from 2 single-arm Phase 2 studies: a 144-week study in 14 adult patients conducted by Ultragenyx in the United States and an 88-week study in 13 adult patients conducted by Kyowa Kirin in Japan and South Korea. In both studies, Crysvita® was associated with increases in serum phosphorus and serum 1,25-dihydroxyvitamin D levels. Increased

phosphate levels led to improvements in osteomalacia. Additionally, whole body bone scans demonstrated reduced tracer uptake with long-term treatment suggesting healing of bone lesions. The most common adverse reactions (>10%) in TIO patients were: tooth abscess, muscle spasms, dizziness, constipation, injection site reaction, rash, and headache.

Recommendations

The College of Pharmacy recommends updating the prior authorization criteria for Crysvita® (burosumab-twza) based on the FDA label expansion and the new FDA approved indication with the following criteria (changes and additions shown in red):

Crysvita® (Burosumab-twza) Approval Criteria [X-Linked Hypophosphatemia (XLH) Diagnosis]:

1. An FDA approved indication for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric members ~~1 year~~ 6 months of age and older. Diagnosis of XLH must be confirmed by 1 of the following:
   a. Genetic testing; or
   b. Elevated serum fibroblast growth factor 23 (FGF23) level; and
2. Member's serum phosphorus level must be below the normal range for member age; and
3. Member must not have any contraindications to taking Crysvita® including the following:
   a. Concomitant use with oral phosphate and active vitamin D analogs; and
   b. Serum phosphorus within or above the normal range for member age; and
   c. Severe renal impairment or end-stage renal disease; and
4. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
   a. Crysvita® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
   b. Crysvita® must be shipped via cold chain supply to the member's home and administered by a home health care provider if the member's caregiver has been trained on the proper storage of Crysvita®; and
5. Member must have clinical signs and symptoms of XLH (symptoms beyond hypophosphatemia alone); and
6. Every 2 week dosing will not be approved for members 18 years of age or older; and

7. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment, and thereafter as appropriate; and
8. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and
9. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; 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.

Crysvita® (Burosumab-twza) Approval Criteria [Tumor-Induced Osteomalacia (TIO) Diagnosis]:

1. An FDA approved diagnosis for the treatment of fibroblast growth factor 23 (FGF-23)-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in members 2 years of age and older; and
2. Member's diagnosis must be confirmed by elevated serum FGF23 level that was not amendable to cure by surgical excision of the underlying tumor/lesion; and
3. Member's serum phosphorus level must be below the normal range for member age; and
4. Member must not have any contraindications to taking Crysvita® including the following:
    a. Concomitant use with oral phosphate and active vitamin D analogs; and
    b. Serum phosphorus within or above the normal range for member age; and
    c. Severe renal impairment or end-stage renal disease; and
5. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
    a. Crysvita® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Crysvita® must be shipped via cold chain supply to the member's home and administered by a home health care provider if the

member's caregiver has been trained on the proper storage of Crysvita®; and

6. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment and thereafter as appropriate and follow the Crysvita® *Prescribing Information* for dose adjustments; and
7. The prescriber must agree to monitor 25-hydroxy vitamin D levels; and
8. Crysvita® must be prescribed by an endocrinologist or specialist with expertise in the treatment of TIO (or an advanced care practitioner with a supervising physician who is an endocrinologist or specialist with expertise in treating TIO); and
9. The member's recent weight (within the last 3 months) 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 authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; and
11. Early refill requests for dose changes more frequently than every 4 weeks will not be approved; and
12. The maximum approvable dosing regimen is 180mg every 2 weeks; and
13. A quantity limit of 12 single-dose vials per month will apply.

Utilization Details of Crysvita® (Burosumab-twza): Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
CRYSVITA INJ 10MG/ML	36	3	$166,980.46	$165.66	$16.04
CRYSVITA INJ 20MG/ML	17	3	$262,769.47	$552.04	$13.56
CRYSVITA INJ 30MG/ML	14	2	$484,913.66	$1,237.02	$263.19
TOTAL	**67**	**7***	**$914,663.59**	**$487.56**	**$13,651.70**

INJ = injection
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

[1] Scheinman SJ, Drezner MK. Hereditary Hypophosphatemic Rickets and Tumor-Induced Osteomalacia. *UpToDate*. Available online at: https://www.uptodate.com/contents/hereditary-hypophosphatemic-rickets-and-tumor-induced-osteomalacia. Last revised 10/15/2020. Last accessed 01/07/2021.
[2] Ultragenyx Pharmaceutical Inc. Ultragenyx and Kyowa Kirin Announce U.S. FDA Approves Label Update for Crysvita® (Burosumab) for the Treatment of X-Linked Hypophosphatemia (XLH). *Globe Newswire*. Available online at: https://ir.ultragenyx.com/news-releases/news-release-details/ultragenyx-and-kyowa-kirin-announce-us-fda-approves-label-update. Issued 09/30/2019. Last accessed 01/07/2021.
[3] Ultragenyx Pharmaceutical Inc. Ultragenyx and Kyowa Kirin Announce U.S. FDA Approval of Crysvita® (Burosumab) for the Treatment of Tumor-Induced Osteomalacia (TIO). *Globe Newswire*. Available online at: https://ir.ultragenyx.com/news-releases/news-release-details/ultragenyx-and-kyowa-kirin-announce-us-fda-approval-crysvitar. Issued 06/18/2020. Last accessed 01/07/2021.

Appendix K

Fiscal Year 2020 Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Inqovi® (Decitabine/Cedazuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx)

Oklahoma Health Care Authority
February 2021

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 72 years. CLL/SLL is the most prevalent adult leukemia in western countries. In 2020, there were an estimated 21,040 new diagnoses and 4,060 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 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 [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As a single-agent.

Calquence® (Acalabrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) 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. In combination with low-dose cytarabine (LDAC); and
3. Members 75 years of age or older or who have significant comorbid conditions [severe cardiac disease, ECOG performance status ≥2, or serum creatinine (SCr) >1.3].

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 all other 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 in members 75 years of age or older or who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. *IDH2* mutation; or
2. Relapsed/refractory AML; and
    a. *IDH2* mutation; and
    b. As a single-agent.

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 [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 [Chronic Graft-Versus-Host Disease (cGVHD) Diagnosis]:

1. Failure of 1 or more lines of therapy.

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 [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 [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 [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 [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 [Hairy Cell Leukemia (HCL) Diagnosis]:

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

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.

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.

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 patients who have relapsed; or
c. T315I mutation; or
d. Members who are intolerant or resistant to ≥2 or more 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 in members 75 years of age or older or who have comorbidities that preclude use of intensive chemotherapy; and
   a. As a single-agent; and
   b. *IDH1* 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 must be 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; and
3. In combination with azacitidine, decitabine, or low-dose cytarabine (LDAC).

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

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

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.

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

1. Relapsed/refractory AML; and
2. FLT3 mutation; and
3. 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.

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 [Erdheim-Chester Disease (ECD) Diagnosis]:

1. Diagnosis of ECD; and
2. *BRAF* V600E or V600K mutation; and
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.

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.

Utilization of Leukemia Medications: Fiscal Year 2020

The following utilization data includes medications indicated for leukemia; 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
2019	43	264	$3,070,021.60	$11,628.87	$394.60	14,096	7,780
2020	49	324	$4,269,946.28	$13,178.85	$446.09	16,322	9,572
% Change	**14.00%**	**22.70%**	**39.10%**	**13.30%**	**13.00%**	**15.80%**	**23.00%**
Change	**6**	**60**	**$1,199,924.68**	**$1,549.98**	**$51.49**	**2,226**	**1,792**

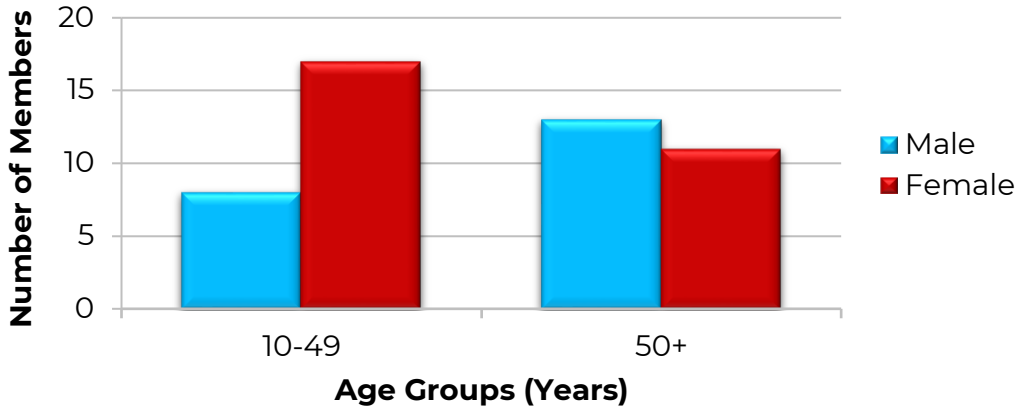
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Fiscal Year Comparison: Medical Claims

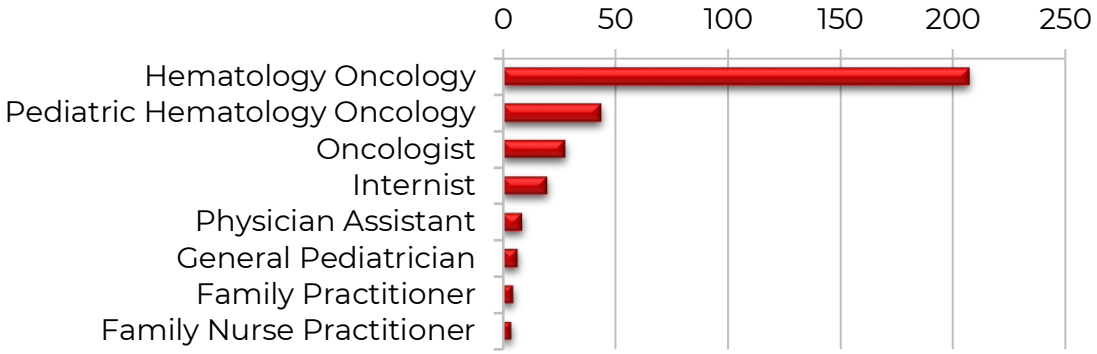
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	6	17	$250,557.04	$14,738.65	2,134
2020	10	31	$378,691.17	$12,215.84	2,696
% Change	**66.67%**	**82.35%**	**51.14%**	**-17.12%**	**26.34%**
Change	**4**	**14**	**$128,134.13**	**-$2,522.81**	**562**

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

Demographics of Members Utilizing Leukemia Medications: Pharmacy Claims

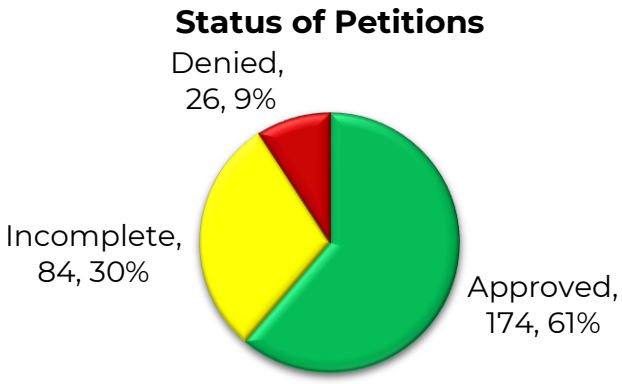


Top Prescriber Specialties of Leukemia Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Leukemia Medications

There were 284 prior authorization requests submitted for leukemia medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



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

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

- **March 2020:** AbbVie announced the trial of Venclexta® (venetoclax) in combination with azacitidine versus azacitidine in combination with placebo, VIALE-A, met its dual primary endpoints of statistically significant improvement of overall survival (OS) and composite complete remission rate for patients with previously-untreated AML who are ineligible for intensive chemotherapy.
- **March 2020:** The National Comprehensive Cancer Network (NCCN) AML Guidelines and the NCCN Drugs and Biologics Compendium were updated to expand the appropriate utilization of Venclexta® (venetoclax) to include relapsed/refractory AML patients.
- **April 2020:** The FDA approved an expanded indication for Imbruvica® (ibrutinib) to include its use in combination with rituximab for the initial treatment of adult patients with CLL or SLL.
- **June 2020:** The FDA approved an expanded indication for Mylotarg™ (gemtuzumab ozogamicin) for newly-diagnosed CD33-positive AML to include pediatric patients 1 month of age and older.
- **July 2020:** The FDA approved Inqovi® (decitabine/cedazuridine) for the treatment of adult patients with myelodysplastic syndromes (MDS).
- **September 2020:** The FDA approved Onureg® (azacitidine) for continued treatment of patients with AML who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.
- **October 2020:** The FDA granted regular approval to Venclexta® (venetoclax) in combination with azacitidine, decitabine, or low-dose cytarabine (LDAC) for newly-diagnosed AML in adults 75 years of age or older, or who have comorbidities precluding intensive induction chemotherapy. Venclexta® was initially granted accelerated approval

for this indication in November 2018. Efficacy was confirmed in 2 randomized, double-blind, placebo-controlled trials.

- **December 2020:** The FDA approved the supplemental New Drug Application (sNDA) for Iclusig® (ponatinib) for the treatment of adults with chronic-phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least 2 prior kinase inhibitors.
- **December 2020:** The FDA approved Riabni™ (rituximab-arrx), a biosimilar to Rituxan® (rituximab), for the treatment of adult patients with non-Hodgkin lymphoma (NHL), CLL, granulomatosis with polyangiitis (GPA; Wegener's granulomatosis), and microscopic polyangiitis (MPA). Riabni™, a CD20-directed cytolytic antibody, was proven to be highly similar to Rituxan® based on a totality of evidence, which included comparative analytical, nonclinical, and clinical data, with no clinically meaningful differences in safety or effectiveness.

Product Summaries[13,14,15]

Inqovi® (Decitabine/Cedazuridine):

- **Therapeutic Class:** Combination of a nucleoside metabolic inhibitor (decitabine) and a cytidine deaminase inhibitor (cedazuridine)
- **Indication(s):** Treatment of adult patients with MDS, including previously treated and untreated, de novo and secondary MDS with French-American-British subtypes [refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia (CMML)] and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups
- **How Supplied:** 35mg decitabine/100mg cedazuridine oral tablets
- **Dose:** One tablet (35mg decitabine/100mg cedazuridine) taken once daily on days 1 through 5 of each 28-day cycle
- **Cost:** The Wholesale Acquisition Cost (WAC) is $1,499.00 per tablet, resulting in a cost of $7,495.00 per 28 days based on the recommended dosing of 1 tablet daily on days 1 through 5 of each 28-day cycle

Onureg® (Azacitidine):

- **Therapeutic Class:** Nucleoside metabolic inhibitor
- **Indication(s):** Treatment of adult patients with AML who achieved first CR or CRi following intensive induction chemotherapy and are not able to complete intensive curative therapy
- **How Supplied:** 200mg and 300mg oral tablets
- **Dose:** 300mg once daily on days 1 through 14 of each 28-day cycle; 200mg strength available for dose modification if needed
- **Cost:** The WAC is $1,511.29 per tablet for either strength, resulting in a cost of $21,158.06 per 28 days based on the recommended dosing of 1 tablet daily on days 1 through 14 of each 28-day cycle

Riabni™ (Rituximab-arrx):

- **Therapeutic Class:** CD20-directed cytolytic antibody; biosimilar to Rituxan® (rituximab)
- **Indication(s):**
  - Treatment of adult patients with NHL:
    - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single-agent after first-line cyclophosphamide, vincristine, and prednisone (CVP)
    - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
  - Treatment of adult patients with CLL:
    - Previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC)
  - Treatment of adult patients with GPA and MPA in combination with corticosteroids
- **How Supplied:** 100mg/10mL and 500mg/50mL solution for intravenous (IV) infusion in a single-dose vial (SDV)
- **Dose:**
  - NHL: 375mg/m^2 IV infusion; see Riabni™ *Prescribing Information* for dosing schedules specific to type of NHL being treated
  - CLL: 375mg/m^2 in the first cycle and 500mg/m^2 in cycles 2 through 6, in combination with FC, administered every 28 days
  - GPA and MPA: For induction, 375mg/m^2 once weekly for 4 weeks with corticosteroids; then (2) 500mg IV infusions separated by 2 weeks; then 500mg IV every 6 months thereafter
- **Cost:** The WAC is $71.68 per milliliter (mL) for both vial sizes, with a cost per vial of $716.80 (100mg/10mL) and $3,584.00 (500mg/50mL); cost will vary depending on patient weight, diagnosis, and treatment duration

Recommendations

The College of Pharmacy recommends the prior authorization of Inqovi® (decitabine/cedazuridine), Onureg® (azacitidine), and Riabni™ (rituximab-arrx) with the following criteria (shown in red):

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 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).

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.

Riabni™ (Rituximab-arrx) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Rituxan® (rituximab) must be provided.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Iclusig® (ponatinib) based on FDA approval; changes noted in red:

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 ~~all other~~ 2 or more tyrosine kinase inhibitors (TKIs); or
    c. Post-hematopoietic stem cell transplantation in members with prior accelerated or blast phase prior to transplant or who have relapsed.

Finally, the College of Pharmacy recommends updating the prior authorization criteria for Venclexta® (venetoclax) based on NCCN compendia approval; changes and new criteria noted in red (only criteria with updates are listed):

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

1. Member meets 1 of the following:
    a. Member must be 75 years of age or older; or

b. If the member is younger than 75 years of age, they must be unable to tolerate intensive induction chemotherapy; and

2. ~~Must be used~~ As first-line therapy or in relapsed/refractory disease; and
3. Must be used in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC).

Utilization Details of Leukemia Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
DASATINIB PRODUCTS					
SPRYCEL TAB 100MG	109	16	$1,477,575.81	6.81	$13,555.74
SPRYCEL TAB 140MG	16	2	$227,332.18	8	$14,208.26
SPRYCEL TAB 70MG	8	2	$54,613.55	4	$6,826.69
SPRYCEL TAB 50MG	7	3	$67,833.44	2.33	$9,690.49
SPRYCEL TAB 20MG	6	2	$63,097.69	3	$10,516.28
SUBTOTAL	**146**	**25**	**$1,890,452.67**	**5.84**	**$12,948.31**
IBRUTINIB PRODUCTS					
IMBRUVICA TAB 420MG	35	6	$441,610.75	5.83	$12,617.45
IMBRUVICA TAB 280MG	16	3	$199,576.04	5.33	$12,473.50
IMBRUVICA CAP 140MG	7	2	$51,809.38	3.5	$7,401.34
IMBRUVICA TAB 560MG	5	3	$63,983.13	1.67	$12,796.63
SUBTOTAL	**63**	**14**	**$756,979.30**	**4.5**	**$12,015.54**
NILOTINIB PRODUCTS					
TASIGNA CAP 150MG	26	4	$369,340.94	6.5	$14,205.42
TASIGNA CAP 200MG	9	2	$127,720.99	4.5	$14,191.22
SUBTOTAL	**35**	**6**	**$497,061.93**	**5.83**	**$14,201.77**
PONATINIB PRODUCTS					
ICLUSIG TAB 45MG	14	3	$232,011.58	4.67	$16,572.26
ICLUSIG TAB 15MG	3	1	$66,274.19	3	$22,091.40
SUBTOTAL	**17**	**4**	**$298,285.77**	**4.25**	**$17,546.22**
ACALABRUTINIB PRODUCTS					
CALQUENCE CAP 100MG	17	2	$239,216.35	8.5	$14,071.55
SUBTOTAL	**17**	**2**	**$239,216.35**	**8.5**	**$14,071.55**
VENETOCLAX PRODUCTS					
VENCLEXTA TAB 100MG	13	4	$91,130.00	3.25	$7,010.00
VENCLEXTA TAB STARTER	1	1	$2,534.36	1	$2,534.36
SUBTOTAL	**14**	**5**	**$93,664.36**	**2.8**	**$6,690.31**
BOSUTINIB PRODUCTS					
BOSULIF TAB 100MG	7	2	$81,234.75	3.5	$11,604.96
BOSULIF TAB 500MG	1	1	$15,684.35	1	$15,684.35
BOSULIF TAB 400MG	1	1	$15,684.35	1	$15,684.35
SUBTOTAL	**9**	**4**	**$112,603.45**	**2.25**	**$12,511.49**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ENASIDENIB PRODUCTS					
IDHIFA TAB 100MG	8	1	$212,435.32	8	$26,554.42
SUBTOTAL	**8**	**1**	**$212,435.32**	**8**	**$26,554.42**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	8	1	$86,864.68	8	$10,858.09
SUBTOTAL	**8**	**1**	**$86,864.68**	**8**	**$10,858.09**
IDELALISIB PRODUCTS					
ZYDELIG TAB 150MG	5	1	$53,621.13	5	$10,724.23
SUBTOTAL	**5**	**1**	**$53,621.13**	**5**	**$10,724.23**
ALPELISIB PRODUCTS					
PIQRAY 300MG DAILY DOSE	1	1	$16,363.91	1	$16,363.91
SUBTOTAL	**1**	**1**	**$16,363.91**	**1**	**$16,363.91**
DUVELISIB PRODUCTS					
COPIKTRA CAP 15MG	1	1	$12,397.41	1	$12,397.41
SUBTOTAL	**1**	**1**	**$12,397.41**	**1**	**$12,397.41**
TOTAL	**324**	**49***	**$4,269,946.28**	**6.61**	**$13,178.85**

CAP = capsule; TAB = tablet
*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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
BRENTUXIMAB VEDOTIN J9042	25	7	$336,985.65	3.57	$13,479.43
BLINATUMOMAB J9039	5	2	$23,005.50	2.5	$4,601.10
INOTUZUMAB OZOGAMICIN J9229	1	1	$18,700.02	1	18,700.02
TOTAL	**31**	**10**	**$378,691.17**	**3.1**	**$12,215.84**

+Total number of unduplicated claims.
*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

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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 2.2019. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Last accessed 01/11/2021.
[4] Hallek M. Chronic Lymphocytic Leukemia: 2015 Update on Diagnosis, Risk Stratification, and Treatment. *Am J Hematol* 2015; 90:446-460.
[5] AbbVie. AbbVie Announces Positive Topline Results from Phase 3 Trial of Venclexta® (Venetoclax) in Combination with Azacitidine in Patients with Acute Myeloid Leukemia (AML). *PR Newswire*. Available online at: https://news.abbvie.com/news/press-releases/abbvie-announces-positive-topline-results-from-phase-3-trial-venclexta-venetoclax-in-combination-with-azacitidine-in-patients-with-acute-myeloid-leukemia-aml.htm. Issued 03/23/2020. Last accessed 12/29/2020.
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[7] National Comprehensive Cancer Network (NCCN) Drugs and Biologic Compendium. Available by subscription online at: https://www.nccn.org/professionals/drug_compendium/content/pdf. Last accessed 01/11/2021.
[8] Jonas BA, Pollyea DA. How We Use Venetoclax With Hypomethylating Agents for the Treatment of Newly Diagnosed Patients with Acute Myeloid Leukemia. *Leukemia* 2019; 33:2795-2804.
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[11] Park B. Iclusig Approved for Resistant or Intolerant Chronic-Phase CML. *MPR*. Available online at: https://www.empr.com/home/news/iclusig-approved-for-resistant-or-intolerant-chronic-phase-cml/. Issued 12/22/2020. Last accessed 02/08/2021.
[12] Amgen. FDA Approves Amgen's Riabni™ (Rituximab-arrx), A Biosimilar to Rituxan® (Rituximab). *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-amgens-riabni-rituximab-arrx-a-biosimilar-to-rituxan-rituximab-301195492.html. Issued 12/17/2020. Last accessed 12/30/2020.
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[14] Onureg® Prescribing Information. Celgene Corporation. Available online at: https://packageinserts.bms.com/pi/pi_onureg.pdf. Last revised 09/2020. Last accessed 12/29/2020.
[15] Riabni™ Prescribing Information. Amgen. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761140s000lbl.pdf. Last revised 12/2020. Last accessed 12/30/2020.

Appendix L

Fiscal Year 2020 Annual Review of Azedra® (Iobenguane I-131)

Oklahoma Health Care Authority
February 2021

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. Most are benign, but 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 2020

There was no SoonerCare utilization of Azedra® (iobenguane I-131), including pharmacy and medical claims, during fiscal year 2020 (fiscal year 2020 = 07/01/2019 to 06/30/2020).

Prior Authorization of Azedra® (Iobenguane I-131)

There were no prior authorization requests submitted for Azedra® (iobenguane I-131) during fiscal year 2020.

Market News and Updates[2]

Anticipated Patent Expiration(s):

- Azedra® (iobenguane I-131): 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.
[2] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 01/2021. Last accessed 01/05/2021.

Appendix M

Fiscal Year 2020 Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Fintepla® (Fenfluramine)

Oklahoma Health Care Authority
February 2021

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. The member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. The member must not be taking St. John's wort concurrently with Afinitor®; and
7. The 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 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 1 other anticonvulsant; 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; 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, the member must have failed therapy 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.

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 patients 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 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.

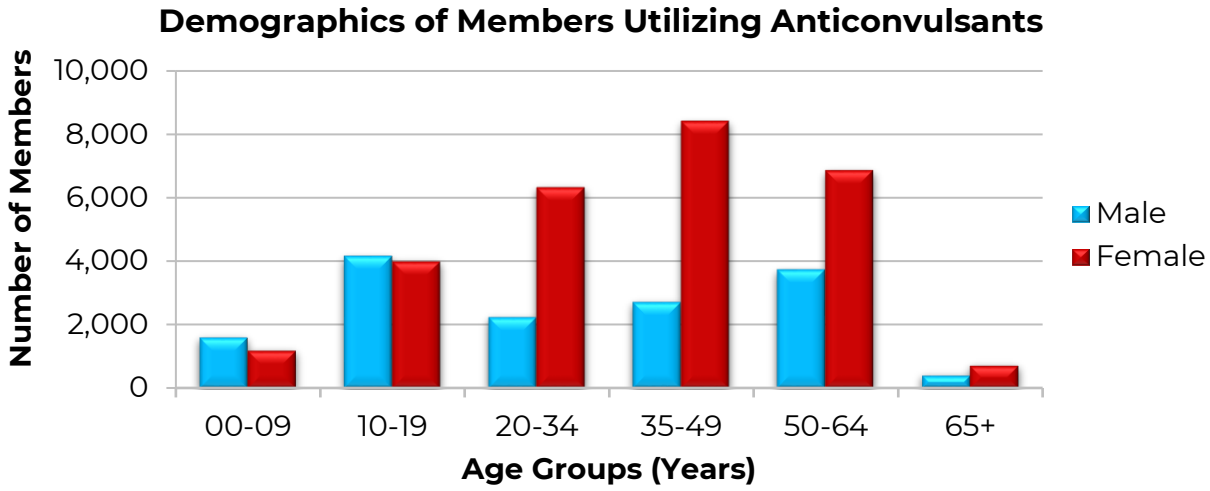
Utilization of Anticonvulsants: Fiscal Year 2020

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

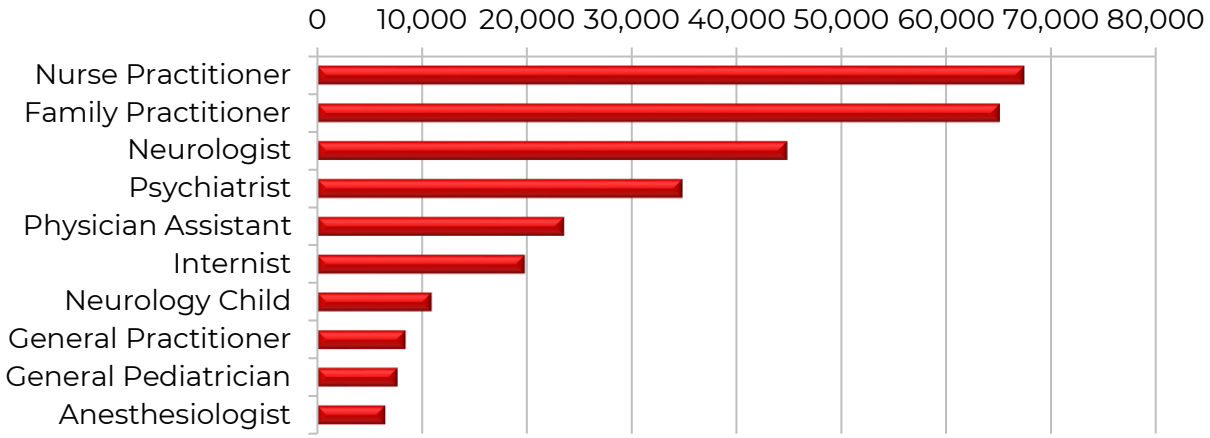
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	44,224	318,779	$26,907,990.78	$84.41	$2.77	31,091,840	9,719,557
2020	42,227	315,101	$28,219,484.87	$89.56	$2.86	31,713,138	9,880,868
% Change	**-4.5%**	**-1.2%**	**4.9%**	**6.1%**	**3.2%**	**2.0%**	**1.7%**
Change	**-1,997**	**-3,678**	**$1,311,494.09**	**$5.15**	**$0.09**	**621,298**	**161,311**

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



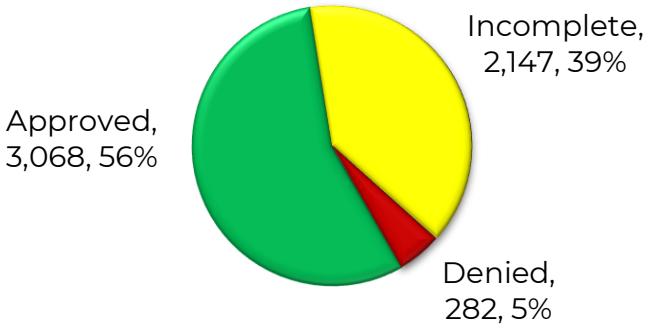
Top Prescriber Specialties of Anticonvulsants by Number of Claims



Prior Authorization of Anticonvulsants

There were 5,497 prior authorization requests submitted for anticonvulsants during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

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
- 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):

- **June 2020:** The FDA approved Fintepla® (fenfluramine) oral solution for the treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older. The effectiveness of fenfluramine in patients with DS was assessed in 2 clinical trials in 202 patients between 2 and 18 years of age. The trials measured the change from baseline in the frequency of convulsive seizures. In both trials, patients treated with Fintepla® had a significantly greater reduction in the frequency of convulsive seizures when compared to placebo, with reductions seen within 3 to 4 weeks that remained generally consistent over the 14 to 15 week treatment periods. Fintepla® is a Schedule IV controlled substance and only available through a risk evaluation and mitigation strategy (REMS) program due to the risk of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH). Cardiac monitoring with an echocardiogram (ECHO) is required before starting treatment with Fintepla®.
- **July 2020:** The FDA approved a new indication for Epidiolex® (cannabidiol) for the treatment of seizures associated with TSC in patients 1 year of age and older. TSC is a rare genetic disease that causes benign tumors to grow in the brain and other parts of the body such as the heart and kidneys. TSC usually affects the central nervous system (CNS) and can results in seizures, development delay, and behavior problems. The effectiveness of cannabidiol for the treatment of seizures associated with TSC was assessed in a double-blind, placebo-controlled trial with 224 patients. Of the 224 patients, 148 patients received cannabidiol and 76 received placebo. The primary endpoint of the trial was the change from baseline seizure frequency. Patients treated with cannabidiol had a significantly greater reduction in the frequency of seizures during the treatment period than patients who received placebo.

News:

- **April 2020:** GW Pharmaceuticals announced that it received notification from the U.S. Drug Enforcement Administration (DEA) that Epidiolex® (cannabidiol) is no longer a controlled substance. Epidiolex®

(cannabidiol) was initially placed in Schedule V of the Controlled Substance Act (CSA) when it was first FDA approved in November 2018.

- **July 2020:** Results from a Phase 2a trial published in *Lancet Psychiatry* showed that prescription grade cannabidiol (CBD) was safe and more effective than placebo at reducing cannabis use when administered at daily doses of 400mg and 800mg. The trial included 82 adult patients who met Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria for cannabis use disorder of at least moderate severity, who expressed a desire to quit cannabis, and who had at least 1 prior unsuccessful attempt at quitting. In the first phase of the dose-finding trial, 48 patients were randomly allocated to receive oral CBD at 200mg, 400mg, and 800mg daily or placebo. CBD at 200mg was eliminated from the trial as it was found to be an inefficacious dose. In the second phase, 34 new patients were randomly assigned to receive 4 weeks of CBD at 400mg, 800mg, or placebo daily. Both doses of CBD, 400mg and 800mg, were associated with reduced cannabis intake with a decrease in tetrahydrocannabinol (THC) levels in the urine by -94.21ng/mL and -72.02ng/mL, respectively. Abstinence from cannabis use increased by an average of 0.5 days per week with 400mg CBD daily and 0.3 days per week with 800mg CBD daily. There were no severe adverse events recorded for patients taking CBD. It is important to note that CBD does not produce intoxicating or reward effects that are associated with THC and has contrasting effects on a patient's cannabinoid system.
- **August 2020:** Findings from the DIET trial that compared the ketogenic, modified Atkins, and low glycemic index therapy diets showed a reduction in seizures for children with drug-resistant epilepsy. The trial included 158 patients from 1 to 15 years of age with 4 or more seizures a month, who had failed 2 or more anticonvulsants, and who had not been treated with any of the diets previously mentioned. Patients were enrolled between April 2016 and August 2017 at a tertiary care referral center in India and were randomly assigned to 1 of the previously listed diets in addition to their ongoing anticonvulsant therapy. Of the 158 patients, 52 were randomized to the ketogenic diet, 52 to the modified Atkins diet, and 54 to the low glycemic index therapy diet. Patients were supplemented with vitamins and minerals and each patient's caregiver kept a daily log of meals, seizure frequency, urinary ketones, and dietary intolerances. The primary outcome studied was the percent change in seizure frequency after 24 weeks of the dietary therapy. After 24 weeks of therapy, the median change in seizure frequency was -66% in the ketogenic diet group, -45% in the modified Atkins group, and -54% in the low glycemic index therapy group. Treatment-related adverse events were similar between the ketogenic (56.4%) and

modified Atkins groups (56.9%), but were significantly lower in the low glycemic index group (33.3%). The most common adverse event seen in the clinical trial was vomiting.

Pipeline:

- **Ganaxolone:** Ganaxolone is a gamma-amino butyric acid $(GABA)_A$ receptor modulator that acts by regulating brain activity which includes inhibiting abnormal electrical discharges that cause seizures. Ganaxolone is being developed in oral and IV formulations and is in Phase 2 and Phase 3 trials for the treatment of multiple indications including cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD), protocadherin 19 (PCDH19)-related epilepsy, TSC, and refractory status epilepticus. Marinus Pharmaceuticals is anticipating a new drug application (NDA) submission to the FDA for ganaxolone mid-2021 for the treatment of CDD.

Fintepla® (Fenfluramine) Product Summary[9,10,11,12,13]

Indication(s): Fintepla® (fenfluramine) is indicated for the treatment of seizures associated with DS in patients 2 years of age and older.

Dosing:

- Fintepla® (fenfluramine) is available as a 2.2mg/mL oral solution.
- The initial and maintenance dosing of fenfluramine is 0.1mg/kg twice daily and can be increased weekly based on efficacy and tolerability.
- The maximum daily maintenance dosage of fenfluramine is 0.35mg/kg twice daily (maximum daily dosage of 26mg) for patients not on concomitant stiripentol.
- For patients taking concomitant stiripentol plus clobazam, the maximum daily maintenance dosage of fenfluramine is 0.2mg/kg (maximum daily dosage of 17mg).
- Fenfluramine may be given with or without food.

Mechanism of Action: Fenfluramine and the metabolite norfenfluramine increase extracellular levels of serotonin through interaction with serotonin transporter proteins and exhibit agonist activity at serotonin 5HT-2 receptors. The exact mechanisms of how fenfluramine exhibits its therapeutic effects in seizures associated with DS are unknown.

Warnings and Precautions:

- Valvular Heart Disease (VHD): Due to the association between serotonergic drugs and VHD, cardiac monitoring is required. Patients should undergo an ECHO to evaluate for VHD before starting treatment. If VHD is observed, the prescriber should weigh the risks and benefits of initiating therapy. ECHOs should be repeated every 6 months and once 3 to 6 months after treatment is discontinued.

- Pulmonary Arterial Hypertension (PAH): Due to the association between serotonergic drugs and PAH, cardiac monitoring is required prior to starting treatment, during treatment, and after treatment is discontinued.
- Fintepla® Risk Evaluation and Mitigation Strategy (REMS) Program: Fintepla® is only available through a restricted distribution program because of the risk of VHD and PAH. Requirements of the REMS program include:
  - Prescriber must be enrolled in the Fintepla® REMS program.
  - Prescribers must counsel patients about the risk of VHD and PAH, including signs and symptoms of each and the need for cardiac monitoring.
  - Patients must enroll in the REMS program and comply with ongoing cardiac monitoring requirements.
  - The pharmacy must be certified by enrolling in the REMS program and must only dispense to patients who are enrolled in the REMS program.
  - Wholesalers and distributors must only distribute to certified pharmacies.
- Decreased Appetite and Weight: In clinical trials, a decrease in appetite was reported as an adverse reaction in approximately 37% of patients taking fenfluramine compared to 8% of patients on placebo. Decreased weight was seen in 9% of the patients taking fenfluramine, compared to 1% in patients on placebo. Given the frequency of those adverse reactions, the growth of pediatric patients should be carefully monitored. Weights should be monitored regularly during treatment and dose adjustments may be considered as clinically appropriate.
- Somnolence, Sedation, and Lethargy: In clinical trials, somnolence, sedation, and lethargy were seen in 25% of patients taking fenfluramine, compared to 11% of patients on placebo. In general, these effects may diminish with continued treatment. Other CNS depressants could potentiate the effects of fenfluramine.
- Suicidal Behavior and Ideation: Antiepileptic drugs (AEDs) can increase the risk of suicidal thoughts or behaviors in patients taking these drugs for any indication. Patients on any AEDs for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior.
- Withdrawal of AEDs: Fenfluramine should be withdrawn gradually due to the risk of increased seizure frequency and status epilepticus. Rapid discontinuation may be considered for life threatening adverse reactions.
- Serotonin Syndrome: Serotonin syndrome may occur with fenfluramine and an increased risk of serotonin syndrome can occur with concomitant use of other serotonergic drugs such as selective

serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs). Patients should be monitored for signs and symptoms of serotonin syndrome, including mental status changes, autonomic instability, neuromuscular signs (e.g., hyperreflexia), and/or gastrointestinal (GI) symptoms. Fenfluramine should be discontinued immediately if serotonin syndrome is suspected.

- Increased Blood Pressure (BP): An increase in BP can occur with treatment with fenfluramine, and monitoring of BP is recommended.
- Glaucoma: Fenfluramine can cause mydriasis and can precipitate glaucoma. Treatment may need to be discontinued if acute decreases in visual acuity or ocular pain occur.

Adverse Reactions:

- The most common adverse reactions seen in the clinical trials (incidence at least 10% and greater than placebo) were decreased appetite; somnolence, sedation, lethargy; diarrhea; constipation; abnormal ECHO; fatigue, malaise, asthenia; ataxia, balance disorder, gait disturbance; BP increased; drooling, salivary hypersecretion; pyrexia; upper respiratory tract infection; vomiting; decreased weight; fall; and status epilepticus.

Drug Interactions:

- Stiripentol Plus Clobazam: Coadministration of fenfluramine with stiripentol plus clobazam, with or without valproate, increases fenfluramine plasma concentrations and decreases its metabolite, norfenfluramine, due to an inhibition of fenfluramine metabolism.
- Strong CYP1A2 and CYP2B6 Inducers: Coadministration with rifampin or strong CYP1A2 and CYP2B6 inducers will lower the efficacy of fenfluramine due to decreased plasma concentrations.
- Serotonin Receptor Antagonists: Coadministration of serotonin receptor antagonists, such as cyproheptadine, can decrease the efficacy of fenfluramine.
- Serotonergic Drugs: Concomitant use of fenfluramine and other serotonergic drugs can increase the risk of serotonin syndrome.

Efficacy: The safety and efficacy of fenfluramine for adjunctive treatment of seizures associated with DS were assessed in 2 randomized, double-blind, placebo-controlled trials in patients 2 to 18 years of age. In both trials, patients were inadequately controlled on at least 1 AED or other anti-seizure treatment, including vagal nerve stimulation or ketogenic diet. Patients also underwent a 6-week baseline observation period, during which a minimum of 6 convulsive seizures while on a stable AED therapy was required to be included in either trial.

- Study 1: Study 1 was a 14-week, Phase 3 trial that included 119 patients with DS, not on stiripentol therapy, who were randomized (1:1:1) to

receive either fenfluramine 0.2mg/kg/day (N=39), 0.7mg/kg/day (N=40), or placebo (N=40). The maximum dose of fenfluramine in each treatment arm was 30mg/day. Randomization was stratified by age group (<6 years and ≥6 to 18 years), and patients were titrated to the randomized dose over a 2 week titration period. Once titrated, the patients continued treatment for a 12-week maintenance period.

- Inclusion Criteria: Enrolled patients included men and non-pregnant, non-lactating women 2 to 18 years of age with a clinical diagnosis of DS with uncontrolled convulsive seizures on current AED therapy and not receiving stiripentol. Patients had to be free of cardiovascular disease (CVD) on an ECHO, electrocardiogram (ECG), or physical examination.
- Primary Endpoint: The primary endpoint was the change in mean monthly convulsive seizure frequency (MCSF) comparing the baseline with the combined titration and maintenance period for fenfluramine at 0.7mg/kg/day compared with placebo. Fenfluramine 0.2mg/kg/day versus placebo was assessed as a key secondary outcome.
- Results: The trial met its primary endpoint with fenfluramine 0.7mg/kg/day showing a 62.3% greater reduction in mean MCSF compared with placebo [95% confidence interval (CI): 47.7%, 72.8%; P<0.0001]. For the secondary endpoint, fenfluramine 0.2mg/kg/day showed a 32.4% reduction in mean MCSF when compared with placebo (95% CI: 6.2%, 52.3%; P=0.0209). A median reduction in seizure frequency was seen in all groups [fenfluramine 0.7mg/kg/day (74.9%; from median 20.7 seizures per 28 days to 4.7 seizures per 28 days), fenfluramine 0.2mg/kg/day (42.3%; from median 17.5 seizures per 28 days to 12.6 seizures per 28 days), and placebo (19.2%; from median 27.3 seizures per 28 days to 22.0 seizures per 28 days)].

- Study 2: Study 2 was a 15-week, Phase 3 trial that included 87 patients with DS, on stiripentol-containing AED regimens, who were randomized (1:1) to receive either fenfluramine 0.4mg/kg/day (N=43) or placebo (N=44). The maximum dose of fenfluramine was 17mg/day. Randomization was stratified by age group (<6 years and ≥6 years of age), and patients were titrated to the randomized dose over a 3 week titration period. Once titrated, the patients continued treatment for a 12-week maintenance period.
  - Inclusion Criteria: Similar criteria to Study 1, except patients had to be on a stable, stiripentol-inclusive AED regimen.
  - Primary Endpoint: The primary endpoint was the change in mean MCSF comparing the baseline with the combined titration and maintenance period for fenfluramine compared with placebo.

- Results: Patients receiving fenfluramine achieved a 54.0% greater reduction in mean MCSF compared to those receiving placebo (95% CI: 35.6%, 67.2%; P<0.001).

Cost Comparison: Anticonvulsant Therapies for DS[14]

Medication	Unit Cost*	FDA Maximum Dose	Cost of Therapy for 4 Weeks
Fintepla® (fenfluramine) 2.2mg/mL oral solution	**$42.60**	**26mg/day**	**$14,096.72**
Diacomit® (stiripentol) 500mg capsule	$50.00	3,000mg/day	$8,400.00
Epidiolex® (cannabidiol) 100mg/mL oral solution	$13.10	20mg/kg/day	$2,567.60
clobazam 2.5mg/mL oral suspension	$0.47	40mg/day	$210.56
valproic acid 250mg/5mL oral solution	$0.02	60mg/kg/day	$23.52
levetiracetam 100 mg/mL oral solution	$0.03	3,000mg/day	$25.20
topiramate 200mg tablet	$0.09	400mg/day	$5.04

Cost of therapy calculated based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC) or State Maximum Allowable Costs (SMAC).
Costs do not reflect rebated prices or net costs.
*Unit = tablet, capsule, or mL
A weight of 35kg was used as a comparison for medications that did not have a specific total dose per day listed as the FDA maximum dose.

Recommendations

The College of Pharmacy recommends the prior authorization of Fintepla® (fenfluramine) with the following criteria shown in red:

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. 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.

Additionally, the College of Pharmacy recommends updating the current approval criteria for Epidiolex® (cannabidiol) based on the new FDA approved indication (changes noted in red):

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 with at least 2* other anticonvulsants (*The manufacturer of Epidiolex® has currently provided a supplemental rebate to require a trial with 2 other anticonvulsant therapies; however, Epidiolex® will follow the original criteria and require trials with 3 other anticonvulsant therapies if the manufacturer chooses not to participate in supplemental rebates.); and
6. Members currently stable on Epidiolex® and who have a seizure diagnosis will be grandfathered; and
7. Member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and

8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Utilization Details of Anticonvulsants: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
ACETAZOLAMIDE PRODUCTS					
ACETAZOLAMIDE TAB 250MG	353	108	$23,205.11	$65.74	3.3
ACETAZOLAMIDE CAP 500MG ER	240	88	$13,786.21	$57.44	2.7
ACETAZOLAMIDE TAB 125MG	76	28	$4,187.44	$55.10	2.7
SUBTOTAL	**669**	**224**	**$41,178.76**	**$61.55**	**3.0**
BRIVARACETAM PRODUCTS					
BRIVIACT TAB 100MG	440	56	$484,180.61	$1,100.41	7.9
BRIVIACT TAB 50MG	284	48	$271,003.43	$954.24	5.9
BRIVIACT SOL 10MG/ML	96	15	$106,213.65	$1,106.39	6.4
BRIVIACT TAB 25MG	23	8	$28,164.32	$1,224.54	2.9
BRIVIACT TAB 10MG	8	2	$9,456.30	$1,182.04	4.0
BRIVIACT TAB 75MG	7	3	$7,043.70	$1,006.24	2.3
SUBTOTAL	**858**	**132**	**$906,062.01**	**$1,056.02**	**6.5**
CANNABIDIOL PRODUCTS					
EPIDIOLEX SOL 100MG/ML	1,370	178	$2,503,024.60	$1,827.03	7.7
SUBTOTAL	**1,370**	**178**	**$2,503,024.60**	**$1,827.03**	**7.7**
CARBAMAZEPINE PRODUCTS					
CARBAMAZEPINE TAB 200MG	3,071	586	$103,319.94	$33.64	5.2
CARBAMAZEPINE CHW 100MG	568	97	$21,128.13	$37.20	5.9
CARBAMAZEPINE TAB 400MG ER	493	76	$74,356.54	$150.82	6.5
CARBAMAZEPINE CAP 300MG ER	353	54	$43,135.71	$122.20	6.5
CARBAMAZEPINE TAB 200MG ER	333	72	$24,539.81	$73.69	4.6
CARBAMAZEPINE CAP 200MG ER	242	44	$29,602.90	$122.33	5.5
CARBAMAZEPINE SUS 100/5ML	233	26	$20,548.80	$88.19	9.0
CARBAMAZEPINE TAB 100MGER	204	61	$10,434.98	$51.15	3.3
CARBAMAZEPINE CAP 100MG ER	109	35	$6,621.95	$60.75	3.1
TEGRETOL TAB 200MG	68	9	$27,609.48	$406.02	7.6
CARBATROL CAP 200MG	66	7	$11,460.67	$173.65	9.4
TEGRETOL-XR TAB 400MG	52	6	$19,180.53	$368.86	8.7
TEGRETOL SUS 100/5ML	48	7	$21,739.55	$452.91	6.9
TEGRETOL-XR TAB 200MG	32	3	$13,377.64	$418.05	10.7
CARBATROL CAP 300MG	22	2	$3,912.25	$177.83	11.0
EPITOL TAB 200MG	14	9	$608.64	$43.47	1.6
TEGRETOL-XR TAB 100MG	5	1	$425.24	$85.05	5.0

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
SUBTOTAL	**5,913**	**1,095**	**$432,002.76**	**$73.06**	**5.4**
CLOBAZAM PRODUCTS					
CLOBAZAM SUS 2.5MG/ML	1,250	162	$237,434.25	$189.95	7.7
CLOBAZAM TAB 10MG	1,247	185	$41,180.63	$33.02	6.7
CLOBAZAM TAB 20MG	1,059	121	$73,114.12	$69.04	8.8
ONFI TAB 20MG	99	12	$311,290.09	$3,144.34	8.3
ONFI TAB 10MG	67	9	$90,188.95	$1,346.10	7.4
ONFI SUS 2.5MG/ML	60	10	$154,858.08	$2,580.97	6.0
SYMPAZAN MIS 5MG	3	1	$2,081.73	$693.91	3.0
SUBTOTAL	**3,785**	**500**	**$910,147.85**	**$240.46**	**7.6**
CLONAZEPAM PRODUCTS					
CLONAZEPAM TAB 1MG	11,159	2,167	$121,771.92	$10.91	5.1
CLONAZEPAM TAB 0.5MG	9,990	2,443	$106,782.35	$10.69	4.1
CLONAZEPAM TAB 2MG	2,784	481	$31,292.65	$11.24	5.8
CLONAZEPAM ODT 0.25MG	1,139	339	$36,935.57	$32.43	3.4
CLONAZEPAM ODT 0.5MG	616	209	$22,194.69	$36.03	2.9
CLONAZEPAM ODT 0.125MG	590	210	$22,303.41	$37.80	2.8
CLONAZEPAM ODT 1MG	359	132	$13,211.25	$36.80	2.7
CLONAZEPAM ODT 2MG	43	19	$1,910.22	$44.42	2.3
KLONOPIN TAB 2MG	12	1	$2,991.54	$249.30	12.0
SUBTOTAL	**26,692**	**6,001**	**$359,393.60**	**$13.46**	**4.4**
DIAZEPAM PRODUCTS					
DIAZEPAM GEL 10MG	1,255	779	$529,292.98	$421.75	1.6
DIAZEPAM GEL 20MG	395	190	$195,081.47	$493.88	2.1
DIASTAT ACDL GEL 5-10MG	140	120	$75,079.02	$536.28	1.2
DIAZEPAM GEL 2.5MG	81	69	$31,484.76	$388.70	1.2
DIASTAT ACDL GEL 12.5-20MG	67	37	$39,207.90	$585.19	1.8
DIASTAT PED GEL 2.5MG	20	16	$5,692.97	$284.65	1.3
VALTOCO LIQ 15MG	2	2	$411.98	$205.99	1.0
VALTOCO SPR 10MG	1	1	$1,131.41	$1,131.41	1.0
SUBTOTAL	**1,961**	**1,214**	**$877,382.49**	**$447.42**	**1.6**
DIVALPROEX, VALPROATE, AND VALPROIC ACID PRODUCTS					
DIVALPROEX TAB 500MG DR	7,856	1,406	$148,235.60	$18.87	5.6
DIVALPROEX TAB 500MG ER	6,318	1,198	$176,459.91	$27.93	5.3
DIVALPROEX TAB 250MG DR	5,153	1,185	$74,885.93	$14.53	4.3
DIVALPROEX TAB 250MG ER	3,258	691	$77,049.87	$23.65	4.7
VALPROIC ACID SOL 250MG/5ML	2,148	291	$44,016.99	$20.49	7.4
DIVALPROEX CAP 125MG	1,949	298	$137,912.83	$70.76	6.5
DIVALPROEX TAB 125MG DR	1,643	370	$23,484.82	$14.29	4.4

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
VALPROIC ACID CAP 250MG	859	182	$25,234.54	$29.38	4.7
DEPAKOTE SPR CAP 125MG	108	13	$41,863.56	$387.63	8.3
DEPAKOTE ER TAB 500MG	65	6	$39,850.02	$613.08	10.8
DEPAKOTE ER TAB 250MG	45	4	$9,433.02	$209.62	11.3
DEPAKOTE TAB 500MG DR	35	4	$22,704.71	$648.71	8.8
DEPAKOTE TAB 250MG DR	23	2	$4,801.96	$208.78	11.5
VALPROATE INJ 500MG/5ML	1	1	$17.08	$17.08	1.0
SUBTOTAL	**29,461**	**5,651**	**$825,950.84**	**$28.04**	**5.2**
ESLICARBAZAPINE PRODUCTS					
APTIOM TAB 800MG	97	16	$104,048.38	$1,072.66	6.1
APTIOM TAB 600MG	83	12	$115,794.37	$1,395.11	6.9
APTIOM TAB 400MG	10	6	$7,646.12	$764.61	1.7
APTIOM TAB 200MG	5	2	$4,703.18	$940.64	2.5
SUBTOTAL	**195**	**36**	**$232,192.05**	**$1,190.73**	**5.4**
ETHOSUXIMIDE PRODUCTS					
ETHOSUXIMIDE CAP 250MG	729	122	$53,990.76	$74.06	6.0
ETHOSUXIMIDE SOL 250MG/5ML	496	81	$35,142.33	$70.85	6.1
ZARONTIN CAP 250MG	6	2	$1,842.90	$307.15	3.0
SUBTOTAL	**1,231**	**205**	**$90,975.99**	**$73.90**	**6.0**
FELBAMATE PRODUCTS					
FELBAMATE TAB 600MG	197	21	$41,377.70	$210.04	9.4
FELBAMATE SUS 600MG/5ML	112	10	$47,179.59	$421.25	11.2
FELBAMATE TAB 400MG	57	8	$4,185.87	$73.44	7.1
FELBATOL TAB 600MG	21	2	$38,648.56	$1,840.41	10.5
FELBATOL TAB 400MG	14	2	$17,630.28	$1,259.31	7.0
SUBTOTAL	**401**	**43**	**$149,022.00**	**$371.63**	**9.3**
GABAPENTIN PRODUCTS					
GABAPENTIN CAP 300MG	32,719	9,341	$445,869.51	$13.63	3.5
GABAPENTIN TAB 600MG	23,200	4,500	$400,454.66	$17.26	5.2
GABAPENTIN TAB 800MG	18,094	2,944	$373,265.15	$20.63	6.1
GABAPENTIN CAP 100MG	10,101	3,523	$123,980.86	$12.27	2.9
GABAPENTIN CAP 400MG	6,203	1,526	$86,456.07	$13.94	4.1
GABAPENTIN SOL 250MG/5ML	1113	222	$53,499.08	$48.07	5.0
NEURONTIN CAP 300MG	4	1	$4,925.59	$1,231.40	4.0
SUBTOTAL	**91,434**	**22,057**	**$1,488,450.92**	**$16.28**	**4.1**
LACOSAMIDE PRODUCTS					
VIMPAT TAB 200MG	2,299	267	$1,994,785.29	$867.68	8.6
VIMPAT TAB 100MG	1,307	245	$1,054,292.01	$806.65	5.3
VIMPAT SOL 10MG/ML	1,200	157	$930,118.61	$775.10	7.6

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
VIMPAT TAB 150MG	1050	152	$852,423.63	$811.83	6.9
VIMPAT TAB 50MG	622	132	$308,407.85	$495.83	4.7
VIMPAT INJ 200MG/20ML	2	1	$173.00	$86.50	2.0
SUBTOTAL	**6,480**	**954**	**$5,140,200.39**	**$793.24**	**6.8**
LAMOTRIGINE PRODUCTS					
LAMOTRIGINE TAB 100MG	9,857	2,130	$116,225.26	$11.79	4.6
LAMOTRIGINE TAB 25MG	7,338	2,480	$87,041.06	$11.86	3.0
LAMOTRIGINE TAB 200MG	6,946	1,154	$90,348.00	$13.01	6.0
LAMOTRIGINE TAB 150MG	3,750	734	$46,083.62	$12.29	5.1
LAMOTRIGINE CHW 25MG	264	49	$9,121.10	$34.55	5.4
LAMOTRIGINE TAB 300MG ER	139	21	$25,323.77	$182.19	6.6
LAMOTRIGINE TAB 200MG ER	132	23	$16,721.91	$126.68	5.7
LAMOTRIGINE CHW 5MG	108	29	$2,566.77	$23.77	3.7
LAMICTAL TAB 200MG	98	9	$109,696.59	$1,119.35	10.9
LAMICTAL TAB 150MG	81	8	$98,617.58	$1,217.50	10.1
LAMOTRIGINE TAB 50MG ER	79	16	$6,318.53	$79.98	4.9
LAMOTRIGINE TAB 25MG ODT	76	15	$53,230.63	$700.40	5.1
LAMOTRIGINE TAB 100MG ER	72	17	$6,030.52	$83.76	4.2
LAMOTRIGINE TAB 50MG ODT	65	14	$16,629.07	$255.83	4.6
LAMOTRIGINE TAB 100MG	59	11	$18,641.47	$315.96	5.4
LAMICTAL XR TAB 200MG	58	7	$95,845.06	$1,652.50	8.3
LAMICTAL TAB 100MG	50	5	$57,213.11	$1,144.26	10.0
LAMOTRIGINE TAB 250MG ER	42	7	$15,073.14	$358.88	6.0
LAMOTRIGINE TAB 200MG	27	5	$7,502.10	$277.86	5.4
LAMICTAL ODT TAB 100MG	17	2	$5,565.47	$327.38	8.5
LAMICTAL CHW 25MG	15	2	$101,606.26	$6,773.75	7.5
LAMOTRIGINE ODT TAB 100MG	12	2	$4,213.55	$351.13	6.0
LAMICTAL ODT TAB 25MG	11	1	$3,926.51	$356.96	11.0
LAMOTRIGINE TAB 25MG ER	10	3	$2,435.21	$243.52	3.3
LAMICTAL ODT TAB 50MG	9	1	$6,075.66	$675.07	9.0
LAMICTAL ODT TAB 200MG	8	1	$6,886.56	$860.82	8.0
SUBVENITE TAB 150MG	7	5	$82.74	$11.82	1.4
LAMICTAL XR TAB 250MG	5	1	$8,646.36	$1,729.27	5.0
SUBVENITE TAB 100MG	4	1	$34.64	$8.66	4.0
LAMICTAL TAB 25MG	2	2	$1,881.03	$940.52	1.0
SUBVENITE TAB 200MG	2	2	$29.98	$14.99	1.0
SUBVENITE TAB 25MG	1	1	$13.01	$13.01	1.0
SUBTOTAL	**29,344**	**6,758**	**$1,019,626.27**	**$34.75**	**4.3**
LEVETIRACETAM PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
LEVETIRACETAM SOL 100MG/ML	10,919	1,605	$232,084.02	$21.26	6.8
LEVETIRACETAM TAB 500MG	9,461	2,010	$153,827.72	$16.26	4.7
LEVETIRACETAM TAB 1000MG	5,927	941	$145,621.78	$24.57	6.3
LEVETIRACETAM TAB 750MG	4,340	769	$100,121.05	$23.07	5.6
LEVETIRACETAM TAB 250MG	1,532	318	$23,071.03	$15.06	4.8
LEVETIRACETAM TAB 500MG ER	481	94	$14,663.96	$30.49	5.1
LEVETIRACETAM TAB 750MG ER	275	58	$11,255.09	$40.93	4.7
KEPPRA XR TAB 500MG	76	10	$57,931.87	$762.26	7.6
KEPPRA TAB 1000MG	62	6	$74,205.71	$1,196.87	10.3
KEPPRA XR TAB 750MG	62	11	$66,666.55	$1,075.27	5.6
LEVETIRACETAM INJ 500MG/5ML	51	1	$3,455.83	$67.76	51.0
KEPPRA TAB 750MG	44	4	$49,393.72	$1,122.58	11.0
KEPPRA TAB 500MG	33	6	$15,471.85	$468.84	5.5
KEPPRA SOL 100MG/ML	32	5	$14,781.88	$461.93	6.4
KEPPRA TAB 250MG	11	1	$10,423.98	$947.63	11.0
ROWEEPRA TAB 500MG	5	4	$107.85	$21.57	1.3
ROWEEPRA TAB 750MG	3	1	$64.26	$21.42	3.0
ROWEEPRA XR TAB 500MG XR	2	1	$83.64	$41.82	2.0
SUBTOTAL	**33,316**	**5,845**	**$973,231.79**	**$29.21**	**5.7**
METHSUXIMIDE PRODUCTS					
CELONTIN CAP 300MG	29	4	$8,274.98	$285.34	7.3
SUBTOTAL	**29**	**4**	**$8,274.98**	**$285.34**	**7.3**
MIDAZOLAM PRODUCTS					
NAYZILAM SPR 5MG	184	129	$137,352.20	$746.48	1.4
SUBTOTAL	**184**	**129**	**$137,352.20**	**$746.48**	**1.4**
OXCARBAZEPINE PRODUCTS					
OXCARBAZEPINE TAB 300MG	9,987	1,970	$190,762.53	$19.10	5.1
OXCARBAZEPINE TAB 600MG	8,303	1,283	$246,352.67	$29.67	6.5
OXCARBAZEPINE TAB 150MG	6,386	1,564	$111,413.17	$17.45	4.1
OXCARBAZEPINE SUS 300MG/5MG	3,231	494	$358,886.55	$111.08	6.5
TRILEPTAL SUS 300MG/5MG	313	89	$192,617.37	$615.39	3.5
OXTELLAR XR TAB 600MG	160	24	$225,111.05	$1,406.94	6.7
OXTELLAR XR TAB 300MG	47	5	$13,401.28	$285.13	9.4
TRILEPTAL TAB 600MG	44	4	$78,519.42	$1,784.53	11.0
OXTELLAR XR TAB 150MG	26	4	$5,357.19	$206.05	6.5
SUBTOTAL	**28,497**	**5,437**	**$1,422,421.23**	**$49.91**	**5.2**
PERAMPANEL PRODUCTS					
FYCOMPA TAB 4MG	132	33	$108,239.92	$820.00	4.0
FYCOMPA TAB 8MG	127	21	$109,071.42	$858.83	6.0

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
FYCOMPA SUS 0.5MG/ML	117	28	$111,820.95	$955.73	4.2
FYCOMPA TAB 6MG	100	22	$84,951.20	$849.51	4.5
FYCOMPA TAB 10MG	76	8	$72,829.03	$958.28	9.5
FYCOMPA TAB 12MG	61	9	$61,149.47	$1,002.45	6.8
FYCOMPA TAB 2MG	61	18	$25,559.31	$419.01	3.4
SUBTOTAL	**674**	**139**	**$573,621.30**	**$851.07**	**4.8**
PHENOBARBITAL (PHENOBARB) PRODUCTS					
PHENOBARB ELX 20MG/5ML	714	137	$41,853.95	$58.62	5.2
PHENOBARB TAB 64.8MG	497	61	$17,229.55	$34.67	8.1
PHENOBARB TAB 32.4MG	422	48	$14,385.89	$34.09	8.8
PHENOBARB TAB 97.2MG	165	21	$7,224.34	$43.78	7.9
PHENOBARB TAB 30MG	129	23	$2,443.27	$18.94	5.6
PHENOBARB TAB 60MG	104	20	$2,205.03	$21.20	5.2
PHENOBARB TAB 16.2MG	102	13	$2,938.50	$28.81	7.8
PHENOBARB SOL 20MG/5ML	65	14	$3,195.25	$49.16	4.6
PHENOBARB TAB 100MG	23	5	$403.19	$17.53	4.6
PHENOBARB TAB 15MG	19	3	$217.86	$11.47	6.3
SUBTOTAL	**2,240**	**345**	**$92,096.83**	**$41.11**	**6.5**
PHENYTOIN AND FOSPHENYTOIN PRODUCTS					
PHENYTOIN EX CAP 100MG	3,185	474	$94,369.26	$29.63	6.7
PHENYTOIN SUS 125MG/5ML	243	24	$6,767.55	$27.85	10.1
DILANTIN CAP 100MG	234	31	$41,481.31	$177.27	7.5
PHENYTOIN CHW 50MG	188	33	$7,414.41	$39.44	5.7
PHENYTOIN EX CAP 200MG	140	26	$10,739.10	$76.71	5.4
DILANTIN CAP 30MG	109	19	$13,277.22	$121.81	5.7
PHENYTOIN EX CAP 300MG	57	15	$3,368.17	$59.09	3.8
DILANTIN CHW 50MG	33	4	$3,388.73	$102.69	8.3
FOSPHENYTOIN INJ 100MG/2ML	21	2	$2,344.29	$111.63	10.5
DILANTIN-125 SUS 125MG/5ML	6	1	$1,490.23	$248.37	6.0
PHENYTEK CAP 200MG	6	3	$565.22	$94.20	2.0
PHENYTEK CAP 300MG	1	1	$142.45	$142.45	1.0
SUBTOTAL	**4,223**	**633**	**$185,347.94**	**$43.89**	**6.7**
PREGABALIN PRODUCTS					
LYRICA CAP 150MG	2,105	499	$1,169,159.27	$555.42	4.2
PREGABALIN CAP 150MG	1,360	470	$24,195.88	$17.79	2.9
LYRICA CAP 75MG	1,334	495	$670,216.83	$502.41	2.7
LYRICA CAP 100MG	1,178	363	$669,711.01	$568.52	3.2
PREGABALIN CAP 75MG	1034	493	$17,418.43	$16.85	2.1
PREGABALIN CAP 100MG	900	345	$15,920.59	$17.69	2.6

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
LYRICA CAP 50MG	748	320	$399,995.04	$534.75	2.3
LYRICA CAP 300MG	705	137	$322,053.65	$456.81	5.1
LYRICA CAP 200MG	553	137	$296,444.98	$536.07	4.0
PREGABALIN CAP 50MG	507	275	$8,420.68	$16.61	1.8
PREGABALIN CAP 200MG	483	137	$9,407.44	$19.48	3.5
PREGABALIN CAP 300MG	360	106	$6,273.32	$17.43	3.4
LYRICA CAP 225MG	146	37	$68,492.42	$469.13	3.9
LYRICA CAP 25MG	146	64	$66,056.61	$452.44	2.3
PREGABALIN CAP 225MG	116	32	$1,865.88	$16.09	3.6
PREGABALIN CAP 25MG	90	61	$1,437.88	$15.98	1.5
LYRICA SOL 20MG/ML	13	2	$12,060.83	$927.76	6.5
PREGABALIN SOL 20MG/ML	2	1	$121.76	$60.88	2.0
SUBTOTAL	**11,780**	**3,974**	**$3,759,252.50**	**$319.12**	**3.0**
PRIMIDONE PRODUCTS					
PRIMIDONE TAB 50MG	562	114	$8,694.12	$15.47	4.9
PRIMIDONE TAB 250MG	223	30	$4,311.55	$19.33	7.4
MYSOLINE TAB 250MG	21	2	$79,251.61	$3,773.89	10.5
SUBTOTAL	**806**	**146**	**$92,257.28**	**$114.46**	**5.5**
RUFINAMIDE PRODUCTS					
BANZEL TAB 400MG	324	39	$1,186,158.90	$3,660.98	8.3
BANZEL SUS 40MG/ML	230	33	$464,299.77	$2,018.69	7.0
BANZEL TAB 200MG	87	11	$94,653.33	$1,087.97	7.9
SUBTOTAL	**641**	**83**	**$1,745,112.00**	**$2,722.48**	**7.7**
STIRIPENTOL PRODUCTS					
DIACOMIT CAP 500MG	1	1	$3,011.41	$3,011.41	1.0
SUBTOTAL	**1**	**1**	**$3,011.41**	**$3,011.41**	**1.0**
TIAGABINE PRODUCTS					
TIAGABINE TAB 4MG	48	6	$14,461.43	$301.28	8.0
TIAGABINE TAB 2MG	27	3	$7,007.70	$259.54	9.0
TIAGABINE TAB 12MG	23	2	$6,110.20	$265.66	11.5
TIAGABINE TAB 16MG	6	2	$1,879.58	$313.26	3.0
SUBTOTAL	**104**	**13**	**$29,458.91**	**$283.26**	**8.0**
TOPIRAMATE PRODUCTS					
TOPIRAMATE TAB 50MG	8,802	2,495	$108,580.39	$12.34	3.5
TOPIRAMATE TAB 25MG	8,094	2,815	$95,714.69	$11.83	2.9
TOPIRAMATE TAB 100MG	7,400	1,488	$99,004.68	$13.38	5.0
TOPIRAMATE TAB 200MG	2,882	464	$43,203.12	$14.99	6.2
TOPIRAMATE CAP 25MG	434	74	$23,951.38	$55.19	5.9
TOPIRAMATE CAP 15MG	391	104	$14,443.05	$36.94	3.8

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TROKENDI XR CAP 200MG	151	20	$205,630.41	$1,361.79	7.6
TROKENDI XR CAP 100MG	110	20	$84,069.61	$764.27	5.5
TROKENDI XR CAP 50MG	51	15	$19,972.51	$391.62	3.4
TOPIRAMATE CAP ER 100MG	37	9	$18,396.62	$497.21	4.1
TROKENDI XR CAP 25MG	36	7	$11,249.00	$312.47	5.1
TOPAMAX TAB 200MG	31	3	$50,756.88	$1,637.32	10.3
TOPAMAX TAB 100MG	29	4	$32,011.88	$1,103.86	7.3
TOPIRAMATE CAP ER 50MG	25	7	$19,147.00	$765.88	3.6
TOPIRAMATE CAP ER 200MG	24	3	$14,528.40	$605.35	8.0
TOPAMAX SPR CAP 25MG	14	3	$36,980.55	$2,641.47	4.7
TOPAMAX TAB 50MG	13	2	$8,611.15	$662.40	6.5
QUDEXY XR CAP 100MG/24HR	9	4	$5,562.03	$618.00	2.3
TOPIRAMATE CAP ER 150MG	9	2	$4,661.31	$517.92	4.5
QUDEXY XR CAP 50MG/24HR	3	2	$975.67	$325.22	1.5
TOPIRAMATE CAP ER 25MG	2	2	$653.90	$326.95	1.0
QUDEXY XR CAP 25MG/24HR	1	1	$265.11	$265.11	1.0
SUBTOTAL	**28,548**	**7,544**	**$898,369.34**	**$31.47**	**3.8**
VIGABATRIN PRODUCTS					
SABRIL POW 500MG	139	19	$2,845,578.58	$20,471.79	7.3
VIGABATRIN PAK 500MG	26	3	$98,967.06	$3,806.43	8.7
SABRIL TAB 500MG	12	3	$271,787.34	$22,648.95	4.0
VIGADRONE POW 500MG	12	2	$14,466.92	$1,205.58	6.0
SUBTOTAL	**189**	**27**	**$3,230,799.90**	**$17,094.18**	**7.0**
ZONISAMIDE PRODUCTS					
ZONISAMIDE CAP 100MG	3,018	428	$60,101.62	$19.91	7.1
ZONISAMIDE CAP 50MG	633	128	$10,043.83	$15.87	4.9
ZONISAMIDE CAP 25MG	411	87	$6,846.33	$16.66	4.7
ZONEGRAN CAP 100MG	13	2	$16,274.95	$1,251.92	6.5
SUBTOTAL	**4,075**	**645**	**$93,266.73**	**$22.89**	**6.3**
TOTAL	**315,101**	**42,227***	**$28,219,484.87**	**$89.56**	**7.5**

*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
ACDL = AcuDial; CAP = Capsule; CHW = Chewable; ELX = Elixir; ER = Extended-Release; EX = Extended; INJ = Injection; LIQ = Liquid; MIS = Miscellaneous; ODT = Orally Disintegrating Tablet; PED = Pediatric; POW = Powder; SOL = Solution; SPR = Spray or Sprinkle; SUS = Suspension; TAB = Tablet; XR = Extended-Release
Please note, 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. However, 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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Appendix N

Fiscal Year 2020 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr)

Oklahoma Health Care Authority
February 2021

Current Prior Authorization Criteria

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Relpax® brand name only (eletriptan)	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)			eletriptan (generic Relpax®)
sumatriptan/naproxen (Treximet®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan tablet (Reyvow®)
			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) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
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 any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zembrace® SymTouch® or Tosymra® will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. 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.
4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
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® (i.e., 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 generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
7. Use of Reyvow® (lasmiditan) or Ubrelvy® (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications.

Aimovig® (Erenumab-aooe) and Ajovy® (Fremanezumab-vfrm) 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. Member has failed medical migraine preventive therapy with at least 3 agents with different mechanisms of action. 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®, Ajovy®) 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. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. A patient-specific, clinically significant reason why member cannot use Emgality® (galcanezumab-gnlm) must be provided; and
14. 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
15. 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 Ajovy®, a quantity limit of 1 syringe or 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.

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.

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. Member has failed medical migraine preventive therapy with at least 2¥ agents with different mechanisms of action. (¥The manufacturer of Emgality® has currently provided a supplemental rebate to require a trial with 2 other migraine preventative therapies; however, Emgality® will follow the original criteria and require trials with 3 other migraine preventative therapies if the manufacturer chooses 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. Medication must be prescribed by or in consultation with 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. Prescriber must verify that 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. 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.

**The manufacturer of Emgality® has currently provided a supplemental rebate to be the preferred calcitonin gene-related peptide (CGRP) inhibitor; however, Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.*

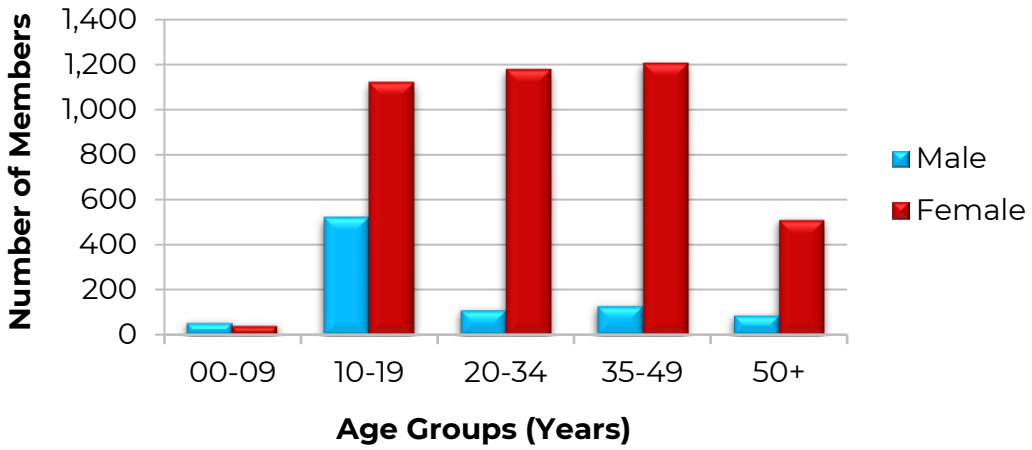
Utilization of Anti-Migraine Medications: Fiscal Year 2020

Comparison of Fiscal Years

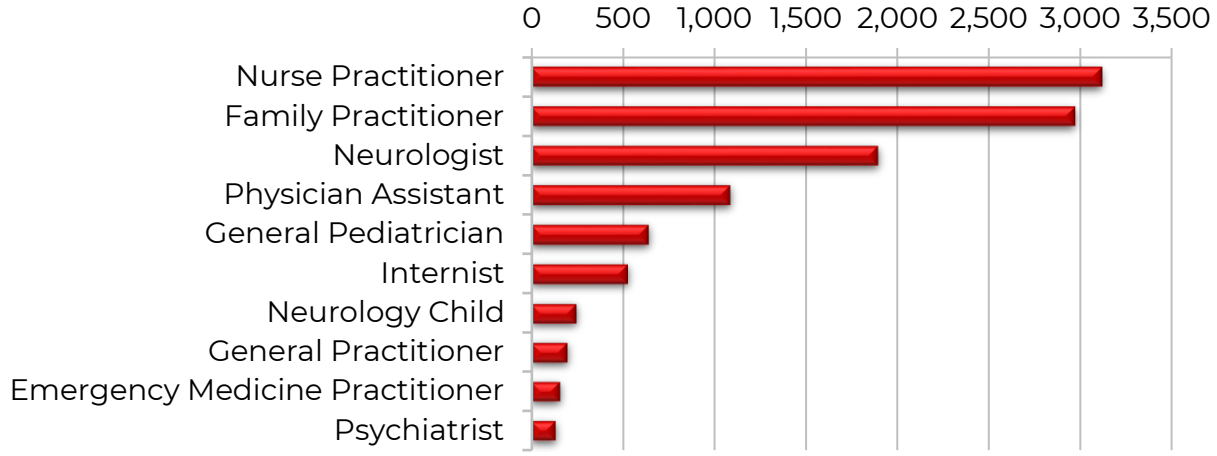
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	5,038	11,251	$375,000.48	$33.33	$1.99	121,390	188,873
2020	4,951	11,633	$768,531.74	$66.06	$3.71	120,394	207,189
% Change	**-1.70%**	**3.40%**	**104.90%**	**98.20%**	**86.40%**	**-0.80%**	**9.70%**
Change	**-87**	**382**	**$393,531.26**	**$32.73**	**$1.72**	**-996**	**18,316**

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

Demographics of Members Utilizing Anti-Migraine Medications



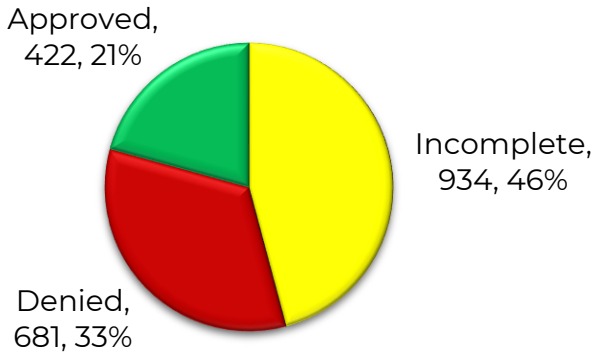
Top Prescriber Specialties of Anti-Migraine Medications by Number of Claims



Prior Authorization of Anti-Migraine Medications

There were 2,037 prior authorization requests submitted for anti-migraine medications during fiscal year 2020. 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 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Zomig® (zolmitriptan nasal spray): May 2021
- Reyvow® (lasmiditan tablet): April 2025
- Treximet® (sumatriptan/naproxen tablet): April 2026
- Tosymra® (sumatriptan nasal spray): July 2031
- Nurtec™ ODT [rimegepant orally disintegrating tablet (ODT)]: February 2033
- Onzetra® Xsail® (sumatriptan nasal powder): October 2034
- Ubrelvy® (ubrogepant tablet): January 2035
- Zembrace® SymTouch® [sumatriptan subcutaneous (sub-Q) injection]: January 2036

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

- **February 2020:** The FDA approved Vyepti® (eptinezumab-jjmr) for the preventive treatment of migraine in adults. Vyepti® is the first FDA-approved intravenous (IV) treatment for migraine prevention.
- **February 2020:** The FDA approved Nurtec™ ODT (rimegepant) for treatment of acute migraine with or without aura in adults. Rimegepant is the first calcitonin gene-related peptide (CGRP) receptor antagonist available in a fast-acting ODT.

News:

- **April 2020:** Ajovy® (fremanezumab-vfrm) is now available in an autoinjector device for the preventive treatment of migraine in adults. The autoinjector device includes a button-free, push-down mechanism, as well as audible clicks to guide patients and caregivers through successful administration into the upper arm, thigh, or abdomen. The autoinjector is for one-time use only and locks after use; a viewing window displays when the dose has been delivered. Ajovy® is available as a 225mg/1.5mL solution in a single-dose prefilled autoinjector and in a single-dose prefilled syringe. For the dosing regimen of Ajovy® 675mg every 3 months, 3 separate autoinjectors or 3 separate syringes must be used and administered as 3 consecutive sub-Q injections of 225mg each.
- **October 2020:** The FDA cleared the first dual-purpose, external trigeminal nerve stimulation device to treat and prevent acute migraine for over-the-counter (OTC) use in adults 18 years of age and older. This device, Cefaly® Dual, was previously only available with a prescription. Most migraines involve the trigeminal nerve, which can be accessed through the skin on the forehead. Cefaly® Dual stimulates the trigeminal nerve using a reusable self-adhesive electrode placed on the forehead. The device has 2 settings, acute and prevent. In the acute setting, the individual wears the device for 60 minutes at the onset or during a migraine attack. In the prevent setting, the individual wears the device for 20 minutes daily to help prevent future episodes. The FDA's OTC clearance of Cefaly® Dual was based on several randomized, controlled clinical studies supporting the efficacy and safety of the device.
- **October 2020:** Biohaven Pharmaceutical announced that the FDA has accepted their supplemental New Drug Application (sNDA) for Nurtec™ ODT (rimegepant) for the preventive treatment of migraine. The sNDA filing was based on the outcomes of a pivotal migraine preventive treatment study of patients with migraines (Study 305) as well as the rimegepant long-term, open-label safety study that supported the approval of rimegepant for the acute treatment of migraine. Study 305 achieved its primary endpoint demonstrating a statistically significant reduction from baseline in monthly migraine days (MMD) in patients treated with rimegepant compared with placebo during the third month of treatment. Those receiving rimegepant 75mg every other day (N=348) experienced a 4.3 day reduction from baseline in MMD, compared to a 3.5 day reduction in the placebo group (N=347; $P<0.05$). If approved, rimegepant will be the first CGRP-targeting therapy with indications for both preventive and acute treatment of migraine. The Prescription Drug User Fee Act

(PDUFA) goal date for completion of the FDA review of the preventive sNDA is set for the second quarter of 2021.

- **January 2021:** Results from the pivotal migraine preventive treatment study of patients with migraines supporting the use of rimegepant for the preventive treatment of migraine have been published in *The Lancet*. As previously mentioned, in this United States-based Phase 2/3 study, rimegepant demonstrated a statistically significant reduction from baseline in MMD in patients treated with rimegepant compared with placebo during weeks 9 to 12 of treatment. Investigators observed that about half of patients treated with rimegepant showed ≥50% reduction in the number of moderate-to-severe MMD. The most common adverse events (AEs) were nausea (2% in patients receiving rimegepant and 0.5% in those receiving placebo) and hypersensitivity, including dyspnea and rash, occurring in <1% of patients treated with rimegepant.
- **January 2021:** An FDA analysis of postmarketing case reports suggested the migraine prevention drug, Aimovig® (erenumab), was associated with elevated blood pressure (BP). Of 61 erenumab-linked hypertension (HTN) cases submitted to the FDA Adverse Event Reporting System (FAERS), 41 were associated with a serious outcome according to regulatory criteria, including 7 cases that specified hospitalization. About half of the 61 cases reported baseline BP measurements. In those patients, median systolic BP increase was 39mm Hg and median diastolic BP increase was 28mm Hg. Elevated BP occurred within a week of the first dose of erenumab in 46% of cases. Nearly a third (31%) of all cases reported a history of pre-existing HTN. Based on the findings, the *Warning and Precautions* section of the Aimovig® *Prescribing Information* has been updated to include HTN. It has not been determined if this is a class effect as more information is needed. Elizabeth Loder, MD, MPH, of Brigham and Women's Hospital and Harvard Medical School, pointed out that "erenumab was the first of the CGRP monoclonal antibodies to market and thus has accumulated the largest number of FAERS reports."

Pipeline:

- **Atogepant:** AbbVie announced topline results from the ADVANCE study, which evaluated atogepant 10, 30, and 60mg. These results showed all 3 doses were associated with a significant reduction from baseline in mean MMD compared with placebo, meeting the primary endpoint in this Phase 3 trial for migraine prevention. The Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group trial was designed to evaluate the efficacy, safety, and tolerability of oral atogepant for the prevention of migraine in those who experienced 4 to 14 migraine days per month. A total of 910 patients

were randomized to 1 of 4 treatment groups: 10, 30, or 60mg of atogepant once daily or placebo. The primary endpoint was change from baseline in mean MMD during the 12-week treatment period. All atogepant dose groups met the primary endpoint and demonstrated significantly greater decreases in mean MMD compared with placebo. The most common adverse events (reported in ≥5% of patients and at least 1 atogepant group, and at a rate greater than placebo), across all doses versus placebo, were constipation (6.9 to 7.7% vs 0.5%), nausea (4.4 to 6.1% vs 1.8%), and upper respiratory tract infection (3.9 to 5.7% vs 4.5%).

Nurtec™ ODT (Rimegepant) Product Summary[10]

Indication(s): Nurtec™ ODT (rimegepant) is a CGRP receptor antagonist indicated for the acute treatment of migraine with or without aura in adults.

Limitation(s) of Use: Nurtec™ ODT is not indicated for the preventive treatment of migraine.

Dosing and Administration:

- Nurtec™ ODT is supplied as a 75mg ODT, available in cartons containing a blister pack of (8) 75mg ODTs.
- The recommended dose is 75mg as needed, with a maximum dose of 75mg in 24 hours.
- The safety of treating >15 migraines with Nurtec™ ODT in a 30-day period has not been established.
- Dry hands should be used when opening the Nurtec™ ODT blister pack; immediately after opening the blister pack the ODT should be placed on or under tongue. The ODT will disintegrate in saliva, no additional liquid is needed.

Contraindication(s): Patients with a history of hypersensitivity reaction to rimegepant, Nurtec™ ODT, or any of its components

Safety:

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including dyspnea and rash, occurred with rimegepant in clinical studies. Hypersensitivity reactions can occur days after administration, and delayed serious hypersensitivity has occurred. If a hypersensitivity reaction occurs, discontinuation of rimegepant and initiation of appropriate therapy is recommended.
- **Drug Interactions:** Concomitant administration of rimegepant with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole), strong and moderate CYP3A inducers (e.g., phenobarbital, rifabutin), and inhibitors of P-gp or BCRP inhibitors (e.g., amiodarone, carvedilol,

ritonavir) should be avoided. If taken with a moderate CYP3A4 inhibitor (e.g., diltiazem, fluconazole), a second dose of rimegepant within 48 hours should be avoided.

- **Pregnancy:** There are no adequate data on the developmental risk associated with the use of rimegepant in pregnant women. In animal studies, oral administration of rimegepant during organogenesis resulted in adverse effects on development in rats (decreased fetal body weight and increased incidence of fetal variations) at exposures greater than those used clinically and which were associated with maternal toxicity. The evaluation of developmental effects in rats following oral administration of rimegepant throughout pregnancy and lactation was inadequate.
- **Lactation:** There are no data on the presence of rimegepant or its metabolites in human milk, the effects of rimegepant on the breastfed infant, or the effects of rimegepant on milk production. There are no animal data on the excretion of rimegepant in milk.
- **Pediatric Use:** The safety and effectiveness of rimegepant in pediatric patients have not been established.
- **Geriatric Use:** In pharmacokinetic studies, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects. Clinical studies of rimegepant did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.
- **Hepatic Impairment:** No dosage adjustment of rimegepant is required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Plasma concentrations of rimegepant were significantly higher in subjects with severe (Child-Pugh C) hepatic impairment. Rimegepant use should be avoided in patients with severe hepatic impairment.
- **Renal Impairment:** No dosage adjustment of rimegepant is required in patients with mild, moderate, or severe renal impairment. Rimegepant has not been studied in patients with end-stage renal disease (ESRD) and in patients on dialysis. Rimegepant use should be avoided in patients with ESRD (creatinine clearance <15mL/min).

Adverse Reactions: The most common adverse reaction in the clinical study was nausea (2% in patients who received rimegepant compared to 0.4% of patients who received placebo). Hypersensitivity, including dyspnea and severe rash, occurred in <1% of patients treated with rimegepant.

Efficacy: The efficacy of rimegepant for the acute treatment of migraine with and without aura in adults was demonstrated in a randomized, double-blind, placebo-controlled study. The study randomized patients to 75mg of rimegepant (N=732) or placebo (N=734). Patients were instructed to treat a

migraine of moderate-to-severe headache pain intensity. Rescue medication [i.e., nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and/or an antiemetic] was allowed 2 hours after the initial treatment. Other forms of rescue medication such as triptans were not allowed within 48 hours of initial treatment. Approximately 14% of patients were taking preventive medications for migraine at baseline; however, none of the patients were on concomitant preventive medication that act on the CGRP pathway.
The primary efficacy analyses were conducted in patients who treated a migraine with moderate-to-severe pain. Rimegepant 75mg demonstrated an effect on pain freedom and most bothersome symptom (MBS) freedom at 2 hours after dosing, compared to placebo. Pain freedom was defined as a reduction of moderate or severe headache pain to no headache pain, and MBS freedom was defined as the absence of the self-identified MBS (i.e., photophobia, phonophobia, nausea). The percentage of patients achieving headache pain freedom and MBS freedom 2 hours after a single dose was statistically significantly greater in patients who received rimegepant compared to those who received placebo (P<0.001 and P=0.001, respectively, for pain freedom and MBS freedom).

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Nurtec™ ODT (rimegepant) 75mg ODT	**$101.90**	**$101.90**
Ubrelvy® (ubrogepant) 100mg tablet	$81.54	$163.08
rizatriptan 10mg tablet	$0.69	$2.07
sumatriptan 100mg tablet	$0.60	$1.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per maximum cumulative dose based on FDA recommended dosing in a 24-hour period.
ODT = orally disintegrating tablet

Vyepti® (Eptinezumab-jjmr) Product Summary[11]

Indication(s): Vyepti® (eptinezumab-jjmr) is a CGRP antagonist indicated for the preventive treatment of migraine in adults.

Dosing and Administration:

- Vyepti® is supplied as 100mg/mL solution in a 1mL single-dose vial (SDV).
- Vyepti® requires dilution with 100mL 0.9% sodium chloride injection prior to administration.
- Vyepti® should be stored refrigerated at 2°C to 8°C (36°F to 46°F) until time of use.
- The recommended dosage is 100mg administered by IV infusion every 3 months. Some patients may benefit from a dosage of 300mg administered by IV infusion every 3 months.

Contraindication(s): Patients with serious hypersensitivity to eptinezumab or to any of the excipients in Vyepti®

Safety:

- **Hypersensitivity:** Hypersensitivity reactions, including angioedema, urticaria, facial flushing, and rash, have occurred with eptinezumab in clinical trials. Most hypersensitivity reactions occurred during infusion and were not serious, but often led to discontinuation or required treatment. Serious hypersensitivity reactions may occur. If a hypersensitivity reaction occurs, consider discontinuing eptinezumab, and instituting appropriate therapy.
- **Immunogenicity:** In patients receiving eptinezumab 100mg or 300mg every 3 months, the incidence of anti-eptinezumab antibody development in Study 1 (up to 56 weeks) was 20.6% (92/447), and 41.3% (38/92) of those patients developed anti-eptinezumab neutralizing antibodies. In Study 2 (up to 32 weeks), the incidence of anti-eptinezumab antibody development was 18.3% (129/706), and 34.9% (45/129) of those patients developed anti-eptinezumab neutralizing antibodies. Although the results from both studies showed no clear evidence of an impact from development of anti-eptinezumab antibodies, including neutralizing antibodies, on the safety and efficacy profiles of eptinezumab, the available data are too limited to make definitive conclusions.
- **Pregnancy:** There are no adequate data on developmental risks associated with the use of eptinezumab in pregnant women. No adverse developmental effects were observed following administration of eptinezumab to pregnant animals at doses greater than those used clinically.
- **Lactation:** There are no data on the presence of eptinezumab in human milk, the effects on the breastfed infant, or the effects on milk production.
- **Pediatric Use:** The safety and effectiveness of eptinezumab in pediatric patients have not been established.
- **Geriatric Use:** Clinical studies of eptinezumab did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.

Adverse Reactions: The most common (incidence ≥2% and at least 2% greater than placebo) adverse reactions in the clinical trials of eptinezumab for the preventive treatment of migraine were nasopharyngitis and hypersensitivity.

Efficacy: The efficacy of eptinezumab was evaluated as a preventive treatment of episodic and chronic migraine in 2 randomized, multicenter,

placebo-controlled studies, both with 6-month double-blind periods. Eptinezumab was administered by IV infusion every 3 months in both studies; however, the primary endpoint was measured at 12 weeks. Both studies excluded patients with a history of cardiovascular disease (hypertension, ischemic heart disease), neurological disease, or cerebrovascular disease. The primary efficacy endpoint, in both studies, was the change from baseline in mean MMD over months 1 to 3. Secondary endpoints, in both studies, included the percentages of patients with ≥50% and ≥75% reductions from baseline in MMD over months 1 to 3.

- **Study 1 – Episodic Migraine:** Study 1 included adults with a history of episodic migraine (4 to 14 headache days per month, of which at least 4 were migraine days). A total of 665 patients were randomized to receive placebo (N=222), 100mg eptinezumab (N=221), or 300mg eptinezumab (N=222) every 3 months for 12 months. Patients were allowed to use concurrent acute migraine or headache medications, including migraine-specific medications (i.e., triptans, ergotamine derivatives), during the study. The mean migraine frequency at baseline was approximately 8.6 MMD and was similar across treatment groups.
  - Primary Endpoint: Eptinezumab treatment demonstrated statistically significant improvements compared to placebo for the primary efficacy endpoint (100mg eptinezumab -3.9, P=0.018; 300mg eptinezumab -4.3, P<0.001).
  - Secondary Endpoints: The 300mg dose showed statistically significant improvements compared to placebo (P<0.001), while the 100mg dose showed results that were nominally statistically significant or not statistically significant.
- **Study 2 – Chronic Migraine:** Study 2 included adults with a history of chronic migraine (15 to 26 headache days per month, of which at least 8 were migraine days). A total of 1,072 patients were randomized to receive placebo (N=366), 100mg eptinezumab (N=356), or 300mg eptinezumab (N=350) every 3 months for 6 months. Patients were allowed to use and to continue an established stable regimen of acute migraine or headache preventive medication (except onabotulinumtoxinA); 41% percent of patients were taking concomitant preventive medication for migraine. Patients with a dual diagnosis of chronic migraine and medication overuse headache attributable to acute medication overuse (triptans, ergotamine, or combination analgesics >10 days per month) were included in the study population. Patients using opioids or butalbital-containing products >4 days per month were not allowed. The mean migraine frequency at baseline was approximately 16.1 MMD and was similar across treatment groups.
  - Primary Endpoint: Eptinezumab treatment demonstrated statistically significant improvements compared to placebo for the

primary efficacy endpoint (100mg eptinezumab -7.7, P<0.001; 300mg eptinezumab -8.2, P<0.001).
- Secondary Endpoints: Both doses showed statistically significant improvements compared to placebo (P<0.001).

Cost Comparison:

Medication	Cost Per mL	Cost Per Maintenance Dose	Cost Per Year
Vyepti® (eptinezumab-jjmr) 100mg/mL vial	**$1,495.00**	**$1,495.00 -$4.485.00***	**$5,980 -$17,940.00***
Emgality® (galcanezumab-gnlm) 120mg/mL pen	$583.84	$583.84⁺	$8,173.76⁺
Ajovy® (fremanezumab-vfrm) 225mg/1.5mL autoinjector	$389.00	$583.50 - $1,750.50△	$7,002.00△

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per maintenance and cost per year based on recommended dosing of 100mg to 300mg every 3 months.
⁺Cost per maintenance dose and cost per year based on recommended dosing of 120mg every month. Cost per year includes loading dose of 240mg (as 2 consecutive 120mg doses) required for initiation of treatment.
△Cost per maintenance dose and cost per year based on recommended dosing of 225mg every month or alternative dosing of 675mg every 3 months.

Recommendations

The College of Pharmacy recommends the placement of Nurtec™ ODT (rimegepant) into the Special Prior Authorization (PA) Tier of the Anti-Migraine Product Based Prior Authorization (PBPA) category with the following criteria and recommends updating the Reyvow® (lasmiditan) and Ubrelvy® (ubrogepant) criteria based on net cost and to clarify the use of concomitant medications based on clinical studies (proposed additions and changes are shown in red in the following criteria and Tier chart):

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zembrace® SymTouch® or Tosymra® will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. 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.

4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
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 generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
7. For use of Nurtec™ ODT (rimegepant), 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
    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 calcitonin gene-related peptide (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.)
8. 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.

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Relpax® brand name only (eletriptan)	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)			eletriptan (generic Relpax®)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
sumatriptan/naproxen (Treximet®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan tablet (Reyvow®)
			rimegepant (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) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
PA = prior authorization

Additionally, the College of Pharmacy recommends the prior authorization of Vyepti® (eptinezumab-jjmr), updating the Ajovy® (fremanezumab-vfrm) criteria based on net cost, and updating the CGRP prophylactic treatment criteria to be consistent with treatment guidelines with the following criteria (additions and changes are shown in red):

Aimovig® (Erenumab-aooe) and ~~Ajovy® (Fremanezumab-vfrm)~~ 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
9. 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
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; 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 this 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 Ajovy®, a quantity limit of 1 syringe 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.~~
    c. 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 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. Medication must be prescribed by or in consultation with 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. Prescriber must verify that 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.
    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.

**The manufacturer of Ajovy® and Emgality® has provided a supplemental rebate to be the preferred calcitonin gene-related peptide (CGRP) inhibitor(s); however, Ajovy® and Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.*

Utilization Details of Anti-Migraine Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-1 MEDICATIONS						
SUMATRIPTAN PRODUCTS						
SUMATRIPTAN TAB 50MG	2,977	1,567	$48,111.19	$16.16	1.9	6.26%
SUMATRIPTAN TAB 100MG	2,845	1,134	$45,390.26	$15.95	2.51	5.91%
SUMATRIPTAN TAB 25MG	1,770	1,054	$32,383.45	$18.30	1.68	4.21%
SUBTOTAL	**7,592**	**3,755**	**$125,884.90**	**$16.58**	**2.02**	**16.38%**
RIZATRIPTAN PRODUCTS						
RIZATRIPTAN TAB 10MG	1,244	529	$19,568.19	$15.73	2.35	2.55%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
RIZATRIPTAN TAB 10MG ODT	824	384	$18,701.62	$22.70	2.15	2.43%
RIZATRIPTAN TAB 5MG	459	254	$7,127.45	$15.53	1.81	0.93%
RIZATRIPTAN TAB 5MG ODT	377	207	$7,238.69	$19.20	1.82	0.94%
SUBTOTAL	**2,904**	**1,374**	**$52,635.95**	**$18.12**	**2.11**	**6.85%**
ELETRIPTAN PRODUCTS						
RELPAX TAB 40MG	132	49	$72,032.25	$545.70	2.69	9.37%
RELPAX TAB 20MG	68	28	$32,869.86	$483.38	2.43	4.28%
SUBTOTAL	**200**	**77**	**$104,902.11**	**$524.51**	**2.6**	**13.65%**
SUMATRIPTAN/NAPROXEN COMBINATION PRODUCTS						
SUMAT-NAPROX TAB 85-500MG	32	20	$8,277.02	$258.66	1.6	1.08%
SUBTOTAL	**32**	**20**	**$8,277.02**	**$258.66**	**1.6**	**1.08%**
TIER-1 SUBTOTAL	**10,728**	**4,848***	**$291,699.98**	**$27.19**	**2.12**	**37.96%**
TIER-2 MEDICATIONS						
ZOLMITRIPTAN PRODUCTS						
ZOLMITRIPTAN TAB 5MG	37	9	$828.39	$22.39	4.11	0.11%
ZOMIG SPR 5MG	16	6	$7,925.54	$495.35	2.67	1.03%
ZOLMITRIPTAN TAB 2.5MG	10	3	$245.29	$24.53	3.33	0.03%
ZOLMITRIPTAN TAB 5MG ODT	6	4	$155.71	$25.95	1.5	0.02%
ZOMIG SPR 2.5MG	4	2	$1,995.12	$498.78	2	0.26%
ZOLMITRIPTAN TAB 2.5 MG	2	2	$60.07	$30.04	1	0.01%
SUBTOTAL	**75**	**26**	**$11,210.12**	**$149.47**	**2.88**	**1.35%**
NARATRIPTAN PRODUCTS						
NARATRIPTAN TAB 2.5MG	23	7	$653.04	$28.39	3.29	0.08%
NARATRIPTAN TAB 1MG	3	2	$109.57	$36.52	1.5	0.01%
SUBTOTAL	**26**	**9**	**$762.61**	**$29.33**	**2.88**	**0.09%**
TIER-2 SUBTOTAL	**101**	**33***	**$11,972.73**	**$118.54**	**3.06**	**1.44%**
TIER-3 MEDICATIONS						
ALMOTRIPTAN PRODUCTS						
ALMOTRIPTAN TAB 12.5MG	7	1	$1,620.42	$231.49	7	0.21%
SUBTOTAL	**7**	**1**	**$1,620.42**	**$231.49**	**7**	**0.21%**
FROVATRIPTAN PRODUCTS						
FROVATRIPTAN TAB 2.5MG	3	1	$634.76	$211.59	3	0.08%
SUBTOTAL	**3**	**1**	**$634.76**	**$211.59**	**3**	**0.08%**
TIER-3 SUBTOTAL	**10**	**2***	**$2,255.18**	**$225.52**	**5**	**0.29%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
SUMATRIPTAN PRODUCTS						
SUMATRIPTAN INJ 6MG/0.5ML	18	4	$5,342.99	$296.83	4.5	0.70%
SUMATRIPTAN SPR 20MG/ACT	13	1	$5,721.28	$440.10	13	0.74%
SUBTOTAL	**31**	**5**	**$11,064.27**	**$356.92**	**6.2**	**1.44%**
ELETRIPTAN PRODUCTS						
ELETRIPTAN TAB 40MG	3	1	263.34	483.38	3	0.03%
SUBTOTAL	**3**	**1**	**263.34**	**483.38**	**3**	**0.03%**
UBROGEPANT PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
UBRELVY TAB 50MG	2	2	$1,072.68	$536.34	1	0.14%
SUBTOTAL	**2**	**2**	**$1,072.68**	**$536.34**	**1**	**0.14%**
SPECIAL PA SUBTOTAL	**36**	**8***	**$12,400.29**	**$344.45**	**4.5**	**1.61%**
CALCITONIN GENE-RELATED PEPTIDE (CGRP) INJECTABLE PRODUCTS						
GALCANEZUMAB PRODUCTS						
EMGALITY INJ 120MG/ML	696	172	$413,440.26	$593.84	4.05	53.80%
EMGALITY INJ 100MG/ML	1	1	$1,463.22	$1,463.22	1	0.19%
SUBTOTAL	**697**	**173**	**$414,903.48**	**$595.27**	**4.03**	**53.99%**
ERENUMAB PRODUCTS						
AIMOVIG INJ 70MG/ML	29	9	$16,709.04	$576.17	3.22	2.17%
AIMOVIG INJ 140MG/ML	26	8	$15,012.93	$577.42	3.25	1.95%
SUBTOTAL	**55**	**17**	**$31,721.97**	**$576.76**	**3.24**	**4.12%**
FREMANEZUMAB PRODUCTS						
AJOVY INJ 225MG/1.5ML	6	2	$3,578.11	$596.35	3	0.47%
SUBTOTAL	**6**	**2**	**$3,578.11**	**$596.35**	**3**	**0.47%**
CGRP INJ SUBTOTAL	**758**	**176***	**$450,203.56**	**$593.94**	**4.31**	**58.58%**
TOTAL	**11,633**	**4,951***	**$768,531.74**	**$66.06**	**2.35**	**100.00%**

TAB = tablet; SUMAT = sumatriptan; NAPROX = naproxen; SPR = nasal spray; ODT = orally disintegrating tablet; ACT = actuation; INJ = injection
*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

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Appendix O

Fiscal Year 2020 Annual Review of Systemic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System)

Oklahoma Health Care Authority
February 2021

Current Prior Authorization Criteria

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	**Tier-2**	**Special PA**
celecoxib (Celebrex®) 50mg, 100mg, & 200mg caps	diclofenac potassium (Cataflam®)	celecoxib (Celebrex®) 400mg caps
diclofenac epolamine (Flector® Patch)	diclofenac sodium/ misoprostol (Arthrotec®)	diclofenac (Zorvolex®)
diclofenac ER (Voltaren® XR)	diclofenac sodium (Voltaren®) 25mg tabs	diclofenac potassium (Cambia®) powder pack
diclofenac sodium (Voltaren®) 50mg & 75mg tabs	etodolac (Lodine®) 200mg & 300mg caps	diclofenac potassium (Zipsor®) caps
diclofenac sodium 1% (Voltaren® Gel)	etodolac ER (Lodine® XL)	diclofenac sodium (Dyloject™) inj
etodolac (Lodine®) 400mg & 500mg tabs	naproxen sodium (Anaprox®) 275mg & 550mg tabs	diclofenac sodium (Pennsaid®) topical drops
flurbiprofen (Ansaid®)	oxaprozin (Daypro®)	fenoprofen (Nalfon®)
ibuprofen (Motrin®)	piroxicam (Feldene®)	ibuprofen (Caldolor®) inj
ketoprofen (Orudis®)	tolmetin (Tolectin®)	ibuprofen/famotidine (Duexis®)
meloxicam (Mobic®)		indomethacin (Indocin®) susp & ER caps
nabumetone (Relafen®)		indomethacin (Tivorbex®)
naproxen (Naprosyn®)		ketoprofen ER (Oruvail®)
naproxen EC (Naprosyn®)		ketorolac tromethamine (Sprix®) nasal spray
sulindac (Clinoril®)		meclofenamate (Meclomen®)
		mefenamic acid (Ponstel®)
		meloxicam (Vivlodex®) caps
		meloxicam ODT (Qmiiz ODT™)
		nabumetone 1,000mg (Relafen DS®)

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	**Tier-2**	**Special PA**
		naproxen sodium ER (Naprelan®)
		naproxen/esomeprazole (Vimovo®)

caps = capsules; ER = extended-release; EC = enteric-coated; inj = injection; ODT = orally disintegrating tablet; PA = prior authorization; susp = suspension; tabs = tablets
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

NSAIDs Tier-2 Approval Criteria:

1. Previous use of at least 2 Tier-1 NSAID products (from different product lines) plus a proton pump inhibitor (PPI) within the last 120 days.

NSAIDs Special Prior Authorization (PA) Approval Criteria:

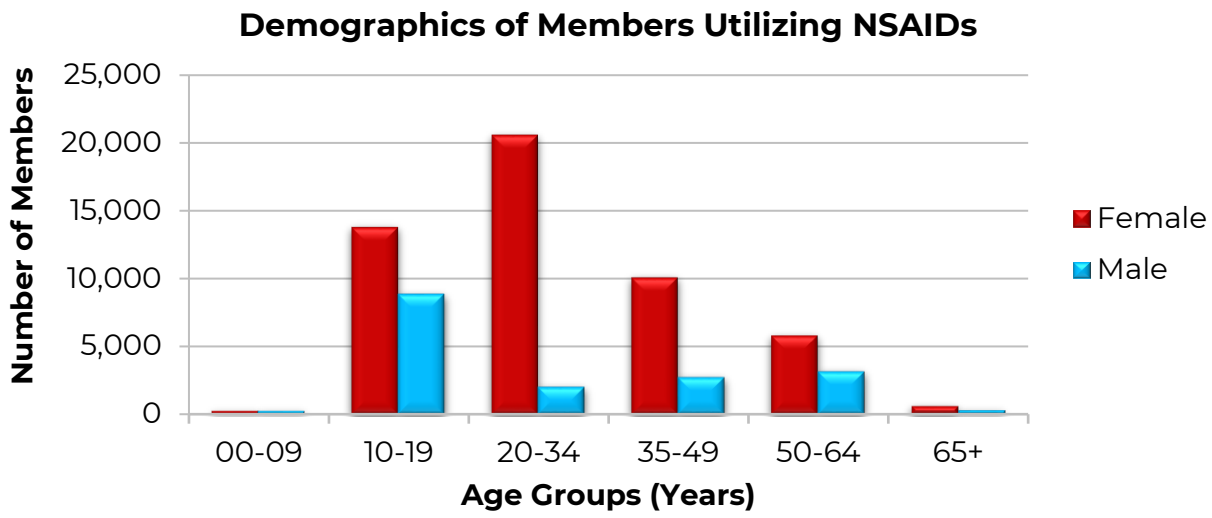
1. A unique indication for which a Tier-1 or Tier-2 product is not appropriate; or
2. Previous use of at least 2 Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 product must be provided; and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

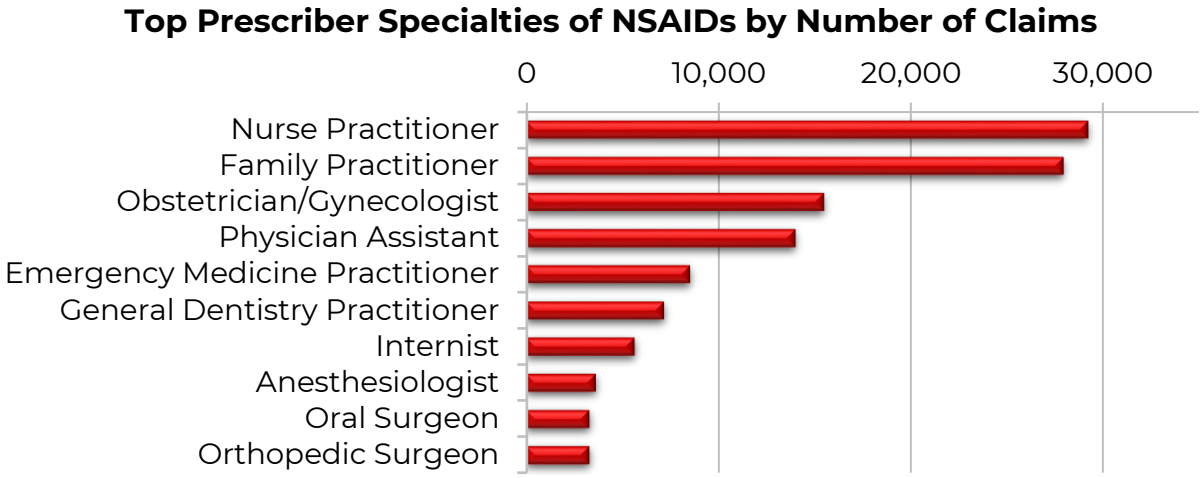
Utilization of NSAIDs: Fiscal Year 2020

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	72,132	137,032	$1,949,651.58	$14.23	$0.62	6,750,036	3,124,304
2020	68,449	132,163	$2,002,975.18	$15.16	$0.67	6,797,156	3,003,035
% Change	**-5.10%**	**-3.60%**	**2.70%**	**6.50%**	**8.10%**	**0.70%**	**-3.90%**
Change	**-3,683**	**-4,869**	**$53,323.60**	**$0.93**	**$0.05**	**47,120**	**-121,269**

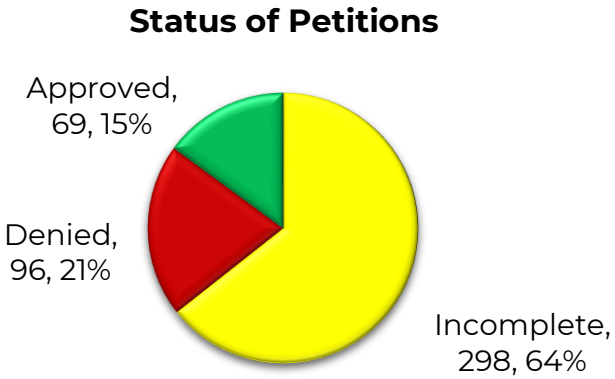
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020





Prior Authorization of NSAIDs

There were 463 prior authorization requests submitted for NSAIDs during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11]

Anticipated Patent Expiration(s):

- Licart™ (diclofenac epolamine topical system): December 2021
- Cambia® (diclofenac potassium powder packs): June 2026
- Duexis® (ibuprofen/famotidine tablets): July 2026
- Dyloject™ (diclofenac sodium injection): March 2027
- Zipsor® (diclofenac potassium capsules): February 2029
- Tivorbex® (indomethacin capsules): April 2030
- Zorvolex® (diclofenac capsules): April 2030
- Anjeso® (meloxicam injection): May 2030
- Pennsaid® (diclofenac sodium 2% topical drops): August 2030
- Qmiiz™ ODT (meloxicam orally disintegrating tablets): August 2030
- Caldolor® (ibuprofen injection): September 2030
- Vimovo® (naproxen/esomeprazole tablets): October 2031
- Vivlodex® (meloxicam capsules): March 2035

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

- **December 2018:** The FDA approved Licart™ (diclofenac epolamine topical system) for the treatment of acute pain due to minor strains, sprains, and contusions. In October 2020, IBSA Pharma launched Licart™ in the United States. Licart™ is the only topical NSAID approved by the FDA for once-daily application. Each topical system (patch) can be applied to the skin for a full 24 hours and has been shown to provide pain relief within 1 to 3 hours after application and continues to relieve pain for 24 hours.
- **February 2020:** The FDA approved GlaxoSmithKline's Voltaren® Arthritis Pain (diclofenac sodium 1% topical gel) for over-the-counter (OTC) use as part of the Rx-to-OTC switch process. The OTC product is approved for the temporary relief of arthritis pain in upper body areas (including hand, wrist, and elbow) and lower body areas (including foot, ankle, and knee). Voltaren® Arthritis Pain is the first and only prescription strength NSAID gel to be available OTC.
- **February 2020:** The FDA approved Anjeso® (meloxicam injection) for the management of moderate-to-severe pain, alone or in combination with non-NSAIDs, in adult patients. Anjeso® is administered as a once-daily intravenous (IV) bolus injection. The safety and efficacy of Anjeso® were evaluated in 2 double-blind, placebo-controlled Phase 3 studies in patients with postoperative pain (bunionectomy surgery or elective abdominoplasty surgery) for a maximum of 3 doses. Because the onset of clinically-meaningful analgesia is delayed, Anjeso® should not be used alone when rapid pain relief is required. Patient-reported meaningful analgesia occurred at 2 and 3 hours after administration of Anjeso® in the 2 Phase 3 studies. Oral oxycodone 5mg was allowed in both studies as rescue medication and was used by 50% and 78% of

patients who received Anjeso® and 49% and 78% of patients who received placebo in the 2 Phase 3 studies.

Guideline Update(s):

- **August 2020:** The American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) released new guidelines for the nonpharmacologic and pharmacologic management of acute pain from non-low back, musculoskeletal injuries in adults. Acute musculoskeletal pain was defined as pain lasting <4 weeks and included a variety of injuries such as strains, sprains, soft tissue injuries, whiplash, nonsurgical fractures, contusions, and others. The guideline was developed based on a review of 2 systematic evidence reviews: a meta-analysis of 207 studies which included 32,959 patients and evaluated the comparative efficacy and safety of nonpharmacologic and pharmacologic treatments, and a systematic review of 13 observational studies which included 13,263,393 patients and evaluated the predictors of prolonged opioid use. Some key recommendations from the ACP/AAFP guidelines include:
  - Topical NSAIDs (with or without menthol gel) are recommended as the first-line option to reduce or relieve symptoms, improve physical function, and improve patient treatment satisfaction (strong recommendation; moderate-certainty evidence).
  - Oral NSAIDs are also recommended to reduce or relieve symptoms and to improve physical function, or oral acetaminophen is recommended to reduce pain (conditional recommendation; moderate-certainty evidence).
  - Opioids, including tramadol, are recommended against use in this setting (conditional recommendation; low-certainty evidence).

  In the studies evaluated, opioid interventions were associated with significant increases in neurologic and gastrointestinal (GI) adverse effects with only small effects on symptom relief and pain. Additionally, a substantial number of patients prescribed opioids for acute pain continued using opioids long-term (27% in high-risk populations; 6% in the general population). Predictors of risk for prolonged opioid use included a longer prescribing period (>7 days vs. 1-3 days) and higher morphine milligram equivalents (MME) per day. Therefore, opioids should be avoided for the treatment of acute musculoskeletal injuries except in cases of severe injury or intolerance of first-line therapies.

Pipeline:

- **ATB-352:** Antibe Therapeutics is currently in the pre-clinical phase of development for ATB-352, a hydrogen sulfide-releasing derivative of ketoprofen for the treatment of acute post-operative pain. Pre-clinical animal studies of ATB-352 have shown that ATB-352 causes negligible

GI damage with potentially enhanced analgesic potency relative to ketoprofen. Investigational New Drug (IND)-enabling studies of ATB-352 are currently ongoing.

- **NMT-001:** Neumentum is initiating Phase 3 studies of NMT-001, a novel pre-mixed bag formulation of ketorolac tromethamine intended for continuous IV infusion for moderately severe post-surgical pain that necessitates opioid-level analgesia. NMT-001 has the potential to become the first continuously-infused, 24-hour non-opioid analgesic option for post-operative pain. Neumentum anticipates receiving FDA approval for NMT-001 in 2021.
- **Otenaproxesul (ATB-346):** Antibe Therapeutics has completed Phase 2 studies of otenaproxesul (ATB-346), a hydrogen sulfide-releasing derivative of naproxen. A Phase 2B safety study of otenaproxesul demonstrated superior GI safety relative to naproxen. In June 2020, top-line results were released from a Phase 2B efficacy study in patients with osteoarthritis of the knee. Patients were randomized to 1 of 3 otenaproxesul once-daily doses (150mg, 200mg, or 250mg) or placebo. Results demonstrated a statistically significant reduction in pain as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale scores for the 200mg and 250mg daily doses of otenaproxesul compared to placebo. Antibe Therapeutics plans to initiate Phase 3 studies of otenaproxesul for the treatment of chronic pain and inflammation in the first half of 2021.

Anjeso® (Meloxicam Injection) Product Summary[12]

Indication: Anjeso® (meloxicam injection) is an NSAID indicated for use in adults for the management of moderate-to-severe pain, alone or in combination with non-NSAID analgesics.

- Limitation of Use: Use of Anjeso® alone is not recommended when rapid onset of analgesia is required due to delayed onset of efficacy. In 2 clinical studies of Anjeso®, the median time to meaningful pain relief was 2 and 3 hours after administration of Anjeso®. Additionally, some patients may not experience adequate pain relief during the entire 24-hour dosing interval. Administration of additional short-acting, non-NSAID analgesics may be required in these cases.

How Supplied: Opaque, pale-yellow, aqueous dispersion containing 30mg/mL of meloxicam in a single-dose vial (SDV)

Dosing and Administration:

- 30mg once daily administered by IV bolus injection over 15 seconds
- Should be used for the shortest duration possible consistent with individual patient treatment goals

- Patients should be well hydrated prior to administration to reduce the risk of renal toxicity

Cost Comparison:

Product	Cost Per Unit*	Cost Per Day+
Anjeso® (meloxicam injection) 30mg/mL	**$94.00**	**$94.00**
meloxicam 7.5mg tablet	$0.02	$0.02
meloxicam 15mg tablet	$0.02	$0.02

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 Cost (SMAC) if NADAC unavailable.
*Unit = 1mL for Anjeso® and 1 tablet for meloxicam tablets.
+Cost per day based on 30mg daily for Anjeso® and 1 tablet daily for meloxicam tablets.

Licart™ (Diclofenac Epolamine Topical System) Product Summary[13]

Indication: Licart™ (diclofenac epolamine topical system) is an NSAID patch indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions.

How Supplied: 1.3% diclofenac epolamine topical system (patch) supplied in re-sealable envelopes, each containing 5 topical systems (10cm x 14cm each), with 3 envelopes per box

Dosing and Administration: 1 topical system applied to the most painful area once daily

Cost Comparison:

Product	Cost Per Unit*	Cost Per Day+
Licart™ (diclofenac epolamine topical system) 1.3%	**$24.86**	**$24.86**
Flector® (diclofenac epolamine patch) 1.3%	$4.81	$9.63
diclofenac sodium 75mg tablet	$0.09	$0.17

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 Cost (SMAC) if NADAC unavailable.
*Unit = 1 topical system or patch for Licart™ and Flector® and 1 tablet for diclofenac sodium tablets.
+Cost per day based on 1 topical system daily for Licart™, 1 patch twice daily for Flector®, and 1 tablet twice daily for diclofenac sodium tablets.

Recommendations

The College of Pharmacy recommends the placement of Anjeso® (meloxicam injection) into the Special Prior Authorization (PA) Tier of the NSAIDs Product Based Prior Authorization (PBPA) category with the following additional criteria in red:

Anjeso® (Meloxicam Injection) Approval Criteria:

1. An FDA approved diagnosis of management of moderate-to-severe pain, alone or in combination with non-nonsteroidal anti-inflammatory (NSAID) analgesics; and
2. Member must be 18 years of age or older; and
3. Member must be well hydrated before Anjeso® administration to reduce the risk of renal toxicity; and
4. Anjeso® should be used for the shortest duration consistent with individual patient treatment goals; and
5. A patient-specific, clinically significant reason the member cannot use oral meloxicam tablets or other Tier-1 NSAIDs must be provided; and
6. A quantity limit of 3 vials per 3 days will apply; and
7. For consideration of a longer duration of use, a patient-specific, clinically significant reason why the member cannot transition to an oral Tier-1 NSAID must be provided, along with the anticipated duration of treatment.

Additionally, the College of Pharmacy recommends the placement of Licart™ (diclofenac epolamine topical system) into the Special PA Tier of the NSAIDs PBPA category. The College of Pharmacy also recommends the addition of an age restriction of 12 years of age or younger for naproxen suspension and recommends moving ketoprofen capsules from Tier-1 to the Special PA Tier of the NSAIDs PBPA category and moving diclofenac ER (Voltaren® XR) from Tier-1 to Tier-2 of the NSAIDs PBPA category based on net cost (additions and changes shown in red):

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	**Tier-2**	**Special PA**
celecoxib (Celebrex®) 50mg, 100mg, & 200mg caps	**diclofenac ER (Voltaren® XR)**	celecoxib (Celebrex®) 400mg caps
diclofenac epolamine (Flector® Patch)	diclofenac potassium (Cataflam®)	diclofenac (Zorvolex®)
~~**diclofenac ER (Voltaren® XR)**~~	diclofenac sodium/ misoprostol (Arthrotec®)	**diclofenac epolamine (Licart™) topical system**
diclofenac sodium (Voltaren®) 50mg & 75mg tabs	diclofenac sodium (Voltaren®) 25mg tabs	diclofenac potassium (Cambia®) powder pack
diclofenac sodium 1% (Voltaren® Gel)	etodolac (Lodine®) 200mg & 300mg caps	diclofenac potassium (Zipsor®) caps
etodolac (Lodine®) 400mg & 500mg tabs	etodolac ER (Lodine® XL)	diclofenac sodium (Dyloject™) inj
flurbiprofen (Ansaid®)	naproxen sodium (Anaprox®) 275mg & 550mg tabs	diclofenac sodium (Pennsaid®) topical drops
ibuprofen (Motrin®)	oxaprozin (Daypro®)	fenoprofen (Nalfon®)

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	**Tier-2**	**Special PA**
~~**ketoprofen (Orudis®)**~~	piroxicam (Feldene®)	ibuprofen (Caldolor®) inj
meloxicam (Mobic®)	tolmetin (Tolectin®)	ibuprofen/famotidine (Duexis®)
nabumetone (Relafen®)		indomethacin (Indocin®) susp & ER caps
naproxen* (Naprosyn®)		indomethacin (Tivorbex®)
naproxen EC (Naprosyn®)		**ketoprofen (Orudis®) caps**
sulindac (Clinoril®)		ketoprofen ER (Oruvail®)
		ketorolac tromethamine (Sprix®) nasal spray
		meclofenamate (Meclomen®)
		mefenamic acid (Ponstel®)
		meloxicam (Anjeso®) inj
		meloxicam (Vivlodex®) caps
		meloxicam ODT (Qmiiz ODT™)
		nabumetone 1,000mg (Relafen DS®)
		naproxen sodium ER (Naprelan®)
		naproxen/esomeprazole (Vimovo®)

caps = capsules; ER = extended-release; EC = enteric-coated; inj = injection; ODT = orally disintegrating tablet; PA = prior authorization; susp = suspension; tabs = tablets
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Naproxen oral suspension is available without prior authorization for members 12 years of age and younger. Members older than 12 years of age will require a reason why a special formulation product is needed in place of the regular tablet formulation.

Utilization Details of NSAIDs: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
IBUPROFEN PRODUCTS						
IBUPROFEN TAB 800MG	45,387	30,030	$558,070.04	$12.30	1.51	27.86%
IBUPROFEN TAB 600MG	11,573	9,646	$132,367.47	$11.44	1.2	6.61%
IBUPROFEN TAB 400MG	2,850	2,043	$34,504.23	$12.11	1.4	1.72%
IBU TAB 800MG	797	625	$10,095.46	$12.67	1.28	0.50%
IBU TAB 600MG	262	238	$3,166.41	$12.09	1.1	0.16%
IBU TAB 400MG	141	106	$1,752.66	$12.43	1.33	0.09%
SUBTOTAL	**61,010**	**42,688**	**$739,956.27**	**$12.13**	**1.43**	**36.94%**
NAPROXEN PRODUCTS						
NAPROXEN TAB 500MG	17,357	11,123	$217,265.67	$12.52	1.56	10.85%
NAPROXEN TAB 375MG	1,897	1,365	$24,640.49	$12.99	1.39	1.23%
NAPROXEN TAB 250MG	1,809	1,137	$23,577.12	$13.03	1.59	1.18%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
NAPROXEN SUS 125MG/5ML	447	263	$103,337.23	$231.18	1.7	5.16%
NAPROXEN DR TAB 500MG	443	303	$8,160.86	$18.42	1.46	0.41%
NAPROXEN DR TAB 375MG	111	63	$1,816.97	$16.37	1.76	0.09%
NAPROXEN SODIUM TAB 550MG	103	64	$3,245.84	$31.51	1.61	0.16%
EC-NAPROXEN TAB 500MG	83	58	$1,489.50	$17.95	1.43	0.07%
NAPROXEN SODIUM TAB 275MG	4	2	$161.84	$40.46	2	0.01%
EC-NAPROXEN TAB 375MG	3	3	$44.47	$14.82	1	0.00%
SUBTOTAL	**22,257**	**14,381**	**$383,739.99**	**$17.24**	**1.55**	**19.16%**
MELOXICAM PRODUCTS						
MELOXICAM TAB 15MG	15,825	7,124	$147,274.56	$9.31	2.22	7.35%
MELOXICAM TAB 7.5MG	7,697	3,923	$74,623.56	$9.70	1.96	3.73%
SUBTOTAL	**23,522**	**11,047**	**$221,898.12**	**$9.43**	**2.13**	**11.08%**
DICLOFENAC PRODUCTS						
DICLOFENAC TAB 75MG DR	5,217	2,424	$77,742.60	$14.90	2.15	3.88%
DICLOFENAC GEL 1%	5,062	2,827	$183,758.50	$36.30	1.79	9.17%
DICLOFENAC TAB 50MG DR	1,973	982	$33,364.70	$16.91	2.01	1.67%
DICLOFENAC TAB 100MG ER	186	95	$14,840.09	$79.79	1.96	0.74%
DICLOFENAC POTASSIUM TAB 50MG	127	68	$5,049.77	$39.76	1.87	0.25%
FLECTOR PATCH 1.3%	111	70	$37,849.45	$340.99	1.59	1.89%
DICLOFENAC PATCH 1.3%	80	40	$16,598.98	$207.49	2	0.83%
DICLOFENAC TAB 25MG DR	20	9	$1,066.61	$53.33	2.22	0.05%
CAMBIA POWDER 50MG	2	1	$1,837.81	$918.91	2	0.09%
DICLOFENAC SOL 1.5%	1	1	$38.73	$38.73	1	0.00%
SUBTOTAL	**12,779**	**6,517**	**$372,147.24**	**$29.12**	**1.96**	**18.58%**
CELECOXIB PRODUCTS						
CELECOXIB CAP 200MG	3,407	1,391	$59,391.06	$17.43	2.45	2.97%
CELECOXIB CAP 100MG	1,296	496	$23,060.18	$17.79	2.61	1.15%
CELECOXIB CAP 50MG	23	15	$498.64	$21.68	1.53	0.02%
SUBTOTAL	**4,726**	**1,902**	**$82,949.88**	**$17.55**	**2.48**	**4.14%**
KETOROLAC PRODUCTS						
KETOROLAC TAB 10MG	2,854	2,468	$66,692.52	$23.37	1.16	3.33%
KETOROLAC INJ 60MG/2ML	24	7	$369.91	$15.41	3.43	0.02%
KETOROLAC INJ 30MG/ML	10	7	$520.44	$52.04	1.43	0.03%
KETOROLAC INJ 15MG/ML	1	1	$13.21	$13.21	1	0.00%
SUBTOTAL	**2,889**	**2,483**	**$67,596.08**	**$23.40**	**1.16**	**3.37%**
NABUMETONE PRODUCTS						
NABUMETONE TAB 750MG	1,319	436	$24,200.15	$18.35	3.03	1.21%
NABUMETONE TAB 500MG	916	380	$14,297.76	$15.61	2.41	0.71%
SUBTOTAL	**2,235**	**816**	**$38,497.91**	**$17.23**	**2.74**	**1.92%**
ETODOLAC PRODUCTS						
ETODOLAC TAB 400MG	1,095	631	$29,292.18	$26.75	1.74	1.46%
ETODOLAC TAB 500MG	448	169	$14,862.05	$33.17	2.65	0.74%
ETODOLAC CAP 300MG	62	36	$2,826.20	$45.58	1.72	0.14%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
ETODOLAC CAP 200MG	40	24	$1,517.60	$37.94	1.67	0.08%
ETODOLAC ER TAB 600MG	13	2	$1,733.65	$133.36	6.5	0.09%
ETODOLAC ER TAB 400MG	10	6	$1,255.90	$125.59	1.67	0.06%
ETODOLAC ER TAB 500MG	4	3	$360.57	$90.14	1.33	0.02%
SUBTOTAL	**1,672**	**871**	**$51,848.15**	**$31.01**	**1.92**	**2.59%**
INDOMETHACIN PRODUCTS						
INDOMETHACIN CAP 50MG	404	252	$6,054.36	$14.99	1.6	0.30%
INDOMETHACIN CAP 25MG	304	183	$4,551.76	$14.97	1.66	0.23%
INDOCIN SUS 25MG/5ML	19	4	$16,111.17	$847.96	4.75	0.80%
INDOMETHACIN CAP 75MG ER	4	3	$65.98	$16.50	1.33	0.00%
SUBTOTAL	**731**	**442**	**$26,783.27**	**$36.64**	**1.65**	**1.34%**
SULINDAC PRODUCTS						
SULINDAC TAB 150MG	145	42	$2,289.88	$15.79	3.45	0.11%
SULINDAC TAB 200MG	83	39	$1,505.08	$18.13	2.13	0.08%
SUBTOTAL	**228**	**81**	**$3,794.96**	**$16.64**	**2.81**	**0.19%**
FLURBIPROFEN PRODUCTS						
FLURBIPROFEN TAB 100MG	44	12	$1,278.71	$29.06	3.67	0.06%
SUBTOTAL	**44**	**12**	**$1,278.71**	**$29.06**	**3.67**	**0.06%**
OXAPROZIN PRODUCTS						
OXAPROZIN TAB 600MG	18	4	$1,092.30	$60.68	4.5	0.05%
SUBTOTAL	**18**	**4**	**$1,092.30**	**$60.68**	**4.5**	**0.05%**
DICLOFENAC/MISOPROSTOL PRODUCTS						
DICLO/MISOPR TAB 75MG/0.2MG	15	4	$1,716.12	$114.41	3.75	0.09%
DICLO/MISOPR TAB 50MG/0.2MG	10	8	$1,063.46	$106.35	1.25	0.05%
SUBTOTAL	**25**	**12**	**$2,779.58**	**$111.18**	**2.08**	**0.14%**
FENOPROFEN PRODUCTS						
FENOPROFEN TAB 600MG	8	2	$588.23	$73.53	4	0.03%
SUBTOTAL	**8**	**2**	**$588.23**	**$73.53**	**4**	**0.03%**
KETOPROFEN PRODUCTS						
KETOPROFEN CAP 25MG	8	6	$325.95	$40.74	1.33	0.02%
SUBTOTAL	**8**	**6**	**$325.95**	**$40.74**	**1.33**	**0.02%**
PIROXICAM PRODUCTS						
PIROXICAM CAP 20MG	5	4	$113.22	$22.64	1.25	0.01%
SUBTOTAL	**5**	**4**	**$113.22**	**$22.64**	**1.25**	**0.01%**
IBUPROFEN/FAMOTIDINE PRODUCTS						
DUEXIS TAB 800MG/26.6MG	3	1	$7,468.83	$2,489.61	3	0.37%
SUBTOTAL	**3**	**1**	**$7,468.83**	**$2,489.61**	**3**	**0.37%**
MEFENAMIC ACID PRODUCTS						
MEFENAMIC ACID CAP 250MG	2	1	$71.06	$35.53	2	0.00%
SUBTOTAL	**2**	**1**	**$71.06**	**$35.53**	**2**	**0.00%**
PIROXICAM PRODUCTS						
PIROXICAM CAP 10MG	1	1	$45.43	$45.43	1	0.00%
SUBTOTAL	**1**	**1**	**$45.43**	**$45.43**	**1**	**0.00%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TOTAL	**132,163**	**68,449***	**$2,002,975.18**	**$15.16**	**1.93**	**100.00%**

CAP = capsule; DICLO/MISOPR = diclofenac/misoprostol; DR = delayed-release; EC = enteric-coated;
ER = extended-release; IBU = ibuprofen; INJ = injection; SOL = solution; SUS = suspension; TAB = tablet
*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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J1741 IBUPROFEN INJ 100MG	9	9	$152.76	$16.97
TOTAL	**9**	**9**	**$152.76**	**$16.97**

INJ = injection
+Total number of unduplicated claims.
*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

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Appendix P

30-Day Notice to Prior Authorize Oxlumo™ (Lumasiran)

Oklahoma Health Care Authority
February 2021

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

Primary hyperoxaluria is a group of rare, autosomal recessive genetic disorders which ultimately result in overproduction of oxalate. Patients with primary hyperoxaluria lack a specific functional enzyme which would normally prevent excess accumulation of oxalate. There are 3 types of primary hyperoxaluria, identified by the specific enzyme affected. Pathogenic mutations in the alanine-glyoxylate aminotransferase (*AGXT*), glyoxylate reductase-hydroxypyruvate reductase (*GRHPR*), and 4-hydroxy-2-oxoglutarate aldolase (*HOGA1*) genes cause primary hyperoxaluria type 1 (PH1), type 2 (PH2), and type 3 (PH3), respectively.

PH1 is the most common type, accounting for approximately 80% of primary hyperoxaluria cases, and is also the most severe form of the disorder. The estimated prevalence of PH1 is 1 to 3 cases per 1 million population, with fewer than 1,000 cases expected in the United States. PH1 is thought to account for 1% to 2% of pediatric end-stage renal disease (ESRD) cases.

PH1 is caused by a variety of different pathogenic mutations in the *AGXT* gene which normally encodes a liver-specific peroxisomal enzyme, alanine-glyoxylate aminotransferase (AGT). When present, AGT catalyzes the conversion of glyoxylate and alanine to pyruvate and glycine. In PH1, AGT is deficient, causing glyoxylate levels to accumulate. Subsequently, glyoxylate is converted to oxalate by lactate dehydrogenase, leading to excessive oxalate production in the liver. Oxalate is a waste product of metabolism that tends to form highly insoluble calcium oxalate salts and is normally excreted almost entirely by the kidneys. Individuals with PH1 have abnormally elevated urinary oxalate excretion (hyperoxaluria) as the kidneys attempt to remove excess oxalate. During excretion, calcium oxalate tends to crystallize and can form kidney stones in the renal tubules (nephrolithiasis) or deposits in the kidney tissue itself (nephrocalcinosis). Over time, this leads to progressive kidney damage including chronic kidney disease (CKD) and ESRD. As kidney function declines, the ability to remove excess oxalate is further impaired. When the estimated glomerular filtration rate (eGFR) falls below 30mL/min/1.73m^2, the plasma concentration of oxalate increases, resulting in systemic oxalosis and calcium oxalate deposits in other tissues such as the retina, myocardium, blood vessels, bones, bone marrow, and subcutaneous (sub-Q) tissue. Without treatment, PH1 results in the eventual progression to oxalosis and death from ESRD or complications of oxalosis.

Treatment options for PH1 are limited. Supportive measure are recommended in all patients with PH1 and include high fluid intake, urine alkalization to reduce calcium oxalate crystallization, and pyridoxine (a cofactor for AGT). Additionally, combined liver and kidney transplantation should be considered prior to CKD Stage 4 (eGFR 15-29mL/min/1.73m^2), before systemic oxalosis occurs. Because the genetic defect in PH1 is isolated to the liver, a transplanted liver can restore the production of the missing AGT enzyme. In November 2020, the U.S. Food and Drug Administration (FDA) approved Oxlumo™ (lumasiran) as the first approved therapy for the treatment of PH1 to lower urinary oxalate levels in pediatric and adult patients.

Oxlumo™ (Lumasiran) Product Summary[7,8,9]

Indication(s): Oxlumo™ (lumasiran) is a small interfering ribonucleic acid (siRNA) therapy directed against hydroxyacid oxidase 1 (HAO1) indicated for the treatment of PH1 to lower urinary oxalate levels in pediatric and adult patients.

How Supplied: Clear, colorless-to-yellow solution containing 94.5mg/0.5mL of lumasiran in a single-dose vial (SDV)

Dosing and Administration:

- Administered as a sub-Q injection according to the following weight-based regimens:
  - Patients <10kg: Loading dose (LD) of 6mg/kg monthly for 3 doses; maintenance dose (MD) of 3mg/kg once monthly thereafter
  - Patients 10kg to <20kg: LD of 6mg/kg monthly for 3 doses; MD of 6mg/kg every 3 months thereafter
  - Patients ≥20kg: LD of 3mg/kg monthly for 3 doses; MD of 3mg/kg every 3 months thereafter
- Should be administered by a health care professional
- Administration sites include the abdomen, thigh, or the side or back of the upper arms; sites should be rotated
  - Areas with scar tissue, areas that are reddened, inflamed, or swollen, and the area around the navel should be avoided
- Injection volumes >1.5mL should be divided equally into multiple syringes and injected into separate sites at least 2cm apart
- Oxlumo™ SDVs can be stored at 2°C to 25°C (36°F to 77°F)

Mechanism of Action: Lumasiran is a siRNA therapy which reduces levels of the enzyme glycolate oxidase (GO) by targeting HAO1 messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. Subsequently, reduced levels of GO enzyme lead to reduced amounts of glyoxylate, a substrate for oxalate production. This results in reduced oxalate production in

the liver. Based on its mechanism of action, lumasiran is not expected to be effective for PH2 or PH3.

Contraindication(s): None

Use in Specific Populations:

- Pregnancy: There are no data available on the use of lumasiran in pregnant women to evaluate the drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Studies in animals did not identify any adverse effects on pregnancy or embryo-fetal development at doses up to 45 times the maximum recommended human dose (MRHD) in rats and 90 times the MRHD in rabbits.
- Lactation: There are no data available on the presence of lumasiran in human milk, the effects on the breastfed child, or the effects of the drug on milk production.
- Pediatric Use: The safety and effectiveness of lumasiran have been established in pediatric patients from birth to 18 years of age. Use in this age range is supported by evidence from 2 studies: a randomized, double-blind, placebo-controlled study in 39 pediatric and adult patients 6 years of age and older and a single-arm study in 18 patients younger than 6 years of age (range: 4 to 74 months of age).
- Geriatric Use: Clinical studies of lumasiran did not include patients 65 years of age and older; therefore, it is not known whether they respond differently than younger patients.
- Hepatic Impairment: No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Lumasiran has not been studied in patients with severe hepatic impairment.
- Renal Impairment: No dose adjustment is necessary in patients with an eGFR ≥30mL/min/1.73m^2. Lumasiran has not been studied in patients with an eGFR <30mL/min/1.73m^2.

Adverse Reactions: The most common adverse reactions, occurring in ≥10% of patients treated with lumasiran (and ≥5% more frequently than in placebo) in the Phase 3 ILLUMINATE-A study, were injection site reaction and abdominal pain (including general abdominal pain, upper abdominal pain, lower abdominal pain, and abdominal discomfort).

Efficacy: The safety and efficacy of lumasiran were assessed in 2 Phase 3 studies, ILLUMINATE-A and ILLUMINATE-B. In both studies, weight-based lumasiran (as described in the Dosing and Administration section of this report) was administered for at least 6 months for assessment of the primary efficacy end point. Additional secondary end points are being assessed in both studies during an ongoing extension phase of up to 60 months.

- ILLUMINATE-A: This study was a randomized, double-blind, placebo-controlled study in 39 patients 6 years of age and older (median: 15 years of age; range: 6 to 61 years of age).
    - Inclusion Criteria: All patients had confirmed PH1 and an eGFR ≥30mL/min/1.73m^2.
    - Exclusion Criteria: Patients were excluded if they had an eGFR <30mL/min/1.73m^2 at screening, evidence of systemic oxalosis, or a history of kidney or liver transplant.
    - Primary Endpoint: The primary efficacy endpoint was the percent reduction from baseline in 24-hour urinary oxalate excretion corrected for body surface area (BSA) averaged over months 3 through 6.
    - Results: The least squares (LS) mean percent change from baseline in the lumasiran group was -65% [95% confidence interval (CI): -71, -59] vs. -12% (95% CI: -20, -4) in the placebo group. The between-group LS mean difference was 53% (95% CI: 45, 62) and was statistically significant (P<0.0001). Additionally, by month 6, normal 24-hour urinary oxalate excretion was achieved in 52% (95% CI: 31, 72) in the lumasiran group vs. 0% (95% CI: 0, 25) in the placebo group (P=0.001).
- ILLUMINATE-B: This study was a single-arm study in 18 patients younger than 6 years of age (median: 47 months of age; range: 4 to 74 months of age).
    - Inclusion Criteria: All patients had confirmed PH1 and an eGFR ≥45mL/min/1.73m^2 (for patients ≥12 months of age) or a normal serum creatinine (for patients <12 months of age).
    - Exclusion Criteria: Patients were excluded if they did not have relatively preserved kidney function (or had an abnormal serum creatinine level at screening for patients <1 year of age), had clinical evidence of systemic oxalosis, or a history of kidney or liver transplant.
    - Primary Endpoint: The primary efficacy endpoint was the percent reduction from baseline in spot urinary oxalate:creatinine ratio averaged over months 3 through 6.
    - Results: The patients treated with lumasiran achieved a reduction in spot urinary oxalate:creatinine ratio from baseline of 71% (95% CI: 65, 77).

Cost: The Wholesale Acquisition Cost (WAC) of Oxlumo™ is $110,000 per 1mL or $55,000 per 94.5mg/0.5mL SDV. Cost will vary due to weight-based dosing. For an 80kg adult, estimated costs are $165,000 per dose, $990,000 for the first year of treatment, and $660,000 per year for maintenance dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Oxlumo™ (lumasiran) with the following criteria:

Oxlumo™ (Lumasiran) Approval Criteria:

1. An FDA approved indication for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels. Diagnosis of PH1 must be confirmed by:
    a. Molecular genetic testing identifying biallelic pathogenic variants in the *AGXT* gene; or
    b. Liver biopsy confirming alanine-glyoxylate aminotransferase (AGT) catalytic deficiency if the results of genetic testing are not diagnostic; and
2. Oxlumo™ must be prescribed by a nephrologist, geneticist, or other specialist with expertise in the treatment of PH1 (or an advanced care practitioner with a supervising physician who is a nephrologist, geneticist, or other specialist with expertise in the treatment of PH1); and
3. The prescriber must verify the member has an estimated glomerular filtration rate (eGFR) of ≥30mL/min/1.73m^2 prior to starting Oxlumo™ and must agree to monitor renal function regularly during treatment with Oxlumo™; and
4. The member must not have a history of kidney or liver transplant; and
5. The member must not have evidence of systemic oxalosis; and
6. The prescriber must verify that Oxlumo™ will be administered by a health care professional; 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 the Oxlumo™ *Prescribing Information*; and
8. Initial approvals will be for the duration of 6 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by a reduction in urinary oxalate excretion.

[1] U.S. National Library of Medicine. Primary Hyperoxaluria. *MedlinePlus*. Available online at: https://medlineplus.gov/genetics/condition/primary-hyperoxaluria/. Last revised 08/18/2020. Last accessed 12/29/2020.
[2] National Organization for Rare Disorders (NORD). Primary Hyperoxaluria. Available online at: https://rarediseases.org/rare-diseases/primary-hyperoxaluria/. Last accessed 12/29/2020.
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[4] Cochat P, Rumsby G. Primary Hyperoxaluria. *N Engl J Med* 2013; 369(7):649-58.
[5] Cochat P, Hulton SA, Acquaviva C, et al. Primary Hyperoxaluria Type 1: Indications for Screening and Guidance for Diagnosis and Treatment. *Nephrol Dial Transplant* 2012; 27(5):1729-36.
[6] Alnylam Pharmaceuticals, Inc. Alnylam Announces U.S. Food and Drug Administration (FDA) Approval of Oxlumo™ (Lumasiran), the First and Only Treatment Approved for Primary Hyperoxaluria Type 1 to Lower Urinary Oxalate Levels in Pediatric and Adult Patients. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20201124005407/en/Alnylam-Announces-U.S.-Food-and-Drug-Administration-FDA-Approval-of-OXLUMO%E2%84%A2-lumasiran-the-First-and-Only-Treatment-Approved-for-Primary-Hyperoxaluria-Type-1-to-Lower-Urinary-Oxalate-Levels-in-Pediatric-and-Adult-Patients. Issued 11/24/2020. Last accessed 01/05/2021.
[7] Oxlumo™ (Lumasiran) Prescribing Information. Alnylam Pharmaceuticals, Inc. Available online at: https://www.alnylam.com/wp-content/uploads/pdfs/OXLUMO-Prescribing-Information.pdf. Last revised 11/2020. Last accessed 12/29/2020.
[8] A Study to Evaluate Lumasiran in Children and Adults with Primary Hyperoxaluria Type 1 (ILLUMINATE-A). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/study/NCT03681184. Last revised 12/17/2020. Last accessed 01/07/2021.
[9] A Study of Lumasiran in Infants and Young Children with Primary Hyperoxaluria Type 1 (ILLUMINATE-B). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT03905694. Last revised 12/09/2020. Last accessed 01/07/2021.

Appendix Q

Fiscal Year 2020 Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Teriparatide

Oklahoma Health Care Authority
February 2021

Current Prior Authorization Criteria

Osteoporosis Medications*		
Tier-1	**Tier-2**	**Special PA¥**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax® + D)	abaloparatide inj (Tymlos®)
calcium + vitamin D†	risedronate tabs (Actonel®)	alendronate effervescent tabs (Binosto®)
ibandronate tabs (Boniva®)		alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)		alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		romosozumab-aqqg inj (Evenity®)
		teriparatide inj (Forteo®)

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization
†OTC calcium and vitamin D must be used at recommended doses in conjunction with Tier-1 bisphosphonates for trial to be accepted unless member has a recent laboratory result showing adequate vitamin D or member is unable to tolerate calcium. OTC calcium and vitamin D are only covered for members with osteoporosis that are being treated with a bisphosphonate.
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
¥Unique criteria applies to medications in the Special PA Tier.

Osteoporosis Medications Tier-2 Approval Criteria:

1. A trial of at least 1 Tier-1 bisphosphonate medication, compliantly used for at least 6 months concomitantly with calcium and vitamin D, that failed to prevent fracture or improve bone mineral density (BMD) scores; or
2. Hypersensitivity to or intolerable adverse effect(s) with all Tier-1 bisphosphonate medications; and
3. Quantity limits apply based on FDA approved maximum doses.

Actonel® (Risedronate 30mg Tablets), Atelvia® [Risedronate Delayed-Release (DR) Tablets], and Binosto® (Alendronate Effervescent Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 bisphosphonate medications must be provided; or
2. Members with a diagnosis in history of Paget's disease will not require prior authorization.

Boniva® [Ibandronate Intravenous (IV) Solution] and Prolia® (Denosumab) Approval Criteria:

1. A minimum of a 12-month trial with a Tier-1 or Tier-2 bisphosphonate plus adequate calcium and vitamin D; or
2. Contraindication to or intolerable adverse effects with Tier-1 and Tier-2 bisphosphonate medications.

Evenity® (Romosozumab-aqqg) Approval Criteria:

1. An FDA approved diagnosis of osteoporosis in postmenopausal women at high-risk for fracture; and
2. Member meets 1 of the following:
    a. History of osteoporotic fracture; or
    b. Multiple risk factors for fracture (e.g., T-score ≤-2.5 at the total hip or femoral neck, smoking, corticosteroid use, rheumatoid arthritis); or
    c. Failed or intolerant to other available osteoporosis therapy; and
3. Prescriber must verify member has not had a myocardial infarction or stroke within the preceding year; and
4. Prescriber must verify calcium levels will be monitored and pre-existing hypocalcemia will be corrected prior to starting therapy; and
5. Prescriber must verify that the member will take adequate calcium and vitamin D supplements during treatment with Evenity® to reduce the risk of hypocalcemia; and
6. Evenity® must be administered by a health care provider; and
7. Approval will be limited to a total duration of 1 year of therapy.

Fosamax® (Alendronate Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of osteoporosis or Paget's disease; and
2. A patient-specific, clinically significant reason why the member cannot use the oral tablet formulation must be provided.

Fosamax® (Alendronate 40mg Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 bisphosphonate medications including a 35mg alendronate tablet in combination with a 5mg alendronate tablet to achieve a 40mg dose must be provided; or

2. Members with a diagnosis in history of Paget's disease will not require prior authorization.

Forteo® (Teriparatide) Approval Criteria:

1. A diagnosis of 1 of the following:
    a. Treatment of postmenopausal women with osteoporosis at high risk for fracture; or
    b. To increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture; or
    c. Treatment of men and women with osteoporosis associated with sustained systemic corticosteroid therapy at high risk for fracture; or
    d. Treatment of non-healing fracture; and
2. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D or a patient-specific, clinically significant reason why the member cannot use a bisphosphonate must be provided; and
3. The diagnosis of non-healing fracture may be approved for 6 months; and
4. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
5. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy.

Tymlos® (Abaloparatide) Approval Criteria:

1. A diagnosis of postmenopausal osteoporosis confirmed by the following:
    a. History of vertebral fracture(s) or low trauma or fragility fracture(s) (e.g., prior fracture from minor trauma such as falling from standing height or less) within the past 5 years; or
    b. A Bone Mineral Density test (T-score at or below -2.5) within the last month in the spine, femoral neck, total hip, or 33% radius; or
    c. A T-score between -1.0 and -2.5 in the spine, femoral neck, total hip, or 33% radius, with a FRAX® 10-year probability for major osteoporotic fracture ≥20% or the 10-year probability of hip fracture ≥3%; and
2. One of the following [if a 12-month bisphosphonate trial is inappropriate for the member, the member must have a trial of Prolia® or a selective estrogen receptor modulatory (SERM) or a patient-specific, clinically significant reason why Prolia® or a SERM is not appropriate must be provided]:
    a. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D; or
    b. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or

c. A 12-month trial of a SERM, unless contraindicated, intolerant, or allergic, that did not yield adequate results; and

3. A patient-specific, clinically significant reason why the member cannot use Forteo® (teriparatide) must be provided; and
4. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
5. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy; and
6. A quantity limit of 1 pen per 30 days will apply.

Utilization of Osteoporosis Medications: Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	581	2,377	$277,674.87	$116.82	$2.68	18,558	103,642
2020	526	2,107	$356,776.02	$169.33	$3.39	22,751	105,396
% Change	**-9.50%**	**-11.40%**	**28.50%**	**44.90%**	**26.50%**	**22.60%**	**1.70%**
Change	**-55**	**-270**	**$79,101.15**	**$52.51**	**$0.71**	**4,193**	**1,754**

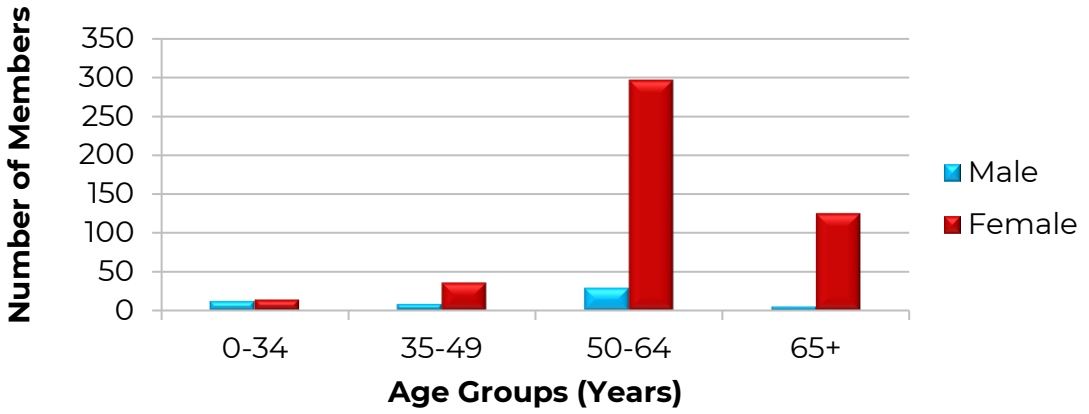
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Comparison of Fiscal Years: Medical Claims

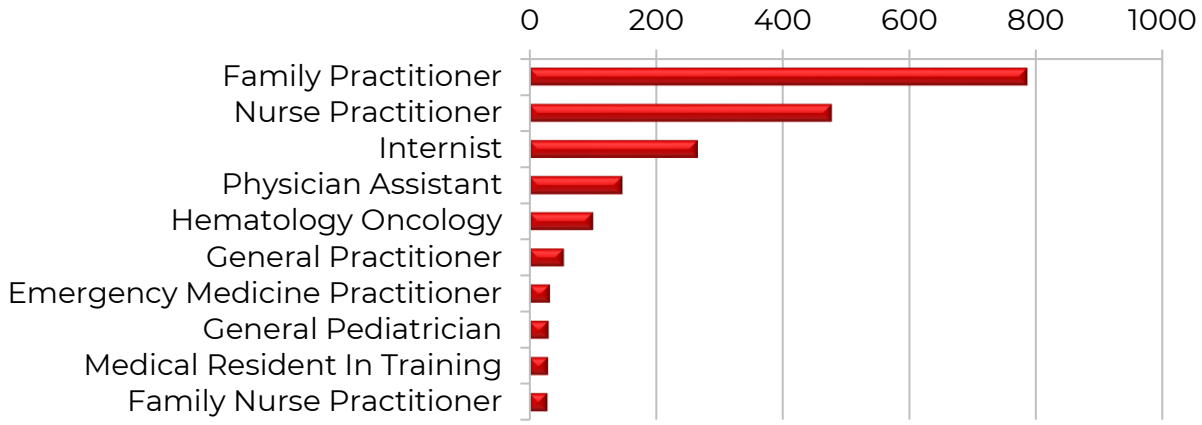
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2019	173	537	$688,191.33	$1,281.55	3.10
2020	193	524	$686,015.41	$1,309.19	2.72
% Change	**11.56%**	**-2.42%**	**-0.32%**	**2.16%**	**-12.58%**
Change	**20**	**-13**	**-$2,175.92**	**$27.64**	**-0.39**

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

Demographics of Members Utilizing Osteoporosis Medications: Pharmacy Claims



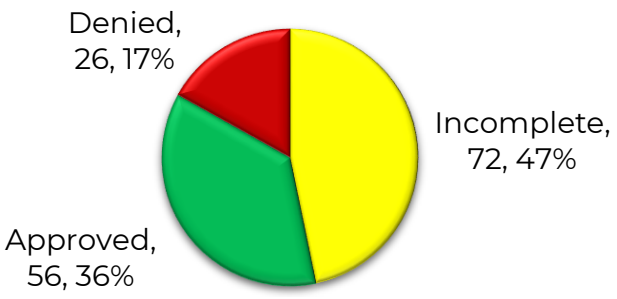
Top Prescriber Specialties of Osteoporosis Medications by Number of Claims: Pharmacy Claims



Prior Authorization of Osteoporosis Medications

There were 154 prior authorization requests submitted for osteoporosis medications during fiscal year 2020. Computer edits are in place to detect lower tiered medications in a 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 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Binosto® (alendronate effervescent tablets): August 2023
- Forteo® (teriparatide injection): March 2025
- Tymlos® (abaloparatide injection): April 2031

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

- **October 2019:** The FDA approved the New Drug Application (NDA) for PF708 (also known as Bonsity™ and teriparatide injection) submitted under the 505(b)(2) regulatory pathway using Forteo® as the reference drug. Teriparatide is a parathyroid hormone analog (PTH 1-34) indicated for treatment of postmenopausal women with osteoporosis at high risk for fracture, to increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture, and treatment of men and women with osteoporosis associated with sustained systemic corticosteroid therapy at high risk for fracture. Teriparatide is administered as a 20mcg subcutaneous (sub-Q) injection into the thigh or abdominal wall once a day, and use for more than 2 years during a patient's lifetime is not recommended. Pfenex is also asking the FDA to designate teriparatide as therapeutically equivalent ("A" rated) to Forteo®. A comparative human factors study between teriparatide and Forteo® is currently underway in order to be granted therapeutic equivalence.

News:

- **June 2020:** Pfenex announced that its commercialization partner, Alvogen, has launched teriparatide injection in the United States. Teriparatide injection (also referred to as PF708 and Bonsity™) is the first approved teriparatide product since Forteo® (teriparatide injection). The Alvogen product is pharmaceutically equivalent to Forteo® in that it has the same active ingredient in the same strength, dosage form, and route of administration. It has also been shown to have comparable bioavailability to Forteo®. These characteristics allowed the product to be approved under a 505(b)(2) NDA with Forteo® as the reference drug. It may provide a lower-cost teriparatide option for increasing bone density in patients at high risk for fracture and is FDA-approved for the same indications as Forteo®.
- **July 2020:** In response to the COVID-19 pandemic and the impact on outdoor physical activity and leisure time, the American Bone and Mineral Research (ASBMR), American Association of Clinical Endocrinologist (AACE), Endocrine Society, European Calcified Tissue Society (ECTS), National Osteoporosis Society (NOF), and International Osteoporosis Foundation (IOF) remind individuals of the importance of obtaining the daily recommended dosage of vitamin D. ASBMR, AACE,

Endocrine Society, ECTS, NOF, and IOF recommend that most adults 19 years of age and older obtain between 400-1,000 international units (IUs) of vitamin D daily from food and/or supplements. In addition, while recent observational studies have suggested associations between low vitamin D concentrations and higher rates of COVID-19 infection, these are likely related to ethnicity, age, and general health rather than a causal relationship.

Pipeline:

- **Evenity® (Romosozumab-aqqg):** Evenity® is currently FDA approved for the treatment of osteoporosis in postmenopausal women at high risk for fracture or patients who have failed or are intolerant to other available osteoporosis therapies. However, a Phase 3 trial is underway to expand the indication to include treatment of male osteoporosis. The Phase 3 trial was a randomized, placebo-controlled trial to evaluate the efficacy and safety in men with osteoporosis. The primary efficacy endpoint was percentage change from baseline in lumbar spine (LS) bone mineral density (BMD) at month 12. Results from the trial showed that the mean percentage change from baseline in the LS and total hip (TH) was significantly greater for the romosozumab group than for the placebo group (LS: 12.1% vs 1.2%; TH: 2.5% vs -0.5%; P<0.001).
- **Prolia® (Denosumab):** A Phase 3 trial is currently recruiting to evaluate the safety and efficacy of denosumab in pediatric patients with corticosteroid-induced osteoporosis. The trial will be a randomized, double-blind, placebo-controlled, parallel-group trial in children 5 to 17 years of age. The primary outcome will be the effect of denosumab on LS BMD Z-score as assessed by dual-energy X-ray absorptiometry (DXA) at 12 months. The trial has an estimated primary completion date of May 2026. A separate trial evaluated denosumab as a treatment option for pediatric osteogenesis imperfecta. The trial was the first prospective trial evaluating the safety and efficacy of denosumab in 10 children 5 to 11 years of age with at least 2 years of prior bisphosphonate treatment. Denosumab was administered sub-Q every 12 weeks at a dose of 1mg/kg. The primary endpoint was change of areal BMD using DXA of the LS after 48 weeks. The study found a mean relative change of LS BMD of +19% and LS Z-scores increased from -2.23 ± 2.03 to -1.27 ± 2.37 (P=0.0006).

Teriparatide Product Summary[9]

Indication(s): Teriparatide is indicated for the following:

- Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture

- Treatment of men and women with osteoporosis associated with sustained systemic corticosteroid therapy at high risk for fracture

Dosing:

- Teriparatide is administered as a 20mcg subcutaneous (sub-Q) injection into the thigh or abdominal wall once a day.
- Because symptoms of orthostatic hypotension may occur, teriparatide should initially be administered under circumstances in which the patient can sit or lie down.
- Use of teriparatide for >2 years during a patient's lifetime is not recommended.
- Teriparatide is available as a 620mcg/2.48mL (250mcg/mL) single-patient-use pen containing 28 daily doses of 20mcg.

Mechanism of Action: Teriparatide is a synthetic recombinant human parathyroid hormone (PTH) that mimics the biologically active 34 N-terminal region of endogenous PTH, which is the primary regulator of calcium and phosphate in the bones and kidneys. Teriparatide binds with high affinity to cell surface receptors similarly to endogenous PTH, and leads to increased skeletal mass, increased markers of bone formation and resorption, and increased bone strength. With once-daily use, teriparatide stimulates osteoblast activity over osteoclast activity, resulting in new bone formation on trabecular and cortical bone surfaces.

Contraindication(s):

- Patients with hypersensitivity to teriparatide or any of its excipients

Warnings and Precautions:

- <u>The Following Individuals Should Not Be Treated With Teriparatide:</u>
  - Patients with Paget's disease of bone, pediatric and young adult patients with open epiphyses, and patients with prior external beam or implant radiation involving the skeleton
  - Patients with bone metastases, history of skeletal malignancies, metabolic bone disease other than osteoporosis, or hypercalcemia disorders
- <u>Treatment Duration:</u> Use of teriparatide for >2 years during a patient's lifetime is not recommended.
- <u>Laboratory Alterations:</u> Teriparatide may increase serum calcium, urinary calcium, and serum uric acid.
- <u>Urolithiasis:</u> Teriparatide should be used with caution in patients with active or recent urolithiasis because of the risk of exacerbation.
- <u>Orthostatic Hypotension:</u> Transient orthostatic hypotension may occur with initial doses of teriparatide.

Boxed Warning: Potential Risk of Osteosarcoma

- In rats, teriparatide caused an increase in the incidence of osteosarcoma, a malignant bone tumor.
- Due to the uncertain relevance of the rat osteosarcoma finding to humans, teriparatide should only be prescribed for patients for whom potential benefits outweigh potential risk.
- Teriparatide should not be prescribed for patients at increased baseline risk for osteosarcoma (e.g., patients with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, patients with prior external beam or implant radiation therapy involving the skeleton).

Adverse Reactions: In controlled trials, the most common adverse reactions reported (>10%) included arthralgia, pain, and nausea. In addition, adverse reactions have been voluntarily reported since post-approval of teriparatide and include osteosarcoma and hypercalcemia. Since these were reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Efficacy: The efficacy of teriparatide was demonstrated using the clinical trials for Forteo® (teriparatide) and was approved as a NDA under the 505(b)(2) regulatory pathway using Forteo® as the reference drug. Pfenex is currently conducting a comparative human factors study between teriparatide and Forteo® to allow teriparatide to be designated as therapeutically equivalent ("A" rated) to Forteo®, which would permit it to be automatically substituted for Forteo® in many states.

Cost Comparison:

Medication	Cost Per mL	Cost Per 28 Days†	Cost Per 2 Years
Teriparatide injection pen	**$997.98**	**$2,474.99**	**$64,349.74**
Forteo® (teriparatide injection) pen	$1,499.10	$3,597.84	$93,543.84

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
†Cost is based off a dosing regimen of 20mcg per day.

Recommendations

The College of Pharmacy recommends the prior authorization of teriparatide injection with the following criteria:

Forteo® (Teriparatide) and Teriparatide Approval Criteria:

1. A diagnosis of 1 of the following:
   a. Treatment of postmenopausal women with osteoporosis at high risk for fracture; or

b. To increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture; or
c. Treatment of men and women with osteoporosis associated with sustained systemic corticosteroid therapy at high risk for fracture; or
d. Treatment of non-healing fracture (this indication only pertains to Forteo®); and

2. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D or a patient-specific, clinically significant reason why the member cannot use a bisphosphonate must be provided; and
3. Use of teriparatide will require a patient-specific, clinically significant reason why the member cannot use Forteo® (teriparatide); and
4. The diagnosis of non-healing fracture may be approved for 6 months; and
5. Treatment duration, including other parathyroid hormone analogs, has not exceeded a total of 24 months during the patient's lifetime; and
6. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy.

Osteoporosis Medications*		
Tier-1	**Tier-2**	**Special PA**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax® + D)	abaloparatide inj (Tymlos®)
calcium + vitamin D†	risedronate tabs (Actonel®)	alendronate effervescent tabs (Binosto®)
ibandronate tabs (Boniva®)		alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)		alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		romosozumab-aqqg inj (Evenity®)
		teriparatide inj (Forteo®)
		teriparatide inj

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization
†OTC calcium and vitamin D must be used at recommended doses in conjunction with Tier-1 bisphosphonates for trial to be accepted unless member has a recent laboratory result showing adequate vitamin D or member is unable to tolerate calcium. OTC calcium and vitamin D are only covered for members with osteoporosis that are being treated with a bisphosphonate.
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization Details of Osteoporosis Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
ALENDRONATE PRODCUTS					
ALENDRONATE TAB 70MG	1,601	397	$17,413.26	$0.23	$10.88
ALENDRONATE TAB 35MG	115	33	$1,532.64	$0.24	$13.33
ALENDRONATE TAB 10MG	60	15	$909.18	$0.31	$15.15
ALENDRONATE TAB 5MG	9	4	$153.53	$0.35	$17.06
SUBTOTAL	**1,785**	**449**	**$20,008.61**	**$0.24**	**$11.21**
IBANDRONATE PRODCUTS					
IBANDRONATE TAB 150MG	121	6,952	$2,535.96	$0.36	$20.96
SUBTOTAL	**121**	**6,952**	**$2,535.96**	**$0.36**	**$20.96**
ZOLEDRONIC ACID PRODUCTS					
ZOLEDRONIC INJ 5MG/100ML	2	2	$144.14	$0.20	$72.07
SUBTOTAL	**2**	**2**	**$114.14**	**$0.20**	**$72.07**
TIER-1 SUBTOTAL	**1,908**	**486**	**$22,688.71**	**$0.25**	**$11.89**
TIER-2 PRODUCTS					
RISEDRONATE PRODUCTS					
RISEDRONATE TAB 35MG	17	2	$548.69	$1.15	$32.28
RISEDRONATE TAB 150MG	12	1	$512.68	$1.42	$42.72
RISEDRONATE TAB 5MG	10	1	$1,102.46	$3.67	$110.25
SUBTOTAL	**39**	**4**	**$2,163.83**	**$1.90**	**$55.48**
TIER-2 SUBTOTAL	**39**	**4**	**$2,163.83**	**$1.90**	**$55.48**
SPECIAL PA PRODUCTS					
ABALOPARATIDE PRODUCTS					
TYMLOS INJ 2,000MCG/ML	14	3	$25,380.01	$60.43	$1,812.86
SUBTOTAL	**14**	**3**	**$25,380.01**	**$60.43**	**$1,812.86**
ROMOSOZUMAB-AQQG PRODUCTS					
EVENITY INJ 105MG/1.17ML	5	1	$9,164.55	$61.10	$1,832.91
SUBTOTAL	**5**	**1**	**$9,164.55**	**$61.10**	**$1,832.91**
TERIPARATIDE PRODUCTS					
FORTEO SOL 600MCG/2.4ML	70	12	$236,872.64	$120.85	$3,383.89
SUBTOTAL	**70**	**12**	**$236,872.64**	**$120.85**	**$3,383.89**
DENOSUMAB PRODUCTS					
PROLIA SOL 60MG/ML	48	30	$55,872.52	$6.50	$1,164.01
SUBTOTAL	**48**	**30**	**$55,872.52**	**$6.50**	**$1,164.01**
ALENDRONATE PRODUCTS					
ALENDRONATE SOL 70MG/75ML	23	3	$4,633.76	$5.58	$201.47
SUBTOTAL	**23**	**3**	**$4,633.76**	**$5.58**	**$201.47**
SPECIAL PA SUBTOTAL	**160**	**49**	**$331,923.48**	**$27.75**	**$2,074.52**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TOTAL	**2,107**	**526***	**$356,776.02**	**$3.39**	**$169.33**

SOL = solution; INJ = injection; TAB = tablet: PA = prior authorization
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
XGEVA J0897	282	66	$637,296.73	$2,259.92	4.27
ZOLEDRONIC ACID J3489	179	76	$8,669.71	$48.43	2.36
PROLIA J0897	60	50	$39,647.78	$660.80	1.20
IBANDRONATE SODIUM J1740	3	1	$401.19	$133.73	3.00
TOTAL	**524⁺**	**193***	**$686,015.41**	**$1,309.19**	**2.72**

⁺Total number of unduplicated claims.
*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

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Appendix R

30-Day Notice to Prior Authorize Zokinvy™ (Lonafarnib)

Oklahoma Health Care Authority
February 2021

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

Hutchinson-Gilford Progeria Syndrome (HGPS)/Progeroid Laminopathies (PL) are rare, debilitating, autosomal dominant genetic diseases that cause premature aging and death. Classic HGPS, frequently referred to as "progeria", has an estimated incidence of 1 in 4 to 8 million births and an estimated prevalence of 1 in 20 million. It is estimated that there are 400 children worldwide with HGPS and 200 children with PL. Of these patients, approximately 180 children and young adults have been identified, including 18 with HGPS and 13 with PL in the United States. HGPS and PL cause patients to experience accelerated cardiovascular disease (CVD) from the buildup of defective progerin or progerin-like protein in cells. Progeria is caused by a genetic mutation in the lamin A/C (*LMNA)* gene. This mutation usually arises as a new change in the genetic material and is not inherited from a parent. The *LMNA* gene on chromosome 1q encodes prelamin A. Prelamin A is ultimately converted to lamin A, a structural protein component of the nuclear lamina that stabilizes the nuclear membrane. Mutant lamin A protein, a 50-amino acid internal deletion, is known as progerin. Pathogenic variants of *LMNA* cause a group of degenerative disorders known as laminopathies, which include HGPS and at least 12 other known diseases.

The symptoms begin within a year of life with poor growth and weight gain. Children with progeria have a characteristic facial appearance with a large head, small mouth and chin, narrow nose, and large eyes. Other symptoms include baldness, loss of fat under the skin, and dental and joint abnormalities. They also often have symptoms typically seen in much older adults including joint stiffness, hip dislocations, and severe, progressive CVD. Intelligence is typically normal. Most people with progeria die in their teens (range 8-20 years of age) from severe atherosclerosis leading to heart attacks or strokes. Diagnosis is based on symptoms and clinical exam and is confirmed by genetic testing. Treatment for progeria is focused on managing the symptoms and may include diet modifications, treatment of CVD, and physical therapy.

Market News and Updates[6,7,8]

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

- **November 2020:** The FDA approved Zokinvy™ (lonafarnib) capsules to reduce the risk of death due to HGPS and for the treatment of certain processing-deficient PL in patients 1 year of age and older. Zokinvy™ is not approved for use in patients with other progeroid syndromes or laminopathies. Zokinvy™ is an oral farnesyltransferase inhibitor that helps prevent the buildup of defective progerin or progerin-like protein. Before Zokinvy™, the only treatment options included supportive care and therapies directed towards the complications from the disease.

Pipeline:

- **Lonafarnib/Everolimus:** A Phase 1/2 dose-escalation trial of everolimus in combination with lonafarnib in HGPS and PL is currently being conducted. 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. Trial visits are expected to end in April 2021, followed by several months of data analysis and eventual publication of results in a peer-reviewed, scientific publication. 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; 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 mechanism of actions.

Zokinvy™ (Lonafarnib) Product Summary[9]

Indication(s): Zokinvy™ (lonafarnib) is a farnesyltransferase inhibitor indicated in patients 12 months of age and older with a body surface area (BSA) ≥0.39m^2:

- To reduce risk of mortality in HGPS
- For treatment of processing-deficient PL with either:
  - Heterozygous *LMNA* mutation with progerin-like protein accumulation; or
  - Homozygous or compound heterozygous *ZMPSTE24* mutations

- Limitation(s) of Use: Zokinvy™ is not indicated for other Progeroid Syndromes or processing-proficient PL. Zokinvy™ would not be expected to be effective in these populations based upon its mechanism of action.

Dosing:

- Zokinvy™ (lonafarnib) is an oral capsule available in 2 strengths: 50mg and 75mg.
- The recommended starting dose for Zokinvy™ is 115mg/m^2 twice daily with morning and evening meals.
- After 4 months of treatment, the dose should be increased to 150mg/m^2 twice daily.
- All total daily doses should be rounded to the nearest 25mg increment.
- Capsules should be swallowed whole. If patients are unable to swallow capsules, the capsule contents may be mixed with Ora Blend SF®, Ora-Plus®, orange juice, or applesauce. Zokinvy™ should not be mixed with juice containing grapefruit or Seville oranges. The mixture must be prepared fresh for each dose and taken within approximately 10 minutes of mixing.
- If a dose is missed, it should be taken as soon as possible with food, up to 8 hours prior to the next scheduled dose. If <8 hours remains before the next scheduled dose, the missed dose should be skipped, and the patient should resume taking Zokinvy™ at the next scheduled dose.
- For patients who have increased their dose of Zokinvy™ to 150mg/m^2 twice daily and are experiencing repeated episodes of vomiting and/or diarrhea resulting in dehydration or weight loss, the Zokinvy™ dose can be reduced to the starting dose of 115mg/m^2 twice daily. Zokinvy™ should be taken with morning and evening meals and with an adequate amount of water.

Mechanism of Action: Lonafarnib inhibits farnesyltransferase to prevent farnesylation and subsequent accumulation of progerin and progerin-like proteins in the inner nuclear membrane.

Drug Interaction(s):

- **Weak CYP3A Inhibitors:** If concomitant use of Zokinvy™ with a weak CYP3A inhibitor is unavoidable:
    - Reduce to or continue Zokinvy™ at the starting dosage of 115mg/m^2 twice daily
    - Resume the previous Zokinvy™ dosage 14 days after discontinuing the concomitant use of the weak CYP3A4 inhibitor
- **Strong/Moderate CYP3A Inhibitors:** Concomitant use with Zokinvy™ is contraindicated.
- **CYP2C9 Inhibitors:** Coadministration of Zokinvy™ with a CYP2C9 inhibitor should be avoided; it may increase the risk of Zokinvy™ adverse reactions.
    - If coadministration is unavoidable, the patient should be closely monitored for arrhythmias and events such as syncope and heart

palpitations because the effect of increased Zokinvy™ exposures on the QT interval is unknown.

- **Midazolam:** Zokinvy™ should be temporarily discontinued for 10 to 14 days before and 2 days after administration of midazolam.
- **Lovastatin, Simvastatin, or Atorvastatin:** Coadministration with Zokinvy™ is contraindicated.
- **Loperamide:** Loperamide is contraindicated in patients younger than 2 years of age. When Zokinvy™ is coadministered with loperamide, do not exceed loperamide 1mg once daily when first administered. The loperamide dosage should slowly be increased with caution in accordance with its approved product labeling.
- **P-gp Substrates:** Zokinvy™ is a weak P-gp inhibitor. When Zokinvy™ is coadministered with P-gp substrates (e.g., digoxin, dabigatran) where minimal concentration changes may lead to serious or life-threatening toxicities, monitor for adverse reactions and reduce the dosage of the P-gp substrate in accordance with its approved product labeling.

Contraindication(s):

- **Strong or Moderate CYP3A Inhibitors or Inducers:** Coadministration of Zokinvy™ with a strong CYP3A inhibitor increases lonafarnib area under the curve (AUC) and maximum serum concentration (Cmax) which may increase the risk of Zokinvy™ adverse reactions.
- **Midazolam/Lovastatin/Simvastatin/Atorvastatin:** Coadministration of with Zokinvy™ is contraindicated. Lonafarnib is a strong CYP3A mechanism-based inhibitor. Coadministration of Zokinvy™ with a CYP3A substrate increases the AUC and Cmax of the CYP3A substrate which may increase the risk of the CYP3A substrate's adverse reactions, including extreme sedation or respiratory depression (midazolam) and myopathy or rhabdomyolysis (listed statins).

Warnings and Precautions:

- Risk of Reduced Efficacy or Adverse Reactions Due to Drug Interactions: Prior to and during treatment, the potential for drug interactions should be considered and concomitant medications reviewed; patients should be monitored for adverse reactions.
- Laboratory Abnormalities: Patients should be monitored for changes in electrolytes, complete blood counts, and liver enzymes.
- Nephrotoxicity: Zokinvy™ caused nephrotoxicity in rats. Patients' renal function should be monitored at regular intervals.
- Retinal Toxicity: Zokinvy™ caused rod-dependent, low-light vision decline in monkeys. Ophthalmological evaluations should be performed at regular intervals and at the onset of any new visual changes.

- Impaired Fertility: Zokinvy™ caused impaired fertility in female rats, impaired fertility and testicular toxicity in male rats, and toxicity in the male reproductive tract in monkeys. Females and males of reproductive potential should be advised of the animal fertility findings.
- Embryo-Fetal Toxicity: Zokinvy™ can cause fetal harm. Females of reproductive potential should be advised of the risk to a fetus and to use effective contraception.

Adverse Reactions: The most common adverse reactions (incidence ≥25%) were vomiting, diarrhea, infection, nausea, decreased appetite, fatigue, upper respiratory tract infection, abdominal pain, musculoskeletal pain, electrolyte abnormalities, decreased weight, headache, myelosuppression, increased aspartate aminotransferase, decreased blood bicarbonate, cough, hypertension, and increased alanine aminotransferase.

Efficacy: The efficacy of Zokinvy™ was based on results from the observational cohort survival study, which retrospectively compared survival data from 2 Phase 2 studies in patients with HGPS to those from a natural history cohort.

- **Study 1** was a Phase 2 open-label, single-arm study that evaluated the efficacy of Zokinvy™ in 28 patients (26 with classic HGPS, 1 with non-classic HGPS, and 1 with processing-deficient PL with *LMNA* heterozygous mutation with progerin-like protein accumulation). Patients received Zokinvy™ for 24 to 30 months. Patients initiated treatment with Zokinvy™ 115mg/m^2 twice daily. After 4 months of treatment, patients who tolerated treatment had an increase in dose to 150mg/m^2 twice daily. Among the 28 patients treated, 27 patients with HGPS (16 females, 11 males) were included in the survival assessment. The median age at treatment initiation for the 27 patients was 7.5 years (range: 3 to 16 years). The body weight range was 6.6 to 17.6kg and the BSA range was 0.38 to 0.75m^2. Zokinvy™ is not indicated in patients with a BSA <0.39m^2 because the appropriate dosage strength is not available for this population.
- Following completion of Study 1, 26 patients enrolled in a second Phase 2 open label, single-arm study, **Study 2**, which consisted of 2 study phases. In the first phase of Study 2, patients received Zokinvy™ with additional therapies for about 5 years. In the second phase of Study 2, patients received Zokinvy™ 150mg/m^2 twice daily for a period of up to 3 years. There were 35 treatment naïve patients with HGPS enrolled into the second phase of Study 2. Among the 35 treated patients (22 males, 13 females), 34 (97.1%) patients had classic HGPS and 1 (2.9%) patient had non-classic HGPS. The median age was 6 years (range: 2 to 17 years). The body weight range was 6.7 to 22kg and the BSA range was 0.42 to 0.90m^2.

- The retrospective survival analysis was based on the mortality data from 62 treated patients (27 patients in Study 1 and 35 treatment-naïve patients in Study 2) and data from matched, untreated patients in a separate natural history cohort.
- The mean lifespan of HGPS patients treated with Zokinvy™ increased by an average of 3 months through the first 3 years of follow-up and 2.5 years through the last follow-up time (11 years) compared to untreated patients.
- The approval of Zokinvy™ for the treatment of certain processing-deficient PL that are very rare took into account similarities in the underlying genetic mechanism of disease and other available data.

Cost Comparison: Zokinvy™ 50mg capsules have a Wholesale Acquisition Cost (WAC) of $717.00 per capsule and Zokinvy™ 75mg capsules have a WAC of $1,075.50 per capsule. The maximum dose is 300mg/m^2 per day. For a patient with a BSA of 1m^2 at the maximum dose of 300mg/m^2 per day, the estimated cost is $129,060.00 per month and $1,548,720.00 per year for 150mg [(2) 75mg capsules] twice daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Zokinvy™ (lonafarnib) with the following 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 or 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 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 be 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.

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Appendix S

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 21, 2021

FDA Approves First Extended-Release, Injectable Drug Regimen for Adults Living with HIV

The FDA approved Cabenuva (cabotegravir and rilpivirine, injectable formulation) as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace a current antiretroviral regimen in those who are virologically suppressed on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine. This is the first FDA-approved injectable, complete regimen for HIV-infected adults that is administered once a month.

The FDA also approved Vocabria (cabotegravir, tablet formulation), which should be taken in combination with oral rilpivirine (Edurant) for 1 month prior to starting treatment with Cabenuva to ensure the medications are well-tolerated before switching to the extended-release injectable formulation.

"Currently, the standard of care for patients with HIV includes patients taking daily pills to adequately manage their condition. This approval will allow some patients the option of receiving once-monthly injections in lieu of a daily oral treatment regimen," said John Farley, M.D., M.P.H., director of the Office of Infectious Diseases in the FDA's Center for Drug Evaluation and Research. "Having this treatment available for some patients provides an alternative for managing this chronic condition."

The safety and efficacy of Cabenuva were established through 2 randomized, open-label, controlled clinical trials in 1,182 HIV-infected adults who were virologically suppressed (HIV-1 RNA less than 50 copies/mL) before initiation of treatment with Cabenuva. Patients in both trials continued to show virologic suppression at the conclusion of each study, and no clinically relevant change from baseline in CD4+ cell counts was observed.

The most common adverse reactions with Cabenuva were injection site reactions, fever, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness and rash. Cabenuva should not be used if there is a known previous hypersensitivity reaction to cabotegravir or rilpivirine, or in patients who are not virally suppressed (HIV-1 RNA greater than 50 copies/mL).

Cabenuva and Vocabria were granted Fast Track and Priority Review designations by the FDA. The FDA granted the approval of Cabenuva and Vocabria to ViiV Healthcare.

FDA NEWS RELEASE

For Immediate Release: January 8, 2021

FDA Issues Alert Regarding SARS-CoV-2 Viral Mutation to Health Care Providers and Clinical Laboratory Staff

The FDA is alerting clinical laboratory staff and health care providers that the FDA is monitoring the potential impact of viral mutations, including an emerging variant from the United Kingdom known as the B.1.1.7 variant, on authorized SARS-CoV-2 molecular tests, and that false negative results can occur with any molecular test for the detection of SARS-CoV-2 if a mutation occurs in the part of the virus's genome assessed by that test. The SARS-CoV-2 virus can mutate over time, like all viruses, resulting in genetic variation in the population of circulating viral strains, as seen with the B.1.1.7 variant. The FDA is taking additional actions to ensure authorized tests remain accurate by working with test developers and conducting ongoing data analysis to evaluate all currently authorized molecular tests. The FDA believes the risk that these mutations will impact overall testing accuracy is low.

"The FDA will continue to monitor SARS-CoV-2 genetic viral variants to ensure authorized tests continue to provide accurate results for patients," said FDA Commissioner Stephen M. Hahn, M.D. "While these efforts continue, we are working with authorized test developers and reviewing incoming data to ensure that health care providers and clinical staff can quickly and accurately diagnose patients infected with SARS-CoV-2, including those with emerging genetic variants. At this time, we believe the data suggests that the currently authorized COVID-19 vaccines may still be effective against this strain. The FDA will continue to keep health care providers and the public informed of any new information as it becomes available."

The FDA has been monitoring SARS-CoV-2 viral mutations, and potential impact on testing, throughout the pandemic. The presence of SARS-CoV-2 genetic variants in a patient sample can potentially change the performance of a SARS-CoV-2 test. Tests that rely on the detection of multiple regions of the genome may be less impacted by genetic variation in the SARS-CoV-2 genome than tests that rely on detection of only a single region.

Three currently authorized molecular tests, MesaBiotech Accula, TaqPath COVID-19 Combo Kit, and Linea COVID-19 Assay Kit, may be impacted by genetic variants of SARS-CoV-2, but the impact does not appear to be significant. Importantly, the detection pattern that appears with the TaqPath and Linea diagnostic tests when certain genetic variants are present may help with early identification of new variants in patients to reduce further spread of infection. The recently identified B.1.1.7 variant has been associated with an increased risk of transmission, therefore early

identification of this variant in patients may help reduce further spread of infection.

The FDA has reminded clinical laboratory staff and health care providers about the risk of false negative results with all laboratory tests, including molecular tests. Laboratories should expect some false results to occur even when very accurate SARS-CoV-2 tests are used. Today's announcement also provides important information and recommendations for clinical laboratory staff and health care providers who use molecular tests for the detection of SARS-CoV-2.

The FDA will continue to communicate with the public as we have additional information to share. The FDA encourages stakeholders to report any adverse events or suspected adverse events experienced with molecular tests for detection of SARS-CoV-2. Voluntary reports can be submitted through MedWatch, the FDA Safety Information and Adverse Event Reporting program. Health care personnel and clinical laboratory staff employed by facilities that are performing COVID-19 testing should follow the reporting requirements for authorized laboratories as specified in the test's Emergency Use Authorization. Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices.

FDA NEWS RELEASE

For Immediate Release: December 28, 2020

FDA Approves First Generic of Drug Used to Treat Severe Hypoglycemia

The FDA approved the first generic of glucagon for injection USP, 1mg/vial packaged in an emergency kit, for the treatment of severe hypoglycemia, which may occur in patients with diabetes mellitus. The drug is also indicated as a diagnostic aid in the radiologic examination of the stomach, duodenum, small bowel and colon when diminished intestinal motility would be advantageous.

"Glucagon for injection has been approved for use in the United States. for more than 20 years, but until today, there has been no approved generic of this important drug that can save the lives of people who may experience the serious condition of very low blood sugar," said Sally Choe, Ph.D., director of the Office of Generic Drugs in FDA's Center for Drug Evaluation and Research. "Today's approval reflects the FDA's continued commitment to advancing patient access to lower-cost, high-quality generic drug products that are as safe and effective as their brand name counterparts. Supporting development and expanding opportunities to bring generic copies of complex drugs, like glucagon, to the market has been a major focus of our efforts to improve competition and help lower drug prices."

Severe hypoglycemia occurs when a patient's blood sugar falls to a level where he or she becomes confused or unconscious, or suffers from other symptoms that require assistance from another person to treat.

Typically, severe hypoglycemia occurs in people with diabetes who are using insulin treatment.

The generic glucagon for injection is a synthetic version of human glucagon. Glucagon is a hormone that causes the liver to quickly increase blood sugar levels. This hormone also slows down movement of the gastrointestinal tract. The most common side effects associated with glucagon for injection are nausea and vomiting, a temporary increase in heart rate, as well as redness and swelling of the injection site.

The FDA regularly takes steps to help guide industry through the development process for generic drug products, including complex products such as glucagon. The development of complex products can be more difficult due to their complex active ingredient, formulation, or mode of delivery. As a result, many complex drugs lack generic competition even after patents and exclusivities no longer block generic approval.

The FDA maintains a list of off-patent, off-exclusivity drug products without an approved generic to improve transparency and encourage the development and submission of applications for drugs with limited competition. Glucagon is included on this list. The FDA also prioritizes the review of submissions for generic drugs for which there are fewer than 3 approved generics of the reference listed drug (RLD) and for which there are no blocking patents or exclusivities on the RLD.

Under the Generic Drug User Fee Amendments (GDUFA), individual companies can meet with the FDA as part of its pre-Abbreviated New Drug Application (ANDA) program to support the development of such complex generic drug products. The FDA also publishes guidance documents describing the steps the FDA recommends companies take to submit complete applications for generic drug products.

The FDA requires sponsors to submit appropriate data and information to demonstrate that complex generic drug products meet the agency's rigorous approval standards. These standards ensure that quality generic drug products are as safe and effective as their brand name counterparts.

Addressing the challenges related to complex generics, and promoting more generic competition to these medicines, is a key part of the FDA's Drug Competition Action Plan, and the agency's efforts to promote patient access and more affordable medicines.

The FDA granted approval of this generic glucagon for injection to Amphastar Pharmaceuticals, Inc. of Rancho Cucamonga, Calif.

FDA NEWS RELEASE

For Immediate Release: December 23, 2020

FDA Takes Further Steps to Confront Opioid Crisis through Risk Evaluation and Mitigation Strategy Programs

While the FDA's efforts to combat COVID-19 remain at the forefront of our day-to-day activities, the FDA also continues its work on a number of

important public health issues and, in particular, the opioid crisis. We remain committed to using all facets of our regulatory authority to lessen the impact of opioid addiction, misuse, and abuse while also striking a careful balance between patient access and safety to ensure that patients suffering from significant pain have access to appropriate medication.

To that end, the FDA has been and continues to address this public health crisis on a number of fronts, including efforts to:

- Decrease unnecessary exposure to prescription opioids and prevent new addiction;
- Support the treatment of those with opioid use disorder;
- Foster the development of new and effective pain therapies; and
- Take action against those who contribute to the illegal importation and sale of opioid products.

Part of our regulatory authority efforts include requiring Risk Evaluation and Mitigation Strategies (REMS) for various opioid analgesics to help mitigate the serious risks associated with their use.

Today, we took further steps to strengthen the REMS program for transmucosal immediate-release fentanyl (TIRF) products to help ensure that the benefits of these drugs continue to outweigh the risks.

TIRF medicines contain fentanyl, a powerful opioid, and are used to manage breakthrough pain in adults with cancer who are routinely taking other opioid pain medicines around-the-clock for pain. To use the TIRF medicines safely, these patients must be opioid tolerant based on concurrent regular use of another opioid medication.

Despite the decline in the use of TIRF medicines in recent years, data have suggested that prescribing of TIRF medicines still occurs in patients who are not opioid tolerant. With this in mind, the FDA finalized modifications to the REMS program to address the persistence of these concerning prescribing practices. These changes will also improve our ability to monitor for adverse events and ensure safe use of these medicines.

In particular, this program has been strengthened to:

- Require that prescribers document a patient's opioid tolerance with each prescription of a TIRF medicine for outpatient use;
- Require outpatient pharmacies dispensing TIRF medicines to document and verify a patient's opioid tolerance before dispensing;
- Require inpatient pharmacies to develop internal policies and procedures to verify opioid tolerance in patients who require TIRF medicines while hospitalized; and
- Require a new patient registry for use, along with other data sources, to monitor for accidental exposure, misuse, abuse, addiction, and overdose.

In addition to the modifications to fortify the TIRF REMS program, the FDA also continues efforts to evaluate the opioid analgesic (OA) REMS. Earlier this month, we hosted a workshop inviting scientific discussions about methods to evaluate the impact of the OA REMS on prescriber behavior and patient

outcomes. The goal of the OA REMS is to educate prescribers and other health care providers (including pharmacists) on the treatment and monitoring of patients with pain. The public workshop served as a forum for public scientific discussion of innovative, multidisciplinary methods to consider when evaluating the OA REMS education program. The FDA will use these discussions to ensure that the methods ultimately used to evaluate the OA REMS are scientifically sound.

Effectively addressing the opioid crisis requires continued focus and collaboration across many different stakeholders. The FDA's REMS are an important tool, and it's critical we ensure they are continuing to fulfill their purpose.

FDA NEWS RELEASE

For Immediate Release: December 18, 2020

FDA Takes Additional Action in Fight against COVID-19 by Issuing Emergency Use Authorization for Second COVID-19 Vaccine

The FDA issued an emergency use authorization (EUA) for the second vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The EUA allows the Moderna COVID-19 Vaccine to be distributed in the United States for use in individuals 18 years of age and older.

"With the availability of 2 vaccines now for the prevention of COVID-19, the FDA has taken another crucial step in the fight against this global pandemic that is causing vast numbers of hospitalizations and deaths in the United States each day," said FDA Commissioner Stephen M. Hahn, M.D. "Through the FDA's open and transparent scientific review process, 2 COVID-19 vaccines have been authorized in an expedited timeframe while adhering to the rigorous standards for safety, effectiveness, and manufacturing quality needed to support EUA that the American people have come to expect from the FDA. These standards and our review process, which are the same we have used in reviewing the first COVID-19 vaccine and intend to use for any other COVID-19 vaccines, included input from independent scientific and public health experts as well as a thorough analysis of the data by the agency's career staff."

The FDA has determined that the Moderna COVID-19 Vaccine has met the statutory criteria for issuance of an EUA. The totality of the available data provides clear evidence that the Moderna COVID-19 Vaccine may be effective in preventing COVID-19. The data also show that the known and potential benefits outweigh the known and potential risks, supporting the company's request for the vaccine's use in people 18 years of age and older. In making this determination, the FDA can assure the public and medical community that it has conducted a thorough evaluation of the available safety, effectiveness, and manufacturing quality information.

The Moderna COVID-19 Vaccine contains messenger RNA (mRNA), which is genetic material. The vaccine contains a small piece of the SARS-CoV-2 virus's mRNA that instructs cells in the body to make the virus's distinctive "spike" protein. After a person receives this vaccine, their body produces copies of the spike protein, which does not cause disease, but triggers the immune system to learn to react defensively, producing an immune response against SARS-CoV-2.

"Guided by science and data, the agency's career staff determined that the vaccine's known and potential benefits clearly outweigh its known and potential risks, and although not an FDA approval, the FDA's expectations described in our June and October guidance documents have been met," said Peter Marks, M.D., Ph.D., Director of the FDA's Center for Biologics Evaluation and Research. "Today's authorization demonstrates our steadfast commitment to the health of the American people, with the assurance that our scientific standards and the integrity of our review process have been maintained. This achievement is yet another testament to the dedication of FDA's career scientists and physicians, who have been working urgently to conduct comprehensive and rigorous evaluations of the data submitted for vaccines to prevent COVID-19."

FDA Evaluation of Available Safety Data

Moderna COVID-19 Vaccine is administered as a series of 2 doses, 1 month apart. The available safety data to support the EUA include an analysis of 30,351 participants enrolled in an ongoing randomized, placebo-controlled study conducted in the United States. These participants, 15,185 of whom received the vaccine and 15,166 of whom received saline placebo, were followed for a median of more than 2 months after receiving the second dose. The most commonly reported side effects, which typically lasted several days, were pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, swollen lymph nodes in the same arm as the injection, nausea and vomiting, and fever. Of note, more people experienced these side effects after the second dose than after the first dose, so it is important for vaccination providers and recipients to expect that there may be some side effects after either dose, but even more so after the second dose.

It is mandatory for ModernaTX, Inc. and vaccination providers to report the following to the Vaccine Adverse Event Reporting System (VAERS) for Moderna COVID-19 Vaccine: all vaccine administration errors, serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS), and cases of COVID-19 that result in hospitalization or death.

FDA Evaluation of Available Effectiveness Data

The effectiveness data to support the EUA include an analysis of 28,207 participants in the ongoing randomized, placebo-controlled United States study who did not have evidence of SARS-CoV-2 infection prior to the first dose of vaccine. Among these participants, 14,134 received the vaccine and 14,073 received placebo. The vaccine was 94.1% effective in preventing COVID-

19 disease among these clinical trial participants with 11 cases of COVID-19 in the vaccine group and 185 in the placebo group. At the time of the analysis of these 196 COVID-19 cases, none in the vaccine group and 30 in the placebo group were classified as severe. After the analysis of these 196 cases was completed, 1 severe case in the vaccine group was identified and is awaiting confirmation. At this time, data are not available to determine how long the vaccine will provide protection, nor is there evidence that the vaccine prevents transmission of SARS-CoV-2 from person to person.

The EUA Process

On the basis of the determination by the Secretary of the Department of Health and Human Services on February 4, 2020, that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and issued declarations that circumstances exist justifying the authorization of emergency use of unapproved products, the FDA may issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent COVID-19 when there are no adequate, approved, and available alternatives.

The issuance of an EUA is different from an FDA approval of a vaccine, in that a vaccine available under an EUA is not approved. In determining whether to issue an EUA for a product, the FDA evaluates the available evidence to determine whether the product may be effective and also assesses any known or potential risks and any known or potential benefits. If the product meets the effectiveness standard and the benefit-risk assessment is favorable, the product is made available during the emergency. Once a manufacturer submits an EUA request for a COVID-19 vaccine to the FDA, the agency then evaluates the request and determines whether the relevant statutory criteria are met, taking into account the totality of the scientific evidence about the vaccine that is available to the FDA.

The EUA also requires that fact sheets that provide important information, including dosing instructions, and information about the benefits and risks of the Moderna COVID-19 Vaccine, be made available to vaccination providers and vaccine recipients.

ModernaTX, Inc. has submitted a pharmacovigilance plan to the FDA to monitor the safety of Moderna COVID-19 Vaccine. The pharmacovigilance plan includes a plan to complete longer-term safety follow-up for participants enrolled in ongoing clinical trials. The pharmacovigilance plan also includes other activities aimed at monitoring the safety profile of the Moderna COVID-19 vaccine and ensuring that any safety concerns are identified and evaluated in a timely manner.

The FDA also expects manufacturers whose COVID-19 vaccines are authorized under an EUA to continue their clinical trials to obtain additional safety and effectiveness information and pursue approval.

The EUA for the Moderna COVID-19 Vaccine was issued to ModernaTX, Inc. The authorization will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated. The EUA for Moderna COVID-19 Vaccine may be revised or revoked if it is determined the EUA no longer meets the statutory criteria for issuance.

FDA NEWS RELEASE

For Immediate Release: December 18, 2020

FDA Approves First Adjuvant Therapy for Most Common Type of Lung Cancer

The FDA approved Tagrisso (osimertinib) as the first adjuvant treatment for patients with non-small cell lung cancer whose tumors have a specific type of genetic mutation.

"Today's approval of Tagrisso demonstrates how additional research on therapies approved in later stages of cancer can eventually improve treatment options for patients in earlier stages," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "With this approval, patients may be treated with this targeted therapy in an earlier and potentially more curative stage of non-small cell lung cancer."

Lung cancer is the most common cancer type and the leading cause of cancer-related deaths worldwide. In the United States, approximately 229,000 adults will be diagnosed with lung cancer in 2020, of which 76% of cases will be non-small cell lung cancer. Approximately 20% of patients with non-small cell lung cancer will have epidermal growth factor receptor (EGFR) mutations, which are mutations on a protein that causes rapid cell growth, and consequently, helps cancer spread. Although most patients who are diagnosed with non-small cell lung cancer have unremovable tumors, 30% have resectable disease; thus, more than 10,000 patients nationwide each year may be candidates for Tagrisso as adjuvant therapy after tumor removal. Tagrisso was approved in 2018 for the first-line treatment of patients with metastatic non-small cell lung cancer whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.

Tagrisso was evaluated in a randomized, double-blind, placebo-controlled trial of 682 patients with early stage non-small cell lung cancer and EGFR exon 19 deletions or exon 21 L858R mutation-positive who had undergone complete tumor removal. A total of 339 patients received Tagrisso orally once daily and 343 received a placebo following recovery from surgery and standard adjuvant chemotherapy, if given. The main outcome measure was the amount of time it took for the cancer to come back or for death to occur from any cause. In the overall trial population, patients who received

Tagrisso had an 80% decrease in chance of disease recurrence compared with patients who received a placebo.

The most common side effects of Tagrisso include diarrhea, rash, musculoskeletal pain, dry skin, skin inflammation around nails, sore mouth, fatigue and cough. Tagrisso should be withheld if patients develop symptoms of interstitial lung disease, and permanently discontinued if interstitial lung disease is confirmed. Tagrisso may affect the heart's electrical system and can also cause issues such as heart failure so periodic monitoring should be conducted. Tagrisso may also cause inflammation of the cornea. Tagrisso can cause fetal harm when administered to a pregnant woman; therefore, the pregnancy status of females of reproductive potential should be confirmed before treatment with Tagrisso is started. Tagrisso should be withheld if Stevens-Johnson syndrome or erythema multiforme major is suspected.

Tagrisso received Orphan Drug designation for treatment of EGFR mutation-positive non-small cell lung cancer. Orphan Drug designation provides incentives to assist and encourage drug development for rare diseases. Additionally, the agency granted Tagrisso a Breakthrough Therapy designation for this indication. The FDA granted approval of Tagrisso to AstraZeneca.

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

FDA NEWS RELEASE

For Immediate Release: December 18, 2020

FDA Approves First Oral Hormone Therapy for Treating Advanced Prostate Cancer

The FDA approved Orgovyx (relugolix) for the treatment of adult patients with advanced prostate cancer.

"Today's approval marks the first oral drug in this class and it may eliminate some patients' need to visit the clinic for treatments that require administration by a health care provider," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "This potential to reduce clinic visits can be especially beneficial in helping patients with cancer stay home and avoid exposure during the coronavirus pandemic."

The American Cancer Society estimates that in 2020, there will have been more than 190,000 cases of prostate cancer in the United States. One of the treatment options for advanced prostate cancer is androgen deprivation

therapy, which uses drugs to lower levels of the hormones that help prostate cancer cells grow. Current FDA-approved treatments of this type are injected or placed as small implants under the skin. Orgovyx is an orally administered treatment that works by blocking the pituitary gland from making hormones called luteinizing hormone and follicle-stimulating hormone, thereby reducing the amount of testosterone the testicles are able to make.

The safety and efficacy of Orgovyx was evaluated in a randomized, open-label trial in men with advanced prostate cancer. The patients randomly received either Orgovyx once daily or injections of leuprolide, another hormone-targeting drug, every 3 months for 48 weeks. The objective was to determine if Orgovyx achieved and maintained low enough levels of testosterone, by day 29 through end of the treatment course. In the 622 patients who received Orgovyx, the castration rate was 96.7%.

The most common side effects of Orgovyx include: hot flush, increased glucose, increased triglycerides, musculoskeletal pain, decreased hemoglobin, fatigue, constipation, diarrhea and increased levels of certain liver enzymes. Androgen deprivation therapies such as Orgovyx may affect the heart's electrical properties or cause electrolyte abnormalities, therefore healthcare providers should consider periodic monitoring of electrocardiograms and electrolytes. Based on findings in animals and the mechanism of action, Orgovyx can cause fetal harm and loss of pregnancy when administered to a pregnant female; it is advised that males with female partners of reproductive potential use effective contraception during treatment and for 2 weeks after the last dose of Orgovyx. Due to the drug's suppression of the pituitary gonadal system, diagnostic test results of the pituitary gonadotropic and gonadal functions conducted during and after taking Orgovyx may be affected.

The FDA granted approval of Orgovyx to Myovant Sciences.

FDA NEWS RELEASE

For Immediate Release: December 15, 2020

Coronavirus (COVID-19) Update: FDA Authorizes Antigen Test as First Over-the-Counter Fully At-Home Diagnostic Test for COVID-19

The FDA issued an emergency use authorization (EUA) for the first over-the-counter (OTC) fully at-home diagnostic test for COVID-19. The Ellume COVID-19 Home Test is a rapid, lateral flow antigen test, a type of test that runs a liquid sample along a surface with reactive molecules. The test detects fragments of proteins of the SARS-CoV-2 virus from a nasal swab sample from any individual 2 years of age or older.

"Today's authorization is a major milestone in diagnostic testing for COVID-19. By authorizing a test for OTC use, the FDA allows it to be sold in places like drug stores, where a patient can buy it, swab their nose, run the test and find out their results in as little as 20 minutes," said FDA Commissioner Stephen M. Hahn, M.D. "As we continue to authorize additional

tests for home use, we are helping expand Americans' access to testing, reducing the burden on laboratories and test supplies, and giving Americans more testing options from the comfort and safety of their own homes."

The announcement today of the first fully at-home OTC COVID-19 diagnostic test follows last month's authorization of the first prescription COVID-19 test for home use and last week's announcement of the first non-prescription test system, in which a lab processes the self-collected sample. The FDA has authorized more than 225 diagnostic tests for COVID-19 since the start of the pandemic, including more than 25 tests that allow for home collection of samples, which are then sent to a lab for testing. The Ellume COVID-19 Home Test is the first COVID-19 test that can be used completely at home without a prescription.

"The FDA strongly supports innovation in test development and we have worked tirelessly with test developers to support the shared goal of getting more accurate and reliable tests to Americans who need them. Today is a promising step forward and we are eager to continue advancing additional innovation in COVID-19 testing that the science supports," said Jeff Shuren, M.D., J.D., director of FDA's Center for Devices and Radiological Health. "This test, like other antigen tests, is less sensitive and less specific than typical molecular tests run in a lab. However, the fact that it can be used completely at home and return results quickly means that it can play an important role in response to the pandemic."

Similar to other antigen tests, a small percentage of positive and negative results from this test may be false. Therefore, for patients without symptoms, positive results should be treated as presumptively positive until confirmed by another test as soon as possible. This is especially true if there are fewer infections in a particular community, as false positive results can be more common when antigen tests are used in populations where there is little COVID-19.

The FDA reminds patients that all tests can experience false negative and false positive results. Individuals with positive results should self-isolate and seek additional care from their health care provider. Individuals who test negative and experience COVID-like symptoms should follow up with their health care provider as negative results do not preclude an individual from SARS-CoV-2 infection.

The Ellume COVID-19 Home Test uses a mid-turbinate nasal swab (sample is collected further back than the usual nasal swab, but not as far back as nasopharyngeal swabs, which are only appropriate for use by a trained health care provider) to detect certain proteins of the virus known as antigens. The Ellume COVID-19 Home Test correctly identified 96% of positive samples and 100% of negative samples in individuals with symptoms. In people without symptoms, the test correctly identified 91% of positive samples and 96% of negative samples. The Ellume COVID-19 Home Test uses an analyzer that connects with a software application on a smartphone to

help users perform the test and interpret results. Results are delivered in as little as 20 minutes to individuals via their smartphone. The mobile application requires individuals to input their zip code and date of birth, with optional fields including name and e-mail address, and reports the results as appropriate to public health authorities to monitor disease prevalence. Ellume expects to produce more than 3 million tests in January 2021.

The FDA continues to work with test developers to expand access to COVID-19 testing and supports further development of COVID-19 tests that can be used completely at home.

Current Drug Shortages Index (as of January 21, 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***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
AVYCAZ® (ceftazidime and avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Azacitidine for Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Ceftolozane and Tazobactam (Zerbaxa) Injection	***Currently in Shortage***

Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***
Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Floxuridine for Injection, USP	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydralazine Hydrochloride Injection, USP	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***

Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Misoprostol Tablets	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***

Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sertraline Hydrochloride Oral Solution, USP	***Currently in Shortage***
Sertraline Hydrochloride Tablets	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Teprotumumab-trbw	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Timolol Maleate Ophthalmic Solution	***Currently in Shortage***
Tobramycin Lyophilized Powder for Injection	***Currently in Shortage***
Valproate Sodium Injection, USP	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***
Zinc Acetate Capsules	***Currently in Shortage***