OKLAHOMA
Health Care Authority

Drug Utilization Review Board

# OHCA Webinar
# Wednesday,
# March 10, 2021
# 4:00pm

Please register for the webinar at:
https://zoom.us/s/97305655255
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 – March 10, 2021

DATE: February 22, 2021

NOTE: In response to COVID-19, the March 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/s/97305655255
After registering, you will receive a confirmation email containing information about joining the webinar.

*Enclosed are the following items related to the March 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**

**Quarterly Review of the Medication Therapy Management (MTM) Program – Appendix B**

**Update on Medication Coverage Authorization Unit/Spring 2021 Pipeline Update – Appendix C**

**Action Item – Vote to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System) – Appendix D**

**Action Item – Vote to Prior Authorize Oxlumo™ (Lumasiran) – Appendix E**

**Action Item – Vote to Prior Authorize Fintepla® (Fenfluramine) – Appendix F**

**Action Item – Vote to Prior Authorize Teriparatide – Appendix G**

**Action Item – Vote to Prior Authorize Zokinvy™ (Lonafarnib) – Appendix H**

**Action Item – Vote to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr) – Appendix I**

**Action Item – Vote to Prior Authorize Inqovi® (Decitabine/Cedazuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx) – Appendix J**

**Action Item – Annual Review of Qutenza® (Capsaicin 8% Patch) – Appendix K**

**Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel), Monjuvi® (Tafasitamab-cxix), Romidepsin 27.5mg/5.5mL Vial, Tecartus™ (Brexucabtagene Autoleucel), and Ukoniq™ (Umbralisib) – Appendix L**

**Annual Review of Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – Appendix M**

**Annual Review of Hemophilia Medications and 30-Day Notice to Prior Authorize Sevenfact® [Coagulation Factor VIIA (Recombinant)-jncw] – Appendix N**

**Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Bafiertam™ (Monomethyl Fumarate), Kesimpta® (Ofatumumab), and Zeposia® (Ozanimod) – Appendix O**

**Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Orladeyo™ (Berotralstat) – Appendix P**

**Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Nyvepria™ (Pegfilgrastim-apgf) – Appendix Q**

**Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Barhemsys® (Amisulpride) – Appendix R**

**Annual Review of Growth Hormone Products and 30-Day Notice to Prior Authorize Sogroya® (Somapacitan-beco) – Appendix S**

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

**Future Business**

**Adjournment**

# Oklahoma Health Care Authority

**Drug Utilization Review Board**
**(DUR Board)**
**Meeting – March 10, 2021 @ 4:00pm**

**Oklahoma Health Care Authority (OHCA) Webinar**
Please register for the meeting at:
https://zoom.us/s/97305655255
After registering, you will receive a confirmation email containing information about joining the webinar.

## AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Mitchell, Vice Chairwoman:

**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/s/97305655255

Or join by phone:
Dial: +1-253-215-8782 or +1-346-248-7799
Webinar ID: 973 0565 5255
Passcode: 92831084

**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. Mitchell, Vice Chairwoman:

**2. Public Comment Forum**

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Mitchell, Vice Chairwoman:

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

A. February 17, 2021 DUR Minutes – Vote
B. February 17, 2021 DUR Recommendation Memorandum
C. Correspondence

Items to be presented by Dr. Smith, Dr. Mitchell, Vice Chairwoman:

**4. Quarterly Review of the Medication Therapy Management (MTM) Program – See Appendix B**

A. Medication Therapy Management Program Update

Items to be presented by Dr. Nawaz, Dr. Wilson, Dr. Mitchell, Vice Chairwoman:

**5. Update on Medication Coverage Authorization Unit/Spring 2021 Pipeline Update – See Appendix C**

A. Pharmacy Helpdesk Activity for February 2021
B. Medication Coverage Activity for February 2021
C. Spring 2021 Pipeline Update

Items to be presented by Dr. Wilson, Dr. Mitchell, Vice Chairwoman:

**6. Action Item – Vote to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System) – See Appendix D**

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

Items to be presented by Dr. Wilson, Dr. Mitchell, Vice Chairwoman:

**7. Action Item – Vote to Prior Authorize Oxlumo™ (Lumasiran) – See Appendix E**

A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Ha, Dr. Mitchell, Vice Chairwoman:

**8. Action Item – Vote to Prior Authorize Fintepla® (Fenfluramine) – See Appendix F**

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

Items to be presented by Dr. Daniel, Dr. Mitchell, Vice Chairwoman:

**9. Action Item – Vote to Prior Authorize Teriparatide – See Appendix G**

A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Nawaz, Dr. Mitchell, Vice Chairwoman:

**10. Action Item – Vote to Prior Authorize Zokinvy™ (Lonafarnib) – See Appendix H**

A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Chandler, Dr. Mitchell, Vice Chairwoman:

**11. Action Item – Vote to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr) – See Appendix I**

A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Borders, Dr. Mitchell, Vice Chairwoman:

**12. Action Item – Vote to Prior Authorize Inqovi® (Decitabine/Cedazuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx) – See Appendix J**

A. Introduction
B. New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)

C. College of Pharmacy Recommendations

Items to be presented by Dr. Wilson, Dr. Mitchell, Vice Chairwoman:

**13. Action Item – Annual Review of Qutenza® (Capsaicin 8% Patch) – See Appendix K**

A. Current Prior Authorization Criteria
B. Utilization of Qutenza® (Capsaicin 8% Patch)
C. Prior Authorization of Qutenza® (Capsaicin 8% Patch)
D. Market News and Updates
E. College of Pharmacy Recommendations

Items to be presented by Dr. Borders, Dr. Mitchell, Vice Chairwoman:

**14. Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel), Monjuvi® (Tafasitamab-cxix), Romidepsin 27.5mg/5.5mL Vial, Tecartus™ (Brexucabtagene Autoleucel), and Ukoniq™ (Umbralisib) – See Appendix L**

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

Items to be presented by Dr. Borders, Dr. Mitchell, Vice Chairwoman:

**15. Annual Review of Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – See Appendix M**

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)
D. Prior Authorization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)
E. Market News and Updates
F. College of Pharmacy Recommendations

Items to be presented by Dr. Ratterman, Dr. Mitchell, Vice Chairwoman:

**16. Annual Review of Hemophilia Medications and 30-Day Notice to Prior Authorize Sevenfact® [Coagulation Factor VIIA (Recombinant)-jncw] – See Appendix N**

A. Current Prior Authorization Criteria
B. Utilization of Hemophilia Medications
C. Prior Authorization of Hemophilia Medications
D. Market News and Updates
E. Sevenfact® [Coagulation Factor VIIA (Recombinant)-jncw] Product Summary
F. Cost Comparison
G. College of Pharmacy Recommendations
H. Utilization Details of Hemophilia Medications

Items to be presented by Dr. Nawaz, Dr. Mitchell, Vice Chairwoman:

**17. Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Bafiertam™ (Monomethyl Fumarate), Kesimpta® (Ofatumumab), and Zeposia® (Ozanimod) – See Appendix O**

A. Current Prior Authorization Criteria
B. Utilization of MS Medications
C. Prior Authorization of MS Medications
D. Market News and Updates

E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of MS Medications

Items to be presented by Dr. Chandler, Dr. Mitchell, Vice Chairwoman:

**18. Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Orladeyo™ (Berotralstat) – See Appendix P**

A. Current Prior Authorization Criteria
B. Utilization of HAE Medications
C. Prior Authorization of HAE Medications
D. Market News and Updates
E. Orladeyo™ (Berotralstat) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of HAE Medications

Items to be presented by Dr. Ha, Dr. Mitchell, Vice Chairwoman:

**19. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Nyvepria™ (Pegfilgrastim-apgf) – See Appendix Q**

A. Current Prior Authorization Criteria
B. Utilization of G-CSFs
C. Prior Authorization of G-CSFs
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of G-CSFs

Items to be presented by Dr. Ha, Dr. Mitchell, Vice Chairwoman:

**20. Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Barhemsys® (Amisulpride) – See Appendix R**

A. Current Prior Authorization Criteria
B. Utilization of Anti-Emetic Medications
C. Prior Authorization of Anti-Emetic Medications
D. Market News and Updates
E. Barhemsys® (Amisulpride) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Emetic Medications

Items to be presented by Dr. Wilson, Dr. Mitchell, Vice Chairwoman:

**21. Annual Review of Growth Hormone Products and 30-Day Notice to Prior Authorize Sogroya® (Somapacitan-beco) – See Appendix S**

A. Current Prior Authorization Criteria
B. Utilization of Growth Hormone Products
C. Prior Authorization of Growth Hormone Products
D. Market News and Updates
E. Sogroya® (Somapacitan-beco) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Growth Hormone Products

Items to be presented by Dr. Nawaz, Dr. Mitchell, Vice Chairwoman:

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

Items to be presented by Dr. Adams, Dr. Mitchell, Vice Chairwoman:

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

A. Annual Review of the Pharmacy Benefit
B. Anti-Diabetic Medications

C. Antihypertensive Medications
D. Muscular Dystrophy Medications
**Future product and class reviews subject to change.*

**24. Adjournment**

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

# Appendix A

**OKLAHOMA HEALTH CARE AUTHORITY**
**DRUG UTILIZATION REVIEW (DUR) BOARD MEETING**
**MINUTES OF MEETING FEBRUARY 17, 2021**

| 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 |
| Jill Ratterman, D.Ph.; Clinical Pharmacist | x | |
| Paula Root, M.D.; Senior Medical Director | | x |
| Michelle Tahah, Pharm.D.; Clinical Pharmacist | x | |

| OTHERS PRESENT: | |
|---|---|
| Adam Kopp, Zogenix | Marilyn Semenchuk, Biocodex |
| Dave Miley, Teva | Melanie Curlett, Takeda |
| Dave Poskey, UCB | Nima Nabavi, Amgen |
| David Large, Biohaven Pharmaceuticals | Ray Kong, Ultragenyx |
| Doug Pierce, Genentech | Rick Dabner, Alnylam |
| Jason Skinner, Ph.D.; Amgen | Steven Isaki, Lundbeck |
| Jeff O'Dell, Ultragenyx | Tony Salicos, Greenwich Biosciences |
| Joe Garcia, AbbVie | William Eicholzer, Alexion |
| John Churnetski, Alexion | Kristi Kemp, Allergan |
| Jomy Joseph, Sanofi | Lindsey Walter, Novartis |
| Kathy Gornatti, Greenwich Biosciences | Mahesh Tawney, Alnylam |
| Mahesh Tawney, Alnylam | |

| PRESENT FOR PUBLIC COMMENT: | |
|---|---|
| Jason Skinner, Ph.D. | Amgen |
| Mahesh Tawney | Alnylam |

**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. 16 JASON SKINNER, PH.D.**

**2B: AGENDA ITEM NO. 18 MAHESH TAWNEY**

**ACTION: NONE REQUIRED**

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

**3A: NOVEMBER 4, 2020 DUR MINUTES – VOTE**

Materials included in agenda packet; presented by Dr. Muchmore

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

**ACTION: MOTION CARRIED**

**3B: NOVEMBER 4, 2020 DUR RECOMMENDATIONS MEMORANDUM**

**3C: DECEMBER 9, 2020 DUR MINUTES – VOTE**

Materials included in agenda packet; presented by Dr. Muchmore

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

**ACTION: MOTION CARRIED**

**3D: DECEMBER 9, 2020 DUR RECOMMENDATIONS MEMORANDUM**

**3E. JANUARY 13, 2021 DUR RECOMMENDATIONS MEMORANDUM**

**AGENDA ITEM NO. 4:** **NARROW THERAPEUTIC INDEX (NTI) DRUG LIST**

**4A: INTRODUCTION**

**4B: SOONERCARE NTI DRUG LIST**

Materials included in agenda packet; presented by Dr. Wilson

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 5:** **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/MONTELUKAST IN ALLERGIC RHINITIS SAFETY MAILING UPDATE**

**5A: PHARMACY HELPDESK ACTIVITY FOR JANUARY 2021**

**5B: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2021**

**5C: MONTELUKAST IN ALLERGIC RHINITIS SAFETY MAILING UPDATE**

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

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 6:** **APPROVAL OF NOVEMBER 2020 DUR RECOMMENDATIONS**

**6A: 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**

Materials included in agenda packet; presented by Dr. Nawaz

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

**ACTION: MOTION CARRIED**

**6B: 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**

Materials included in agenda packet; presented by Dr. Borders

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

**ACTION: MOTION CARRIED**

**6C: VOTE TO PRIOR AUTHORIZE LENVIMA® (LENVATINIB)**

- **I. LENVIMA® (LENVATINIB) PRODUCT SUMMARY**
- **II. COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Borders

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 7:** **APPROVAL OF DECEMBER 2020 DUR RECOMMENDATIONS**

**7A: 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**

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**7B: 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**

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**7C: 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**

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**7D: VOTE TO PRIOR AUTHORIZE PIZENSY™ (LACTITOL)**

**I. INTRODUCTION**
**II. COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**7E: 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**

Materials included in agenda packet; presented by Dr. Ha
Dr. Broyles moved to approve; seconded by Dr. Garton

**ACTION: MOTION CARRIED**

**7F: 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**

Materials included in agenda packet; presented by Dr. Ha
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 8:</u> VOTE TO PRIOR AUTHORIZE NEXLETOL® (BEMPEDOIC ACID) AND NEXLIZET™ (BEMPEDOIC ACID/EZETIMIBE)**

**8A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND INDICATION(S)**
**8B: PRODUCT SUMMARIES**
**8C: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Ha
Dr. Mitchell moved to approve; seconded by Dr. Garton

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 9:</u> VOTE TO PRIOR AUTHORIZE IMCIVREE™ (SETMELANOTIDE)**

**9A: INTRODUCTION**

**9B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler
Dr. Broyles moved to approve; seconded by Dr. Garton

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 10:</u> VOTE TO PRIOR AUTHORIZE FENSOLVI® (LEUPROLIDE ACETATE) AND ORIAHNN™ (ELAGOLIX/ESTRADIOL/ NORETHINDRONE AND ELAGOLIX)**

**10A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)**

**10B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Wilson
Dr. Garton moved to approve; seconded by Dr. Hanner

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 11:</u> VOTE TO PRIOR AUTHORIZE DURYSTA™ (BIMATOPROST IMPLANT)**

**11A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)**

**11B: COLLEGE OF PHARMACY RECOMMENDATIONS**

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

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 12:</u> ANNUAL REVIEW OF CRYSVITA® (BUROSUMAB-TWZA)**

**12A: INTRODUCTION**

**12B: UTILIZATION OF CRYSVITA® (BUROSUMAB-TWZA)**

**12C: PRIOR AUTHORIZATION OF CRYSVITA® (BUROSUMAB-TWZA)**

**12D: MARKET NEWS AND UPDATES**

**12E: COLLEGE OF PHARMACY RECOMMENDATIONS**

**12F: UTILIZATION DETAILS OF CRYSVITA® (BUROSUMAB-TWZA)**

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 13:</u> ANNUAL REVIEW OF LEUKEMIA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE INQOVI® (DECITABINE/ CEDAZURIDINE), ONUREG® (AZACITIDINE), AND RIABNI™ (RITUXIMAB-ARRX)**

**13A: INTRODUCTION**

**13B: CURRENT PRIOR AUTHROIZATION CRITERIA**

**13C: UTILIZATION OF LEUKEMIA MEDICATIONS**

**13D: PRIOR AUTHORIZATION OF LEUKEMIA MEDIATIONS**

**13E: MARKET NEWS AND UPDATES**

**13F: PRODUCT SUMMARIES**

**13G: COLLEGE OF PHARMACY RECOMMENDATIONS**

**13H: UTILZATION DETAILS OF LEUKEMIA MEDICATIONS**

Materials included in agenda packet; presented by Dr. Borders

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 14:** **ANNUAL REVIEW OF AZEDRA® (IOBENGUANE I-131)**

**14A: INTRODUCTION**
**14B: CURRENT PRIOR AUTHORIZATION CRITERIA**
**14C: UTILIZATION OF AZEDRA® (IOBENGUANE I-131)**
**14D: PRIOR AUTHORIZATION OF AZEDRA® (IOBENGUANE I-131)**
**14E: MARKET NEWS AND UPDATES**
**14F: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Borders

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 15:** **ANNUAL REVIEW OF ANTICONVULSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE FINTEPLA® (FENFLURAMINE)**

**15A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**15B: UTILIZATION OF ANTICONVULSANTS**
**15C: PRIOR AUTHORIZATION OF ANTICONVULSANTS**
**15D: MARKET NEWS AND UPDATES**
**15E: FINTEPLA® (FENFLURAMINE) PRODUCT SUMMARY**
**15F: COST COMPARISON: ANTICONVULSANT THERAPIES FOR DRAVET SYNDROME**
**15G: COLLEGE OF PHARMACY RECOMMENDATIONS**
**15H: UTILIZATION DETAILS OF ANTICONVULSANTS**

Materials included in agenda packet; presented by Dr. Ha

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 16:** **ANNUAL REVIEW OF ANTI-MIGRAINE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NURTEC™ ODT (RIMEGEPANT) AND VYEPTI® (EPTINEZUMAB-JJMR)**

**16A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**16B: UTILIZATION OF ANTI-MIGRAINE MEDICATIONS**
**16C: PRIOR AUTHORIZATION OF ANTI-MIGRAINE MEDICATIONS**
**16D: MARKET NEWS AND UPDATES**
**16E: PRODUCT SUMMARIES**
**16F: COLLEGE OF PHARMACY RECOMMENDATIONS**
**16G: UTILIZATION DETAILS OF ANTI-MIGRAINE MEDICATIONS**

Materials included in agenda packet; presented by Dr. Chandler

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 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)**

**17A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**17B: UTILIZATION OF NSAIDS**
**17C: PRIOR AUTHORIZATION OF NSAIDS**
**17D: MARKET NEWS AND UPDATES**
**17E: PRODUCT SUMMARIES**
**17F: COLLEGE OF PHARMACY RECOMMENDATIONS**
**17G: UTILIZATION DETAILS OF NSAIDS**

Materials included in agenda packet; presented by Dr. Wilson

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 18:** **30-DAY NOTICE TO PRIOR AUTHORIZE OXLUMO™ (LUMASIRAN)**

**18A: INTRODUCTION**
**18B: OXLUMO™ (LUMASIRAN) PRODUCT SUMMARY**
**18C: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Wilson

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 19:** **ANNUAL REVIEW OF OSTEOPOROSIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TERIPARATIDE**

**19A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**19B: UTILIZATION OF OSTEOPOROSIS MEDICATIONS**
**19C: PRIOR AUTHORIZATION OF OSTEOPOROSIS MEDICATIONS**
**19D: MARKET NEWS AND UPDATES**
**19E: TERIPARATIDE PRODUCT SUMMARY**
**19F: COLLEGE OF PHARMACY RECOMMENDATIONS**
**19G: UTILIZATION DETAILS OF OSTEOPOROSIS MEDICATIONS**

Materials included in agenda packet; presented by Dr. Daniel

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 20:** **30-DAY NOTICE TO PRIOR AUTHORIZE ZOKINVY™ (LONAFARNIB)**

**20A: INTRODUCTION**
**20B: MARKET NEWS AND UPDATES**
**20C: ZOKINVY™ (LONAFARNIB) PRODUCT SUMMARY**
**20D: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Nawaz

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 21:** **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Nawaz

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 22:** **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

**22A: MULTIPLE SCLEROSIS MEDICATIONS**
**22B: HEREDITARY ANGIOEDEMA (HAE) MEDICATIONS**
**22C: GRANULOCYTE COLONY-STIMULATING FACTORS (G-CSFS)**
**22D: HEMOPHILIA MEDICATIONS**

**Future business subject to change.*

Materials included in agenda packet; presented by Dr. Adams

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 23:** **ADJOURNMENT**

The meeting was adjourned at 6:08pm.

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

# Memorandum

**Date:** February 18, 2021

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

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

**Subject:** DUR Board Recommendations from Meeting of February 17, 2021

## Recommendation 1: Narrow Therapeutic Index (NTI) Drug List

NO ACTION REQUIRED.

## Recommendation 2: Montelukast in Allergic Rhinitis Safety Mailing Update

NO ACTION REQUIRED.

## Recommendation 3A: Approval of November 2020 DUR Recommendations: 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)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 3B: Approval of November 2020 DUR Recommendations: 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)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 3C: Approval of November 2020 DUR Recommendations: Vote to Prior Authorize Lenvima® (Lenvatinib)

MOTION CARRIED by unanimous approval.

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 4A: Approval of December 2020 DUR Recommendations: Vote to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon) and to Update the Approval Criteria for Soliris® (Eculizumab)

MOTION CARRIED by unanimous approval.

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~~
15. 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
16. 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.

## Recommendation 4B: Approval of December 2020 DUR Recommendations: 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)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the removal of the trial requirement of a mesalamine product for a diagnosis of Crohn's disease (CD) or ulcerative colitis (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 systemic lupus erythematosus (SLE) and to reflect the new FDA approved indication of lupus nephritis (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 adult-onset Still's disease (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™)± |
| 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)** |

| Targeted Immunomodulator Agents*± | | |
|---|---|---|
| **Tier-1 (DMARDs appropriate to disease state)** | **Tier-2*** | **Tier-3** |
| | | 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).
πUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome (CRS).
≠Orencia® ClickJect™ requires a patient-specific, clinically significant reason why the member cannot use the typical pre-filled syringe formulation.
** Unique criteria applies to this medication for approval.

## Recommendation 4C: Approval of December 2020 DUR Recommendations: Vote to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule]

MOTION CARRIED by unanimous approval.

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.

## Recommendation 4D: Approval of December 2020 DUR Recommendations: Vote to Prior Authorize Pizensy™ (Lactitol)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 4E: Approval of December 2020 DUR Recommendations: Vote to Update the Approval Criteria for Spravato® (Esketamine)

MOTION CARRIED by unanimous approval.

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.~~

## Recommendation 4F: Approval of December 2020 DUR Recommendations: Vote to Update the Approval Criteria for Bavencio® (Avelumab), Braftovi® (Encorafenib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), and Yervoy® (Ipilimumab)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 5: Vote to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 6: Vote to Prior Authorize Imcivree™ (Setmelanotide)

MOTION CARRIED by unanimous approval.

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 ≥95$^{th}$ 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/1.73$m^2$]; 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.

## Recommendation 7: Vote to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/ Norethindrone and Elagolix)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 8: Vote to Prior Authorize Durysta™ (Bimatoprost Implant)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 9: Annual Review of Crysvita® (Burosumab-twza)

MOTION CARRIED by unanimous approval.

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 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 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.

## Recommendation 10: Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Inqovi® (Decitabine/ Cedazuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx)

NO ACTION REQUIRED.

## Recommendation 11: Annual Review of Azedra® (Iobenguane I-131)

NO ACTION REQUIRED.

## Recommendation 12: Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Fintepla® (Fenfluramine)

NO ACTION REQUIRED.

## Recommendation 13: Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr)

NO ACTION REQUIRED.

## Recommendation 14: 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)

NO ACTION REQUIRED.

## Recommendation 15: 30-Day Notice to Prior Authorize Oxlumo™ (Lumasiran)

NO ACTION REQUIRED.

## Recommendation 16: Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Teriparatide

NO ACTION REQUIRED.

## Recommendation 17: 30-Day Notice to Prior Authorize Zokinvy® (Lonafarnib)

NO ACTION REQUIRED.

## Recommendation 18: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

## Recommendation 19: Future Business

NO ACTION REQUIRED.

VIELABIO

Viela Bio
One MedImmune Way
Gaithersburg, MD 20878

Tel: 240-558-0038
Fax: 240-772-9578
www.vielabio.com

John Mutchmore, MD, Drug Utilization Review Board, Chair
Oklahoma Health Care Authority
John Muchmore, MD, Chairman- DUR Board
P. O. Box 26901
Oklahoma City, OK 73126-0901

Dear Dr. Mutchmore,

Thank you very much for the opportunity to attend the December OK DUR meeting on NMOSD drug utilization. It was clear from that meeting that further discussion on this topic was planned. Therefore, we at Viela Bio would like to respectfully address the committee by sending a brief letter to elaborate on UPLIZNA® (inebilizumab-cdon) clinical data in advance of the February meeting.

As you are no doubt aware, NMOSD is a rare autoimmune disease that can lead to profound disability. It causes recurrent attacks/relapses that lead to central nervous system inflammatory damage. The disease has a predilection for the optic nerves and spinal cord and can lead to blindness, motor dysfunction, severe pain and death [Mealy et al., 2012]. Disability accrues with each relapse, so prevention of relapses is key to avoid increasing disability over time [Mealy et al., 2019].

The pivotal N-MOmentum trial of UPLIZNA was the largest randomized controlled trial to be conducted in NMOSD to date, with a total of 230 participants (213 AQP4+) [Cree et al., 2019]. UPLIZNA reduced the risk of inflammatory attacks by over 77% compared to placebo in AQP4+ participants during the randomized controlled period, and the long-term data demonstrates that 80% of trial participants remain attack-free roughly 4 years into treatment. Additionally, there was a 71% reduction in disease-related hospitalizations during the randomized controlled period in those treated with UPLIZNA compared to placebo. The most common adverse reactions (at least 10% of patients treated with UPLIZNA and greater than placebo) were urinary tract infection and arthralgia.

As mentioned in Dr. Pardo's eloquent letter at the December committee meeting, there are variables that may or may not make selection of one NMOSD therapy over another advisable. These variables include mechanism of action, NMOSD disease history, previous therapy history including adherence, and comorbidities, to name a few. Therefore, we echo the call to avoid step edit therapy restriction for any of the FDA-approved NMOSD medications, in order to

VIELABIO

Viela Bio
One MedImmune Way
Gaithersburg, MD 20878

Tel: 240-558-0038
Fax: 240-772-9578
www.vielabio.com

ensure that healthcare providers serve the patients' best interest when determining which of the three new therapies is most appropriate.

Thank you for the opportunity to contribute to the discourse in this case; we look forward to the committee's decision.

Sincerely,

Maureen A. Mealy PhD, RN

Field Medical Affairs Director, Viela Bio

Please refer to the following citations listed in the letter herein, including two from my previous role as an NMOSD clinician scientist in academia:

1. Mealy MA, Greenberg BM, Wingerchuk DM, Levy M. Epidemiology of neuromyelitis optica in the United States: a multicenter analysis. *Arch Neurol.* 2012 Sep;69(9):1176-80. doi: 10.1001/archneurol.2012.314. PMID: 22733096
2. Mealy MA, Mossburg SE, Kim SH, Messina S, Borisow N, Levy M. Long-term disability in neuromyelitis optica spectrum disorder with a history of myelitis is associated with age at onset, delay in diagnosis/preventive treatment, MRI lesion length and presence of symptomatic brain lesions. *Mult Scler Relat Disord.* 2019 Feb;28:64-68. doi: 10.1016/j.msard.2018.12.011. Epub 2018 Dec 9.
3. Cree BAC, Bennett JL, Kim HJ, Weinshenker BG, Pittock SJ… N-MOmentum study investigators. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. *Lancet.* 2019 Oct 12;394(10206):1352-1363. doi: 10.1016/S0140-6736(19)31817-3. Epub 2019 Sep 5. PMID: 31495497

# Appendix B

# Medication Therapy Management Program Update

**Oklahoma Health Care Authority**
**March 2021**

## Background[1,2]

The Oklahoma Health Care Authority (OHCA) is responsible for controlling costs of state-purchased health care while continuing to protect and improve the health of Oklahoma SoonerCare members. The University of Oklahoma College of Pharmacy: Pharmacy Management Consultants (PMC) collaborates with OHCA to continually identify members who may be at an increased risk for poor outcomes due to existing conditions and other factors. SoonerCare members with these high-risk and correspondingly high-cost conditions can improve their health outcomes and reduce cost to the health care system by optimizing their medications through medication therapy management (MTM) services. MTM is defined by the Centers for Disease Control and Prevention (CDC) as a "distinct service or group of services provided by health care providers, including pharmacists, to ensure the best therapeutic outcomes for patients." The CDC recommends MTM programs include the following 5 core elements:

- Medication therapy review
- Personal medication record
- Medication-related action plan
- Intervention or referral
- Documentation and follow-up

The costs of prescription medications continue to rise in the United States, and the cost associated with a particular medication is not limited to the cost of the drug itself. A recent study found annual third-party payer costs of drug-related morbidity and mortality from non-optimized medication therapy to be $528.4 billion in the United States. This amount has doubled over the past 20 years and contributes to 16% of the total United States health care expenditures. MTM services are an important tool to help combat this problem.

In December 2019, under the direction of OHCA and in partnership with Arine, PMC developed and implemented an MTM program for SoonerCare members. PMC's clinical pharmacists use Arine's virtual pharmacist platform to perform telephonic MTM services for SoonerCare members across the state of Oklahoma. The goals of the MTM program include:

- Increased member understanding of and adherence to medication therapy
- Optimized therapeutic outcomes

- Decreased medication-related adverse effects
- Reduced overall health care spending

Member selection criteria for the MTM program includes members 18 years of age or older who are currently receiving ≥4 chronic medications or have had ≥1 inpatient or emergency department admission(s) in the preceding 12 months. Member demographic information is shown in Figure 1 and is based on the 826 MTM reviews completed as of November 12, 2020. The average age of members receiving MTM services was 41.4±13.4 years. The average number of inpatient and/or emergency department visits (in the past 12 months) across identified eligible members was 3.7 per member. The average number of medications (in the past 6 months) across identified eligible members was 9 per member.

**Figure 1: MTM Program Member Demographics**

| Characteristic | Percent |
|---|---|
| Female | 79.6% |
| Congestive Heart Failure | 6.3% |
| Diabetes | 23.0% |
| Cardiovascular Disease | 42.1% |
| Hypertension | 50.0% |
| Stroke | 5.7% |
| Anxiety | 52.0% |
| Depression | 43.8% |
| Asthma/COPD | 33.7% |

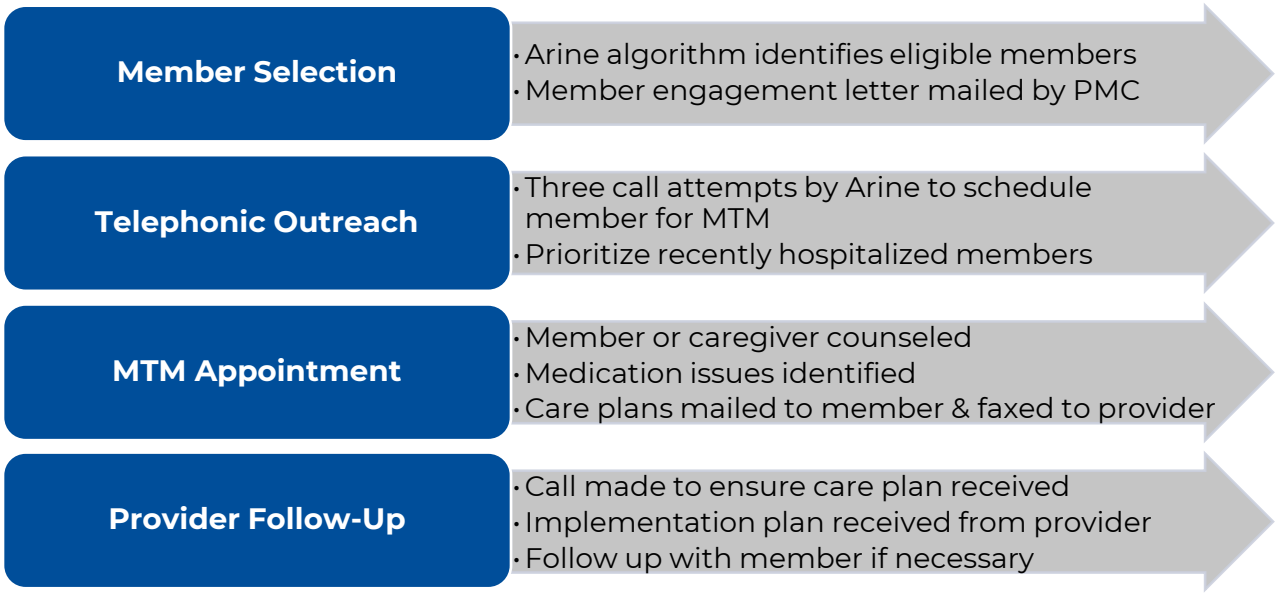
MTM = medication therapy management; COPD= chronic obstructive pulmonary disease

## Workflow[3]

The following figure (Figure 2) describes the workflow for MTM services. Once the members are selected, Arine begins telephonic outreach to members to schedule a review with a clinical pharmacist at PMC. During the review, the clinical pharmacist identifies any drug-related problems (DRPs) and counsels the member or caregiver appropriately.

After the review is complete, care plans are sent to both the member and provider. The member report includes an updated medication list and a summary of the discussion that occurred during the MTM review. The provider care plan contains an updated medication list and a report of the DRPs identified. Each DRP contains both an evidence-based assessment and recommendation for the provider.

**Figure 2: MTM Workflow**




The DRPs identified are organized into categories that were based on the Pharmacy Quality Alliance (PQA) Medication Therapy Problem Categories Framework which are listed below:

- Adherence refers to whether the patient is taking the medication as prescribed and addressing any barriers that may be preventing them from taking their medication correctly.
- Effectiveness refers to a medication being ineffective, dosage too low, or additional monitoring needed to establish effectiveness (e.g., blood glucose monitoring).
- Indication refers to unnecessary medication therapy or additional medication therapy needed.
- Safety refers to adverse drug reactions, dosage too high, or additional monitoring needed to establish safety (e.g., serum potassium monitoring for diuretics).

The last 2 categories were added to the existing PQA framework to address current public health concerns and include:

- Preventative care refers to vaccinations, cancer screenings, nutrition counseling, diabetes screening, and cholesterol screenings.
- SoonerCare resources refers to prior authorization assistance, information regarding covered medications, referral to care coordination, referral to a specialist, or referral to member services to resolve eligibility issues and/or primary care provider selection.

To assess the percentage of care plan implementation by providers, each DRP report asks providers to indicate their planned implementation of the suggested changes. After a reasonable time, providers are contacted to

ensure the reports have been received by the provider and reviewed. Upon verification of receipt and review, clinical pharmacists at PMC review the planned provider changes and communicate new information to members as necessary. Changes in prescription drug regimens are verified in each member's pharmacy claims history.

## Results

The results of the program are based on 826 MTM reviews completed through November 12, 2020. Figure 3 represents program engagement. Of the members scheduling MTM appointments, 80.6% of members completed reviews, and on average, 6 DRPs were identified per member. A total of 525 unique providers received MTM reports. Providers stated their intention to implement 86% of the changes recommended by the clinical pharmacists.

| **Figure 3: Program Engagement** | |
|---|---|
| Number of eligible members | 6,050 |
| Total number of outreach calls to members | 18,601 |
| Unique members receiving outreach calls | 5,810 |
| Percentage of members answering outreach calls | 30.2% |
| Total number of members scheduling and/or rescheduling MTM services | 1,855 |
| Unique members scheduling MTM services | 1,024 |
| Percentage of members completing MTM services | 80.6% |
| Unique DRPs identified | 4,847 |
| Total number of providers receiving MTM reports | 525 |
| Percentage of DRPs implemented by providers* | 86% |

*Implementation of 43% of all recommendations sent through 11/12/2020 are currently being assessed through validation of claims or follow-up.
MTM = medication therapy management; DRPs = drug related problems

Figure 4 includes the total number of DRPs identified based on the disease areas listed below.

| **Figure 4: Recommendations Sent to Members & Providers – Disease Areas** | |
|---|---|
| **Disease** | **Total Number of DRPs** |
| Behavioral health | 730 |
| Cardiovascular disease | 722 |
| Asthma/COPD | 636 |
| Diabetes | 622 |
| Women's health | 185 |
| Gastrointestinal disease | 172 |
| Pain management | 102 |

DRPs = drug related problems; COPD = chronic obstructive pulmonary disease

Figure 5 includes the number of DRPs identified based on the medication therapy problem identified.

| Figure 5: Recommendations Sent to Members & Providers – Category | |
|---|---|
| **Medication Therapy Problem Category** | **Total Number of DRPs** |
| Preventative care | 1,205 |
| Indication | 832 |
| Effectiveness | 680 |
| Safety | 631 |
| Adherence | 492 |
| SoonerCare resources | 132 |

DRPs = drug related problem

## Case Study

Member is a 57 year old female with chronic kidney disease stage 3, hypertension, diabetes, persistent asthma, chronic obstructive pulmonary disease (COPD), and history of myocardial infarction (MI).

DRPs identified by pharmacist:

- Member confusion on proper administration of rescue inhaler
- Aggressively treating hypoglycemia which resulted in hyperglycemia
- Metformin being taken without renal dose adjustment
- Diagnosis of both persistent asthma and COPD without controller inhaler
- History of MI without aspirin
- Excessive daytime drowsiness associated with Benadryl® (diphenhydramine) to self-treat allergies
- Missing key vaccinations – influenza and shingles

DRPs resolved by pharmacist:

- Counseled member on proper rescue inhaler technique and proper treatment of hypoglycemia
- Referred to Care Coordination program at OHCA, and member was assigned to case manager in the Chronic Care Unit

DRPs resolved by provider after report sent:

- Kidney function was evaluated leading to discontinuation of metformin
- Existing basal/bolus insulin was continued
- Dulera® (mometasone/formoterol) 100mcg/5mcg, 1 inhalation twice daily, was started for persistent asthma and COPD
- Aspirin 81mg was started for secondary prevention of MI
- Benadryl® (diphenhydramine) was discontinued and Zyrtec® (cetirizine) was started for allergies
- Provider agreed to administer influenza and shingles vaccines

## Summary

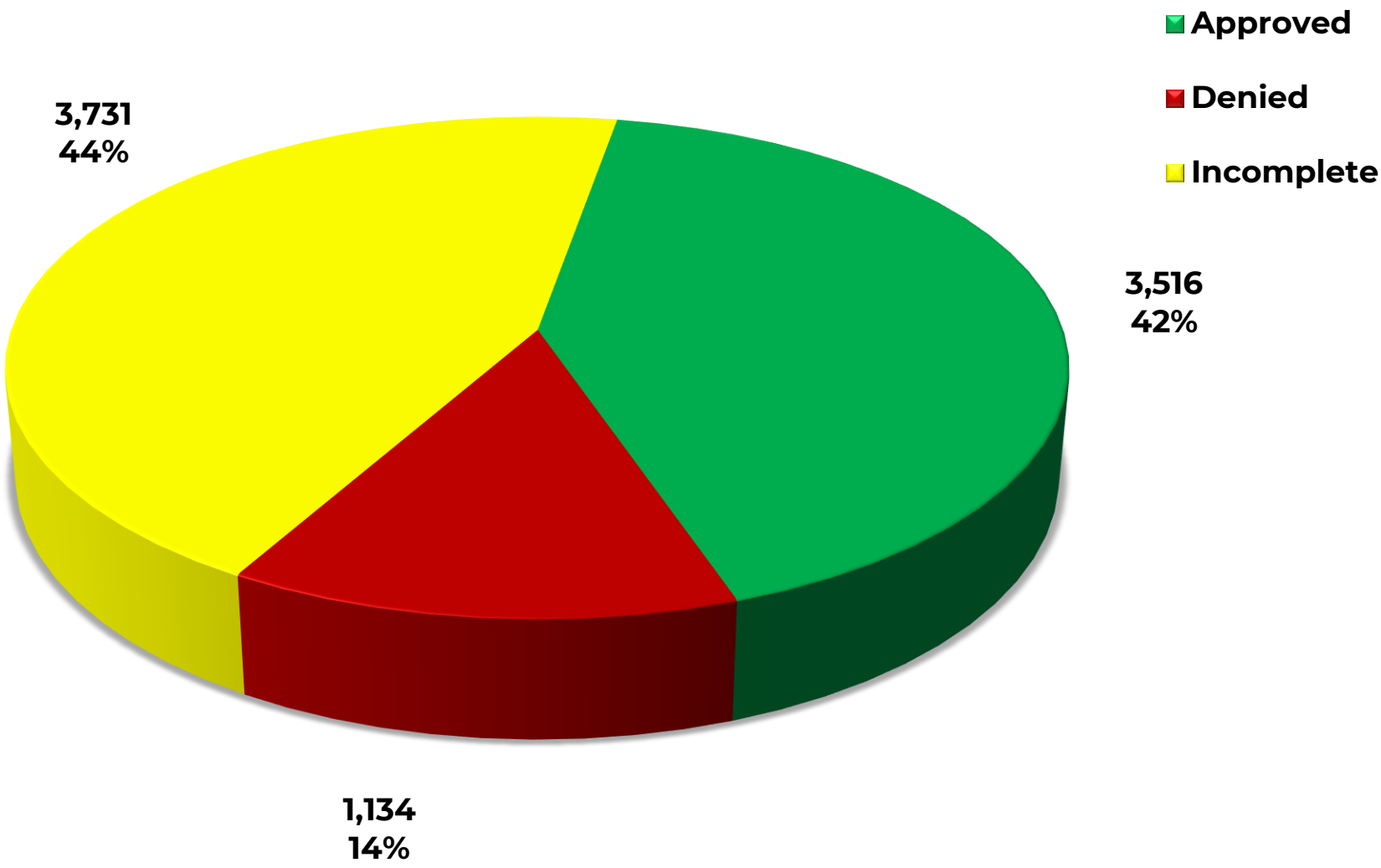
As the cost associated with non-optimized medication therapy continues to grow, PMC is dedicated to finding innovative solutions to this urgent health care issue. The MTM program is well-accepted by SoonerCare members as evidenced by the 80.6% completion rate. Members are receiving care that is more closely aligned with the existing evidence as demonstrated by the identification of 6 DRPs identified per member. Further, providers value the service as evidenced by their 86% acceptance rate.

PMC continues to complete MTM reviews on a daily basis. Since reporting these results, additional reviews have been completed totaling more than 1,100 MTM reviews since December 2019. PMC will continue to work with OHCA to identify SoonerCare members who may benefit from MTM services with the goal of promoting evidence-based use of medications thus improving the quality of care for these members. Future results of the MTM services will be reviewed with the Drug Utilization Review (DUR) Board as they become available.

[1] Centers for Disease Control and Prevention (CDC). Community Pharmacists and Medication Therapy Management. Available online at: https://www.cdc.gov/dhdsp/pubs/guides/best-practices/pharmacist-mtm.htm. Last accessed 02/08/2021.
[2] Watanabe JH, McInnis T, Hirsch JD. Cost of Prescription Drug-Related Morbidity and Mortality. *Ann Pharmacother* 2018; 52(9):829-837. doi: 10.1177/1060028018765159.
[3] Pharmacy Quality Alliance (PQA). PQA Medication Therapy Problem Categories Framework. Available online at: https://pqa.memberclicks.net/assets/Measures/PQA_MTP_Categories_Framework.pdf. Last revised 08/2017. Last accessed 02/08/2021.

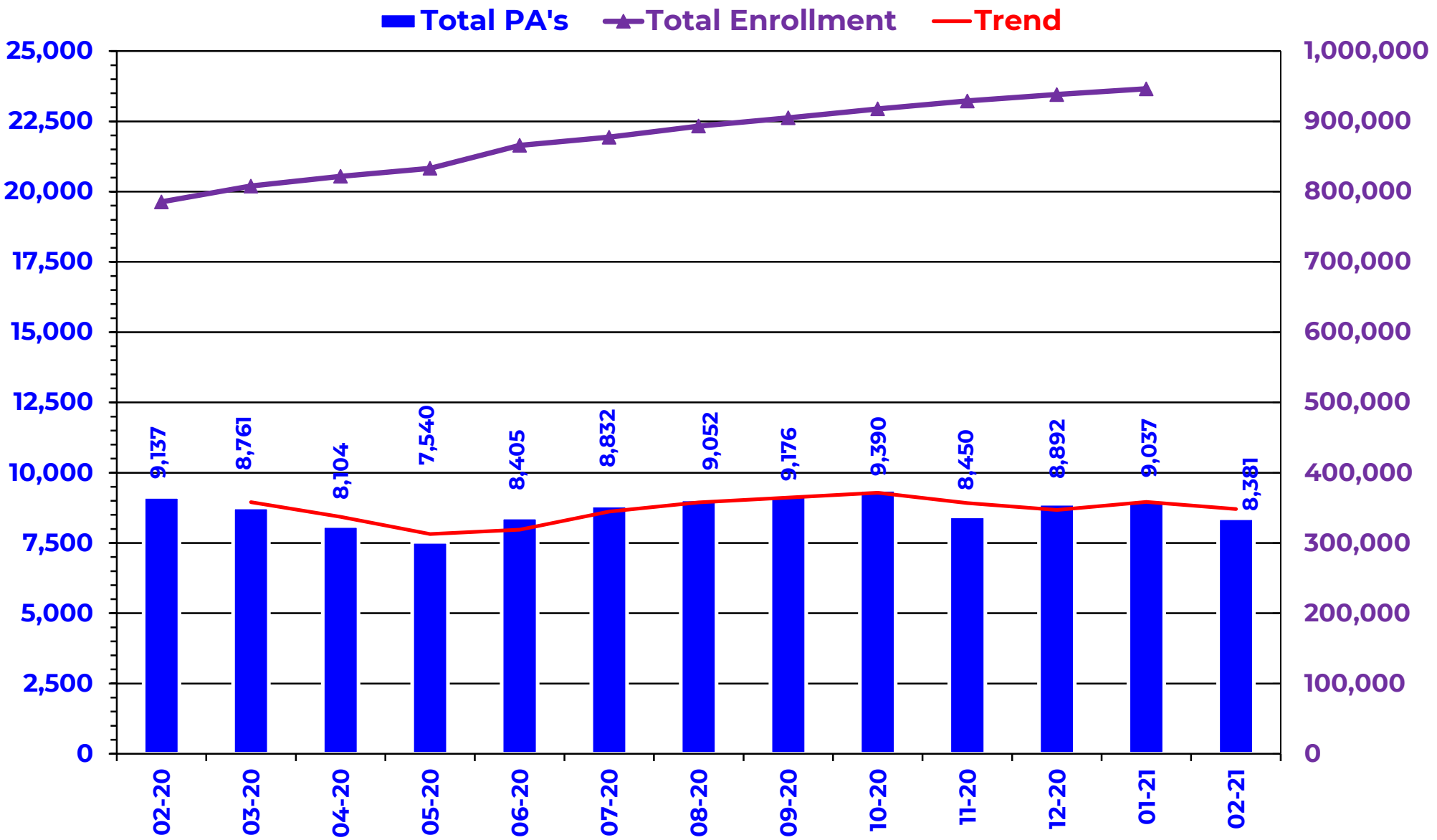
# Appendix C

# PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY 2021



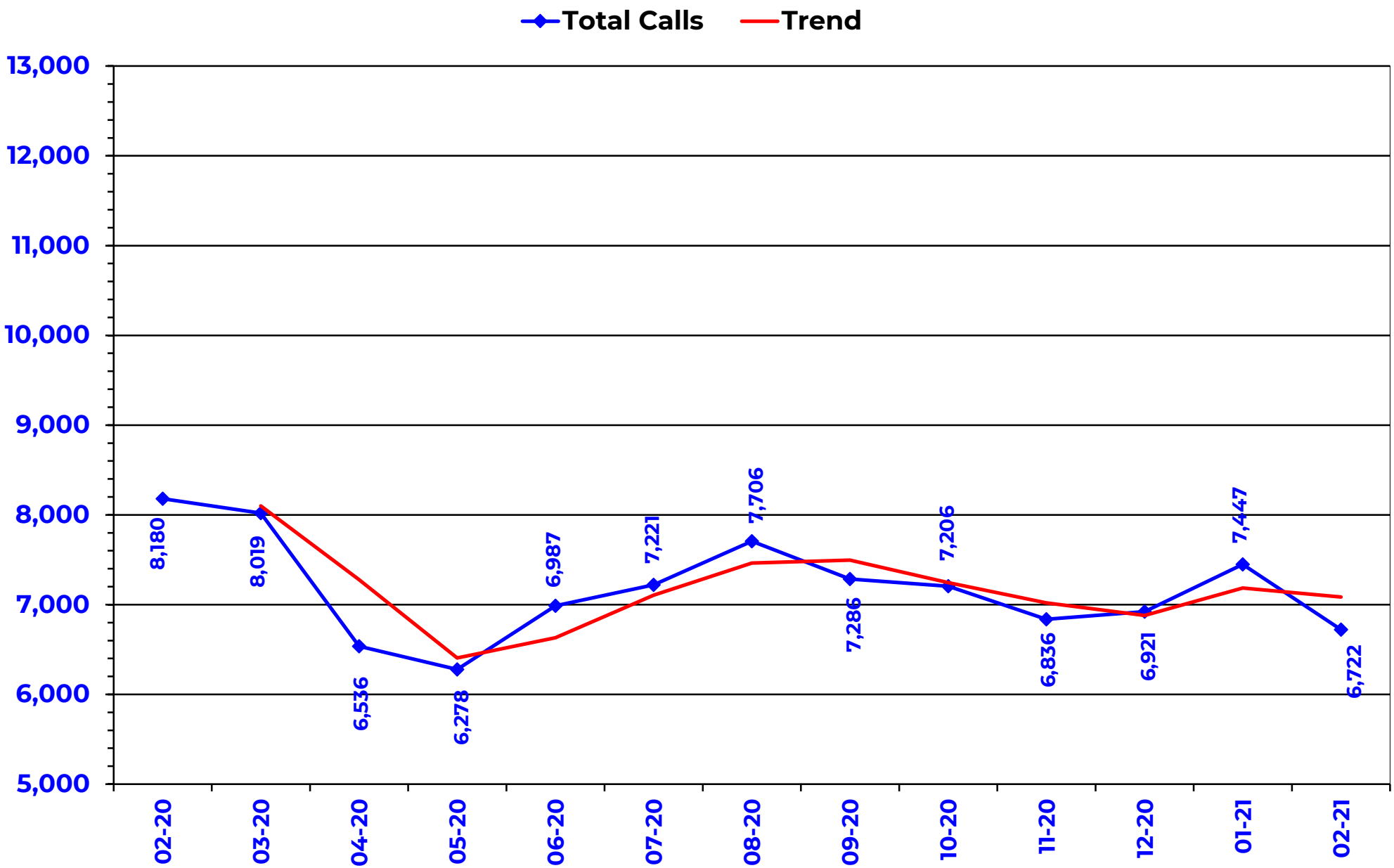

*PA totals include approved/denied/incomplete/overrides*

# PRIOR AUTHORIZATION REPORT: FEBRUARY 2020 – FEBRUARY 2021




*PA totals include approved/denied/incomplete/overrides*

# CALL VOLUME MONTHLY REPORT: FEBRUARY 2020 – FEBRUARY 2021



# Prior Authorization Activity

## 2/1/2021 Through 2/28/2021

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Advair/Symbicort/Dulera | 62 | 8 | 8 | 46 | 358 |
| Analgesic - NonNarcotic | 16 | 0 | 2 | 14 | 0 |
| Analgesic, Narcotic | 336 | 130 | 33 | 173 | 154 |
| Angiotensin Receptor Antagonist | 14 | 4 | 3 | 7 | 359 |
| Antiasthma | 51 | 14 | 11 | 26 | 261 |
| Antibiotic | 51 | 19 | 1 | 31 | 129 |
| Anticonvulsant | 164 | 55 | 16 | 93 | 295 |
| Antidepressant | 189 | 40 | 37 | 112 | 303 |
| Antidiabetic | 322 | 108 | 52 | 162 | 351 |
| Antihistamine | 18 | 2 | 5 | 11 | 358 |
| Antimigraine | 208 | 31 | 69 | 108 | 179 |
| Antineoplastic | 125 | 64 | 14 | 47 | 161 |
| Antiparasitic | 15 | 3 | 1 | 11 | 15 |
| Antiulcers | 59 | 7 | 15 | 37 | 95 |
| Anxiolytic | 26 | 3 | 3 | 20 | 144 |
| Atypical Antipsychotics | 278 | 114 | 32 | 132 | 348 |
| Biologics | 180 | 105 | 15 | 60 | 275 |
| Bladder Control | 44 | 6 | 9 | 29 | 358 |
| Blood Thinners | 331 | 182 | 22 | 127 | 332 |
| Botox | 54 | 28 | 21 | 5 | 322 |
| Buprenorphine Medications | 113 | 24 | 8 | 81 | 77 |
| Calcium Channel Blockers | 12 | 2 | 3 | 7 | 82 |
| Cardiovascular | 52 | 25 | 7 | 20 | 330 |
| Chronic Obstructive Pulmonary | 152 | 27 | 32 | 93 | 335 |
| Constipation/Diarrhea | 205 | 36 | 64 | 105 | 174 |
| Contraceptive | 23 | 10 | 3 | 10 | 330 |
| Dermatological | 298 | 92 | 78 | 128 | 184 |
| Diabetic Supplies | 693 | 364 | 58 | 271 | 259 |
| Endocrine & Metabolic Drugs | 90 | 49 | 6 | 35 | 144 |
| Erythropoietin Stimulating Agents | 16 | 6 | 2 | 8 | 106 |
| Fibromyalgia | 4 | 2 | 0 | 2 | 358 |
| Fish Oils | 11 | 0 | 3 | 8 | 0 |
| Gastrointestinal Agents | 142 | 28 | 28 | 86 | 192 |
| Glaucoma | 12 | 3 | 1 | 8 | 154 |
| Growth Hormones | 101 | 59 | 8 | 34 | 146 |
| Hepatitis C | 98 | 57 | 21 | 20 | 9 |
| HFA Rescue Inhalers | 19 | 0 | 1 | 18 | 0 |
| Insomnia | 72 | 7 | 9 | 56 | 153 |
| Insulin | 134 | 35 | 22 | 77 | 325 |
| Multiple Sclerosis | 52 | 17 | 7 | 28 | 216 |
| Muscle Relaxant | 40 | 4 | 8 | 28 | 20 |

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

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Neurological Agents | 72 | 15 | 20 | 37 | 223 |
| Nsaids | 33 | 3 | 7 | 23 | 266 |
| Ophthalmic | 20 | 2 | 7 | 11 | 357 |
| Ophthalmic Anti-infectives | 13 | 4 | 0 | 9 | 15 |
| Osteoporosis | 8 | 7 | 0 | 1 | 358 |
| Other* | 340 | 76 | 64 | 200 | 265 |
| Otic Antibiotic | 17 | 1 | 2 | 14 | 28 |
| Pediculicide | 32 | 10 | 7 | 15 | 9 |
| Respiratory Agents | 43 | 25 | 0 | 18 | 216 |
| Statins | 15 | 4 | 6 | 5 | 219 |
| Stimulant | 779 | 317 | 99 | 363 | 347 |
| Synagis | 56 | 32 | 0 | 24 | 66 |
| Testosterone | 90 | 30 | 21 | 39 | 289 |
| Thyroid | 14 | 3 | 5 | 6 | 277 |
| Topical Antifungal | 41 | 2 | 12 | 27 | 67 |
| Topical Corticosteroids | 73 | 0 | 42 | 31 | 0 |
| Vitamin | 77 | 30 | 22 | 25 | 164 |
| Pharmacotherapy | 49 | 45 | 0 | 4 | 270 |
| Emergency PAs | 0 | 0 | 0 | 0 | |
| Total | 6,718 | 2,386 | 1,071 | 3,261 | |
| | | | | | |
| **Overrides** | | | | | |
| Brand | 27 | 13 | 2 | 12 | 209 |
| Compound | 6 | 4 | 0 | 2 | 27 |
| Diabetic Supplies | 12 | 9 | 0 | 3 | 80 |
| Dosage Change | 295 | 280 | 0 | 15 | 12 |
| High Dose | 7 | 5 | 0 | 2 | 248 |
| Ingredient Duplication | 4 | 2 | 0 | 2 | 15 |
| Lost/Broken Rx | 71 | 62 | 3 | 6 | 20 |
| MAT Override | 281 | 184 | 7 | 90 | 64 |
| NDC vs. Age | 236 | 132 | 24 | 80 | 234 |
| NDC vs. Sex | 4 | 3 | 0 | 1 | 63 |
| Nursing Home Issue | 28 | 27 | 0 | 1 | 18 |
| Opioid MME Limit | 98 | 48 | 1 | 49 | 118 |
| Opioid Quantity | 23 | 21 | 0 | 2 | 159 |
| Other | 67 | 54 | 0 | 13 | 18 |
| Prescriber Temp Unlock | 1 | 1 | 0 | 0 | 360 |
| Quantity vs. Days Supply | 443 | 250 | 21 | 172 | 225 |
| STBS/STBSM | 14 | 6 | 3 | 5 | 74 |
| Step Therapy Exception | 4 | 0 | 2 | 2 | 0 |
| Stolen | 15 | 14 | 0 | 1 | 22 |
| Third Brand Request | 27 | 15 | 0 | 12 | 10 |
| **Overrides Total** | **1,663** | **1,130** | **63** | **470** | |
| **Total Regular PAs + Overrides** | **8,381** | **3,516** | **1,134** | **3,731** | |

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

| **Denial Reasons** | |
|---|---|
| Unable to verify required trials. | 3,069 |
| Does not meet established criteria. | 1,156 |
| Lack required information to process request. | 635 |
| **Other PA Activity** | |
| Duplicate Requests | 743 |
| Letters | 16,587 |
| No Process | 7 |
| Changes to Existing PAs | 666 |
| Helpdesk Initiated Prior Authorizations | 669 |
| PAs Missing Information | 5 |

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

# Spring 2021 Pipeline Update

**Oklahoma Health Care Authority**
**March 2021**

## Introduction

The following report is a pipeline review compiled by the University of Oklahoma College of Pharmacy: Pharmacy Management Consultants. Information in this report is focused on medications not yet approved by the U.S. Food and Drug Administration (FDA). The pipeline report is not an all-inclusive list, and medications expected to be highly utilized or have a particular impact in the SoonerCare population have been included for review. Pipeline data is collected from a variety of sources and is subject to change; dates listed are projections and all data presented are for informational purposes only. Costs listed in the following report do not reflect rebated prices or net costs.

## Ponesimod[1,2,3,4,5,6]

**Anticipated Indication(s):** Treatment of adult patients with relapsing multiple sclerosis (MS)

**Clinical Trial(s):** In March 2020, Janssen submitted a New Drug Application (NDA) to the FDA for ponesimod for the treatment of adult patients with relapsing forms of MS. Ponesimod is a selective sphingosine-1-phosphate receptor 1 (S1P1) modulator. Ponesimod inhibits S1P protein activity and is thought to reduce the number of circulating lymphocytes that can cross the blood-brain barrier. In the central nervous system (CNS), myelin can be damaged by the movement of immune cells, such as lymphocytes, into the brain. The NDA for ponesimod is supported by data from the Phase 3 OPTIMUM study, which was a 2-year head-to-head study that compared the efficacy and safety of oral ponesimod 20mg to oral Aubagio® (teriflunomide) 14mg in adults with relapsing MS. The primary endpoint was the annualized relapse rate (ARR) defined as the number of confirmed relapses per patient-year measured from baseline to the end of the study at week 108. Results of the study showed a statistically significant reduction of 30.5% in the ARR of ponesimod relative to teriflunomide (ARR=0.202 for ponesimod vs. 0.290 for teriflunomide; P=0.0003).

**Place in Therapy:** MS is a chronic autoimmune condition of the CNS characterized by demyelination, axonal loss, and subsequent neurological impairment. MS affects approximately 2.3 million people worldwide and women are more impacted than males. Relapsing forms of MS include

clinically isolated syndrome, relapsing-remitting MS, and active secondary progressive MS and account for approximately 85% of patients with MS. Patients with relapses experience new or worsening neurological symptoms lasting for more than 24 hours with the absence of fever or infections. Although some MS relapses resolve within days or weeks, others lead to residual and progressive neurological deficits, potentially resulting in severe disability.

**Projected FDA Decision:** March 2021

**SoonerCare Impact:** In calendar year 2020, there were 1,032 paid pharmacy claims for MS medications for 137 unique members, which accounted for a total cost of $6,648,914.01 and an average cost per claim of $6,442.75. In addition, there were 194 paid medical claims for MS medications in calendar year 2020 for 58 unique members, accounting for a total cost of $2,580,209.90 and an average cost per claim of $13,300.05. These costs do not reflect rebated prices or net costs.

## Abrocitinib[5,6,7,8,9]

**Anticipated Indication(s):** Treatment of moderate-to-severe atopic dermatitis (AD) in patients 12 years of age and older

**Clinical Trial(s):** In October 2020, Pfizer submitted a NDA for abrocitinib for the treatment of moderate-to-severe AD in patients 12 years of age and older. Abrocitinib is an investigational, oral, small molecule Janus Kinase 1 (JAK1) inhibitor. Abrocitinib is thought to modulate several important cytokines in AD pathophysiology, including interleukin (IL)-4, IL-13, IL-31, and IL-22. The NDA submission is supported by data from the Phase 3 JAK1 Atopic Dermatitis Efficacy and Safety (JADE) development program. JADE MONO-1 and JADE MONO-2 evaluated the efficacy and safety of 2 once-daily doses of abrocitinib (100mg and 200mg) as monotherapy compared with placebo. JADE COMPARE evaluated the efficacy and safety of the same 2 doses of abrocitinib against placebo in patients who were also on background topical therapy. Additionally, JADE COMPARE included patients receiving dupilumab administered subcutaneously (sub-Q) as an active control arm which was compared with placebo. In June 2020, Pfizer also announced positive top-line results from the JADE TEEN study in patients 12 to 17 years of age with moderate-to-severe AD who were also on background topical therapy. The co-primary endpoints were change from baseline in the Investigator's Global Assessment (IGA) score of 0 or 1 (clear or almost clear skin) plus a reduction from baseline of at least 2 points and a change from baseline in the Eczema Area and Severity Index of >75% (EASI-75) improvement. At week 12, both strengths of abrocitinib demonstrated statistical significance compared to placebo for the 2 co-primary endpoints.

**Place in Therapy:** AD is a chronic inflammatory skin disease and is 1 of the most common chronic childhood dermatoses. Additionally, up to 25% of adult patients report adult onset of initial AD symptoms. AD affects up to 10% of adults and up to 20% of children worldwide. Patients with AD frequently experience symptoms such as itch, skin redness and dryness, skin hardening, oozing or crusting of skin lesions, skin pain, sleep disturbance, daytime sleepiness, and fatigue. Patients with severe AD can also experience hospitalization due to AD flares and associated infections. The annual economic burden of AD including medical costs, indirect costs from lost productivity, and quality of life impact is estimated to be $5.3 billion.

**Projected FDA Decision:** April 2021

**SoonerCare Impact:** During calendar year 2020, there were 1,899 unique SoonerCare members with paid claims for AD medications. There were 4,438 paid claims for AD medications, accounting for a total cost of $5,144,709.53 with an average cost per claim of $1,159.24. These costs do not reflect rebated prices or net costs. This cost information includes paid pharmacy claims for all covered indications and does not distinguish between utilization for AD and utilization for other indications for which use may be appropriate.

### Bimekizumab[10,11,12,13,14]

**Anticipated Indication(s):** Treatment of adults with moderate-to-severe plaque psoriasis

**Clinical Trial(s):** In September 2020, UCB submitted a Biologics License Application (BLA) to the FDA for bimekizumab for the treatment of adults with moderate-to-severe plaque psoriasis. Bimekizumab is an investigational humanized monoclonal IgG1 antibody that selectively inhibits both IL-17A and IL-17F which are key cytokines responsible for driving inflammatory processes. Inhibition of IL-17F in addition to IL-17A suppresses inflammation to a greater extent than IL-17A inhibition alone. The NDA is supported by data from the Phase 3 BE VIVID, BE READY, and BE SURE studies. All 3 studies enrolled adult patients with chronic plaque psoriasis for at least 6 months prior to screening, an affected body surface area of ≥10%, a Psoriasis Area and Severity Index (PASI) score of at least 12, and an Investigator Global Assessment (IGA) score of ≥3 on a 5-point scale. The co-primary endpoints in all 3 studies were PASI 90 response (≥90% improvement from baseline in PASI score) at week 16 and an IGA score of 0 or 1 (clear or almost clear skin) with at least a 2-category improvement in IGA score relative to baseline at week 16. The BE VIVID and BE READY studies were both randomized, double-blind, placebo-controlled studies, while the BE SURE study was a randomized, double-blind study comparing bimekizumab to Humira® (adalimumab). All 3 studies met their co-primary endpoints and demonstrated superior skin

clearance relative to placebo and adalimumab. Additionally, 2 studies have demonstrated the superiority of bimekizumab over Stelara® (ustekinumab), another existing biologic treatment for plaque psoriasis. In January 2021, results from the BE VIVID and BE READY Phase 3 studies were published in *The Lancet*.

**Place in Therapy:** Plaque psoriasis is a common, chronic inflammatory disease of the skin. The signs and symptoms of plaque psoriasis frequently include red patches of skin with silvery scales, dry or cracked skin, and thickened, pitted, or ridged nails. Approximately 3% of the population experiences plaque psoriasis, with an estimated 8 million people affected in the United States. In addition to the physical signs and symptoms of the condition, plaque psoriasis also has a significant impact on psychological and quality of life factors, and the potential to affect work, recreation, relationships, sexual functioning, family, and social life. Treatment for plaque psoriasis is based on disease severity and can include targeted immunomodulators and biologics for patients with moderate-to-severe disease after failure of topical therapy. If approved by the FDA, bimekizumab would be the first biologic agent targeting both IL-17A and IL-17F for the treatment of plaque psoriasis.

**Projected FDA Decision:** July 2021

**SoonerCare Impact:** During calendar year 2020, there were 340 unique SoonerCare members with a reported diagnosis of plaque psoriasis. Paid SoonerCare pharmacy claims for biologic and targeted immunomodulator agents indicated for plaque psoriasis accounted for a total cost of $44,063,210.27 with an average cost per claim of $6,631.03. These costs do not reflect rebated prices or net costs. This cost information includes paid pharmacy claims for all covered indications and does not distinguish between utilization for plaque psoriasis and utilization for other indications for which use may be appropriate.

## Pipeline Table[5,6]

| Medication Name* | Manufacturer | Therapeutic Use | Route of Admin | Approval Status | Anticipated FDA Response |
|---|---|---|---|---|---|
| Citrate/taurolidine/ heparin | CorMedix | Catheter-related infections | IV | NDA; Fst Trk | 02/2021 |
| Udenafil | Mezzion Pharma | Congenital single ventricle heart disease | PO | NDA; OD | 02/2021 |

| Medication Name* | Manufacturer | Therapeutic Use | Route of Admin | Approval Status | Anticipated FDA Response |
|---|---|---|---|---|---|
| Eflornithine/ sulindac | Cancer Prevention Pharma | Familial adenomatous polyposis | PO | NDA; Fst Trk; OD | 02/2021 |
| D-threo-methylphenidate controlled-release | KemPharm | ADHD | PO | NDA | 03/2021 |
| Aducanumab | Biogen | Alzheimer's disease | IV | BLA; Fst Trk | 03/2021 |
| Arimoclomol | Orphazyme | Niemann-Pick disease type C | PO | NDA; Brk Thru; Fst Trk; OD | 03/2021 |
| Ponesimod | Johnson & Johnson | MS | PO | NDA | 03/2021 |
| Dasiglucagon | Zealand Pharma | DM | SC | NDA; OD | 03/2021 |
| Roxadustat | AstraZeneca | Anemia due to CKD | PO | NDA | 03/2021 |
| Cabotegravir (long-acting)/ rilpivirine (long-acting) | ViiV Healthcare | HIV | IM | NDA | 1Q2021 |
| Cabotegravir | ViiV Healthcare | HIV | PO | NDA | 1Q2021 |
| Belumosudil | Kadmon | GVHD | PO | NDA; Brk Thru; OD | 1Q2021 |
| Promethazine/ hydrocodone/ acetaminophen | Charleston Laboratories | Nausea/ vomiting/ pain | PO | NDA | 1Q2021 |
| Ropeginterferon alfa-2b | PharmaEssentia | Polycythemia vera | SC | BLA; OD | 03/2021 – 04/2021 |
| Fosdenopterin | BridgeBio Pharma/ Origin Biosciences | Molybdenum cofactor deficiency | IV | NDA; Brk Thru; OD | 04/2021 |
| Estetrol/ drospirenone | Mayne Pharma/ Mithra Pharmaceuticals | Pregnancy prevention | PO | NDA | 04/2021 |
| Benzoyl peroxide | Sol-Gel Technologies | Rosacea | TOP | NDA | 04/2021 |
| Abrocitinib | Pfizer | Atopic dermatitis | PO | NDA; Brk Thru | 04/2021 |
| Pegunigalsidase alfa | Protalix | Fabry disease | IV | BLA; Fst Trk | 04/2021 |
| Avalglucosidase alfa | Sanofi | Pompe disease | IV | BLA; Brk Thru; Fst Trk | 05/2021 |
| Pegcetacoplan | Apellis Pharmaceuticals | PNH | SC | NDA; Fst Trk; OD | 05/2021 |
| Zonisamide oral suspension | Eton | Seizures | PO | NDA | 05/2021 |

| Medication Name* | Manufacturer | Therapeutic Use | Route of Admin | Approval Status | Anticipated FDA Response |
|---|---|---|---|---|---|
| Budesonide oral suspension | Takeda | Eosinophilic esophagitis | PO | NDA; Brk Thru; OD | 05/2021 |
| Cantharidin | Verrica | Molluscum contagiosum | TOP | NDA | 06/2021 |
| Relugolix/estradiol/ norethindrone acetate | Myovant Sciences | Uterine fibroids | PO | NDA | 06/2021 |
| Human plasminogen | Liminal BioSciences | Plasminogen deficiency | IV | BLA; Fst Trk; OD | 06/2021 |
| Ibrexafungerp | Scynexis | Fungal infections | PO | NDA; Fst Trk; OD | 06/2021 |
| Lonapegsomatropin | Ascendis Pharma | Short stature/ GHD | SC | BLA; OD | 06/2021 |
| Cyclosporine | Santen Pharmaceutical | VKC | OPH | NDA; OD | 06/2021 |
| Bromelain | Vericel | Burns/skin injury | TOP | BLA | 06/2021 |
| Multivalent group B Streptococcus vaccine | Pfizer | Bacterial infection | IM | BLA | 06/2021 |
| Tanezumab | Pfizer/Eli Lilly | Osteoarthritis | SC | BLA; Fst Trk | 2Q2021 |
| Tralokinumab | Leo Pharma | Atopic dermatitis | SC | BLA | 2Q2021 |
| Teplizumab | Provention Bio/ MacroGenics | DM | IV | BLA; Brk Thru; OD | 07/2021 |
| Brincidofovir | Chimerix/SymBio Pharmaceuticals | Smallpox | PO | NDA; Fst Trk; OD | 07/2021 |
| Avacopan | ChemoCentryx | Vasculitis | PO | NDA; OD | 07/2021 |
| Selexipag | Janssen | PAH | IV | NDA | 07/2021 |
| Bimekizumab | UCB | Plaque psoriasis | IV | BLA | 07/2021 |
| Topiramate oral solution | Eton | Seizure disorders | PO | NDA | 08/2021 |
| Vosoritide | BioMarin | Achondroplasia | SC | NDA; OD | 08/2021 |
| Paliperidone Palmitate 6-month injection | Johnson & Johnson | Schizophrenia | IM | NDA | 09/2021 |
| POD-dihydroergotamine mesylate (POD-DHE) | Impel NeuroPharma | Acute migraines | IN | NDA | 09/2021 |
| Reltecimod | Atox | NSTI-related organ dysfunction | IV | NDA; Fst Trk; OD | 09/2021 |
| Somatrogon | Pfizer/OPKO | GHD (pediatrics) | SC | BLA; OD | 10/2021 |

| Medication Name* | Manufacturer | Therapeutic Use | Route of Admin | Approval Status | Anticipated FDA Response |
|---|---|---|---|---|---|
| Efgartigimod | Argenx | Myasthenia gravis | IV | BLA; Fst Trk; OD | 4Q2021 |
| Finerenone | Bayer | Diabetic nephropathy | PO | NDA | 11/2021 |
| Sulopenem | Iterum | Uncomplicated UTI (quinolone-resistant) | IV, PO | NDA; Fst Trk | 11/2021 |
| Difelikefalin | Cara | Hemodialysis-related pruritus | IV | NDA; Brk Thru | 12/2021 |
| Odevixibat | Albireo | Progressive familial intrahepatic cholestasis | PO | NDA; Fst Trk; OD | 12/2021 |
| Trivalent hepatitis B vaccine | VBI Vaccines | HBV infection prevention | IM | BLA | 12/2021 |
| Anifrolumab | AstraZeneca | SLE | IV | BLA; Fst Trk | 2H2021 |
| Daridorexant | Idorsia | Insomnia | PO | NDA | 01/2022 |

1H = 1st half; 1Q = 1st quarter; 2Q = 2nd quarter; 4Q = 4th quarter; ADHD = attention-deficit hyperactivity disorder; Admin = administration; BLA = Biologic License Application; Brk Thru = breakthrough; CKD = chronic kidney disease; DM = diabetes mellitus; Fst Trk = fast track; GHD = growth hormone deficiency; GVHD = graft-versus-host disease; HBV = hepatitis B virus; HIV = human immunodeficiency virus; IN = intranasal; IV = intravenous; MDD = major depressive disorder; MS = multiple sclerosis; NDA = New Drug Application; NSTI = necrotizing soft tissue infection; OD = orphan drug; OP = opthalmic; PAH = pulmonary hypertension; PNH = paroxysmal nocturnal hemoglobinuria; PO = by mouth; SC = subcutaneous; SLE = systemic lupus erythematosus; TOP = topical; VKC = Vernal keratoconjunctivitis

*Most biosimilars and oncology medications are excluded from the table. Medications known to have received a Complete Response Letter (CRL) from the FDA that have not resubmitted were also excluded.

[1] Johnson and Johnson. Johnson and Johnson Pipeline: Available online at: https://www.investor.jnj.com/_document/jnj-pipeline-2q-2019?id=0000016b-fa6f-d5ea-abef-ff6f76240000. Last accessed 02/12/2021.
[2] Ernst D. Ponesimod NDA for Relapsing Multiple Sclerosis Submitted for Review. *MPR*. Available online at: https://www.empr.com/home/news/drugs-in-the-pipeline/ponesimod-nda-for-relapsing-multiple-sclerosis-submitted-for-review/. Issued 03/19/2020. Last accessed 02/12/2021.
[3] Janssen Pharmaceutical Company. Janssen Submits Ponesimod New Drug Application to the U.S. FDA for Treatment of Adults with Relapsing Multiple Sclerosis. Available online at: https://www.janssen.com/janssen-submits-ponesimod-new-drug-application-us-fda-treatment-adults-relapsing-multiple-sclerosis. Issued 03/18/2020. Last accessed 02/12/2021.
[4] Janssen Pharmaceutical Company. New Head-to-Head Phase 3 Study Data Show Ponesimod Superiority versus Aubagio® (Teriflunomide) 14mg in Adults with Relapsing Multiple Sclerosis (MS). Available online at: https://www.janssen.com/new-head-head-phase-3-study-data-show-ponesimod-superiority-versus-aubagio-teriflunomide-14-mg. Issued 09/11/2019. Last accessed 02/15/2021.
[5] MagellanRx Management. MRx Pipeline. Available online at: https://issuu.com/magellanrx/docs/mrx_pipeline_jan_0121?fr=sNjU0ODI4ODIzNTU. Issued 01/2021. Last accessed 02/08/2021.
[6] OptumRx. RxOutlook® 4th Quarter 2020. Available online at: https://professionals.optumrx.com/content/dam/optum3/optum/en/resources/PDFs/orx6204_201119_b2b_newsletter_rxoutlook_final.pdf. Issued 11/24/2020. Last accessed 02/08/2021.
[7] Pfizer, Inc. Pfizer Pipeline. Available online at: https://www.pfizer.com/science/drug-product-pipeline. Last accessed 02/10/2021.
[8] Pfizer, Inc. FDA Grants Priority Review and EMA Accepts Regulatory Submission for Pfizer's Abrocitinib, an Oral Once-Daily JAK1 Inhibitor, for Patients 12 and Up with Moderate to Severe Atopic Dermatitis. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/fda-grants-priority-review-and-ema-accepts-regulatory. Issued 10/27/2020. Last accessed 02/10/2021.
[9] National Eczema Association. Eczema Stats. Available online at: https://nationaleczema.org/research/eczema-facts/. Last accessed 02/10/2021.
[10] UCB. UCB Pipeline. Available online at: https://www.ucb.com/our-science/pipeline. Last accessed 02/10/2021.
[11] Park B. Bimekizumab Under Review for Plaque Psoriasis. *MPR*. Available online at: https://www.empr.com/home/news/drugs-in-the-pipeline/bimekizumab-under-review-for-plaque-psoriasis/. Issued 09/22/2020. Last accessed 02/10/2021.
[12] UCB. UCB Achieves Important Regulatory Milestone for Bimekizumab. Available online at: https://www.ucb.com/stories-media/Press-Releases/article/UCB-Achieves-Important-Regulatory-Milestone-for-Bimekizumab. Issued 09/22/2020. Last accessed 02/10/2021.
[13] UCB. Bimekizumab Phase 3 Data Shows Superior Skin Clearance Over Humira® in Moderate-to-Severe Psoriasis Patients. Available online at: https://www.ucb.com/stories-media/Press-Releases/article/Bimekizumab-Phase-3-Data-Shows-Superior-Skin-Clearance-Over-Humira-in-Moderate-to-Severe-Psoriasis-Patients. Issued 10/31/2020. Last accessed 02/10/2021.
[14] UCB. The Lancet Publishes Two Phase 3 Studies Detailing Bimekizumab Data in Moderate-to-Severe Plaque Psoriasis. Available online at: https://www.ucb.com/stories-media/Press-Releases/article/The-Lancet-Publishes-Two-Phase-3-Studies-Detailing-Bimekizumab-Data-in-Moderate-to-Severe-Plaque-Psoriasis. Issued 02/04/2021. Last accessed 02/10/2021.

# Appendix D

# Vote to Prior Authorize Anjeso® (Meloxicam Injection) and Licart™ (Diclofenac Epolamine Topical System)

**Oklahoma Health Care Authority**
**March 2021**

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

**Anjeso® (meloxicam injection)** was approved by the FDA in February 2020 for the management of moderate-to-severe pain, alone or in combination with non-nonsteroidal anti-inflammatory drugs (NSAIDs), in adult patients. Anjeso® is supplied as an aqueous dispersion containing 30mg/mL of meloxicam in a single-dose vial (SDV) and is administered as a once-daily intravenous (IV) bolus injection over 15 seconds. The recommended dose is 30mg once daily. Anjeso® should not be used alone when rapid onset of analgesia is required due to delayed onset of efficacy of 2 or 3 hours after administration seen in 2 clinical trials 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. Anjeso® should be used for the shortest duration possible consistent with individual patient treatment goals, and patients should be well hydrated prior to administration to reduce the risk of renal toxicity. The FDA approval of Anjeso® was based on data from 2 double-blind, placebo-controlled Phase 3 studies in patients with postoperative pain from bunionectomy surgery or elective abdominoplasty surgery who received Anjeso® for a maximum of 3 doses. Oral oxycodone 5mg was allowed in both studies as a 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.

### 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 Costs (SMAC).
*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)** was approved by the FDA in December 2018 for the topical 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. Licart™ 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. Licart™ is supplied as a 1.3% diclofenac epolamine topical system (patch) in re-sealable envelopes, each containing 5 topical systems (10cm x 14cm each), with 3 envelopes per box. The recommended dose is 1 patch 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 Costs (SMAC).
*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. Prescriber must verify member will 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 extended-release (ER) tablets (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®) |
| ~~**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®) |

| 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), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*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.

[1] IBSA Pharma Inc. Licart™ Now Available to Treat Acute Pain Due to Minor Strains, Sprains, and Contusions. *BioSpace*. Available online at: https://www.biospace.com/article/releases/licart-now-available-to-treat-acute-pain-due-to-minor-strains-sprains-and-contusions/. Issued 10/30/2020. Last accessed 02/10/2021.
[2] Ernst D. Anjeso® Approved for Management of Moderate to Severe Pain. *MPR*. Available online at: https://www.empr.com/home/news/anjeso-approved-for-management-of-moderate-to-severe-pain/. Issued 02/21/2020. Last accessed 02/10/2021.
[3] Anjeso® (Meloxicam Injection) Prescribing Information. Baudax Bio, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/210583s000lbl.pdf. Last revised 11/2020. Last accessed 02/10/2021.
[4] Licart™ (Diclofenac Epolamine Topical System) Prescribing Information. IBSA Pharma, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/206976s002lbl.pdf. Last revised 05/2020. Last accessed 02/10/2021.

# Appendix E

# Vote to Prior Authorize Oxlumo™ (Lumasiran)

**Oklahoma Health Care Authority**
**March 2021**

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

**Oxlumo™ (lumasiran)** was approved by the U.S. Food and Drug Administration (FDA) in November 2020 as the first approved therapy for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. PH1 is a rare, autosomal recessive genetic disorder which results in the overproduction of oxalate and is caused by pathogenic mutations in the alanine-glyoxylate aminotransferase (*AGXT*) gene. Oxlumo™ is supplied as a solution containing 94.5mg/0.5mL of lumasiran in a single-dose vial (SDV) and is administered as a subcutaneous (sub-Q) injection with weight-based dosing. Oxlumo™ should be administered by a health care professional into the abdomen, thigh, or the side or back of the upper arms. For patients weighing <10kg, a loading dose (LD) of 6mg/kg should be given monthly for 3 doses, followed by a maintenance dose (MD) of 3mg/kg every month thereafter. For patients weighing 10kg to <20kg, a LD of 6mg/kg should be given monthly for 3 doses, followed by a MD of 6mg/kg every 3 months thereafter. For patients weighing ≥20kg, a LD of 3mg/kg should be given monthly for 3 doses, followed by a MD of 3mg/kg every 3 months thereafter. The most common adverse reactions, occurring in ≥10% of patients treated with lumasiran (and ≥5% more frequently than in placebo) in Phase 3 studies, were injection site reaction and abdominal pain (including general abdominal pain, upper abdominal pain, lower abdominal pain, and abdominal discomfort). Lumasiran has not been studied in patients with an estimated glomerular filtration rate (eGFR) <30mL/min/1.73m$^2$.

The safety and efficacy of lumasiran were assessed in 2 Phase 3 studies, ILLUMINATE-A and ILLUMINATE-B. In both studies, weight-based lumasiran was administered for at least 6 months for assessment of the primary efficacy end point. Additionally, patients were required to have a confirmed diagnosis of PH1 and were excluded if they did not have relatively preserved renal function, had evidence of systemic oxalosis, or a history of kidney or liver transplantation. ILLUMINATE-A was a randomized, double-blind, placebo-controlled study which included 39 patients ranging from 6 to 61 years of age. The primary 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. Patients in the lumasiran group had a 65% reduction in urinary oxalate excretion compared with a 12% reduction in the placebo

group. The between-group mean difference of 53% [95% confidence interval (CI): 45, 62] was statistically significant in favor of lumasiran (P=0.001). ILLUMINATE-B was a single-arm study in 18 patients younger than 6 years of age and included patients ranging from 4 to 74 months of age. The primary endpoint was the percent reduction from baseline in spot urinary oxalate:creatinine ratio averaged over months 3 through 6. Patients in this study had a 71% reduction from baseline in spot urinary oxalate:creatinine ratio (95% CI: 65, 77).

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] Milliner DS, Harris PC, Cogal AG, et al. Primary Hyperoxaluria Type 1. *GeneReviews®*. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK1283/. Last revised 11/30/2017. Last accessed 02/10/2021.
[2] 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 02/10/2021.
[3] 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 02/10/2021.
[4] 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 02/08/2021. Last accessed 02/10/2021.
[5] 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 02/05/2021. Last accessed 02/10/2021.

# Appendix F

# Vote to Prior Authorize Fintepla® (Fenfluramine)

**Oklahoma Health Care Authority**
**March 2021**

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

- **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 tuberous sclerosis complex (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, developmental 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 statistically significant greater reduction in the frequency of seizures during the treatment period than patients who received placebo.

## Fintepla® (Fenfluramine) Product Summary[3]

- **Therapeutic Class:** Serotonin 5HT-2 receptor agonist
- **Indication(s):** Treatment of seizures associated with DS in patients 2 years of age and older

- **How Supplied:** 2.2mg/mL oral solution
- **Dose:** The initial and maintenance dosing of fenfluramine is 0.1mg/kg twice daily and can be increased weekly based on efficacy and tolerability
  - For patients not on concomitant stiripentol therapy, the maximum daily maintenance dosage of fenfluramine is 0.35mg/kg twice daily (maximum daily dosage of 26mg)
  - For patients on stiripentol plus clobazam therapy, the maximum daily maintenance dosage of fenfluramine is 0.2mg/kg twice daily (maximum daily dosage of 17mg)
- **Cost:** Wholesale Acquisition Cost (WAC) of $42.60 per mL

## Cost Comparison: Anticonvulsant Therapies for DS[4]

| 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 100mg/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.

[1] U.S. Food and Drug Administration (FDA). FDA Approves New Therapy for Dravet Syndrome. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-therapy-dravet-syndrome. Issued 06/25/2020. Last accessed 02/09/2021.
[2] U.S. FDA. FDA Approves New Indication for Drug Containing an Active Ingredient Derived from Cannabis to Treat Seizures in Rare Genetic Disease. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-indication-drug-containing-active-ingredient-derived-cannabis-treat-seizures-rare. Issued 07/31/2020. Last accessed 02/09/2021.
[3] Fintepla® (Fenfluramine) Prescribing Information. Zogenix, Inc. Available online at: https://www.fintepla.com/pdf/Fintepla-prescribing-information.pdf. Last revised 06/2020. Last accessed 02/09/2021.
[4] Andrade DM, Nascimento FA. Dravet syndrome: Management and Prognosis. *UpToDate*. Available online at: https://www.uptodate.com/contents/dravet-syndrome-management-and-prognosis?search=dravet%20syndrome&source=search_result&selectedTitle=1~33&usage_type=default&display_rank=1#H422616694. Last revised 08/03/2020. Last accessed 02/09/2021.

# Appendix G

# Vote to Prior Authorize Teriparatide

**Oklahoma Health Care Authority**
**March 2021**

## Introduction[1]

In October 2019, the U.S. Food and Drug Administration (FDA) approved the New Drug Application (NDA) for teriparatide injection (formerly known as Bonsity™) submitted under the 505(b)(2) regulatory pathway using Forteo® as the reference drug. After FDA approval, teriparatide was launched in the United States by Alvogen in June 2020. Teriparatide is a parathyroid hormone analog (PTH 1-34) indicated for the 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 for the 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 daily. Use of teriparatide for more than 2 years during a patient's lifetime is not recommended. Teriparatide carries a *Boxed Warning* for the potential risk of osteosarcoma that was observed in rats, with an unknown risk in humans; therefore, teriparatide should not be prescribed for patients at an increased baseline risk for osteosarcoma and should only be prescribed for other patients when the potential benefits outweigh the potential risk.

### Cost Comparison:

| Medication | Cost Per mL | Cost Per 28 Days† | Cost Per 2 Years |
|---|---|---|---|
| **Teriparatide 20mcg injection pen** | **$997.98** | **$2,474.99** | **$64,349.74** |
| Forteo® (teriparatide injection) 20mcg 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), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
†Cost per 28 days based on a dosing regimen of 20mcg daily.

## Recommendations

The College of Pharmacy recommends the prior authorization of teriparatide injection with the following criteria:

### Forteo® (Teriparatide) and Teriparatide Approval Criteria:

1. An FDA approved indication 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 (Evenity®) |
| | | teriparatide inj (Forteo®) |
| | | **teriparatide inj** |

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
†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.

[1] Bonsity™ Prescribing Information. Pfenex. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211939s000lbl.pdf. Last revised 10/2019. Last accessed 02/10/2021.

# Appendix H

# Vote to Prior Authorize Zokinvy™ (Lonafarnib)

**Oklahoma Health Care Authority**
**March 2021**

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

**Hutchinson-Gilford Progeria Syndrome (HGPS) and 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.

## New U.S. Food and Drug Administration (FDA) Approval(s)[4,6]

- **Zokinvy™ (lonafarnib):** In 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 with a body surface area (BSA) ≥0.39$m^2$. 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. Zokinvy™ is available as a 50mg and 75mg oral capsule. The recommended starting dose of 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. 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. 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 in a separate natural history cohort. 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 1$m^2$ 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 of action, Zokinvy™ would not be effective in these populations); and
4. Member must be 1 year of age or older; and
5. Member must have a body surface area (BSA) ≥0.39$m^2$; and
6. Member must have clinical signs of progeria (e.g., characteristic facial features, growth deficiency, atherosclerosis); and
7. Zokinvy™ must be prescribed by, or in consultation with, a specialist with expertise in treating HGPS or PL (or an advanced care practitioner with a supervising physician who is a specialist in treating HGPS or PL); and
8. Member must not be taking any of the following medications: strong/moderate CYP3A inhibitors, CYP2C9 inhibitors, midazolam, lovastatin, simvastatin, atorvastatin, or loperamide if younger than 2 years of age; and
9. Prior to and during treatment, the potential for drug interactions should be considered, concomitant medications reviewed, and members should be monitored for adverse reactions; and
10. Member should have ophthalmological evaluations performed at regular intervals and at the onset of any new visual changes; and
11. Prescriber must verify the member will be monitored for changes in electrolytes, complete blood counts, renal function, and liver enzymes; and
12. Member's recent BSA must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to the package labeling; and
13. The maximum approvable dose of Zokinvy™ is 300mg/$m^2$ per day; and
14. Initial approvals will be for 6 months. After 6 months of utilization, compliance and information regarding efficacy, such as a positive response to treatment including no new or worsening heart failure and no stroke incidence, will be required for continued approval. Subsequent approvals will be for 12 months and compliance and documentation of a positive response to Zokinvy™ therapy will be required on each continuation request.

[1] National Institutes of Health (NIH). Progeria. Available online at: https://rarediseases.info.nih.gov/diseases/7467/progeria. Last revised 01/01/2021. Last accessed 02/15/2021.
[2] U.S. Food and Drug Administration (FDA). FDA Approves First Treatment for Hutchinson-Gilford Progeria Syndrome and Some Progeroid Laminopathies. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-hutchinson-gilford-progeria-syndrome-and-some-progeroid-laminopathies. Issued 11/20/2020. Last accessed 02/15/2021.
[3] Introne W, et al. Hutchinson-Gilford Progeria Syndrome. *UpToDate*. Available online at: https://www.uptodate.com/contents/hutchinson-gilford-progeria-syndrome?search=Progeroid%20Laminopathies&source=search_result&selectedTitle=1~7&usage_type=default&display_rank=1. Last revised 12/03/2019. Last accessed 02/15/2021.
[4] Eiger BioPharmaceuticals, Inc. Eiger BioPharmaceuticals Announces FDA Approval of Zokinvy™ (Lonafarnib): The First Treatment for Hutchinson-Gilford Progeria Syndrome and Processing-Deficient Progeroid Laminopathies. *PR Newswire*. Available online at: https://ir.eigerbio.com/news-releases/news-release-details/eiger-biopharmaceuticals-announces-fda-approval-zokinvytm. Issued 11/20/2020. Last accessed 02/15/2021.
[5] Progeria Research Foundation (PRF). PRF By the Numbers. Available online at: https://www.progeriaresearch.org/wp-content/uploads/2020/11/PRF-By-the-Numbers_-FINAL-October2020.pdf. Issued 10/2020. Last accessed 02/15/2021.
[6] Zokinvy™ Prescribing Information. Eiger Biopharmaceuticals, Inc. Available online at: https://www.zokinvy.com/pdf/ZOKINVY_US_PRESCRIBING_INFORMATION.pdf. Last revised 11/2020. Last accessed 02/15/2021.

# Appendix I

# Vote to Prior Authorize Nurtec™ ODT (Rimegepant) and Vyepti® (Eptinezumab-jjmr)

**Oklahoma Health Care Authority**
**March 2021**

## Introduction[1,2]

**Nurtec™ ODT (rimegepant)** is a calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine with or without aura in adults. Nurtec™ ODT is supplied as a 75mg orally disintegrating tablet (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. Nurtec™ ODT is not indicated for the preventive treatment of migraine. 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). 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 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).

### Cost Comparison:

| Medication | Cost Per Dose | Cost Per Maximum Cumulative Dose* |
|---|---|---|
| **Nurtec™ ODT (rimegepant) 75mg ODT** | **$107.00** | **$107.00** |
| Ubrelvy® (ubrogepant) 100mg tablet | $85.62 | $171.24 |
| rizatriptan 10mg tablet | $0.50 | $1.50 |
| sumatriptan 100mg tablet | $0.70 | $1.40 |

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

**Vyepti® (eptinezumab-jjmr)** is a CGRP antagonist indicated for the preventive treatment of migraine in adults. Vyepti® is supplied as 100mg/mL solution in a 1mL single-dose vial (SDV). The recommended dosage is 100mg administered by intravenous (IV) infusion every 3 months. Some patients may benefit from a dosage of 300mg administered by IV infusion every 3 months. The most common (incidence ≥2% and at least 2% greater than placebo) adverse reactions in the clinical studies of eptinezumab for the preventive treatment of migraine were nasopharyngitis and hypersensitivity. 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. For both studies, eptinezumab treatment demonstrated statistically significant improvements compared to placebo for the primary efficacy endpoint, the change from baseline in mean monthly migraine days (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. In study 1, 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. In study 2, 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 | $607.06 | $607.06⁺ | $8,498.84⁺ |
| Ajovy® (fremanezumab-vfrm) 225mg/1.5mL autoinjector | $408.45 | $612.68 - $1,838.25△ | $7,352.16△ |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
*Cost per maintenance dose 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 (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® (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®) |
| 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), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
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 the member must be provided; and
16. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
17. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig®, a quantity limit of 1 syringe or autoinjector per 30 days will apply; and
    ~~b. For 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 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 manufacturers of Ajovy® and Emgality® have 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 manufacturers chooses not to participate in supplemental rebates.*

[1] Nurtec™ ODT Prescribing Information. Biohaven Pharmaceuticals, Inc. Available online at: https://www.nurtec.com/pi. Last revised 03/2020. Last accessed 02/08/2021.
[2] Vyepti™ Prescribing Information. Lundbeck. Available online at: https://www.lundbeck.com/upload/us/files/pdf/Products/Vyepti_PI_US_EN.pdf. Last revised 02/2020. Last accessed 02/08/2021.

# Appendix J

# Vote to Prior Authorize Inqovi® (Decitabine/ Cedazuridine), Onureg® (Azacitidine), and Riabni™ (Rituximab-arrx)

**Oklahoma Health Care Authority**
**March 2021**

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

**News:**

- **March 2020:** The National Comprehensive Cancer Network (NCCN) Acute Myeloid Leukemia (AML) Guidelines and the NCCN Drugs and Biologics Compendium were updated to expand the appropriate utilization of Venclexta® (venetoclax) to include patients with relapsed/refractory AML.

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

- **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.
- **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), chronic lymphocytic leukemia (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.

## 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 the recent 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).

---

[1] National Comprehensive Cancer Network (NCCN) Guidelines. AML V 2.2021. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Last accessed 01/11/2021.
[2] NCCN Drugs and Biologic Compendium. Available by subscription online at: https://www.nccn.org/professionals/drug_compendium/content/pdf. Last accessed 01/11/2021.
[3] 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.
[4] 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 02/05/2021. Last accessed 02/08/2021.
[5] 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.
[6] 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 02/08/2021.

# Appendix K

# Calendar Year 2020 Annual Review of Qutenza® (Capsaicin 8% Patch)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Qutenza® (Capsaicin 8% Patch) Approval Criteria:**

1. An FDA approved diagnosis of postherpetic neuralgia; and
2. Documented treatment attempts at recommended dosing or contraindication(s) to at least 1 agent from each of the following drug classes:
   a. Tricyclic antidepressants; and
   b. Anticonvulsants; and
   c. Topical lidocaine; and
3. Qutenza® must be administered by a health care provider; and
4. A quantity limit of no more than 4 patches per treatment every 90 days will apply.

## Utilization of Qutenza® (Capsaicin 8% Patch): Calendar Year 2020

There was no SoonerCare utilization of Qutenza® (capsaicin 8% patch) during calendar year 2020.

## Prior Authorization of Qutenza® (Capsaicin 8% Patch)

There were no prior authorization requests submitted for Qutenza® (capsaicin 8% patch) during calendar year 2020.

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

**Anticipated Patent Expiration(s):**

- Qutenza® (capsaicin 8% patch): March 2030

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

- **July 2020:** The FDA approved Qutenza® (capsaicin 8% patch) for a new indication for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet. Qutenza® was previously FDA approved in 2009 for the treatment of neuropathic pain due to postherpetic neuralgia. The new indication was supported by data from a 12-week, double-blind, placebo-controlled study in 369 patients with DPN. Patients were randomized to receive Qutenza® (N=186) or placebo (N=183), each administered as a single 30-minute application. Concomitant medications for neuropathic pain were taken

during the study by 47.2% of participants and included anticonvulsants and non-selective serotonin reuptake inhibitor (SSRI) antidepressants. For patients who were already stable on other pain control medications prior to study entry, stable dosing of the pain control medications throughout the study period was required. Use of opioid medications other than short-acting rescue medications was not allowed during the study. The primary efficacy end point was the change from baseline to the mean score over weeks 2 through 8 in the Numeric Pain Rating Scale (NPRS) average daily pain score. Patients were required to call in daily to report their average daily pain score over the previous 24 hours on a numerical scale ranging from 0 to 10. The results of the study demonstrated a statistically significant reduction in average daily pain from baseline to between weeks 2 through 8 in the Qutenza® group relative to placebo (-27.4% vs. -20.9%, respectively; P=0.025). An additional analysis showed this difference between the Qutenza® group and placebo was also maintained from baseline to between weeks 2 through 12 (-28.0% vs. -21.0%, respectively; P=0.018). The recommended dosing of Qutenza® for DPN is a single 30-minute application on the feet using up to a maximum of 4 patches. Prior to application, the feet should be examined to detect skin lesions related to underlying neuropathy or vascular insufficiency. Treatment may be repeated every 3 months or as needed by the return of pain, but should not be repeated more frequently than every 3 months.

## Recommendations

The College of Pharmacy recommends updating the approval criteria for Qutenza® (capsaicin 8% patch) based on the new FDA approved indication, with the following changes shown in red:

**Qutenza® (Capsaicin 8% Patch) Approval Criteria:**

1. An FDA approved diagnosis of postherpetic neuralgia or diabetic peripheral neuropathy of the feet; and
2. Documented treatment attempts at recommended dosing or contraindication(s) to at least 1 agent from each of the following drug classes:
    a. For postherpetic neuralgia:
        i. Tricyclic antidepressants; and
        ii. Anticonvulsants; and
        iii. Topical lidocaine; or
    b. For diabetic peripheral neuropathy of the feet:
        i. Duloxetine or tricyclic antidepressants; and
        ii. Anticonvulsants; and
        iii. Topical lidocaine; and
3. Qutenza® must be administered by a health care provider; and

4. For a diagnosis of diabetic peripheral neuropathy of the feet, the prescriber must verify that they will examine the feet to detect skin lesions related to underlying neuropathy or vascular insufficiency prior to application of Qutenza®; and
5. Initial approvals will be for 1 treatment (for the duration of 90 days). For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
6. A quantity limit of no more than 4 patches per treatment every 90 days will apply.

---

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 02/2021. Last accessed 02/08/2021.
[2] Park B. Qutenza® Approved for Painful Diabetic Peripheral Neuropathy of the Feet. *MPR.* Available online at: https://www.empr.com/home/news/qutenza-capsaicin-approved-pain-diabetic-peripheral-neuropathy-of-feet. Issued 07/22/2020. Last accessed 02/08/2021.
[3] Simpson DM, Robinson-Papp JR, Van J, et al. Capsaicin 8% Patch in Painful Diabetic Peripheral Neuropathy: A Randomized, Double-Blind, Placebo-Controlled Study. *J Pain* 2017; 18(1):42-53.
[4] Qutenza® (Capsaicin Patch) Prescribing Information. Averitas Pharma, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/022395s019lbl.pdf. Last revised 07/2020. Last accessed 02/08/2021.

# Appendix L

# Calendar Year 2020 Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Breyanzi® (Lisocabtagene Maraleucel), Monjuvi® (Tafasitamab-cxix), Romidepsin 27.5mg/5.5mL Vial, Tecartus™ (Brexucabtagene Autoleucel), and Ukoniq™ (Umbralisib)

**Oklahoma Health Care Authority**
**March 2021**

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

Lymphoma is a general term for cancers that develop in the lymphatic system. Lymphomas that do not start in white blood cells (WBCs) are called non-Hodgkin's lymphoma (NHL). NHL consists of a diverse group of neoplasms derived from B-cell progenitors, mature B-cells, mature T-cells, T-cell progenitors, or natural killer (NK) cells. The majority of NHL types develop in B-cells and the most common forms of B-cell NHL include diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), and marginal zone lymphoma (MZL). The clinical presentation of NHL varies widely depending on the type of lymphoma and the areas involved. Common presentations include lymphadenopathy, hepatosplenomegaly, fever, weight loss, and night sweats. Some NHLs behave indolently with waxing and waning lymphadenopathy for years, while others are highly aggressive and result in death within weeks if left untreated. NHL is the seventh most common cancer in the United States and is slightly more common in Caucasian men. In 2021, there will be an estimated 81,560 new diagnoses of NHL and 20,720 deaths due to NHL in the United States.

Hodgkin's lymphoma (HL) is a type of lymphoma that arises from germinal center or post-germinal center B-cells. Almost all HL cases contain Reed-Sternberg cells, a specific type of cancer cells not found in NHL. Most patients with HL can be treated successfully, even in advanced stages. HL is divided into 2 major types, based on the appearance and immunophenotype of the tumor cells: classic HL (cHL) and nodular lymphocyte-predominant HL (NLPHL). Most patients with cHL present with painless localized peripheral lymphadenopathy. HL has a bimodal age distribution and is most common in young adults (15 to 40 years of age) and older adults (older than 55 years of age). Males are slightly more likely to develop HL. In 2021, there will be an estimated 8,830 new diagnoses of HL and 960 deaths due to HL in the United States.

T-cell lymphomas can develop in lymphoid tissues or outside of lymphoid tissues. A similar lymphocyte called a NK cell shares many features with T-cells and when NK cells become cancerous, the cancer is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. T-cell lymphomas account for approximately 7% of all NHLs in the United States; each particular subtype of T-cell lymphoma is very uncommon. They can be aggressive or indolent. Lymphomas that arise from mature T-cells are sometimes categorized together under the general term peripheral T-cell lymphoma (PTCL). Almost all types of T-cell lymphomas fall under the category of PTCL. The following are among the PTCLs: peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS); anaplastic large cell lymphoma (ALCL), primary systemic type; angioimmunoblastic T-cell lymphoma (AITL); extranodal NK/T-cell lymphoma, nasal type; subcutaneous panniculitis-like T-cell lymphoma; enteropathy associated T-cell lymphoma; and hepatosplenic T-cell lymphoma.

PTCL, NOS accounts for the largest number of patients with PTCL in western countries, accounting for approximately 30% of PTCL and approximately 4% of NHLs overall. It is likely that this group of PTCL, NOS tumors represents a conglomerate of many not yet identified PTCL subtypes. The incidence of PTCL, NOS in the United States was approximately 0.4 cases per 100,000 population in 2006. In the United States, the incidence is highest among blacks, lower among non-Hispanic whites, Hispanic whites, and Asian/Pacific Islanders, and lowest among American Indian/Alaskan natives. The median age at diagnosis is 60 years, and the diagnosis is more common in men than women. Most patients with PTCL, NOS present with generalized lymphadenopathy with or without extranodal disease.

ALCL accounts for approximately 1% of all NHLs. Symptoms associated with ALCL include fever, backache, painless swelling of lymph nodes, loss of appetite, itching, skin rash, and fatigue. ALCL can be systemic or cutaneous; systemic ALCL is typically in an advanced stage at diagnosis and can progress rapidly. The systemic subtype is classified as anaplastic lymphoma kinase (ALK)-positive or ALK-negative, depending on whether or not it contains an abnormal ALK fusion protein that results from a genetic event. The non-systemic subtype is called primary cutaneous ALCL and has a good prognosis. AITL is a rare, aggressive type accounting for approximately 7% of all patients with T-cell lymphomas in the United States. Most patients are diagnosed with advanced stage disease and are middle-aged or elderly. Symptoms include fever, night sweats, skin rash, itching, and some autoimmune disorders (autoimmune hemolytic anemia and immune thrombocytopenia). Cutaneous T-cell lymphomas (CTCL) account for 2 to 3% of all NHL cases and generally affect adults. CTCL describes a group of

typically indolent lymphomas that appear on the skin; mycosis fungoides (MF) is the most common type of CTCL.

## 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 relapsed/refractory disease with regional nodes.

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

1. In previously untreated disease in combination with cyclophosphamide, doxorubicin, and prednisone; or
2. In members who have received ≥1 line of therapy as a single-agent.

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

1. In previously untreated Stage III or IV disease in combination with doxorubicin, vinblastine, and dacarbazine; or
2. In 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. In 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. As a single-agent; and
2. CD30+ disease; and
3. DLBCL relapsed/refractory disease in non-autologous stem cell transplant (SCT) candidates; or
4. In members who have transformed to DLBCL from follicular lymphoma or marginal zone lymphoma and received ≥2 lines of therapy for indolent or transformed disease.

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

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

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

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

**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. In members who have received ≥1 line of therapy as a single-agent.

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

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

**Aliqopa™ (Copanlisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:**

1. A diagnosis of relapsed/refractory FL; and
2. Member must have failed at least 2 prior systemic therapies.

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

1. 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. 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.

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

**Brukinsa™ (Zanubrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:**

1. Adult members with a diagnosis of MCL; and
2. Member must have received at least 1 prior therapy.

**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 or more 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 or more lines of systemic therapy; and
3. As a single-agent.

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

**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.

**Istodax® (Romidepsin) 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.

**Istodax® (Romidepsin) Approval [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.

**Istodax® (Romidepsin) Approval [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:**

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

**Istodax® (Romidepsin) Approval [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:**

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

**Polivy™ (Polatuzumab Vedotin-piiq) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade Lymphoma Diagnosis]:**

1. Relapsed/refractory DLBCL or high grade B-cell lymphoma after at least 2 prior therapies; and
2. Used in combination with bendamustine and rituximab; and
3. Member is not a candidate for transplant.

**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.

**Riabni™ (Rituximab-arrx), Ruxience™ (Rituximab-pvvr), and Truxima® (Rituximab-abbs) 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.

**Riabni™ (rituximab-arrx) was reviewed with the leukemia medications and can be found in the February 2021 Drug Utilization Review (DUR) Board packet; however, going forward it will be reviewed annually with the lymphoma medications.

**Yescarta® (Axicabtagene) Approval Criteria [Lymphoma Diagnosis]:**

1. Diagnosis of 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. Member must be 18 years of age or older; and
3. Relapsed/refractory disease; and

4. Member must not have primary central nervous system lymphoma; and
5. Member must have had 2 or more 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 risk evaluation and mitigation strategy (REMS) requirements.

**Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) (Grade 1-2) Diagnosis]:**

1. As a single-agent; and
2. Relapsed/refractory disease.

**Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) or Marginal Zone Lymphoma (MZL) Transformed to Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:**

1. As a single-agent; and
2. Member meets 1 of the following:
    a. Minimal or no chemotherapy prior to histologic transformation to DLBCL (FISH for MYC and BCL2 and/or BCL6 must show no translocation) and have partial response, no response, or progressive disease after chemoimmunotherapy; or
    b. Member must have received ≥2 prior therapies of chemoimmunotherapy for indolent or transformed disease.

**Zolinza® (Vorinostat) 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.

Approval criteria for Xpovio® (selinexor) for the indication of multiple myeloma can be found in the November 2020 DUR Board packet. Xpovio® is reviewed annually with the multiple myeloma medications.

**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.

Approval criteria for Gazyva® (obinutuzumab), Imbruvica® (ibrutinib), Kymriah® (tisagenlecleucel), Venclexta® (venetoclax), and Zydelig® (idelalisib) for indications other than lymphoma can be found in the February 2021 DUR Board packet. These medications are reviewed annually with the leukemia medications.

**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 CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), 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.

**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 [Follicular Lymphoma (FL) Diagnosis]:**

1. Diagnosis of 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 [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. Diagnosis of 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-Transplant Lymphoproliferative Disorders Diagnosis]:**

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

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

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

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

1. Diagnosis of 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 or more 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 risk evaluation and mitigation strategy (REMS) requirements.

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

1. As first-line therapy in combination with obinutuzumab for a maximum duration of 12 months; or
2. Relapsed/refractory disease in combination with rituximab or as a single-agent.

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

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

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

1. Diagnosis of 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.

The following approval criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) includes only criteria for indications of lymphoma. Complete prior authorization criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) can be found in the December 2020 DUR Board packet. These medications are reviewed annually with the skin cancer medications.

**Keytruda® (Pembrolizumab) Approval Criteria [Classical Hodgkin's 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's lymphoma; or
4. For pediatric members:
    a. Diagnosis of refractory cHL; or
    b. Relapsed disease after ≥2 therapies.

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

1. Diagnosis of PMBCL in adult or pediatric members; and
2. Member must have refractory disease or pembrolizumab must be used in members who have relapsed after 2 or more prior lines of therapy; and

3. Authorizations will not be granted for members who require urgent cytoreduction; and
4. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

**Opdivo® (Nivolumab) Approval Criteria [Classical Hodgkin's Lymphoma (cHL) Diagnosis]:**

1. Diagnosis of relapsed or refractory cHL; and
   a. Exception: lymphocyte-predominant HL
2. Nivolumab must be used as a single-agent; and
3. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)].

## Utilization of Lymphoma Medications: Calendar Year 2020

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

### Calendar Year Comparison: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2019** | 12 | 89 | $968,145.39 | $10,878.04 | $377.59 | 3,506 | 2,564 |
| **2020** | 18 | 94 | $1,178,061.27 | $12,532.57 | $436.00 | 4,126 | 2,702 |
| **% Change** | **50.00%** | **5.60%** | **21.70%** | **15.20%** | **15.50%** | **17.70%** | **5.40%** |
| **Change** | **6** | **5** | **$209,915.88** | **$1,654.53** | **$58.41** | **620** | **138** |

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

### Calendar Year Comparison: Medical Claims

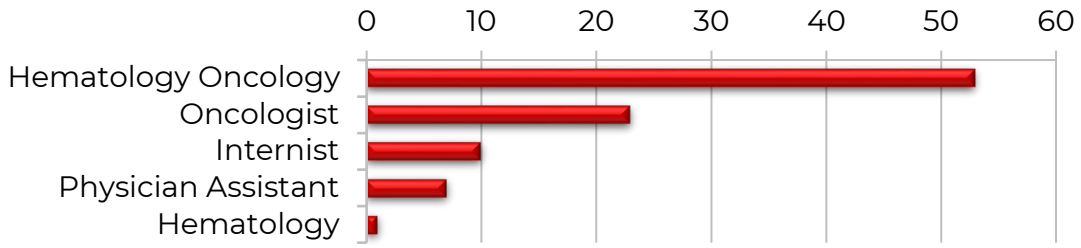
| Calendar Year | *Total Members | †Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|---|
| **2019** | 144 | 663 | $7,123,159.57 | $10,743.83 | 4.60 |
| **2020** | 158 | 748 | $7,578,324.69 | $10,131.45 | 4.73 |
| **% Change** | **9.72%** | **12.82%** | **6.39%** | **-5.70%** | **2.83%** |
| **Change** | **14** | **85** | **$455,165.12** | **-$612.38** | **0.13** |

*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.

### Demographics of Members Utilizing Lymphoma Medications: Pharmacy Claims

- Due to the limited number of members utilizing lymphoma medications, detailed demographic information could not be provided.

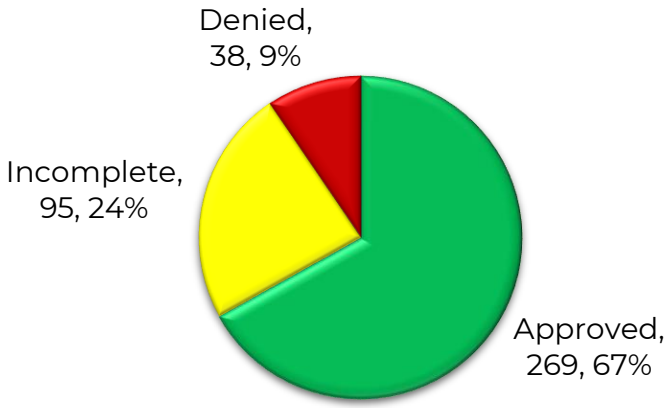
**Top Prescriber Specialties of Lymphoma Medications By Number of Claims: Pharmacy Claims**




## Prior Authorization of Lymphoma Medications

There were 402 prior authorization requests submitted for lymphoma medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

**Status of Petitions**




## Market News and Updates[9,10]

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

- **March 2020:** The FDA approved a New Drug Application (NDA) submitted by Teva Pharmaceuticals for romidepsin 27.5mg/5.5mL. Teva's romidepsin 27.5mg/5.5mL was approved for the same active ingredient, route of administration, concentration of active ingredient, and indications as Istodax® [romidepsin lyophilized powder in a 10mg single-dose vial (SDV)]. Romidepsin 27.5mg/5.5mL differs in its dosage form and presentation. It is supplied as a sterile, clear solution in a SDV. No clinical studies were performed with the Teva formulation. The NDA was approved based on the findings of safety and effectiveness for Istodax®.

- **June 2020:** The FDA granted accelerated approval to Tazverik® (tazemetostat), an EZH2 inhibitor, for adult patients with relapsed or refractory FL whose tumors are positive for an *EZH2* mutation and who have received at least 2 prior systemic therapies, and for adult patients with relapsed or refractory FL who have no satisfactory alternative treatment options.
- **July 2020:** The FDA granted accelerated approval to Tecartus™ (brexucabtagene autoleucel), a CD19-directed genetically modified autologous T-cell immunotherapy, for adult patients with relapsed or refractory MCL.
- **July 2020:** The FDA granted accelerated approval to Monjuvi® (tafasitamab-cxix), a CD19-directed cytolytic antibody, indicated in combination with lenalidomide for adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT).
- **January 2021:** The FDA approved the combination of Opdivo® (nivolumab) and Cabometyx® (cabozantinib) as first-line treatment for patients with advanced renal cell carcinoma (RCC).
- **January 2021:** The FDA approved Xalkori® (crizotinib) for pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic ALCL that is ALK-positive. The safety and efficacy of crizotinib have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.
- **February 2021:** The FDA approved Breyanzi® (lisocabtagene maraleucel) for adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and FL grade 3B.
- **February 2021:** The FDA granted accelerated approval to Ukoniq™ (umbralisib), a kinase inhibitor including PI3K-delta and casein kinase 1 (CK1)-epsilon, for the following indications:
    - Adult patients with relapsed or refractory MZL who have received at least 1 prior anti-CD20-based regimen; and
    - Adult patients with relapsed or refractory FL who have received at least 3 prior lines of systemic therapy.

## Product Summaries[11,12,13,14]

### Breyanzi® (Lisocabtagene Maraleucel):

- **Therapeutic Class:** CD19-directed genetically modified autologous T-cell immunotherapy

- **Indication(s):** Treatment of adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and FL grade 3B
- **How Supplied:** Cell suspension for intravenous (IV) infusion with a patient-specific concentration [each mL contains $1.5 \times 10^6$ to $70 \times 10^6$ chimeric antigen receptor (CAR)-positive viable T-cells]
- **Dose:** Based on the number of CAR-positive viable T-cells, the dose is 50 to $110 \times 10^6$ CAR-positive viable T-cells
- **Cost:** Cost information for Breyanzi® is not yet available

**Monjuvi® (Tafasitamab-cxix):**
- **Therapeutic Class:** CD19-directed cytolytic antibody
- **Indication(s):** Use in combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for ASCT
- **How Supplied:** 200mg lyophilized powder for reconstitution in a SDV
- **Dose:** 12mg/kg via IV infusion as follows:
  - Cycle 1: Days 1, 4, 8, 15, and 22 of the 28-day cycle
  - Cycles 2 and 3: Days 1, 8, 15, and 22 of each 28-day cycle
  - Cycle 4 and Thereafter: Days 1 and 15 of each 28-day cycle
- **Cost:** Wholesale Acquisition Cost (WAC) of $1,200 per SDV; cost will vary due to weight-based dosing

**Tecartus™ (Brexucabtagene Autoleucel):**
- **Therapeutic Class:** CD19-directed genetically modified autologous T-cell immunotherapy
- **Indication(s):** Treatment of adult patients with relapsed or refractory MCL
- **How Supplied:** Cell suspension for IV infusion with a patient-specific concentration with a maximum of $2 \times 10^8$ CAR-positive viable T-cells in approximately 68mL
- **Dose:** Based on the number of CAR-positive viable T-cells, the dose is $2 \times 10^6$ CAR-positive viable T-cells/kg
- **Cost:** WAC of $373,000 per one-time treatment

**Ukoniq™ (Umbralisib):**
- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Relapsed or refractory MZL in patients who have received at least 1 prior anti-CD20-based regimen
  - Relapsed or refractory FL in patients who have received at least 3 prior lines of systemic therapy

- **How Supplied:** 200mg oral tablets
- **Dose:** 800mg once daily
- **Cost:** Cost information for Ukoniq™ is not yet available

## Recommendations

The College of Pharmacy recommends the prior authorization of Breyanzi® (lisocabtagene maraleucel), Monjuvi® (tafasitamab-cxix), Tecartus™ (brexucabtagene autoleucel), and Ukoniq™ (umbralisib) with the following criteria (shown in red):

**Breyanzi® (Lisocabtagene Maraleucel) Approval Criteria [Lymphoma Diagnosis]:**

1. Diagnosis of large B-cell lymphoma; and
2. Relapsed or refractory disease; and
3. Member must have received at least 2 lines of systemic therapy; and
4. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategy (REMS) requirements.

**Monjuvi® (Tafasitamab-cxix) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:**

1. Diagnosis of DLBCL in adults; and
2. Relapsed or refractory disease; and
3. Used in combination with lenalidomide.

**Tecartus™ (Brexucabtagene Autoleucel) Approval Criteria [Lymphoma Diagnosis]:**

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

**Ukoniq™ (Umbralisib) Approval Criteria [Marginal Zone Lymphoma (MZL) Diagnosis]:**

1. Diagnosis of MZL; and
2. Relapsed or refractory disease; and
3. Member must have received at least 1 prior anti-CD20-based regimen.

**Ukoniq™ (Umbralisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:**

1. Diagnosis of FL; and
2. Relapsed or refractory disease; and

3. Member must have received at least 3 prior lines of systemic therapy.

Additionally, the College of Pharmacy recommends the prior authorization of romidepsin 27.5mg/5.5mL vial with the same criteria as Istodax® (romidepsin); changes noted in red:

**Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial 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.

**Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial 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.

**Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:**

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

**Istodax® (Romidepsin) and Romidepsin 27.5mg/5.5mL Vial Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:**

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

Finally, the College of Pharmacy recommends updating the Opdivo® (nivolumab), Tazverik® (tazemetostat), and Xalkori® (crizotinib) prior authorization criteria based on recent FDA approvals; changes and new criteria noted in red (only criteria with updates are listed):

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

1. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
2. For nivolumab monotherapy:
    a. Diagnosis of relapsed or surgically unresectable stage IV disease; and
    b. Failed prior therapy with 1 of the following medications:
        i. Sunitinib; or
        ii. Sorafenib; or
        iii. Pazopanib; or
        iv. Axitinib; or

3. For nivolumab use in combination with ipilimumab:
    a. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; or
4. For nivolumab use in combination with cabozantinib:
    a. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with advanced RCC.
5. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
    b. In combination with ipilimumab: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks thereafter.

**Tazverik® (Tazemetostat) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:**

1. Treatment of adult patients with relapsed/refractory disease; and
2. *EZH2* mutation detected; and
3. Member must have received 2 lines of therapy or as subsequent therapy with no satisfactory alternative treatment options.

**Xalkori® (Crizotinib) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL) Diagnosis]:**

1. Members 1 to 21 years of age:
    a. Diagnosis of systemic ALCL that is anaplastic lymphoma kinase (ALK)-positive; and
    b. Relapsed or refractory disease; or
2. Members older than 21 years of age:
    a. Diagnosis of systemic ALCL that is ALK-positive; and
    b. Second-line or initial palliative intent therapy and subsequent therapy.

## Utilization Details of Lymphoma Medications: Calendar Year 2020

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **IBRUTINIB PRODUCTS** | | | | | |
| IMBRUVICA TAB 420MG | 40 | 6 | $518,998.30 | 6.67 | $12,974.96 |
| IMBRUVICA TAB 280MG | 14 | 3 | $181,673.64 | 4.67 | $12,976.69 |
| IMBRUVICA CAP 140MG | 6 | 2 | $83,401.90 | 3 | $13,900.32 |
| IMBRUVICA TAB 560MG | 4 | 2 | $51,899.54 | 2 | $12,974.89 |
| **SUBTOTAL** | **64** | **13** | **$835,973.38** | **4.92** | **$13,062.08** |
| **ACALABRUTINIB PRODUCTS** | | | | | |
| CALQUENCE CAP 100MG | 18 | 2 | $253,285.38 | 9 | $14,071.41 |
| **SUBTOTAL** | **18** | **2** | **$253,285.38** | **9** | **$14,071.41** |
| **VENETOCLAX PRODUCTS** | | | | | |
| VENCLEXTA TAB 100MG | 11 | 5 | $86,141.76 | 2.2 | $7,831.07 |
| VENCLEXTA TAB START PK | 1 | 1 | $2,660.75 | 1 | $2,660.75 |
| **SUBTOTAL** | **12** | **6** | **$88,802.51** | **2** | **$7,400.21** |
| **TOTAL** | **94** | **18*** | **$1,178,061.27** | **5.22** | **$12,532.57** |

CAP = capsule; TAB = tablet; START PK = starter pack
*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 | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| PEMBROLIZUMAB J9271 | 482 | 103 | $4,934,116.86 | 4.68 | $10,236.76 |
| NIVOLUMAB J9299 | 240 | 45 | $2,271,364.44 | 5.33 | $9,464.02 |
| BRENTUXIMAB VEDOTIN J9042 | 18 | 6 | $344,959.84 | 3 | $19,164.44 |
| OBINUTUZUMAB J9301 | 5 | 2 | $25,631.00 | 2.5 | $5,126.20 |
| RITUXIMAB-ABBS Q5115 | 3 | 2 | $2,252.55 | 1.5 | $750.85 |
| **TOTAL** | **748** | **158** | **$7,578,324.69** | **4.73** | **$10,131.45** |

+Total number of unduplicated claims.
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

[1] Freedman AS, Friedberg JW, Aster JC. Clinical Presentation and Diagnosis of Non-Hodgkin Lymphoma. *UpToDate*. Available online at: https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-non-hodgkin-lymphoma?search=non%20hodgkins%20lymphoma&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Last revised 09/27/2018. Last accessed 02/15/2021.
[2] Cancer Treatment Centers of America. Non-Hodgkin Lymphoma. Available online at: https://www.cancercenter.com/cancer-types/non-hodgkin-lymphoma/types. Last accessed 02/15/2021.
[3] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. *CA Cancer J Clin* 2018; 68:7-30.
[4] MD Anderson Cancer Center. Non-Hodgkin's Lymphoma. Available online at: https://www.mdanderson.org/cancer-types/non-hodgkins-lymphoma.html. Last accessed 02/15/2021.
[5] MD Anderson Cancer Center. Hodgkin's Lymphoma. Available online at: https://www.mdanderson.org/cancer-types/hodgkins-lymphoma.html. Last accessed 02/15/2021.
[6] Aster JC, Pozdnyakova O. Epidemiology, Pathologic Features, and Diagnosis of Classic Hodgkin Lymphoma. *UpToDate*. Available online at: https://www.uptodate.com/contents/epidemiology-pathologic-features-and-diagnosis-of-classic-hodgkin-lymphoma?search=hodgkins%20disease%20adult&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Last revised 06/11/2018. Last accessed 02/15/2021.
[7] Freedman AS, Aster JC. Clinical Manifestations, Pathologic Features, and Diagnosis of Peripheral T Cell Lymphoma, Not Otherwise Specified. *UpToDate*. Available online at: https://www.uptodate.com/contents/clinical-manifestations-pathologic-features-and-diagnosis-of-peripheral-t-cell-lymphoma-not-otherwise-specified?search=t-cell%20lymphoma&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Last revised 04/12/2019. Last accessed 02/15/2021.
[8] Lymphoma Research Foundation. T-Cell Lymphoma. Available online at: https://www.lymphoma.org/aboutlymphoma/nhl/tcell/. Last accessed 02/15/2021.
[9] U.S. Food and Drug Administration (FDA). Center For Drug Evaluation and Research Summary Review. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/208574Orig1s000,Orig2s000SumR.pdf. Issued 02/17/2020. Last accessed 02/11/2021.
[10] U.S. 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 02/09/2021. Last accessed 02/11/2021.
[11] Breyanzi® Prescribing Information. Bristol-Myers Squibb. Available online at: https://packageinserts.bms.com/pi/pi_breyanzi.pdf. Last revised 02/2021. Last accessed 02/11/2021.
[12] Monjuvi® Prescribing Information. MorphoSys US Inc. Available online at: https://www.monjuvi.com/pi/monjuvi-pi.pdf. Last revised 07/2020. Last accessed 02/11/2021.
[13] Tecartus™ Prescribing Information. Kite Pharma. Available online at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf. Last revised 07/2020. Last accessed 02/11/2021.
[14] Ukoniq™ Prescribing Information. TG Therapeutics Inc. Available online at: https://www.tgtherapeutics.com/prescribing-information/uspi-ukon.pdf. Last revised 02/2021. Last accessed 2/11/2021.

# Appendix M

# Calendar Year 2020 Annual Review of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)

**Oklahoma Health Care Authority**
**March 2021**

## Introduction[1,2,3,4]

**Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs):**
GEP-NETs are complex neoplasms that present many clinical challenges. GEP-NETs, also known as carcinoids and islet cell tumors, are tumors derived from neuroendocrine cells that occur anywhere along the gastrointestinal (GI) tract and comprise a heterogeneous family of neoplasms with a wide and complex spectrum of clinical behavior. These tumors have been considered rare diseases; however, data from the United States Surveillance Epidemiology and End Results show an increase of more than 400% in the incidence of GEP-NETs over a period of 29 years (1.09 per 100,000 population in 1973 to 5.25 per 100,000 population in 2004). GEP-NETs are more prevalent than many other tumors of the GI tract, including stomach and pancreatic carcinomas combined. The age at diagnosis is generally younger than for carcinomas (5$^{th}$ decade), and GEP-NETs may arise sporadically or as a result of hereditary predisposition. GEP-NETs have traditionally been divided into foregut, midgut, and hindgut tumors. Survival is dependent on stage and histology. In January 2018, the U.S. Food and Drug Administration (FDA) approved Lutathera® (lutetium Lu-177 dotatate) for the treatment of adult patients with somatostatin receptor-positive GEP-NETs.

**Neurotrophic Tyrosine Receptor Kinase (*NTRK*) Gene Fusions:**
The underlying genomic profile of a tumor has become increasingly important in oncology. Genomic alterations, such as *NTRK* gene fusions, are an area of focus. In tropomyosin receptor kinase (TRK) fusion cancer, the *NTRK* gene fuses with an unrelated gene, causing overexpression of the TRK protein. TRK fusion cancer is rare, but occurs in a broad range of tumor types with varying prevalence across both adult and pediatric patient populations. In November 2018, Vitrakvi® (larotrectinib) was approved by the FDA for use in adults and children with any solid tumor with an *NTRK* gene fusion without a known acquired resistance mutation, that is either metastatic or where surgical resection is likely to result in severe morbidity, and who have no other satisfactory alternative treatments or whose cancer has progressed following treatment. This represents the first new oncology drug to be approved based on a DNA test, instead of based on the tissue of origin.

## Current Prior Authorization Criteria

### Lutathera® (Lutetium Lu-177 Dotatate) Approval Criteria [Gastroenteropancreatic Neuroendocrine Tumor (GEP-NET) Diagnosis]:

1. Diagnosis of progressive locoregional advanced disease or metastatic disease; and
2. Positive imaging of somatostatin receptor; and
3. Used as second-line or subsequent therapy following progression on octreotide or lanreotide; or
4. May be used first-line for treatment of pheochromocytoma/ paraganglioma.

### Vitrakvi® (Larotrectinib) Approval Criteria [Solid Tumors with Neurotrophic Receptor Tyrosine Kinase (*NTRK*) Gene Fusion Diagnosis]:

1. Diagnosis of a solid tumor with a *NTRK* gene fusion without a known acquired resistance mutation; and
2. Disease is metastatic or surgical resection (or radioactive iodine refractory if thyroid carcinoma) is contraindicated; and
3. Documentation of no satisfactory alternative treatments or progression following acceptable alternative treatments.

## Utilization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib): Calendar Year 2020

**Calendar Year 2020 Comparison: Medical Claims**

| Calendar Year | *Total Members | †Total Claims | Total Cost | Cost/ Claim | Total Units |
|---|---|---|---|---|---|
| **2019** | 1 | 2 | $95,000.00 | $47,500.00 | 400 |
| **2020** | 1 | 3 | $125,844.00 | $41,948.00 | 600 |
| **% Change** | **0.00%** | **50.00%** | **32.47%** | **-11.69%** | **50.00%** |
| **Change** | **0** | **1** | **$30,844.00** | **-$5,552.00** | **200** |

*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Cost do not reflect rebated prices or net costs.

- The medical claims information provided is for Lutathera® (lutetium Lu-177 dotatate). There was no pharmacy SoonerCare utilization of Lutathera® (lutetium Lu-177 dotatate) in calendar year 2020. There was no SoonerCare utilization (pharmacy or medical) of Vitrakvi® (larotrectinib) in calendar year 2020.
- Due to the limited number of members utilizing Lutathera® during calendar year 2020, detailed demographic information could not be provided.

## Prior Authorization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)

There were 2 prior authorization requests submitted for 1 unique member for Lutathera® (lutetium Lu-177 dotatate) during calendar year 2020, both of which were approved. There were no prior authorization requests submitted for Vitrakvi® (larotrectinib) during calendar year 2020.

## Market News and Updates[5]

### Anticipated Patent Expiration(s):

- Vitrakvi® (larotrectinib oral capsules): November 2035
- Vitrakvi® (larotrectinib oral solution): April 2037
- Lutathera® (lutetium Lu-177 dotatate intravenous solution): July 2038

## Recommendations

The College of Pharmacy does not recommend any changes to the current Lutathera® (lutetium Lu-177 dotatate) or Vitrakvi® (larotrectinib) prior authorization criteria at this time.

---

[1] Díez M, Teulé A, Salazar R. Gastroenteropancreatic Neuroendocrine Tumors: Diagnosis and Treatment. *Ann Gastroenterol* 2013; 26(1):29-36.
[2] Chan JA, Kulke M. Metastatic Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors: Presentation, Prognosis, Imaging, and Biochemical Monitoring. *UpToDate*. Available online at: https://www.uptodate.com/contents/metastatic-well-differentiated-gastroenteropancreatic-neuroendocrine-tumors-presentation-prognosis-imaging-and-biochemical-monitoring. Last revised 02/2021. Last accessed 02/12/2021.
[3] TRK Fusion Cancer. Bayer and Loxo Oncology, Inc. Available online at: https://trkcancer.com/. Last revised 09/2018. Last accessed 02/12/2021.
[4] Savarese D, Zand J. What's New in Drug Therapy. *UpToDate*. Available online at: https://www.uptodate.com/contents/whats-new-in-drug-therapy. Last revised 02/15/2019. Last accessed 02/12/2021.
[5] 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 02/2021. Last accessed 02/10/2021.

# Appendix N

# Calendar Year 2020 Annual Review of Hemophilia Medications and 30-Day Notice to Prior Authorize Sevenfact® [Coagulation Factor VIIa (Recombinant)-jncw]

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Adynovate®, Afstyla®, Alprolix®, Eloctate®, Esperoct®, Idelvion®, Jivi®, and Rebinyn® Approval Criteria:**

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A patient-specific, clinically significant reason why the member cannot use the following must be provided:
    a. Hemophilia A: Advate® or current factor VIII replacement product; or
    b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of 1 year.

**Coagadex® [Coagulation Factor X (Human)] Approval Criteria:**

1. An FDA approved indication; and
2. Coagadex® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of 1 year.

**Corifact® [Factor XIII Concentrate (Human)] and Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)] Approval Criteria:**

1. An FDA approved indication; and
2. Corifact® or Tretten® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of 1 year.

**Feiba® (Anti-Inhibitor Coagulation Complex) Approval Criteria:**

1. Member must be diagnosed with hemophilia A or B with an inhibitor; and
2. Feiba® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

**Hemlibra® (Emicizumab-kxwh) Approval Criteria:**

1. Member must have a diagnosis of hemophilia A; and
2. Hemlibra® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. Prescriber must be able to monitor appropriate blood clotting tests and levels utilizing testing which accounts for the interaction of Hemlibra® and blood factors by following the Medical and Scientific Advisory Council (MASAC) guidance; and
4. For members with hemophilia A with an inhibitor to factor VIII:
    a. Member must have failed immune tolerance induction (ITI) or is not a good candidate for ITI; and
    b. Member's hemophilia cannot be managed without the use of bypassing agent(s) (e.g., Feiba®, NovoSeven® RT) as prophylaxis for prevention of bleeding episodes, or the member is unable to maintain venous access for daily infusions; and
    c. Member's hemophilia is not currently controlled with the use of bypassing agent(s); and
    d. Prescriber must counsel member and/or caregiver on the risks of utilizing Feiba® for breakthrough bleeding while on Hemlibra®, and member should be monitored closely if any bypassing agent is given; or

5. For members with hemophilia A without an inhibitor:
    a. Member's current prophylaxis therapy is not adequate to prevent spontaneous bleeding episodes, or the member is unable to maintain venous access for prophylactic infusions; and
    b. Treatment plan must be made to address breakthrough bleeds and procedures; and
    c. Routine lab screenings must occur for factor VIII inhibitor while using Hemlibra® since this would change the treatment plan for bleeds and procedures: and
6. First dose must be given in a health care facility; and
7. In order to calculate appropriate dosing, the member's recent weight must be provided and been taken within the last 3 months; and
8. Initial approvals will be for 3 months of therapy. Subsequent approvals will be for the duration of 1 year, if there has been a decrease in the member's spontaneous bleeding episodes since initiating Hemlibra® treatment.

**NovoSeven® RT [Coagulation Factor VIIa (Recombinant)] Approval Criteria:**

1. An FDA approved diagnosis of 1 of the following:
    a. Hemophilia A or B with inhibitors; or
    b. Congenital factor VII deficiency; or
    c. Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets; or
    d. Acquired hemophilia; and
2. NovoSeven® RT must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

**Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence] Approval Criteria:**

1. An FDA approved indication; and
2. Obizur® must be prescribed by a hematologist specializing in hemophilia or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use Feiba® (anti-inhibitor coagulant complex) or NovoSeven® RT [coagulation factor VIIa (recombinant)] must be provided; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approval will be for the duration of the half-life study. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of 1 year.

**Standards-of-Care for Pharmacies Providing Factor Replacement Products** can be found on the Oklahoma Health Care Authority (OHCA) website on the Pharmacy Prior Authorization (PA) page in the Hemophilia Therapeutic Category at https://oklahoma.gov/ohca.

## Utilization of Hemophilia Medications: Calendar Year 2020

### Comparison of Calendar Years: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Total Units | Cost Per Utilizer Per Year |
|---|---|---|---|---|---|---|
| **2019** | 88 | 666 | $19,876,887.41 | $29,845.18 | 10,911,256 | $225,873.72 |
| **2020** | 96 | 772 | $16,552,358.34 | $21,440.88 | 6,681,270 | $172,420.40 |
| **% Change** | **9.1%** | **15.9%** | **-16.7%** | **-28.2%** | **-38.8%** | **-23.7%** |
| **Change** | **8** | **106** | **-$3,324,529.07** | **-$8,404.30** | **-4,229,986** | **-$53,453.52** |

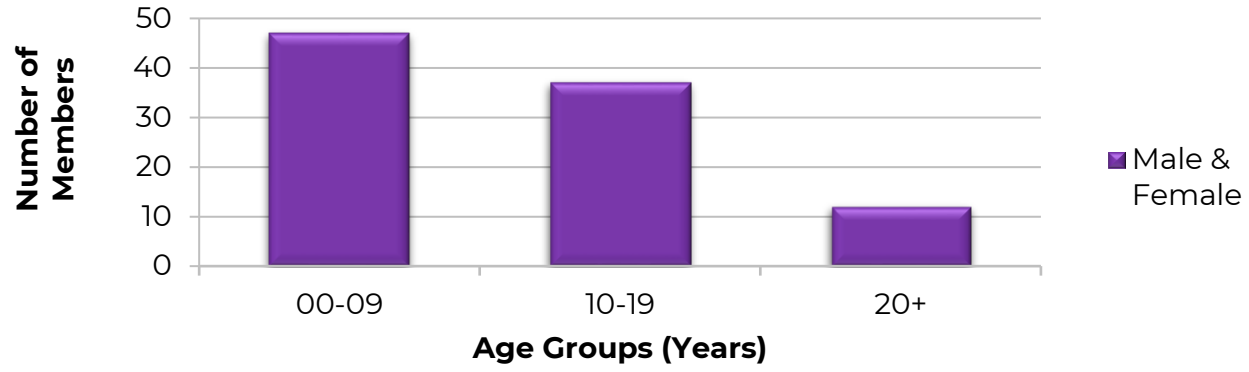
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

### Comparison of Calendar Years: Medical Claims

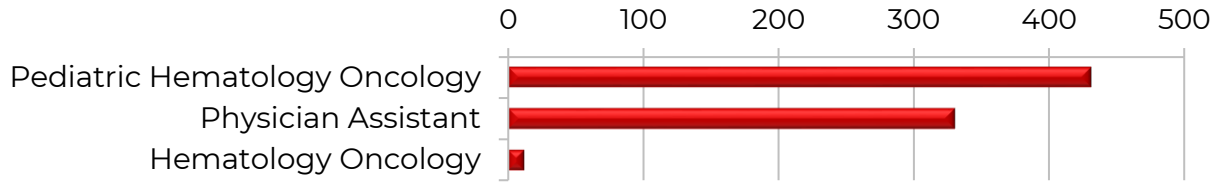
| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Total Units | Cost Per Utilizer Per Year |
|---|---|---|---|---|---|---|
| **2019** | 7 | 60 | $1,034,949.92 | $17,249.17 | 505,222 | $148,849.99 |
| **2020** | 8 | 46 | $752,728.61 | $16,363.66 | 353,337 | $94,091.07 |
| **% Change** | **14.3%** | **-23.3%** | **-27.3%** | **-5.1%** | **-30.1%** | **-36.8%** |
| **Change** | **1** | **14** | **-$282,221.31** | **-$885.51** | **-151,885** | **-$54,758.92** |

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

### Demographics of Members Utilizing Hemophilia Medications

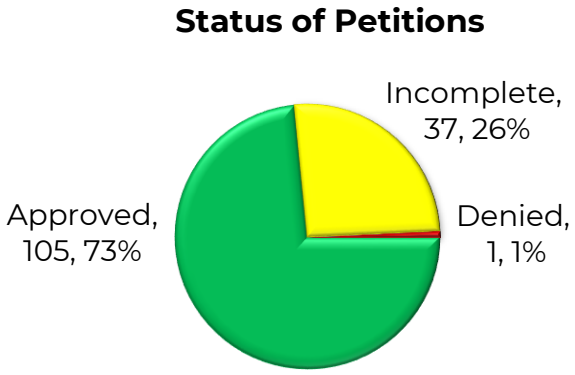



### Top Prescriber Specialties of Hemophilia Medications by Number of Claims



## Prior Authorization of Hemophilia Medications

There were 143 prior authorization requests for 44 unique members submitted for hemophilia medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.




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

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

- **April 2020:** The FDA approved Sevenfact® [coagulation factor VIIa (recombinant)-jncw] for the treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with hemophilia A or B without inhibitors.

**News:**

- **August 2020:** The World Federation of Hemophilia (WFH) published The WFH Guidelines for the Management of Hemophilia, 3rd edition. Since the 2012 edition there have been multiple advancements in the management of hemophilia from genetic assessment to innovative new treatments. Some of those treatments have been brought to market as extended-half life products and a bispecific antibody while others are still in development, including products with novel mechanisms of action and gene therapy.

**Pipeline:**

- **Concizumab:** Concizumab is a monoclonal antibody for hemophilia A or B, irrespective of inhibitor status, which is engineered to create factor X through a series of chemical and molecular reactions. In March 2020, 3 clinical trials [(2) Phase 3 and (1) Phase 2] were placed on hold in response to non-fatal thrombotic events in 3 patients enrolled in an ongoing Phase 3 program. Novo Nordisk announced in August 2020, clinical trials would resume with new safety measures and guidelines in place.

- **Marstacimab:** Marstacimab is a monoclonal antibody designed to treat hemophilia A and B patients, with or without inhibitors, by blocking tissue factor pathway inhibitor (TFPI). Pfizer announced in November 2020, the first participant in the Phase 3 BASIS trial had been dosed.
- **Marzeptacog Alfa (Activated):** Marzeptacog alfa (activated) is a next-generation recombinant factor VIIa variant, administered subcutaneously. In December 2020, marzeptacog alfa (activated) was granted Fast Track designation by the FDA. Catalyst Biosciences announced a Phase 3 clinical trial, CRIMSON 1, which will evaluate the safety and efficacy in adolescents and adults with congenital hemophilia A and B with inhibitors.
- **Gene Therapy:**
  - **Valoctocogene Roxaparvovec:** In August 2020, the FDA rejected BioMarin Pharmaceutical's New Drug Application (NDA) for valoctocogene roxaparvovec, an adeno-associated virus (AAV) vector-mediated gene transfer of human factor VIII (FVIII) intended for patients with hemophilia A, citing the need for longer-term data. The FDA is requesting the completion of a Phase 3 trial with 2-year follow-up safety and efficacy data on all study participants. The NDA was based on a 3-year Phase 1/2 data and an interim analysis of the Phase 3 data. In January 2021, BioMarin announced positive topline results from the ongoing Phase 3 clinical trial, GENEr8-1 which includes 134 participants. With a median follow-up of 71.6 weeks, the annualized bleed rate (ABR) was decreased by 84% which was found to be statistically significant ($P<0.0001$).
  - **Giroctocogene Fitelparvovec:** Giroctocogene fitelparvovec is a recombinant AAV which delivers gene codes to produce FVIII in patients with hemophilia A. In October 2020, Pfizer and Sangamo announced the first patient had been dosed in the Phase 3 AFFINE trial which is a multicenter, single arm trial to evaluate the safety and efficacy. The primary endpoint is the impact on ABR. The trial will follow and evaluate participants for a 5-year period to determine durability and efficacy.
  - **Etranacogene Dezaparvovec:** In November 2020, uniQure announced new data from the Phase 3 HOPE-B trial of etranacogene dezaparvovec, an AAV carrying a gene cassette with the Padua variant of factor IX (FIX) intended for patients with hemophilia B. All 54 participants had an increase in FIX activity from a 2% mean to a 37.2% mean at 26 weeks. Then in December 2020, the FDA placed a clinical hold on the HOPE-3 trial related to a possible serious adverse event associated with a preliminary diagnosis of hepatocellular carcinoma in 1 patient.

## Sevenfact® [Coagulation Factor VIIA (Recombinant)-jncw] Product Summary[1213]

**Indication:** Sevenfact® is a recombinant coagulation factor VIIa concentrate, indicated for the treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with hemophilia A or B with inhibitors.

**Dosing:**

- Mild-to-Moderate Bleeding Episodes:
  - 75mcg/kg given intravenously (IV) and repeated every 3 hours until hemostasis is achieved; or
  - Initial dose of 225mcg/kg IV and if hemostasis is not achieved in 9 hours, then additional doses at 75mcg/kg given every 3 hours as needed.
- Severe Bleeding Episodes: 225mcg/kg IV, followed if necessary 6 hours later with 75mcg/kg every 2 hours.

**Cost Comparison:**

| Factor Product | Unit Cost* | Dosing for Severe Bleeding** | Cost per 24 hours |
|---|---|---|---|
| Sevenfact® | $2.29 | 225mcg/kg, then 75 mcg/kg every 2 hours | $144,270 |
| NovoSeven® RT | $2.40 | 90mcg/kg every 2 hours | $181,440 |

*Wholesale Acquisition Cost (WAC) per 1 mcg
**Dosing per 70kg patient

## Recommendations

The Oklahoma Health Care Authority recommends the prior authorization of Sevenfact® [coagulation factor VIIA (recombinant)-jncw] with the following criteria:

**Sevenfact® [Coagulation Factor VIIA (Recombinant)-jncw] Approval Criteria:**

1. An FDA approved diagnosis; and
2. Sevenfact® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

## Utilization Details of Hemophilia Medications: Calendar Year 2020

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **HEMLIBRA PRODUCTS** | | | | | |
| HEMLIBRA INJ 60MG/0.4ML | 135 | 21 | $2,591,186.42 | $19,193.97 | 6.43 |
| HEMLIBRA INJ 30MG/ML | 116 | 13 | $939,575.25 | $8,099.79 | 8.92 |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| HEMLIBRA INJ 105MG/0.7ML | 68 | 11 | $2,566,326.00 | $37,740.09 | 6.18 |
| HEMLIBRA INJ 150MG/ML | 21 | 5 | $768,840.61 | $36,611.46 | 4.20 |
| **SUBTOTAL** | **340** | **50** | **$6,865,928.28** | **$20,193.91** | **6.80** |
| **KOGENATE PRODUCTS** | | | | | |
| KOGENATE FS INJ 2000U | 49 | 14 | $1,440,386.62 | $29,395.65 | 3.50 |
| KOGENATE FS INJ 500U | 36 | 6 | $296,567.09 | $8,237.97 | 6.00 |
| KOGENATE FS INJ 1000U | 17 | 7 | $169,141.85 | $9,949.52 | 2.43 |
| KOGENATE FS INJ 3000U | 13 | 2 | $878,877.25 | $67,605.94 | 6.50 |
| KOGENATE FS INJ 250U | 1 | 1 | $376.48 | $376.48 | 1.00 |
| **SUBTOTAL** | **116** | **30** | **$2,785,349.29** | **$24,011.63** | **3.87** |
| **ADVATE PRODUCTS** | | | | | |
| ADVATE INJ 2000U | 26 | 8 | $909,215.04 | $34,969.81 | 3.25 |
| ADVATE INJ 1500U | 20 | 9 | $405,503.95 | $20,275.20 | 2.22 |
| ADVATE INJ 1000U | 16 | 5 | $228,433.91 | $14,277.12 | 3.20 |
| ADVATE INJ 3000U | 12 | 2 | $446,065.75 | $37,172.15 | 6.00 |
| ADVATE INJ 500U | 7 | 4 | $21,759.94 | $3,108.56 | 1.75 |
| ADVATE INJ 250U | 4 | 2 | $4,326.65 | $1,081.66 | 2.00 |
| **SUBTOTAL** | **85** | **30** | **$2,015,305.24** | **$23,709.47** | **2.83** |
| **ALPROLIX PRODUCTS** | | | | | |
| ALPROLIX INJ 3000U | 13 | 2 | $378,023.30 | $29,078.72 | 6.50 |
| ALPROLIX INJ 1000U | 12 | 1 | $155,172.12 | $12,931.01 | 12.00 |
| ALPROLIX INJ 4000U | 11 | 1 | $552,047.96 | $50,186.18 | 11.00 |
| ALPROLIX INJ 500U | 9 | 2 | $50,542.47 | $5,615.83 | 4.50 |
| ALPROLIX INJ 2000U | 5 | 2 | $48,461.20 | $9,692.24 | 2.50 |
| ALPROLIX INJ 250U | 4 | 2 | $7,194.11 | $1,798.53 | 2.00 |
| **SUBTOTAL** | **54** | **10** | **$1,191,441.16** | **$22,063.73** | **5.40** |
| **NUWIQ PRODUCTS** | | | | | |
| NUWIQ KIT 1000U | 13 | 4 | $129,539.45 | $9,964.57 | 3.25 |
| NUWIQ KIT 500U | 5 | 4 | $34,330.42 | $6,866.08 | 1.25 |
| NUWIQ KIT 3000U | 4 | 1 | $360,766.15 | $90,191.54 | 4.00 |
| NUWIQ KIT 2500U | 4 | 1 | $313,991.72 | $78,497.93 | 4.00 |
| NUWIQ KIT 250U | 4 | 4 | $3,632.51 | $908.13 | 1.00 |
| NUWIQ KIT 2000U | 2 | 1 | $45,122.29 | $22,561.15 | 2.00 |
| **SUBTOTAL** | **32** | **15** | **$887,382.54** | **$27,730.70** | **2.13** |
| **ADYNOVATE PRODUCTS** | | | | | |
| ADYNOVATE INJ 2000U | 9 | 2 | $288,631.42 | $32,070.16 | 4.50 |
| ADYNOVATE INJ 1500U | 6 | 1 | $166,846.80 | $27,807.80 | 6.00 |
| ADYNOVATE INJ 3000U | 6 | 1 | $377,726.16 | $62,954.36 | 6.00 |
| **SUBTOTAL** | **21** | **4** | **$833,204.38** | **$39,676.40** | **5.25** |
| **WILATE PRODUCTS** | | | | | |
| WILATE INJ 1000-1000U | 26 | 5 | $540,310.67 | $20,781.18 | 5.20 |
| WILATE INJ 500-500U | 14 | 5 | $84,292.88 | $6,020.92 | 2.80 |
| **SUBTOTAL** | **40** | **10** | **$624,603.55** | **$15,615.09** | **4.00** |
| **ELOCTATE PRODUCTS** | | | | | |
| ELOCTATE INJ 1500U | 8 | 1 | $236,923.38 | $29,615.42 | 8.00 |
| ELOCTATE INJ 1000U | 2 | 2 | $67,077.29 | $33,538.65 | 1.00 |
| ELOCTATE INJ 500U | 2 | 2 | $11,747.24 | $5,873.62 | 1.00 |
| **SUBTOTAL** | **12** | **5** | **$315,747.91** | **$26,312.33** | **2.40** |
| **FEIBA PRODUCTS** | | | | | |
| FEIBA INJ 2500U | 2 | 1 | $288,831.28 | $144,415.64 | 2.00 |
| **SUBTOTAL** | **2** | **1** | **$288,831.28** | **$144,415.64** | **2.00** |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **KOVALTRY PRODUCTS** | | | | | |
| KOVALTRY INJ 1000U | 6 | 1 | $129,140.10 | $21,523.35 | 6.00 |
| KOVALTRY INJ 500U | 3 | 1 | $71,543.35 | $23,847.78 | 3.00 |
| **SUBTOTAL** | **9** | **2** | **$200,683.45** | **$22,298.16** | **4.50** |
| **ALPHANATE PRODUCTS** | | | | | |
| ALPHANATE INJ VWF/HUM 1500U | 5 | 1 | $91,787.83 | $18,357.57 | 5.00 |
| ALPHANATE INJ VWF/HUM 1000U | 4 | 1 | $76,630.60 | $19,157.65 | 4.00 |
| ALPHANATE INJ VWF/HUM 250U | 2 | 1 | $7,756.66 | $3,878.33 | 2.00 |
| ALPHANATE INJ VWF/HUM 500U | 1 | 1 | $1,114.03 | $1,114.03 | 1.00 |
| ALPHANATE INJ VWF/HUM 2000U | 1 | 1 | $3,698.40 | $3,698.40 | 1.00 |
| **SUBTOTAL** | **13** | **5** | **$180,987.52** | **$13,922.12** | **2.60** |
| **NOVOSEVEN PRODUCTS** | | | | | |
| NOVOSEVEN RT INJ 1MG | 4 | 3 | $22,069.23 | $5,517.31 | 1.33 |
| NOVOSEVEN RT INJ 5MG | 3 | 2 | $119,393.82 | $39,797.94 | 1.50 |
| NOVOSEVEN RT INJ 2MG | 1 | 1 | $21,577.91 | $21,577.91 | 1.00 |
| **SUBTOTAL** | **8** | **6** | **$163,040.96** | **$20,380.12** | **1.33** |
| **IDELVION PRODUCTS** | | | | | |
| IDELVION SOL 1000U | 4 | 1 | $41,993.86 | $10,498.47 | 4.00 |
| IDELVION SOL 2000U | 2 | 1 | $18,562.26 | $9,281.13 | 2.00 |
| IDELVION SOL 500U | 1 | 1 | $4,704.45 | $4,704.45 | 1.00 |
| **SUBTOTAL** | **7** | **3** | **$65,260.57** | **$9,322.94** | **2.33** |
| **HUMATE PRODUCTS** | | | | | |
| HUMATE-P SOL 500-1200U | 6 | 5 | $7,829.30 | $1,304.88 | 1.20 |
| HUMATE-P SOL 250-600U | 5 | 5 | $3,935.74 | $787.15 | 1.00 |
| HUMATE-P SOL 2400U | 1 | 1 | $25,817.90 | $25,817.90 | 1.00 |
| **SUBTOTAL** | **12** | **11** | **$37,582.94** | **$3,131.91** | **1.09** |
| **CORIFACT PRODUCTS** | | | | | |
| CORIFACT KIT 1000-1600U | 3 | 1 | $33,891.34 | $11,297.11 | 3.00 |
| **SUBTOTAL** | **3** | **1** | **$33,891.34** | **$11,297.11** | **3.00** |
| **RIXUBIS PRODUCTS** | | | | | |
| RIXUBIS INJ 2000U | 3 | 3 | $19,697.26 | $6,565.75 | 1.00 |
| RIXUBIS INJ 1000U | 2 | 2 | $4,354.65 | $2,177.33 | 1.00 |
| RIXUBIS INJ 500U | 1 | 1 | $1,405.40 | $1,405.40 | 1.00 |
| **SUBTOTAL** | **6** | **6** | **$25,457.31** | **$4,242.89** | **1.00** |
| **REBINYN PRODUCTS** | | | | | |
| REBINYN SOL 1000U | 1 | 1 | $3,980.91 | $3,980.91 | 1.00 |
| REBINYN SOL 2000U | 1 | 1 | $8,825.91 | $8,825.91 | 1.00 |
| **SUBTOTAL** | **2** | **2** | **$12,806.82** | **$6,403.41** | **1.00** |
| **KOATE PRODUCTS** | | | | | |
| KOATE INJ 1000U | 4 | 1 | $10,202.99 | $2,550.75 | 4.00 |
| KOATE INJ 500U | 2 | 1 | $1,667.12 | $833.56 | 2.00 |
| **SUBTOTAL** | **6** | **2** | **$11,870.11** | **$1,978.35** | **3.00** |
| **BENEFIX PRODUCTS** | | | | | |
| BENEFIX INJ 2000U | 2 | 1 | $10,622.82 | $5,311.41 | 2.00 |
| **SUBTOTAL** | **2** | **1** | **$10,622.82** | **$5,311.41** | **2.00** |
| **RIASTAP PRODUCTS** | | | | | |
| RIASTAP SOL 1GM | 1 | 1 | $1,269.77 | $1,269.77 | 1.00 |
| **SUBTOTAL** | **1** | **1** | **$1,269.77** | **$1,269.77** | **1.00** |
| **FIBRYGA PRODUCTS** | | | | | |
| FIBRYGA INJ 1GM | 1 | 1 | $1,091.10 | $1,091.10 | 1.00 |
| **SUBTOTAL** | **1** | **1** | **$1,091.10** | **$1,091.10** | **1.00** |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **TOTAL** | **772** | **96*** | **$16,552,358.34** | **$21,440.88** | **8.04** |

FS = formulated with sucrose; HUM = human; INJ = injection; RT = recombinant; SOL = solution; U = units; VMF = von Willebrand factor
*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 |
|---|---|---|---|---|
| J7187 VON WILLEBRAND FACTOR COMPLEX | 3 | 2 | $8,084.01 | $2,694.67 |
| J7189 FACTOR VIIA RT | 31 | 2 | $726,384.42 | $23,431.76 |
| J7192 FACTOR VIII RT | 11 | 3 | $18,061.21 | $1,641.93 |
| J7200 FACTOR IX RT | 1 | 1 | $198.97 | $198.97 |
| **TOTAL** | **46⁺** | **8*** | **$770,789.82** | **$16,363.66** |

RT = recombinant
⁺Total number of unduplicated claims.
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA). FDA Approves Additional Treatment for Adults and Adolescents with Hemophilia A or B and Inhibitors. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-additional-treatment-adults-and-adolescents-hemophilia-or-b-and-inhibitors#:~:text=The%20U.S.%20Food%20and%20Drug%20Administration%20today%20approved,hemophilia%20A%20or%20B%20with%20inhibitors%20%28neutralizing%20antibodies%29. Issued 04/01/2020. Last accessed 02/15/2021.

[2] Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd Edition. *Haemophilia* 2020; 26(S6):1-158. doi: 10.1111/hae.14046.

[3] National Hemophilia Foundation. Three Concizumab Trials Halted by Novo Nordisk. Available online at https://www.hemophilia.org/news/three-concizumab-trials-halted-by-novo-nordisk. Issued 03/17/2020. Last accessed 02/15/2021.

[4] Adams, B. Novo Nordisk's Concizumab Trials Can Resume After Safety Trial. *Fierce Biotech*. Available online at https://www.fiercebiotech.com/biotech/novo-nordisk-s-concizumab-trials-can-resume-after-safety-trial-halt. Issued 08/13/2020. Last accessed 02/15/2021

[5] National Hemophilia Foundation. Pfizer Announces First Participant Dosed Phase 3 Study of Marstacimab. Available online at: https://www.hemophilia.org/news/pfizer-announces-first-participant-dosed-phase-3-study-of-marstacimab. Issued 11/30/2020. Last accessed 02/16/2021.

[6] Catalyst Biosciences, Inc. Catalyst Biosciences Receives FDA Fast Track Designation for Subcutaneous MarzAA for the Treatment of Episodic Bleeding in Hemophilia A or B with Inhibitors. Available online at: https://ir.catalystbiosciences.com/news-releases/news-release-details/catalyst-biosciences-receives-fda-fast-track-designation. Issued 12/02/2020. Last accessed 02/16/2021.

[7] Humer, C. U.S. FDA Rejects BioMarin Hemophilia A Gene Therapy, Shares Dive. *Reuters*. Available online at: https://www.reuters.com/article/us-biomarin-pharma-fda-idUSKCN25F1H6. Issued 08/19/2020. Last accessed 02/16/2021.

[8] BioMarin Pharmaceutical, Inc. BioMarin Announces Positive Phase 3 Gene Therapy Trial Results in Adults with Severe Hemophilia A; Study Met All Primary and Secondary Efficacy Endpoints in One-Year Data Set. Available online at: https://investors.biomarin.com/2021-01-10-BioMarin-Announces-Positive-Phase-3-Gene-Therapy-Trial-Results-in-Adults-with-Severe-Hemophilia-A-Study-Met-All-Primary-and-Secondary-Efficacy-Endpoints-in-One-Year-Data-Set. Issued 01/10/2021. Last accessed 02/16/2021.

[9] National Hemophilia Foundation. First Patient Dosed in Phase 3 Gene Therapy Trial. Available online at: https://www.hemophilia.org/news/first-patient-dosed-in-phase-3-gene-therapy-trial. Issued 10/12/2020. Last accessed 02/16/2021.

[10] National Hemophilia Foundation. UniQure Announces Positive Results from Phase 3 Gene Therapy Trial. Available online at: https://www.hemophilia.org/news/uniqure-announces-positive-results-from-phase-3-gene-therapy-trial. Issued 11/20/2020. Last accessed 02/16/2021.

[11] UniQure. UniQure's Hemophilia B Program has Been Placed on Clinical Hold by the U.S. FDA. Available at: http://www.uniqure.com/patients/clinical-hold-hemophilia-b.php. Issued 12/23/2020. Last accessed 02/16/2021.

[12] Sevenfact® Prescribing Information. Hema Biologics, LLC. Available at: https://www.fda.gov/media/136610/download. Last revised 04/2020. Last accessed 02/16/2021.

[13] NovoSeven® RT Prescribing information. Novo Nordisk. Available at: https://www.novosevenrtpro.com/content/novosevenrtpro/en/dosing-and-administration/quick-reference/bleeding-episodes.html. Last revised 7/2020. Last accessed 2/24/21.

# Appendix O

# Calendar Year 2020 Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Bafiertam™ (Monomethyl Fumarate), Kesimpta® (Ofatumumab), and Zeposia® (Ozanimod)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Multiple Sclerosis (MS) Interferon Medications Approval Criteria:**

1. An FDA approved diagnosis of clinically isolated syndrome, relapsing forms of MS, or secondary progressive forms of MS; and
2. Authorization of Tier-2 medications requires previous failure of preferred Tier-1 medication(s) defined as:
   a. Occurrence of an exacerbation after 6 months; or
   b. Significant increase in magnetic resonance imaging (MRI) lesions after 6 months; or
   c. Adverse reactions or intolerable side effects; and
3. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
4. Compliance will be checked for continued approval every 6 months.

| Multiple Sclerosis (MS) Interferon Medications | |
|---|---|
| **Tier-1** | **Tier-2** |
| interferon β - 1a (Avonex®) | interferon β - 1a (Plegridy®) |
| interferon β - 1b (Betaseron®) | interferon β - 1a (Rebif®) |
| | interferon β - 1b (Extavia®) |

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).

**Ampyra® (Dalfampridine) Approval Criteria:**

1. An FDA approved indication to improve walking in adult members with multiple sclerosis (MS); and
2. Kurtzke Expanded Disability Status Scale (EDSS) score between 3 and 7.5; and
3. Initial approvals will be for the duration of 90 days. If the member has responded well to treatment and the prescriber states the member has shown improvement or the drug was effective, the member may receive authorization for 1 year; and
4. A quantity limit of 60 tablets for 30 days will apply; and
5. Ampyra® may be used with other MS therapies.

**Aubagio® (Teriflunomide) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. All of the following will be required for initiation of treatment:
    a. Verification that female members are not pregnant and are currently using reliable contraception; and
    b. Verification that the member has no active infection(s); and
    c. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
    d. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
    e. Blood pressure (BP) measurement and verification that BP is being monitored; and
    f. Verification that the member does not have tuberculosis (TB), or completion of standard medical treatment for members with TB; and
4. Initial approvals of Aubagio® will be for 6 months, after which time all of the following will be required for further approval:
    a. Medication compliance; and
    b. Repeat CBC and verification that counts are acceptable to the prescriber; and
    c. Repeat LFTs and verification that levels are acceptable to the prescriber; and
    d. Verification that female members are not pregnant and will continue using reliable contraception; and
    e. Verification that BP and signs of renal failure are being monitored; and
5. Compliance will be checked for continued approval every 6 months; and
6. A quantity limit of 30 tablets per 30 days will apply.

**Copaxone® (Glatiramer Acetate) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
3. Approvals for the generic formulation of either strength of Copaxone®, including Glatopa®, will require a patient-specific, clinically significant

reason why the member cannot use the brand formulation (brand formulation is preferred); and
4. Compliance will be checked for continued approval every 6 months.

**Gilenya® (Fingolimod) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS)*, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and
(*The manufacturer of Gilenya® has provided a supplemental rebate to remove the requirement of "at least 1 relapse in the previous 12 months, or transitioning from existing MS therapy"; however, Gilenya® will follow the original criteria if the manufacturer chooses not to participate in supplemental rebates); and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. The first dose should be observed in the prescriber's office for signs and symptoms of bradycardia for 6 hours after the first dose; and
4. Verification from the prescriber that member has no active infection(s); and
5. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
6. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
7. Compliance will be checked for continued approval every 6 months.

**Lemtrada® (Alemtuzumab) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease, in adults; and
2. Member must have had an inadequate response to 2 or more medications indicated for the treatment of MS; and
    a. Lemtrada® must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for 2 hours after each infusion; and
3. The prescriber must agree to monitor complete blood counts (CBC) with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of Lemtrada®; and
4. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada® therapy; and

5. Member, prescriber, pharmacy, and health care facility must all enroll in the Lemtrada® REMS Program and maintain enrollment throughout therapy.

**Mavenclad® (Cladribine) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease, in adults; and
2. Requests for use in patients with clinically isolated syndrome will not generally be approved; and
3. Member must have had at least 1 relapse in the previous 12 months; and
4. Member must have had an inadequate response to 2 or more medications indicated for the treatment of MS; and
5. Prescriber must confirm the member does not have any contraindications for use of cladribine; and
6. Prescriber must confirm the member does not have an active malignancy; and
7. Prescriber must confirm that females members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
8. Prescriber must attest that female and male members of reproductive potential plan to use effective contraception during cladribine dosing and for 6 months after the last dose in each treatment course; and
9. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
10. Verification from the prescriber that member has no active infection(s); and
11. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
12. 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
13. Quantity limits according to package labeling will apply.

**Mayzent® (Siponimod) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Member must have been assessed for CYP2C9 genotype:
    a. Members with a CYP2C9*3/*3 genotype will not generally be approved; or
    b. Members with a CYP2C9*1/*3 or *2/*3 genotype will not be approved for doses exceeding 1mg per day; or

    c. All other genotypes (CYP2C9*1/*1, *1/*2, or *2/*2) will be approved for 2mg per day; and
3. Member must not have any contraindications for use of siponimod including:
    a. CYP2C9*3/*3 genotype; or
    b. Experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or class III/IV HF in the last 6 months; or
    c. Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless member has a functioning pacemaker; and
4. Member must not have received prior treatment with alemtuzumab; and
5. Verification from the prescriber that member has no active infection(s); and
6. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
7. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
8. Ophthalmic evaluation and verification that member will be monitored for changes in vision throughout therapy; and
9. Verification from the prescriber that the member has been assessed for medications and conditions that cause reduction in heart rate (HR) or AV conduction delays and that the member will be followed with appropriate monitoring per package labeling; and
10. Verification from the prescriber that the member has been assessed for previous confirmed history of chickenpox or vaccination against varicella. Members without history of chickenpox or varicella vaccination should receive a full course of the varicella vaccine prior to commencing treatment with Mayzent®; and
11. Verification from the prescriber that members with sinus bradycardia (HR <55 beats per minute), first- or second-degree AV block (Mobitz type I), or a history of HF or MI will be monitored following the first dose for a minimum of 6 hours; and
12. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
13. Female members of reproductive potential must be willing to use effective contraception during treatment with Mayzent® and for at least 10 days after discontinuing treatment; and
14. Member must have had an inadequate response to Gilenya® (fingolimod) or a patient-specific, clinically significant reason why fingolimod is not appropriate for the member must be provided; and
15. Compliance will be checked for continued approval every 6 months; and

16. Quantity limits according to package labeling will apply.

**Ocrevus® (Ocrelizumab) Approval Criteria:**

1. An FDA approved diagnosis of primary progressive forms of multiple sclerosis (MS) or relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Ocrevus® must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for 1 hour after each infusion; and
4. Prescriber must verify hepatitis B virus (HBV) testing has been performed prior to initiating Ocrevus® therapy and member does not have active HBV; and
5. Verification from the prescriber that member has no active infection(s); and
6. Verification from the prescriber that female members are not currently pregnant and will use contraception while receiving Ocrevus® therapy and for 6 months after the last infusion of Ocrevus®; and
7. Compliance will be checked for continued approval.

**Tecfidera® (Dimethyl Fumarate) Approval Criteria:**

1. An FDA approved diagnosis of clinically isolated syndrome, relapsing forms of multiple sclerosis (MS), or secondary progressive forms of MS in adults; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Compliance will be checked for continued approval every 6 months; and
7. A quantity limit of 60 tablets per 30 days will apply.

**Tysabri® (Natalizumab) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, or Crohn's disease in adults; and
2. For a diagnosis of MS, the following criteria will apply:

a. Prescriber must be a neurologist or be an advanced care practitioner with a supervising prescriber that is a neurologist; and
b. Approvals will not be granted for concurrent use with other disease-modifying therapies; or

3. For a diagnosis of Crohn's disease, the following criteria will apply:
   a. Treatment with at least 2 different first-line therapeutic categories for Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first- and second-line alternatives must be provided; and
4. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program; and
5. Compliance will be checked for continued approval every 6 months.

**Vumerity® (Diroximel Fumarate) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no serious active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Verification from the prescriber that member does not have moderate or severe renal impairment; and
7. Verification from the prescriber that the member has been counseled on proper administration of Vumerity® including caloric and fat intake limits at the time of dosing; and
8. Compliance will be checked for continued approval every 6 months; and
9. A quantity limit of 120 capsules per 30 days will apply.

## Utilization of MS Medications: Calendar Year 2020

**Comparison of Calendar Years: Pharmacy Claims**

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2019** | 163 | 1,168 | $6,926,266.04 | $5,930.02 | $202.19 | 40,072 | 34,256 |
| **2020** | 137 | 1,032 | $6,648,914.01 | $6,442.75 | $215.76 | 35,914 | 30,816 |
| **% Change** | **-16.00%** | **-11.60%** | **-4.00%** | **8.60%** | **6.70%** | **-10.40%** | **-10.00%** |
| **Change** | **-26** | **-136** | **-$277,352.03** | **$512.73** | **$13.57** | **-4,158** | **-3,440** |

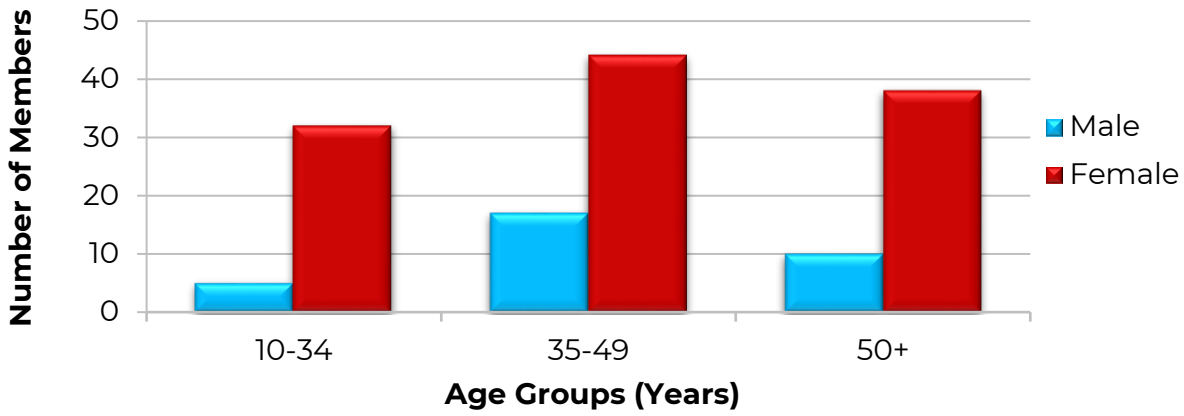
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

## Comparison of Calendar Years: Medical Claims

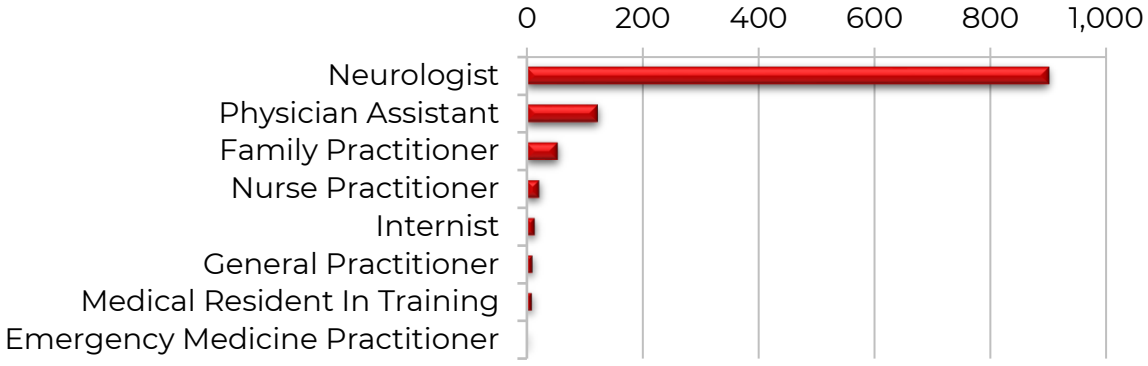
| Calendar Year | *Total Members | †Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|---|
| **2019** | 48 | 184 | $2,066,399.32 | $11,230.43 | 3.8 |
| **2020** | 58 | 194 | $2,580,209.90 | $13,300.05 | 3.34 |
| **% Change** | **20.83%** | **5.43%** | **24.87%** | **18.43%** | **-12.11%** |
| **Change** | **10** | **10** | **$513,810.58** | **$2,069.62** | **-0.46** |

*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.

## Demographics of Members Utilizing MS Medications

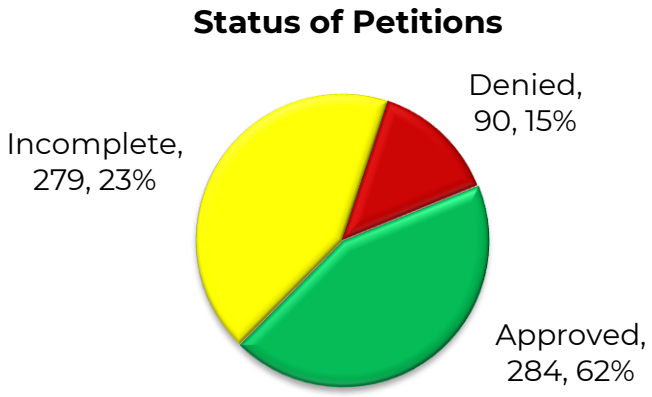



## Top Prescriber Specialties of MS Medications by Number of Claims




## Prior Authorization of MS Medications

There were 653 prior authorization requests submitted for MS medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.




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

**Anticipated Patent Expiration(s):**

- Mavenclad® (cladribine): October 2026
- Tecfidera® (dimethyl fumarate): February 2028
- Zeposia® (ozanimod): May 2029
- Mayzent® (siponimod): November 2030
- Gilenya® (fingolimod): September 2032
- Vumerity® (diroximel fumarate): September 2033
- Aubagio® (teriflunomide): February 2034
- Bafiertam™ (monomethyl fumarate): February 2035

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

- **March 2020:** The FDA approved Zeposia® (ozanimod) oral capsules for the treatment of adults with relapsing forms of MS (RMS), including clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), and active secondary progressive MS (SPMS). Zeposia®, an oral medication taken once daily, is the only approved sphingosine-1-phosphate (S1P) receptor modulator that offers RMS patients treatment initiation with no genetic test and no label-based first-dose observation requirement. An up-titration dosing schedule should be used to reach the maintenance dosage of Zeposia®, as a transient decrease in heart rate (HR) and atrioventricular (AV) conduction delays may occur. The approval of Zeposia® is based on data from the largest pivotal, head-to-head RMS studies with an active comparator to date: the randomized, active-controlled Phase 3 SUNBEAM™ (safety and efficacy of Zeposia® versus interferon beta-1a in RMS) and RADIANCE™ (safety and efficacy of Zeposia® in RMS) Part B clinical studies of more than 2,600 adults. Zeposia® is also in development for additional immune/inflammatory indications, including ulcerative colitis and Crohn's disease.
- **April 2020:** Bafiertam™ (monomethyl fumarate) delayed release (DR) capsules were FDA approved for the treatment of RMS to include CIS, RRMS, and active SPMS, in adults. The FDA granted tentative approval of Bafiertam™ on November 16, 2018 under a New Drug Application

(NDA) submitted under the 505(b)(2) filing pathway. Bafiertam™, a bioequivalent alternative to a prodrug of Tecfidera® (dimethyl fumarate), met the required bioequivalence, safety, efficacy, and quality standards for tentative approval. Final approval was pending the expiration of a United States patent on June 20, 2020 protecting Biogen's Tecfidera®, or the outcome of pending litigation between Banner and Biogen regarding the patent. In January 2019, Banner announced that the United States District Court for the District of Delaware had ruled in favor of Banner's motion for judgment on the pleadings against Biogen deciding Bafiertam™ does not infringe the Tecfidera® patent, thus permitting Banner to seek final FDA approval. On April 21, 2020, Banner announced that the United States Court of Appeals for the Federal Circuit had upheld the earlier Court's decision.

- **August 2020:** The FDA approved Kesimpta® (ofatumumab) as a subcutaneous (sub-Q) injection for the treatment of RMS, to include CIS, RRMS, and active SPMS, in adults. Kesimpta® is a targeted, precisely dosed and delivered B-cell therapy that has demonstrated superiority versus teriflunomide (Aubagio®) in significantly reducing the annualized relapse rate [(ARR), the primary endpoint of ofatumumab's clinical study], 3-month confirmed disability progression (CDP), and the number of gadolinium-enhancing (Gd+) T1 and new or enlarging T2 lesions with a similar safety profile compared with teriflunomide. Traditionally, B-cell treatments, which bind to and deplete B-cells associated with disease activity in MS, have predominantly been available in hospitals or infusion treatment centers. Kesimpta® is the first B-cell therapy that can be self-administered once monthly at home via the Sensoready® autoinjector pen. Kesimpta® provides patients the flexibility of self-administering via once-monthly sub-Q dosing requiring no premedication and eliminating the need to travel to an infusion center. Ofatumumab was first approved by the FDA in 2009 for the treatment of chronic lymphocytic leukemia (CLL) as an intravenous (IV) infusion with a high dose, administered by a health care provider. Ofatumumab was then investigated in an entirely new development program in RMS, as B-cells are known to play a critical role in the development of autoimmune diseases, such as MS. The approval of Kesimpta® is based on results from the 2 identically designed, double-blind, randomized, multi-center Phase 3 ASCLEPIOS I and II studies evaluating the safety and efficacy of Kesimpta® 20mg monthly sub-Q injections versus teriflunomide 14mg oral tablets taken once daily in adults with RMS. The ASCLEPIOS I and II studies enrolled 1,882 patients with MS, between the ages of 18 and 55 years of age, with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5. Results from these 2 studies were recently published in the August 6, 2020 issue of *The New England Journal of Medicine*.

- **February 2021:** The FDA approved a new intramuscular (IM) route of administration for Plegridy® (peginterferon beta-1a injection) for the treatment of RMS. The new IM administration offers patients living with relapsing MS the well-characterized efficacy and safety of Plegridy® with the potential for significantly reduced injection site reactions. The FDA's approval of the IM administration for Plegridy® is based on data evaluating bioequivalence and adverse reactions associated with IM administration compared to sub-Q administration in healthy volunteers. Bioequivalence between the 2 dosing regimens was confirmed, and data shows that participants receiving Plegridy® through IM administration experienced fewer injection site reactions in comparison to participants receiving sub-Q administration (14.4% vs. 32.1%). The overall safety profiles were generally similar, and there were no new safety signals observed. Plegridy® was first approved by the FDA in 2014 and is proven to significantly reduce MS relapses, disability progression, and brain lesions with a well-understood safety and tolerability profile.

**Pipeline:**

- **Ponesimod:** In March 2020, Janssen submitted an NDA to the FDA for ponesimod for the treatment of adult patients with RMS. Ponesimod is a selective S1P1 modulator. Ponesimod inhibits S1P protein activity and is thought to reduce the number of circulating lymphocytes that can cross the blood-brain barrier. In the central nervous system (CNS), myelin can be damaged by the movement of immune cells, such as lymphocytes, into the brain. The NDA for ponesimod is supported by data from the Phase 3 OPTIMUM study, which was a 2-year head-to-head study that compared the efficacy and safety of oral ponesimod 20mg to oral Aubagio® (teriflunomide) 14mg in adults with RMS. The primary endpoint was the ARR defined as the number of confirmed relapses per patient-year measured from baseline to the end of the study at week 108. Results of the study showed a statistically significant reduction of 30.5% in the ARR of ponesimod relative to teriflunomide (ARR=0.202 for ponesimod vs. 0.290 for teriflunomide; P=0.0003). The projected date for the FDA decision on ponesimod is March 2021.
- **Ublituximab:** In December 2020, results from 2 global, active-controlled, Phase 3 studies, ULTIMATE I and II, evaluating ublituximab, a novel anti-CD20 monoclonal antibody, to Aubagio® (teriflunomide) in patients with RMS were announced. Both studies met their primary endpoint with ublituximab treatment demonstrating a statistically significant reduction in ARR over a 96-week period (P<0.005 in each trial). Ublituximab treatment resulted in an ARR of <0.10 in each of ULTIMATE I & II, with a relative reduction in ARR of approximately 60% and 50%, respectively, over teriflunomide. The ULTIMATE I & II studies

investigated the safety and efficacy of a 1-hour 450mg infusion of ublituximab every 6 months, following the day 1 infusion (150mg over 4 hours). The studies were conducted under Special Protocol Assessment (SPA) agreement with the FDA. Further analyses of the ULTIMATE I & II studies including safety and secondary endpoints will be conducted and detailed data will be presented at an upcoming medical congress, targeted in first half of 2021. Additionally, data from these studies are intended to support a Biologics License Application (BLA) submission for ublituximab in RMS targeted in mid-year 2021.

## Bafiertam™ (Monomethyl Fumarate) Product Summary[10]

**Indication(s):** Bafiertam™ (monomethyl fumarate) is indicated for the treatment of RMS, to include CIS, RRMS, and active SPMS, in adults.

**Dosing:**

- Bafiertam™ (monomethyl fumarate) is supplied as a 95mg oral DR capsule.
- Assessments should be done prior to the initiation of treatment with Bafiertam™ which include a complete blood count (CBC), including lymphocyte count, and liver function tests (LFTs).
- The starting dose of Bafiertam™ is 95mg twice daily for 7 days.
- The maintenance dose after 7 days is 190mg [(2) 95mg capsules] twice daily.
- Bafiertam™ capsules should be swallowed whole and intact. Bafiertam™ capsules should not be crushed, chewed, or contents mixed with food.
- Bafiertam™ can be taken with or without food.

**Mechanism of Action:** The mechanism by which monomethyl fumarate exerts its therapeutic effect in MS is unknown. Monomethyl fumarate has been shown to activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway *in vitro* and *in vivo* in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. Monomethyl fumarate has been identified as a nicotinic acid receptor agonist *in vitro*.

**Contraindication(s):**

- Known hypersensitivity to monomethyl fumarate, dimethyl fumarate, diroximel fumarate, or any of the excipients of Bafiertam™
- Concomitant administration with dimethyl fumarate or diroximel fumarate

**Warnings and Precautions:**

- Anaphylaxis and Angioedema: Bafiertam™ should be discontinued and should not be restarted if these occur.

- Progressive Multifocal Leukoencephalopathy (PML): Bafiertam™ should be withheld at the first sign or symptom suggestive of PML.
- Herpes Zoster and Other Serious Opportunistic Infections: Withholding Bafiertam™ should be considered in cases of serious infection until the infection has resolved.
- Lymphopenia: A CBC should be obtained including a lymphocyte count before initiating Bafiertam™, after 6 months, and every 6 to 12 months thereafter. Interrupting Bafiertam™ should be considered if lymphocyte counts $<0.5x10^9$/L persist for >6 months.
- Liver Injury: Serum aminotransferase, alkaline phosphatase, and total bilirubin levels should be obtained prior to treatment with Bafiertam™ and during treatment, as clinically indicated. Bafiertam™ should be discontinued if clinically significant injury induced by Bafiertam™ is suspected.

**Adverse Reactions:** The most common adverse reactions (incidence for dimethyl fumarate [the prodrug of Bafiertam™] ≥10% and ≥2% more than placebo) were flushing, abdominal pain, diarrhea, and nausea.

**Efficacy:** The efficacy of Bafiertam™ is based upon bioavailability studies in healthy subjects comparing oral Tecfidera® to Bafiertam™.

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per Month | Cost Per Year |
|---|---|---|---|
| **Bafiertam™ (monomethyl fumarate) 95mg DR capsule** | **$48.25** | **$5,790.00±** | **$69,480.00±** |
| Tecfidera® (dimethyl fumarate) 240mg tablet | $137.93 | $8,275.80+ | $99,309.60+ |
| Vumerity® (diroximel fumarate) 231mg capsule | $60.27 | $7,232.40* | $86,788.80* |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
Unit = capsule or tablet
±Bafiertam™ cost per month and cost per year based on the recommended maintenance dosage of 190mg [(2) 95mg capsules] twice daily.
+Tecfidera® cost per month and cost per year based on the recommended maintenance dosage of 240mg twice daily.
*Vumerity® cost per month and cost per year based on the recommended maintenance dosage of 462mg [(2) 231mg capsules] twice daily.

## Kesimpta® (Ofatumumab) Product Summary[11,12]

**Indication(s):** Kesimpta® (ofatumumab) a CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of MS, to include CIS, RRMS, and active SPMS, in adults.

**Dosing:**

- Kesimpta® (ofatumumab) is supplied as a 20mg/0.4mL sub-Q injection in a prefilled Sensoready® Pen and as a 20mg/0.4mL single-dose prefilled syringe. Kesimpta® should be stored in the original carton in the refrigerator between 36° and 46°F prior to use.
- Hepatitis B virus (HBV) and quantitative serum immunoglobulins screening are required before the first dose of Kesimpta®.
- Immunizations should be administered according to immunization guidelines at least 4 weeks prior to initiation of Kesimpta® for live or live-attenuated vaccines, and whenever possible, at least 2 weeks prior to initiation of Kesimpta® for inactivated vaccines.
- Kesimpta® should be administered by sub-Q injection only.
- The recommended initial dosing of Kesimpta® is 20mg administered at week 0, 1, and 2.
- The recommended subsequent dosing of Kesimpta® is 20mg administered monthly starting at week 4.

**Mechanism of Action:** The precise mechanism by which ofatumumab exerts its therapeutic effects in MS is unknown, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, ofatumumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

**Contraindication(s):**

- Active HBV infection

**Warnings and Precautions:**

- Infections: Kesimpta® administration should be delayed in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with Kesimpta® and after discontinuation, until B-cell repletion.
- Injection-Related Reactions: Management for injection-related reactions depends on the type and severity of the reaction.
- Reduction in Immunoglobulins: The level of immunoglobulins should be monitored at the beginning, during, and after discontinuation of treatment with Kesimpta® until B-cell repletion. Consider discontinuing Kesimpta® if a patient develops a serious opportunistic infection or recurrent infections if immunoglobulin levels indicate immune compromise.
- Fetal Risk: Kesimpta® may cause fetal harm based on animal data. Females of reproductive potential should be advised of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping Kesimpta®.

**Adverse Reactions:** Most common adverse reactions (incidence >10%) are upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions.

**Efficacy:** The efficacy of Kesimpta® was established in 2 double-blind, active comparator studies in 1,882 patients with RMS. Patients were randomized to Kesimpta® or teriflunomide. The primary endpoint of both studies was the ARR over the treatment period.

- In study 1, the ARR was 0.11 for the Kesimpta® group vs. 0.22 for the teriflunomide group (relative reduction: 51%; P<0.001).
- In study 2, the ARR was 0.10 for the Kesimpta group vs. 0.25 for the teriflunomide group (relative reduction: 59%; P<0.001).

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per Year |
|---|---|---|
| **Kesimpta® (ofatumumab) 20mg/0.4mL Sensoready® Pen** | **$6,916.67/0.4mL** | **$83,000.04⁺** |
| Aubagio® (teriflunomide) 14mg tablet | $268.64/tablet | $96,710.40* |
| Ocrevus® (ocrelizumab) 300mg/10mL SDV | $1,673.75/mL | $66,950.00± |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
SDV = single dose vial
⁺Kesimpta® cost per year based on maintenance dose of 20mg monthly.
*Aubagio® cost per year based on maintenance dose of 14mg once daily.
±Ocrevus® cost per year based on maintenance dose of 600mg every 6 months.

## Zeposia® (Ozanimod) Product Summary[13,14]

**Indication(s):** Zeposia® (ozanimod) is a S1P receptor modulator indicated for the treatment of RMS, to include CIS, RRMS, and active SPMS, in adults.

**Dosing:**

- Zeposia® is supplied as 0.23mg, 0.46mg, and 0.92mg oral capsules.
- Assessments should be done prior to the initiation of treatment with Zeposia® which include CBC, cardiac evaluation, ophthalmic assessment, review of current or prior medications, LFTs, and vaccinations.
- Titration is required for treatment initiation.
- Zeposia® should be initiated with a 7-day titration:
  - Days 1-4: 0.23mg once daily
  - Day 5-7: 0.46mg once daily
  - Days 8 and Thereafter: 0.92mg once daily
- After the initial titration, the recommended maintenance dosage of Zeposia® is 0.92mg taken orally once daily (starting on day 8).
- If a dose is missed within the first 2 weeks of treatment, Zeposia® should be reinitiated with the titration regimen.

**Mechanism of Action:** Ozanimod is a S1P receptor modulator that binds with high affinity to S1P receptors 1 and 5. Ozanimod blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which ozanimod exerts therapeutic effects in MS is unknown but may involve the reduction of lymphocyte migration into the central nervous system (CNS).

**Contraindication(s):**

- Patients who experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or Class III/IV HF in the last 6 months
- Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless patient has a functioning pacemaker
- Severe untreated sleep apnea
- Concomitant use of a monoamine oxidase inhibitor (MAOI)

**Warnings and Precautions:**

- Infections: Zeposia® may increase the risk of infections. A CBC should be obtained before initiating treatment. The patient should be monitored for infection during treatment. Zeposia® should not be started in patients with active infection.
- Bradyarrhythmia and AV Conduction Delays: Zeposia® may result in a transient decrease in HR; for this reason titration is required for treatment initiation. An electrocardiogram (ECG) should be checked to assess for preexisting cardiac conduction abnormalities before starting Zeposia®. The patient's resting heart rate (HR) with concomitant medications that decrease HR should be considered prior to initiation of treatment with Zeposia®; a cardiologist consultation before concomitant use with other drugs that decrease HR should be considered.
- Liver Injury: Liver enzyme results should be obtained before initiation with Zeposia®. Patients with severe hepatic impairment should be closely monitored. Zeposia® should be discontinued if significant liver injury occurs.
- Fetal Risk: Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping Zeposia®.
- Increased Blood Pressure (BP): BP should be monitored during treatment with Zeposia®.
- Respiratory Effects: Zeposia® may cause a decline in pulmonary function. Pulmonary function (e.g., spirometry) should be assessed if clinically indicated.

- Macular Edema: A prompt ophthalmic evaluation is recommended if there is any change in vision while taking Zeposia®. Diabetes mellitus and uveitis increase the risk of macular edema; patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including macula, prior to treatment with Zeposia®.

**Drug Interactions:**

- Vaccines: Live attenuated vaccines should be avoided during and for up to 3 months after treatment with Zeposia®.
- Strong CYP2C8 Inhibitors and Inducers: Concomitant use of Zeposia® is not recommended.
- Breast Cancer Resistance Protein (BCRP) Inhibitors: Concomitant use of Zeposia® is not recommended.

**Adverse Reactions:** The most common adverse reactions (incidence >4%) include upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

**Efficacy:** The efficacy of Zeposia® was established in 2 randomized, double-blind, active comparator-controlled studies in patients with RMS. In both studies, patients were randomized to receive either Zeposia® or Avonex® (interferon beta-1a). The primary endpoint of both study 1 and study 2 was the ARR over the treatment period (study 1; N=895) and 24 months (study 2; N=874).

- In study 1, the ARR was 0.181 and 0.350 for the Zeposia® and Avonex® groups, respectively (relative reduction: 48%; P<0.0001).
- In study 2, the ARR was 0.172 and 0.276 for the Zeposia® and Avonex® groups, respectively (relative reduction: 38%; P<0.0001).
- There was no statistically significant difference in confirmed disability progression between Zeposia® and Avonex® patients over 2 years.

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per Month | Cost Per Year |
|---|---|---|---|
| **Zeposia® (ozanimod) 0.92mg capsule** | **$246.22** | **$7,386.60‡** | **$88,639.20‡** |
| Mayzent® (siponimod) 2mg tablet | $268.59 | $8,057.70+ | $96,692.40+ |
| Gilenya® (fingolimod) 0.5mg capsule | $294.87 | $8,846.10* | $106,153.20* |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
Unit = capsule or tablet
‡Zeposia® cost per month and cost per year based on the recommended maintenance dose of 0.92mg once daily.
+Mayzent® cost per month and cost per year based on the recommended maintenance dosage of 2mg once daily.
*Gilenya® cost per month and cost per year based on the recommended dosage for adults and pediatric patients (10 years of age and older) weighing more than 40kg of 0.5mg once daily.

## Recommendations

The College of Pharmacy recommends the prior authorization of Bafiertam™ (monomethyl fumarate), Kesimpta® (ofatumumab), and Zeposia® (ozanimod) with the following criteria:

**Bafiertam™ (Monomethyl Fumarate) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no serious active infection(s); and
4. Complete blood counts (CBC), including lymphocyte count, and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Intolerable adverse effects associated with a trial of Tecfidera® (dimethyl fumarate) and Vumerity® (diroximel fumarate) that are not expected to occur with Bafiertam™ or a patient-specific, clinically significant reason why a trial of Tecfidera® and Vumerity® is not appropriate for the member must be provided; and
7. Verification that CBC, including lymphocyte count, levels are acceptable to the prescriber in addition to compliance will be required for continued approval every 6 months; and
8. A quantity limit of 120 capsules per 30 days will apply.

**Kesimpta® (Ofatumumab) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Member must have had at least 1 relapse in the previous 12 months; and
3. The prescriber must verify hepatitis B virus (HBV) screening is performed before the first dose of Kesimpta® and the member does not have an active HBV infection; and
4. Prescriber must agree to monitor quantitative serum immunoglobulin level before, during, and after discontinuation of treatment with Kesimpta® until B-cell repletion; and
5. Prescriber must verify the member has no active infection(s); and
6. Prescriber must verify the first injection of Kesimpta® will be administered by a health care professional prepared to manage injection-related adverse reactions; and

7. Kesimpta® must be shipped via cold chain supply and the member or member's caregiver must be trained on the proper storage of Kesimpta®; and
8. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of treatment with Kesimpta®; and
9. Female members of reproductive potential must use an effective method of contraception during treatment and for 6 months after stopping Kesimpta®; and
10. A quantity limit of 1 syringe or prefilled Sensoready® Pen per month will apply. Initial dosing titration will be approved for a quantity limit override upon meeting Kesimpta® approval criteria; and
11. Compliance will be checked for continued approval every 6 months.

**Zeposia® (Ozanimod) Approval Criteria:**

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Member must not have any contraindications for use of Zeposia® including:
    a. Experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or NYHA Class III/IV HF in the last 6 months; or
    b. Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless member has a functioning pacemaker; or
    c. Have severe untreated sleep apnea; or
    d. Concurrent use of monoamine oxidase inhibitors (MAOIs); and
3. Member must not have received prior treatment with alemtuzumab; and
4. Member must not be concurrently using strong CYP2C8 inhibitors/inducers or breast cancer resistance protein (BCRP) inhibitors; and
5. Verification from the prescriber that member has no active infection(s); and
6. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
7. Prescriber must conduct an electrocardiogram (ECG) to determine whether preexisting conduction abnormalities are present before initiating Zeposia®; and
8. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
9. Ophthalmic evaluation and verification that member will be monitored for changes in vision throughout therapy; and

10. Verification from the prescriber that the member has been assessed for medications and conditions that cause reduction in heart rate or AV conduction delays and that the member will be followed with appropriate monitoring per package labeling; and
11. Verification from the prescriber that the member has been assessed for previous confirmed history of chickenpox or vaccination against varicella. Members without a history of chickenpox or varicella vaccination should receive a full course of the varicella vaccine prior to commencing treatment with Zeposia®; and
12. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
13. Female members of reproductive potential must be willing to use effective contraception during treatment with Zeposia® and for at least 3 months after discontinuing treatment; and
14. Member must have had an inadequate response to Gilenya® (fingolimod) or a patient-specific, clinically significant reason why fingolimod is not appropriate for the member must be provided; and
15. Compliance will be checked for continued approval every 6 months; and
16. A quantity limit of 30 capsules per 30 days will apply.

## Utilization Details of MS Medications: Calendar Year 2020

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **INTERFERON BETA-1A PRODUCTS** | | | | | |
| AVONEX PEN KIT 30MCG | 35 | 3 | $239,899.46 | $242.81 | $6,854.27 |
| REBIF INJ 44MCG/0.5ML | 14 | 2 | $111,650.99 | $284.82 | $7,975.07 |
| REBIF REBIDO INJ 44MCG/0.5ML | 11 | 1 | $90,975.54 | $295.38 | $8,270.50 |
| REBIF INJ 22MCG/0.5ML | 9 | 2 | $73,851.18 | $273.52 | $8,205.69 |
| REBIF REBIDO INJ 22MCG/0.5ML | 8 | 1 | $38,733.41 | $217.60 | $4,841.68 |
| **SUBTOTAL** | **77** | **9** | **$555,110.58** | **$259.88** | **$7,209.23** |
| **INTERFERON BETA-1B PRODUCTS** | | | | | |
| BETASERON INJ 0.3MG | 32 | 5 | $247,262.86 | $275.96 | $7,726.96 |
| **SUBTOTAL** | **32** | **5** | **$247,262.86** | **$275.96** | **$7,726.96** |
| **PEGINTERFERON BETA-1A PRODUCTS** | | | | | |
| PLEGRIDY INJ 125MCG/0.5ML | 20 | 3 | $141,156.38 | $252.06 | $7,057.82 |
| **SUBTOTAL** | **20** | **3** | **$141,156.38** | **$252.06** | **$7,057.82** |
| **DALFAMPRIDINE PRODUCTS** | | | | | |
| DALFAMPRIDINE TAB 10MG ER | 168 | 22 | $13,453.02 | $2.67 | $80.08 |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| AMPYRA TAB 10MG | 11 | 1 | $32,357.05 | $98.05 | $2,941.55 |
| **SUBTOTAL** | **179** | **23** | **$45,810.07** | **$8.53** | **$255.92** |
| **TERIFLUNOMIDE PRODUCTS** | | | | | |
| AUBAGIO TAB 14MG | 97 | 16 | $744,280.20 | $255.77 | $7,672.99 |
| AUBAGIO TAB 7MG | 11 | 1 | $84,475.05 | $255.99 | $7,679.55 |
| **SUBTOTAL** | **108** | **17** | **$828,755.25** | **$255.79** | **$7,673.66** |
| **GLATIRAMER ACETATE PRODUCTS** | | | | | |
| COPAXONE INJ 20MG/ML | 201 | 27 | $1,313,283.69 | $220.65 | $6,533.75 |
| COPAXONE INJ 40MG/ML | 82 | 11 | $452,619.12 | $196.96 | $5,519.75 |
| GLATIRAMER INJ 40MG/ML | 2 | 1 | $3,345.26 | $55.75 | $1,672.63 |
| GLATOPA INJ 40MG/ML | 1 | 1 | $1,511.41 | $50.38 | $1,511.41 |
| **SUBTOTAL** | **286** | **40** | **$1,770,759.48** | **$212.32** | **$6,191.47** |
| **FINGOLIMOD PRODUCTS** | | | | | |
| GILENYA CAP 0.5MG | 115 | 15 | $950,934.56 | $275.63 | $8,269.00 |
| **SUBTOTAL** | **115** | **15** | **$950,934.56** | **$275.63** | **$8,269.00** |
| **DIMETHYL FUMARATE PRODUCTS** | | | | | |
| TECFIDERA CAP 240MG | 137 | 23 | $1,133,157.19 | $275.71 | $8,271.22 |
| DIMETHYL FUM CAP 240MG DR | 25 | 11 | $92,908.96 | $123.88 | $3,716.36 |
| TECFIDERA STARTER | 6 | 6 | $49,711.80 | $276.18 | $8,285.30 |
| DIMETHYL FUM STARTER | 1 | 1 | $361.41 | $12.05 | $361.41 |
| **SUBTOTAL** | **169** | **41** | **$1,276,139.36** | **$251.70** | **$7,551.12** |
| **NATALIZUMAB PRODUCTS** | | | | | |
| TYSABRI INJ 300/15ML | 13 | 1 | $82,288.83 | $226.07 | $6,329.91 |
| **SUBTOTAL** | **13** | **1** | **$82,288.83** | **$226.07** | **$6,329.91** |
| **CLADRIBINE PRODUCTS** | | | | | |
| MAVENCLAD 6-PAK 10MG | 4 | 2 | $227,845.64 | $1,998.65 | $56,961.41 |
| MAVENCLAD 7-PAK 10MG | 2 | 1 | $97,657.82 | $1,743.89 | $48,828.91 |
| **SUBTOTAL** | **6** | **3** | **$325,503.46** | **$1,914.73** | **$54,250.58** |
| **OCRELIZUMAB PRODUCTS** | | | | | |
| OCREVUS INJ 300/10ML | 9 | 8 | $262,805.51 | $380.33 | $29,200.61 |
| **SUBTOTAL** | **9** | **8** | **$262,805.51** | **$380.33** | **$29,200.61** |
| **SIPONIMOD PRODUCTS** | | | | | |
| MAYZENT TAB 2MG | 14 | 2 | $107,540.30 | $256.05 | $7,681.45 |
| **SUBTOTAL** | **14** | **2** | **$107,540.30** | **$256.05** | **$7,681.45** |
| **OFATUMUMB PRODUCTS** | | | | | |
| KESIMIPTA INJ 20MG/0.4ML | 3 | 3 | $48,446.92 | $613.25 | $16,148.97 |
| **SUBTOTAL** | **3** | **3** | **$48,446.92** | **$613.25** | **$16,148.97** |
| **TOTAL** | **1,032** | **137*** | **$6,648,914.01** | **$215.76** | **$6,442.75** |

INJ = injection; CAP = capsule; TAB = tablet; PAK = pack; FUM = fumarate; DR = delayed release; ER = extended release
*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 | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **NATALIZUMAB PRODUCTS** | | | | | |
| TYSABRI INJ 300MG/15ML (J2323) | 139 | 22 | $858,071.08 | 6.32 | $6,173.17 |
| **OCRELIZUMAB PRODUCTS** | | | | | |
| OCREVUS INJ 300MG/10ML (J2350) | 55 | 36 | $1,722,138.82 | 1.53 | $31,311.61 |
| **TOTAL** | **194⁺** | **58*** | **$2,580,209.90** | **3.34** | **$13,300.05** |

*Total number of unduplicated utilizing members.
⁺Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 02/2021. Last accessed 02/10/2021.
[2] Bristol-Myers Squibb. United States Food and Drug Administration Approves Bristol Myers Squibb's Zeposia® (Ozanimod), a New Oral Treatment for Relapsing Forms of Multiple Sclerosis. *Business Wire*. Available online at: https://news.bms.com/news/corporate-financial/2020/US-Food-and-Drug-Administration-Approves-Bristol-Myers-Squibbs-ZEPOSIA-ozanimod-a-New-Oral-Treatment-for-Relapsing-Forms-of-Multiple-Sclerosis/default.aspx. Issued 03/26/2020. Last accessed 02/12/2021.
[3] Banner Life Sciences, LLC. Bafiertam™ (Monomethyl Fumarate), the Bioequivalent Alternative to Biogen's Tecfidera® (Dimethyl Fumarate), is a New Oral Treatment Option for Relapsing Forms of Multiple Sclerosis. *Business Wire*. Available online at: https://www.biospace.com/article/releases/banner-life-sciences-announces-final-fda-approval-of-bafiertam-for-multiple-sclerosis/. Issued 04/30/2020. Last accessed 02/15/2021.
[4] Novartis. FDA Approves Kesimpta® (Ofatumumab), the First and Only Self-Administered, Targeted B-Cell Therapy for Patients with Relapsing Multiple Sclerosis. Available online at: https://www.globenewswire.com/news-release/2020/08/20/2081597/0/en/FDA-approves-Novartis-Kesimpta-ofatumumab-the-first-and-only-self-administered-targeted-B-cell-therapy-for-patients-with-relapsing-multiple-sclerosis.html. Issued 08/20/2020. Last accessed 02/15/2021.
[5] Biogen, Inc. Biogen Announces FDA Approval of Plegridy® (Peginterferon Beta-1a) Intramuscular Administration for Multiple Sclerosis. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2021/02/01/2167195/0/en/Biogen-Announces-FDA-Approval-of-PLEGRIDY-peginterferon-beta-1a-Intramuscular-Administration-for-Multiple-Sclerosis.html. Issued 02/01/2021. Last accessed 02/15/2021.
[6] Janssen Pharmaceutical Company. Janssen Submits Ponesimod New Drug Application to the U.S. FDA for Treatment of Adults with Relapsing Multiple Sclerosis. Available online at: https://www.janssen.com/janssen-submits-ponesimod-new-drug-application-us-fda-treatment-adults-relapsing-multiple-sclerosis. Issued 03/18/2020. Last accessed 02/25/2021.
[7] Janssen Pharmaceutical Company. New Head-to-Head Phase 3 Study Data Show Ponesimod Superiority Versus Aubagio® (Teriflunomide) 14mg in Adults with Relapsing Multiple Sclerosis (MS). Available online at: https://www.janssen.com/new-head-head-phase-3-study-data-show-ponesimod-superiority-versus-aubagio-teriflunomide-14-mg. Issued 09/11/2019. Last accessed 02/25/2021.
[8] Prime Therapeutics. March 2021 Decisions Expected from the FDA. Available online at: https://www.primetherapeutics.com/en/news/Stories/2021/Story-Decisions-expected-FDA-March.html. Issued 02/15/2021. Last accessed 02/25/2021.
[9] TG Therapeutics. TG Therapeutics Announced Positive Topline Results from the ULTIMATE I and II Phase 3 Studies Evaluating Ublituximab Monotherapy for the Treatment of Patients with Multiple Sclerosis. Available online at: https://ir.tgtherapeutics.com/news-releases/news-release-details/tg-therapeutics-announces-positive-topline-results-ultimate-i-ii. Issued 12/10/2020. Last accessed 02/25/2021.
[10] Bafiertam™ Prescribing Information. Banner Life Sciences. Available online at: https://bafiertam.com/wp-content/uploads/2020/05/Bafiertam-Prescribing-Information-5-20-2020.pdf. Last revised 04/2020. Last accessed 02/15/2021.
[11] Kesimpta® Prescribing Information. Novartis Pharmaceuticals Corporation. Available online at: https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf. Last revised 08/2020. Last accessed 02/15/2021.
[12] Kesimpta® (Ofatumumab) – New Drug Approval. OptumRx®. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_kesimpta_2020-0821.pdf. Last revised 2020. Last accessed 02/15/2021.
[13] Zeposia® Prescribing Information. Celgene Corporation. Available online at: https://packageinserts.bms.com/pi/pi_zeposia.pdf. Last revised 09/2020. Last accessed 02/15/2021.
[14] Zeposia® (Ozanimod) – New Drug Approval. OptumRx®. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_zeposia_2020-0327.pdf. Last revised 2020. Last accessed 02/15/2021.

# Appendix P

# Calendar Year 2020 Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Orladeyo™ (Berotralstat)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Takhzyro® (Lanadelumab-flyo) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
4. History of at least 1 or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or 3 or more emergency medical treatments per year; or
5. Approval consideration will be given if the member has a recent hospitalization for a severe episode of angioedema; and
6. Authorization of Takhzyro® (lanadelumab-flyo) will also require a patient-specific, clinically significant reason why the member cannot use Cinryze® or Haegarda® (C1 esterase inhibitor); and
7. Cinryze® Dosing:
    a. The recommended dose of Cinryze® is 1,000 units intravenously (IV) every 3 to 4 days, approximately 2 times per week, to be infused at a rate of 1mL/min; and
    b. Initial doses should be administered in an outpatient setting by a health care provider; members can be taught by their health care provider to self-administer Cinryze® IV; and
    c. A quantity limit of 8,000 units per month will apply (i.e., 2 treatments per week or 8 treatments per 28 days); or
8. Haegarda® Dosing:
    a. The recommended dose of Haegarda® is 60 IU/kg subcutaneously (sub-Q) twice weekly; and
    b. 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
    c. A quantity limit of 2 treatments per week or 8 treatments per 28 days will apply; or
9. Takhzyro® Dosing:

a. The recommended dose of Takhzyro® is 300mg sub-Q every 2 weeks (dosing every 4 weeks may be considered in some members); and
b. Prescriber must verify member or caregiver has been trained by a health care professional on proper storage and sub-Q administration of Takhzyro®; and
c. A quantity limit of (2) 300mg/2mL vials per 28 days will apply.

**Berinert® (C1 Esterase Inhibitor) and Firazyr® (Icatibant) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for the *treatment* of acute attacks of HAE.

**Ruconest® (C1 Esterase Inhibitor) and Kalbitor® (Ecallantide) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *treatment* of acute attacks of HAE; and
3. For authorization consideration of Kalbitor® (ecallantide), a patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor) and Firazyr® (icatibant) must be provided.

## Utilization of HAE Medications: Calendar Year 2020

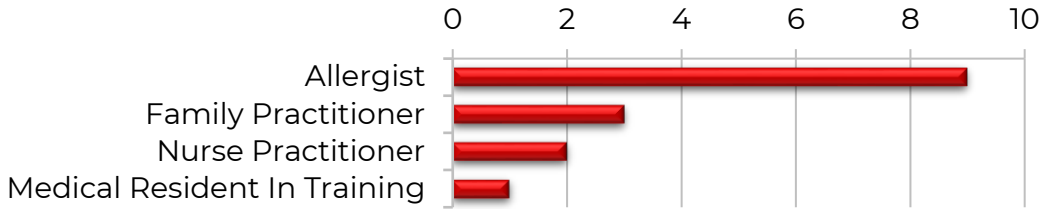
### Comparison of Calendar Years

- There was no SoonerCare utilization of HAE medications in calendar year 2019 to allow for a comparison to calendar year 2020 utilization. The utilization details for calendar year 2020 can be found at the end of this report.

### Demographics of Members Utilizing HAE Medications

- Due to the limited number of members utilizing HAE medications for calendar year 2020, detailed demographic information could not be provided.

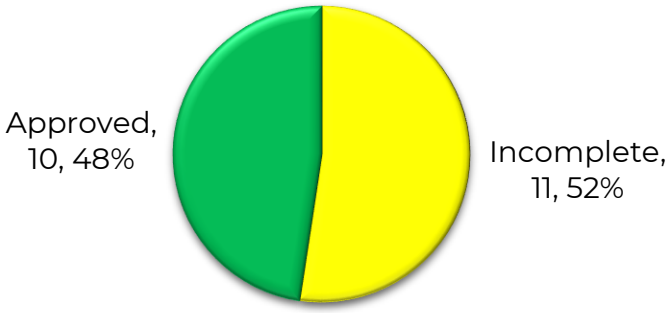
**Top Prescriber Specialties of HAE Medications by Number of Claims**



## Prior Authorization of HAE Medications

There were 21 prior authorization requests submitted for HAE medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

**Status of Petitions**




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

**Anticipated Patent Expiration(s):**

- Orladeyo™ (berotralstat): November 2039

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

- **September 2020:** CSL Behring announced the FDA approved an expanded indication for Haegarda® for routine prophylaxis of HAE attacks in patients 6 years of age and older. HAE affects approximately 1 in 50,000 people in the United States, and children have a 50% chance of inheriting HAE if 1 of their parents has the disease. Haegarda® is the first and only subcutaneous (sub-Q) treatment option for prevention of HAE attacks in patients 6 years of age and older. This FDA approval was based on results from 2 studies. In COMPACT, an international, prospective multi-center, randomized, double-blind, placebo-controlled Phase 3 pivotal study, which included 6 patients 17 years of age or younger with symptomatic HAE, the number of HAE attacks was reduced by a median of 95% relative to placebo. In COMPACT OLE, an open label extension study, there were 126 patients including 9 patients 17 years of age or younger. In this study, all 9 pediatric patients experienced >50% reduction in number of attacks per month versus the pre-study period, with a median of 97% reduction in the median number of attacks per month. In addition to the expanded pediatric indication, the updated label includes clinical safety data regarding Haegarda® use in pregnant women. The new label includes results from a randomized, open-label, active treatment controlled study regarding

4 patients who became pregnant during the study, and received treatment until pregnancy was identified. Patients received Haegarda® for 4 to 8 weeks (9 to 15 doses) during the first trimester. These women reported no complications during delivery and all women delivered healthy babies.

- **November 2020:** Takeda announced the final results from the Phase 3 Hereditary Angioedema Long-term Prophylaxis (HELP) Study™ Open-Label Extension (OLE). The study showed that Takhzyro® (lanadelumab-flyo) helped prevent and reduce the frequency of HAE attacks in patients 12 years of age and older who received treatment for a mean duration of 29.6 months. Results were consistent with the safety and efficacy of Takhzyro® in the pivotal trial. The mean HAE attack rate was reduced by 87.4% overall versus baseline (N=212) and in a pre-specified exploratory endpoint, 68.9% of patients treated with Takhzyro® 300mg every 2 weeks experienced an attack-free period of more than 12 months (N=209).
- **December 2020:** BioCryst Pharmaceuticals announced the FDA approved Orladeyo™ (berotralstat), a once daily oral treatment, for prophylaxis of HAE attacks in adults and pediatric patients 12 years of age and older. Orladeyo™ is the first orally administered non-steroidal option for preventing HAE attacks.

**Guideline Update(s):** The United States Hereditary Angioedema Association Medical Advisory Board (US HAEA MAB) published updated guidelines for HAE management in 2020. Recommendations were made for HAE classification and pathophysiology, HAE diagnosis, considerations for children, specific issues in the management of HAE in women, burden of illness, and the following pertaining to treatment of HAE.

- <u>On-demand treatment of HAE attacks, strong recommendations for the following:</u>
  - Patients must have ready access to effective on-demand medication to administer at the onset of an HAE attack. An FDA-approved on-demand HAE medication [ecallantide, icatibant, plasma-derived C1 inhibitor (pdC1INH), or recombinant human C1IHN (rhC1INH)] should be used as first-line treatment for attacks whenever possible.
  - On-demand treatment of HAE attacks should be self-administered (or administered by a caregiver) whenever feasible except when treating with ecallantide which needs to be administered by a health care provider.
  - All HAE attacks are eligible for treatment irrespective of the location of the swelling or the severity of the attack.
- <u>Prophylactic treatment of HAE attacks, strong recommendations for the following:</u>

- Short-term prophylaxis is indicated when patients are at increased risk of having an attack associated with known triggers such as invasive dental or medical procedures or stressful life events [strong for HAE due to a deficiency of C1INH (HAE-C1INH), weak for HAE with normal C1INH (HAE-nl-C1INH)].
- The decision on when to use long-term prophylactic treatment cannot be made on rigid criteria, but should reflect the needs of the individual patient.
- Long-term prophylactic treatment of HAE-C1INH should include first-line medications [intravenous (IV) C1INH, sub-Q C1INH, or lanadelumab].

▪ Management plans for HAE attacks, strong recommendations for the following:
- HAE management plans must be individualized to each patient's needs due to wide variability in HAE symptoms, response to and tolerance of various HAE medications, and numerous factors impacting clinical course and quality of life. Treatment plans should be monitored regularly and adjusted based on the needs of the patient.
- HAE management plans should include: (A) effective on-demand medication for every patient, (B) consideration of long-term prophylactic medications to prevent HAE attacks, and (C) use of short-term prophylactic medications before medical procedures or other events known to trigger HAE symptoms.
- Consultation with an HAE expert physician is recommended to optimize individualized treatment plans, assist with coordination of care, and provide important patient and family education.

**Pipeline:**

▪ **KVD824:** KalVista Pharmaceuticals plans to submit an Investigational New Drug (IND) application to the FDA in the first quarter of 2021 for a Phase 2 study to evaluating KVD824. KVD824 is a highly potent and selective plasma kallikrein inhibitor. This study is intended to evaluate the efficacy and safety of KVD824 as a twice-daily oral prophylactic treatment for the prevention of HAE attacks.

▪ **KVD900:** In February 2021, KalVista Pharmaceuticals reported positive results from a Phase 2 clinical study of KVD900. The study demonstrated statistically and clinically significant responses for KVD900 for HAE attacks. KVD900 is an oral, on-demand plasma kallikrein inhibitor.

## Orladeyo™ (Berotralstat) Product Summary[8]

**Indication(s):** Orladeyo™ (berotralstat) is a plasma kallikrein inhibitor indicated for the prophylaxis of HAE attacks in adults and pediatric patients 12 years of age and older.

Limitation(s) of Use: Orladeyo™ should not be used for treatment of acute HAE attacks.

**Dosing and Administration:**

- Orladeyo™ is supplied as 110mg and 150mg oral capsules, available in a 28-day supply carton containing (4) 7-capsule blister cards.
- The recommended dosing is 150mg once daily with food.
- A dose of 110mg once daily with food is recommend for patients with moderate or severe hepatic impairment, patients taking P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) inhibitors (e.g., cyclosporine), and patients taking the 150mg dose with persistent gastrointestinal (GI) reactions.

**Contraindication(s):** None

**Safety:**

- **Risk of QT Prolongation with Higher-than-Recommended Dosages:** Berotralstat should not be used for the treatment of acute HAE attacks. Additional doses or doses of berotralstat >150mg once daily are not recommended. An increase in the QT interval was observed at dosages higher than recommended and was concentration dependent.
- **Drug Interactions:** Berotralstat is a substrate of P-gp and BCRP. P-gp inducers (e.g., rifampin, St. John's wort) may decrease berotralstat plasma concentration, leading to reduced efficacy. Use of P-gp inducers with berotralstat is not recommended. Additionally, berotralstat at a dose of 150mg is a moderate inhibitor of CYP2D6 and CYP3A4. For concomitant medications with a narrow therapeutic index that are predominantly metabolized by CYP2D6 (e.g., thioridazine, pimozide) or CYP3A4 (e.g., cyclosporine, fentanyl), appropriate monitoring and dose titration is recommended.
- **Pregnancy:** There are insufficient data in pregnant women available to inform drug-related risks with berotralstat use in pregnancy. Based on animal reproduction studies, no evidence of structural alterations was observed when berotralstat was administered orally to pregnant rats and rabbits during organogenesis at doses up to approximately 10 and 2 times, respectively, the maximum recommended human daily dose (MRHDD).
- **Lactation:** There are no data on the presence of berotralstat in human milk, its effects on the breastfed infant, or its effects on milk production. However, when a drug is present in animal milk, it is likely that the drug

will be present in human milk. Low levels of berotralstat were detected in the plasma of rat pups when rats were dosed with the drug orally during the lactation period. The berotralstat concentration in the rat pup plasma was approximately 2% of the maternal plasma.

- **Pediatric Use:** The safety and effectiveness of berotralstat for the prophylaxis of HAE attacks have been established in pediatric patients 12 years of age and older. Use of berotralstat in this population is supported by evidence from an adequate and well-controlled study that included adults and a total of 6 adolescent patients 12 to 17 years of age.
- **Geriatric Use:** The safety and effectiveness of berotralstat were evaluated in a subgroup of patients (N=9) 65 years of age and older in study 1. Results of the subgroup analysis by age were consistent with overall study results. The safety profile from an additional 5 patients 65 years of age and older enrolled in the open-label, long-term safety study was consistent with data from study 1.
- **Renal Impairment:** No dosage adjustment of berotralstat is recommended for patients with mild, moderate, or severe renal impairment. Berotralstat has not been studied in patients with end-stage renal disease [creatinine clearance (CrCl) <15mL/min or estimated glomerular filtration rate (eGFR) <15 mL/min/1.73m$^2$ or patients requiring hemodialysis], and therefore is not recommended for use in these patient populations.
- **Hepatic Impairment:** No dosage adjustment of berotralstat is recommended for patients with mild hepatic impairment (Child-Pugh Class A). In patients with moderate or severe hepatic impairment (Child-Pugh B or C), the recommended dose of berotralstat is 110mg once daily with food

**Adverse Reactions:** Adverse reactions occurring in ≥10% of patients in any berotralstat treatment group that also occurred at a higher rate than in the placebo treatment group include abdominal pain, vomiting, diarrhea, back pain, and gastroesophageal reflux disease.

**Efficacy:** The efficacy of berotralstat for the prevention of HAE attacks in patients 12 years of age and older with Type I or II HAE was demonstrated in part 1 of a multicenter, randomized, double-blind, placebo-controlled, parallel-group study. The study included 120 adult and adolescent patients who experienced at least 2 investigator confirmed attacks within the first 8 weeks of the run-in period and took at least 1 dose of study treatment. Patients were randomized into 1 of 3 parallel treatment arms, stratified by baseline attack rate, in a 1:1:1 ratio (berotralstat 110mg, berotralstat 150mg, or placebo by oral administration once daily with food) for the 24-week treatment period. Patients discontinued other prophylactic HAE medications

prior to entering the study; however, all patients were allowed to use rescue medications for treatment of breakthrough HAE attacks. Berotralstat 150mg and 110mg produced statistically significant reductions in the rate of HAE attacks compared to placebo for the primary endpoint in the intent-to-treat (ITT) population. In the 110mg group, there was a 30% rate reduction in HAE attacks compared to the placebo group (P=0.024). In the 150mg group there was a 44.2% rate reduction in HAE attacks compared to the placebo group (P<0.001). Reductions in attack rates were observed in the first month of treatment with berotralstat 150mg and 110mg and were sustained through 24 weeks.

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per 28 Days* |
|---|---|---|
| **Orladeyo™ (berotralstat) 150mg capsule** | **$1,332.43** | **$37,308.04** |
| Cinryze® (C1 Esterase Inhibitor) 500mg/5mL vial | $2,841.55 | $45,464.80 |
| Haegarda® (C1 Esterase Inhibitor) 2,000 – 3,000 IU/vial | $1,994.49 - $2,991.73 | $39,889.80Δ |
| Takhzyro® (lanadelumab-flyo) 300mg/2mL vial | $23,414.06 | $46,828.12 |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
Unit = capsule or vial
*Cost per 28 days based on FDA recommended dosing.
ΔCost per 28 days based on FDA recommended dosing of 60 IU/kg twice weekly for a 75kg patient.

## Recommendations

The College of Pharmacy recommends the prior authorization of Orladeyo™ (berotralstat) and recommends updating the Cinryze® (C1 esterase Inhibitor), Haegarda® (C1 esterase Inhibitor), and Takhzyro® (lanadelumab-flyo) approval criteria to be consistent with the current treatment guidelines with the following criteria (changes and additions noted in red):

**Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), Orladeyo™ (Berotralstat), and Takhzyro® (Lanadelumab-flyo) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
4. ~~History of at least 1 or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or 3 or more emergency medical treatments per year; or~~ Based on HAE attack frequency, attack severity, comorbid conditions, and member's access to emergent treatment, the

prescriber has determined long-term prophylaxis is appropriate for the member; or

5. Approval consideration will be given if the member has a recent hospitalization for a severe episode of angioedema; and
6. Authorization of Cinryze® or Haegarda® (C1 esterase inhibitor) will also require a patient-specific, clinically significant reason why the member cannot use Orladeyo™ (berotralstat); and
7. Authorization of Takhzyro® (lanadelumab-flyo) will also require a patient-specific, clinically significant reason why the member cannot use Cinryze® or Haegarda® (C1 esterase inhibitor) or Orladeyo™ (berotralstat); and
8. Cinryze® Dosing:
    a. The recommended dose of Cinryze® is 1,000 units intravenously (IV) every 3 to 4 days, approximately 2 times per week, to be infused at a rate of 1mL/min; and
    b. Initial doses should be administered in an outpatient setting by a health care provider; members can be taught by their health care provider to self-administer Cinryze® IV; and
    c. A quantity limit of 8,000 units per month will apply (i.e., 2 treatments per week or 8 treatments per 28 days); or
9. Haegarda® Dosing:
    a. The recommended dose of Haegarda® is 60 IU/kg subcutaneously (sub-Q) twice weekly; and
    b. 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
    c. A quantity limit of 2 treatments per week or 8 treatments per 28 days will apply; or
10. Orladeyo™ Dosing:
    a. The recommended dose of Orladeyo™ is 150mg by mouth once daily; and
    b. A quantity limit of 28 capsules per 28 days will apply; or
11. Takhzyro® Dosing:
    a. The recommended dose of Takhzyro® is 300mg sub-Q every 2 weeks (dosing every 4 weeks may be considered in some members); and
    b. Prescriber must verify member or caregiver has been trained by a health care professional on proper storage and sub-Q administration of Takhzyro®; and
    c. A quantity limit of (2) 300mg/2mL vials per 28 days will apply.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Berinert® (C1 esterase inhibitor), Firazyr® (icatibant), Kalbitor® (ecallantide), and Ruconest® (C1 esterase inhibitor) based on net costs with the following criteria (changes noted in red):

**Berinert® (C1 Esterase Inhibitor), Firazyr® (Icatibant), Kalbitor® (Ecallantide), and Ruconest® (C1 Esterase Inhibitor) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for the *treatment* of acute attacks of HAE; and
3. For authorization consideration of Firazyr® (icatibant) or Kalbitor® (ecallantide), a patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor) ~~and Firazyr® (icatibant)~~ must be provided; or
4. For authorization consideration of Ruconest® (C1 esterase inhibitor), a patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor), Firazyr® (icatibant), or Kalbitor® (ecallantide) must be provided.

**Utilization Details of HAE Medications: Calendar Year 2020**

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER | % COST |
|---|---|---|---|---|---|---|
| TAKHZYRO INJ 300MG/2ML | 10 | 2 | $454,756.10 | $45,475.61 | 5 | 85.16% |
| ICATIBANT INJ 30MG/3ML | 4 | 2 | $45,790.98 | $11,447.75 | 2 | 8.58% |
| FIRAZYR INJ 30MG/3ML | 1 | 1 | $33,449.90 | $33,449.90 | 1 | 6.26% |
| **TOTAL** | **15** | **3*** | **$533,996.98** | **$35,599.80** | **5** | **100%** |

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

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 02/2021. Last accessed 02/12/2021.
[2] CSL Behring. U.S. Food and Drug Administration Approves Haegarda® (C1 Esterase Inhibitor Subcutaneous [Human]) for Prevention of Hereditary Angioedema (HAE) Attacks in Pediatric Patients. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/us-food-and-drug-administration-approves-haegarda-c1-esterase-inhibitor-subcutaneous-human-for-prevention-of-hereditary-angioedema-hae-attacks-in-pediatric-patients-301138682.html. Issued 09/28/2020. Last accessed 02/12/2021.
[3] Takeda. Final Results from the Phase 3 HELP Study™ Open-Label Extension Support Takhzyro® (Lanadelumab-flyo) Injection as a Long-term Preventive Treatment Option in Patients with Hereditary Angioedema. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20201112006138/en/Final-Results-from-the-Phase-3-HELP-Study%E2%84%A2-Open-Label-Extension-Support-TAKHZYRO%C2%AE-lanadelumab-flyo-Injection-as-a-Long-term-Preventive-Treatment-Option-in-Patients-with-Hereditary-Angioedema. Issued 11/13/2020. Last accessed 02/25/2021.
[4] BioCryst Pharmaceuticals, Inc. BioCryst Announces FDA Approval of Orladeyo™ (Berotralstat), First Oral, Once-daily Therapy to Prevent Attacks in Hereditary Angioedema Patients. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/12/04/2139588/0/en/BioCryst-Announces-FDA-Approval-of-ORLADEYO-berotralstat-First-Oral-Once-daily-Therapy-to-Prevent-Attacks-in-Hereditary-Angioedema-Patients.html. Issued 12/03/2020. Last accessed 02/12/2021.
[5] Busse PG, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guideline for the Management of Hereditary Angioedema. *J Allergy Clin Immunol Pract* 2021; 9:132-50.
[6] KalVista Pharmaceuticals. Products & Pipeline. KVD824 for HAE. Available online at: https://www.kalvista.com/products-pipeline/kvd824-hae. Last accessed 02/15/2021.
[7] KalVista Pharmaceuticals. Products & Pipeline. KVD900 for HAE. Available online at: https://www.kalvista.com/products-pipeline/kvd900-hae. Last accessed 02/15/2021.
[8] Orladeyo™ Prescribing Information. BioCryst Pharmaceuticals. Available online at: https://biocryst.com/wp-ontent/uploads/2020/12/ORLADEYO_PI_V1_2020.pdf?__hstc=132731345.be46e440a98f4eee91d115c244fe1b2c.16134227371 84.16134227371 84.16134227371 84.1&__hssc=132731345.1.16134227371 85&__hsfp=2985976108. Last revised 12/2020. Last accessed 02/12/2021.

# Appendix Q

# Calendar Year 2020 Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Nyvepria™ (Pegfilgrastim-apgf)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Fulphila® (Pegfilgrastim-jmdb), Udenyca® (Pegfilgrastim-cbqv), Ziextenzo® (Pegfilgrastim-bmez) Approval Criteria:**

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

**Granix® (Tbo-filgrastim), Nivestym® (Filgrastim-aafi), and Zarxio® (Filgrastim-sndz) Approval Criteria:**

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

## Utilization of G-CSFs: Calendar Year 2020

### Comparison of Calendar Years: Pharmacy Claims

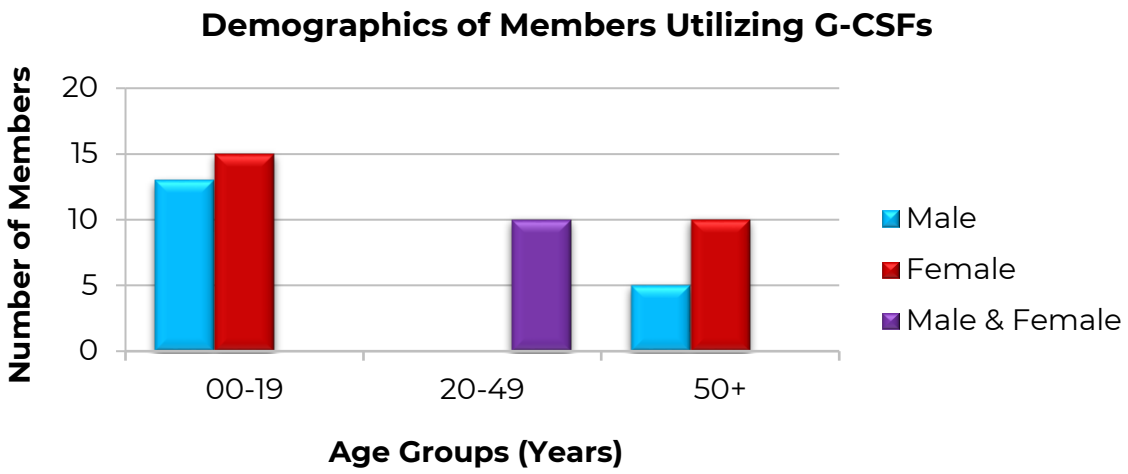
| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2019** | 45 | 174 | $766,853.53 | $4,407.20 | $243.76 | 983 | 3,146 |
| **2020** | 53 | 263 | $734,810.03 | $2,793.95 | $209.41 | 1,108 | 3,509 |
| **% Change** | **17.8%** | **51.1%** | **-4.2%** | **-36.6%** | **-14.1%** | **12.7%** | **11.5%** |
| **Change** | **8** | **89** | **-$32,043.50** | **-$1,613.25** | **-$34.35** | **125** | **363** |

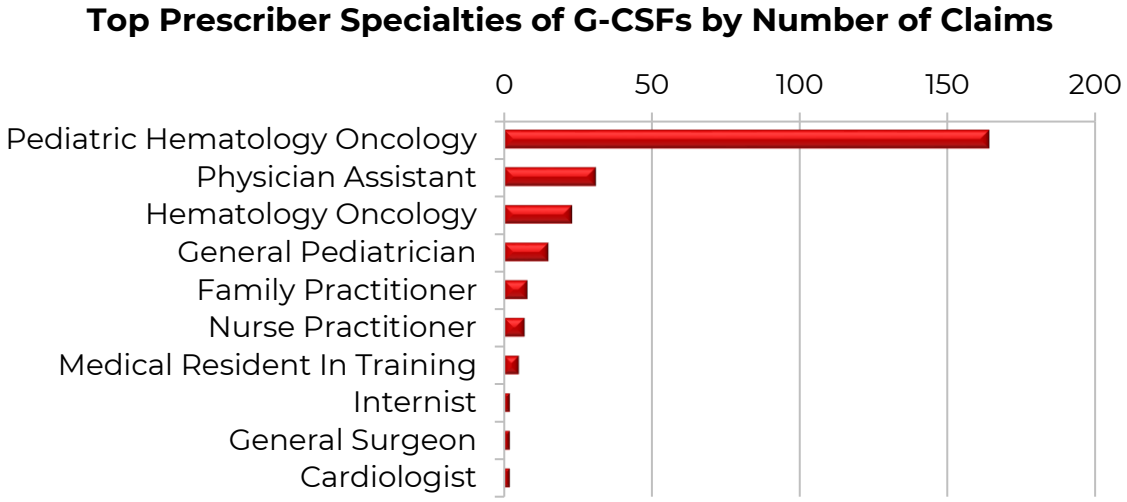
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

### Comparison of Calendar Years: Medical Claims

| Calendar Year | *Total Members | †Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|---|
| **2019** | 218 | 737 | $3,139,993.27 | $4,260.51 | 3.4 |
| **2020** | 249 | 841 | $2,928,049.81 | $3,481.63 | 3.4 |
| **% Change** | **14.22%** | **14.11%** | **-6.51%** | **-18.28%** | **0%** |
| **Change** | **31** | **104** | **-$211,943.46** | **-$778.88** | **0** |

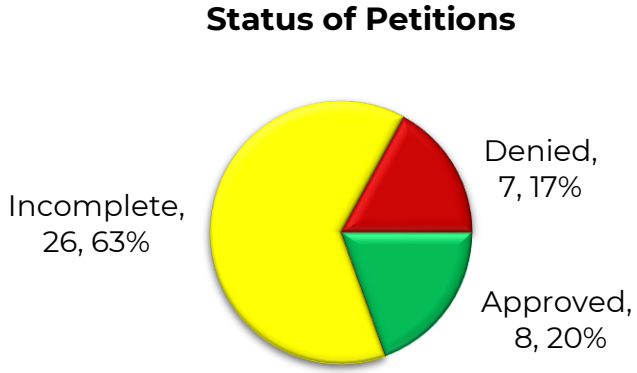
*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.




## Prior Authorization of G-CSFs

There were 41 prior authorization requests submitted for G-CSFs during calendar year 2020. Currently, Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are available without prior authorization. The following chart shows the status of the submitted petitions for calendar year 2020.



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

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

- **June 2020:** The FDA approved Nyvepria™ (pegfilgrastim-apgf) as a biosimilar to Neulasta® (pegfilgrastim) to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. The FDA approval was based on a comprehensive data package and totality of evidence demonstrating a high degree of similarity of Nyvepria™ to Neulasta®. Nyvepria™ is available in a single-dose prefilled syringe and has a Wholesale Acquisition Cost (WAC) of $3,925.00 per 6mg/0.6mL syringe.

### Pipeline:

- **F-627 (Efbemalenograstim Alpha):** Evive Biotech has announced results of its pivotal Phase 3 trial for F-627. The trial was a multi-center, randomized, single dose, double-blind, active-controlled trial comparing the safety and efficacy of F-627 and Neulasta® for the prophylactic treatment of chemotherapy induced neutropenia in women with breast cancer receiving docetaxel plus cyclophosphamide therapy. F-627 was proven to be at least as safe and effective as Neulasta® and could be an alternative to patients who have an allergic reaction to Neulasta® caused by pegylation of pegfilgrastim. F-627's fusion protein structure is thought to decrease the incidence of this allergic reaction.
- **Rolontis® (Eflapegrastim):** Rolontis® is an investigational G-CSF analog comprised of 2 protein components, an analog of G-CSF and an Fc antibody fragment. The Fc fragment interacts with FcRn, which is expressed in the endothelial cells and in bone marrow, and is thought to prolong its retention in these tissues. Results from 2 Phase 3 trials of Rolontis® demonstrated that Rolontis® was non-inferior to pegfilgrastim in the reduction of duration of severe neutropenia in all 4 cycles of chemotherapy treatment. Spectrum Pharmaceuticals submitted a Biologics License Application (BLA) to the FDA and had a Prescription Drug User Fee Act (PDUFA) action date of October 24, 2020; however, the FDA is deferring action on this BLA since they will need to inspect the company's bioplant in South Korea before approval can be considered. Currently, the FDA is unable to conduct this inspection due to travel restrictions from the COVID-19 pandemic.

## Recommendations

The College of Pharmacy recommends the prior authorization of Nyvepria™ (pegfilgrastim-apgf) and recommends removing the prior authorization for

Ziextenzo® (pegfilgrastim-bmez) based on net costs and updating the current pegfilgrastim approval criteria with the following changes shown in red:

**Fulphila® (Pegfilgrastim-jmdb), Nyvepria™ (pegfilgrastim-apgf), and Udenyca® (Pegfilgrastim-cbqv), ~~Ziextenzo® (Pegfilgrastim-bmez)~~ Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Granix® (tbo-filgrastim), Neulasta® (pegfilgrastim), Neupogen® (filgrastim), Zarxio® (filgrastim-sndz), or Ziextenzo® (pegfilgrastim-bmez) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

Additionally, the College of Pharmacy recommends removing the prior authorization for Granix® (tbo-filgrastim) and Zarxio® (filgrastim-sndz) based on net costs and recommends updating the current filgrastim biosimilar approval criteria with the following changes shown in red:

**~~Granix® (Tbo-filgrastim),~~ Nivestym® (Filgrastim-aafi)~~, and Zarxio® (Filgrastim-sndz)~~ Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Granix® (tbo-filgrastim), Neupogen® (filgrastim), or Zarxio® (filgrastim-sndz) must be provided. Biosimilars and/or reference products are preferred based on the lowest net cost product(s) and may be moved to either preferred or non-preferred if the net cost changes in comparison to the reference product and/or other available biosimilar products.

## Utilization Details of G-CSFs: Calendar Year 2020

**Pharmacy Claims**

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **FILGRASTIM PRODUCTS** | | | | | |
| NEUPOGEN INJ 300MCG/ML | 159 | 12 | $260,397.00 | $1,637.72 | 13.25 |
| NEUPOGEN INJ 480MCG/0.8ML PFS | 30 | 19 | $91,436.63 | $3,047.89 | 1.58 |
| NEUPOGEN INJ 300MCG/0.5ML PFS | 16 | 9 | $36,367.76 | $2,272.99 | 1.78 |
| NEUPOGEN INJ 480MCG/1.6ML | 1 | 1 | $6,321.49 | $6,321.49 | 1.00 |
| **SUBTOTAL** | **206** | **41** | **$394,522.88** | **$1915.16** | **5.02** |
| **PEGFILGRASTIM PRODUCTS** | | | | | |
| NEULASTA INJ 6MG/0.6ML PFS | 57 | 17 | $340,287.15 | $5,969.95 | 3.35 |
| **SUBTOTAL** | **57** | **17** | **$340,287.15** | **$5,969.95** | **3.35** |
| **TOTAL** | **263** | **53*** | **$734,810.03** | **$2,793.95** | **4.96** |

INJ = Injection; PFS = Prefilled Syringe
*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 |
|---|---|---|---|---|---|
| **PEGFILGRASTIM PRODUCTS** | | | | | |
| PEGFILGRASTIM INJ (J2505) | 746 | 232 | $2,888,088.99 | $3,871.43 | 3.22 |
| PEGFILGRASTIM-CBQV INJ (Q5111) | 2 | 2 | $280.06 | $140.03 | 1.00 |
| **SUBTOTAL** | **748** | **234** | **$2,888,369.05** | **$3,861.46** | **3.2** |
| **FILGRASTIM PRODUCTS** | | | | | |
| FILGRASTIM INJ (J1442) | 91 | 24 | $39,215.16 | $430.94 | 3.79 |
| FILGRASTIM-SNDZ INJ (Q5101) | 1 | 1 | $235.20 | 235.20 | 1.00 |
| TBO-FILGRASTIM INJ (J1447) | 1 | 1 | $230.40 | $230.40 | 1.00 |
| **SUBTOTAL** | **93** | **26** | **$39,680.76** | **$426.67** | **3.6** |
| **TOTAL** | **841⁺** | **249*** | **$2,928,049.81** | **$3,481.63** | **3.4** |

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

---

[1] Pfizer, Inc. FDA Approves Pfizer's Oncology Supportive Care Biosimilar, Nyvepria™ (Pegfilgrastim-apgf*). Business Wire*. Available online at: https://www.businesswire.com/news/home/20200611005430/en/FDA-Approves-Pfizer%E2%80%99s-Oncology-Supportive-Care-Biosimilar-NYVEPRIA%E2%84%A2-pegfilgrastim-apgf. Issued 06/11/2020. Last accessed 02/09/2021.

[2] Spectrum Pharmaceuticals, Inc. Spectrum Pharmaceuticals Announces Integrated Results from Two Phase 3 ROLONTIS® (Eflapegrastim) Trials Being Presented at the ASCO Annual Meeting. *Business Wire*. Available online at: https://investor.sppirx.com/index.php/news-releases/news-release-details/spectrum-pharmaceuticals-announces-integrated-results-two-phase. Issued 06/02/2019. Last accessed 02/10/2021.

[3] Spectrum Pharmaceuticals, Inc. Rolontis® (Eflapegrastim). Available online at: https://www.sppirx.com/338-spectrum-products-development-rolontis.html. Last accessed 02/10/2021.

[4] Spectrum Pharmaceuticals, Inc. Spectrum Pharmaceuticals Announces that the FDA is Deferring its Action on the BLA for Rolontis® (Eflapegrastim). *Business Wire*. Available online at: https://investor.sppirx.com/news-releases/news-release-details/spectrum-pharmaceuticals-announces-fda-deferring-its-action-bla. Issued 10/26/2020. Last accessed 02/10/2021.

[5] Evive Biotech. Evive Biotech Meets Primary and Secondary Endpoints in Global Phase III Clinical Trial for Their Novel Chemotherapy-Induced Neutropenia Treatment. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/evive-biotech-meets-primary-and-secondary-endpoints-in-global-phase-iii-clinical-trial-for-their-novel-chemotherapy-induced-neutropenia-treatment-301089142.html. Issued 07/07/2020. Last accessed 02/10/2021.

# Appendix R

# Calendar Year 2020 Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Barhemsys® (Amisulpride)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

**Akynzeo® (Netupitant/Palonosetron) and Akynzeo® IV (Fosnetupitant/ Palonosetron) Approval Criteria:**

1. An FDA approved indication for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. For Akynzeo® oral capsules, a previously failed trial of oral aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why oral aprepitant cannot be used must be provided; and
3. For Akynzeo® IV, a previously failed trial of intravenous (IV) fosaprepitant (Emend IV) that resulted in an inadequate response, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
4. Akynzeo® IV will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used; and
5. Approval length will be based on duration of need; and
6. A quantity limit of 1 capsule or vial per chemotherapy cycle will apply; and
7. Akynzeo® oral capsules will not require prior authorization for members with cancer and claims will pay at the point of sale if the member has a reported oncology diagnosis within the past 6 months of claims history.
    a. Based on the current low net cost, Akynzeo® oral capsules will not require prior authorization for members with cancer; however, Akynzeo® oral capsules will follow the original criteria and require a previously failed trial of oral aprepitant if the net cost increases compared to other available products.

**Anzemet® (Dolasetron), Cinvanti® and Emend® (Aprepitant), Emend® IV (Fosaprepitant), and Kytril® and Sancuso® (Granisetron) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A recent trial of ondansetron (within the past 6 months) used for at least 3 days or 1 cycle that resulted in an inadequate response is required for authorization in members receiving moderately emetogenic chemotherapy; and

3. No ondansetron trial is required for authorization of Emend® (aprepitant) in members receiving highly emetogenic chemotherapy; and
4. For Emend® (aprepitant) oral suspension, an age restriction of 6 years and younger will apply. Members older than 6 years of age will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used; and
5. For Cinvanti® [aprepitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
6. Approval length will be based on duration of need.

**Bonjesta® (Doxylamine/Pyridoxine) Approval Criteria:**

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy that is not responsive to conservative management; and
2. Trials with at least 2 non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin B6 (pyridoxine) must be provided; and
4. A patient-specific, clinically significant reason why member cannot use Diclegis® must be provided.

**Cesamet® (Nabilone) and Marinol® and Syndros® (Dronabinol) Approval Criteria:**

1. An FDA approved diagnosis; and
2. Approval length will be based on duration of need; and
3. For Marinol® (dronabinol) and Cesamet® (nabilone), a quantity limit of 60 capsules per 30 days will apply; and
4. Cesamet® (nabilone) will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used; and
5. For Syndros® (dronabinol) oral solution, the quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging; and
6. For Syndros® (dronabinol) oral solution, an age restriction of 6 years and younger will apply. Members older than 6 years of age will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used.

**Doxylamine/Pyridoxine (Generic Diclegis®) Approval Criteria:**

1. Authorization of the generic doxylamine/pyridoxine tablets requires a patient-specific, clinically significant reason why brand formulation Diclegis® (doxylamine/pyridoxine) tablets are not appropriate.

**Palonosetron 0.25mg/5mL Approval Criteria:**

1. A patient-specific, clinically significant reason why the member cannot use generic Aloxi® (palonosetron 0.25mg/5mL), which is available without a prior authorization, must be provided.

**Sustol® (Granisetron Subcutaneous Injection) Approval Criteria:**

1. An FDA approved indication for use in the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens; and
2. Chemotherapy regimen must be listed on the prior authorization request; and
3. A recent trial of ondansetron (within the past 6 months) used for at least 3 days or 1 cycle that resulted in inadequate response is required for authorization in members receiving MEC; and
4. No ondansetron trial is required for authorization of granisetron in members receiving AC combination chemotherapy regimens; and
5. A patient-specific, clinically significant reason why the member cannot use Kytril® (granisetron hydrochloride injection) must be provided; and
6. A quantity limit of 1 injection per chemotherapy cycle will apply.

**Varubi® and Varubi® IV (Rolapitant) Approval Criteria:**

1. An FDA approved indication for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy; and
2. For oral Varubi® (rolapitant oral tablets), a previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. For Varubi® IV [rolapitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
4. Approval length will be based on duration of need; and
5. A quantity limit of 2 tablets or 2 vials per chemotherapy cycle will apply.

**Zuplenz® (Ondansetron) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot take all other available formulations of generic ondansetron must be provided.

## Utilization of Anti-Emetic Medications: Calendar Year 2020

### Comparison of Calendar Years: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2019** | 74,805 | 101,695 | $1,702,835.04 | $16.74 | $2.42 | 1,711,718 | 703,502 |
| **2020** | 54,749 | 78,868 | $1,357,513.24 | $17.21 | $2.26 | 1,445,904 | 599,347 |
| **% Change** | **-26.8%** | **-22.4%** | **-20.3%** | **2.8%** | **-6.6%** | **-15.5%** | **-14.8%** |
| **Change** | **-20,056** | **-22,827** | **-$345,321.80** | **$0.47** | **-$0.16** | **-265,814** | **-104,155** |

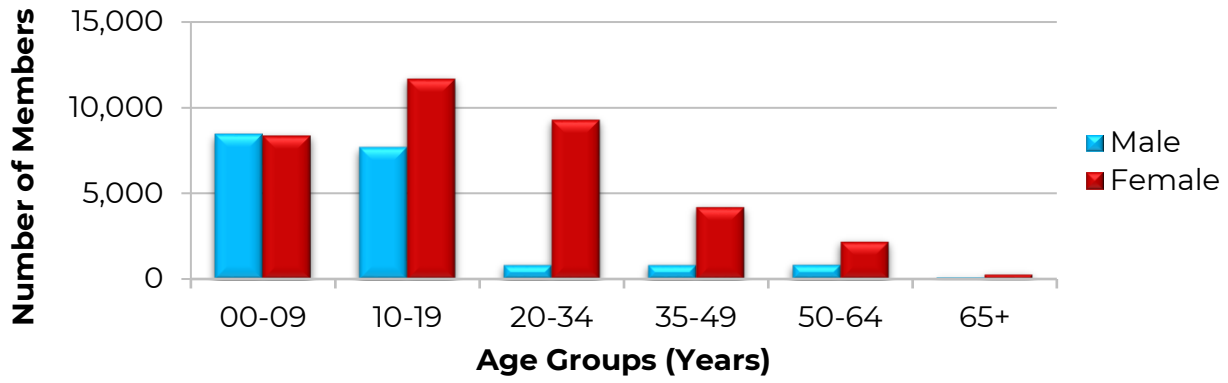
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

### Calendar Year 2020 Utilization: Medical Claims

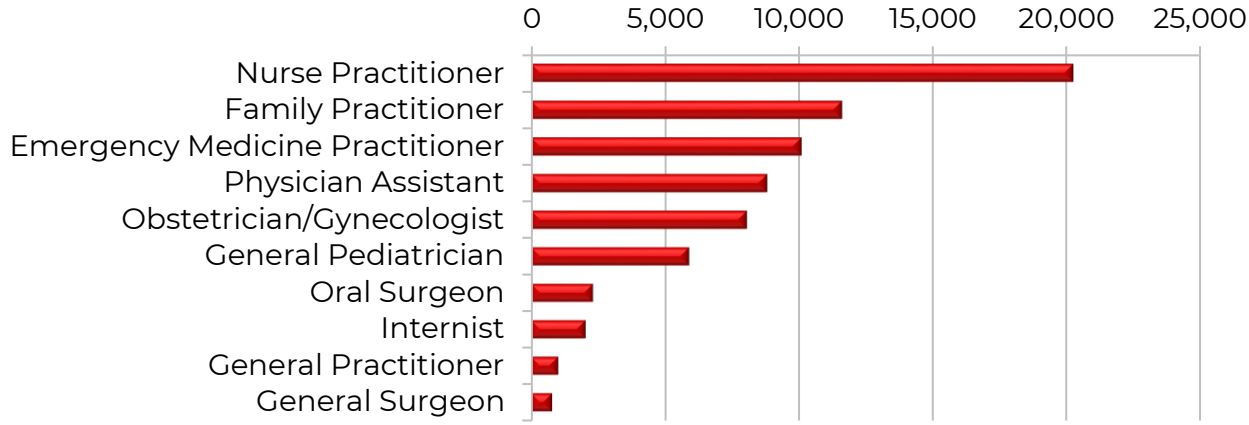
| Calendar Year | *Total Members | †Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|---|
| **2020** | 679 | 4,531 | $454,892.18 | $100.40 | 6.67 |

*Total number of unduplicated utilizing members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.

### Demographics of Members Utilizing Anti-Emetic Medications



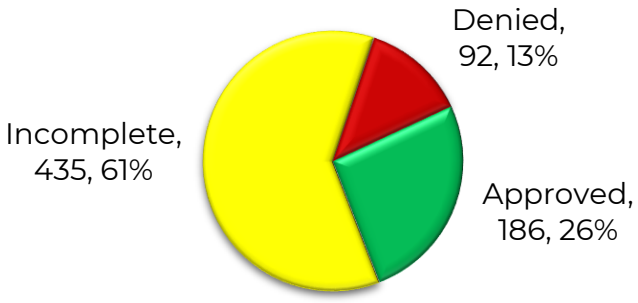

### Top Prescriber Specialties of Anti-Emetic Medications by Number of Claims



## Prior Authorization of Anti-Emetic Medications

There were 713 prior authorization requests submitted for anti-emetic medications during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.

**Status of Petitions**




## Market News and Updates[1,2,34]

**Anticipated Patent Expiration(s):**

- Sustol® [granisetron subcutaneously (sub-Q) injection]: September 2024
- Sancuso® (granisetron transdermal patch): January 2025
- Syndros® (dronabinol oral solution): August 2028
- Varubi® (rolapitant tablet): October 2029
- Zuplenz® (ondansetron oral soluble film): July 2030
- Barhemsys® (amisulpride injection): March 2031
- Bonjesta® [doxylamine/pyridoxine extended-release (ER) tablet]: February 2033
- Akynzeo® (netupitant/palonosetron capsule): September 2035
- Cinvanti® [aprepitant intravenous (IV) emulsion]: September 2035
- Akynzeo® IV (fosnetupitant/palonosetron powder and solution): June 2037

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

- **February 2020:** The FDA announced approval of Barhemsys® (amisulpride) for the prevention and treatment of postoperative nausea and vomiting (PONV) in adult patients. Barhemsys® is a selective dopamine-2 ($D_2$) and dopamine-3 ($D_3$) receptor antagonist that is given via IV infusion. The approval was based on 4 positive Phase 3 studies that studied Barhemsys® for both the prevention and treatment of PONV. The FDA approval covers the prevention of PONV, either alone or in combination with an anti-emetic of a different class and the treatment of PONV in patients who have received anti-emetic prophylaxis with an agent of a different class or who had not received prophylaxis.

- **June 2020:** The FDA announced approval of a new liquid formulation for Akynzeo® IV (fosnetupitant/palonosetron) for the treatment of nausea and vomiting associated with highly emetogenic cancer chemotherapy in combination with dexamethasone in adult patients. Previously, this medication was only available in a powder formulation that required refrigeration and also had to be reconstituted prior to dilution. The newly FDA approved liquid formulation does not need to be refrigerated or reconstituted prior to dilution and can be stored at room temperature for 24 hours after dilution.

**News:**

- **January 2020:** The antipsychotic olanzapine has been used off-label for the treatment of chemotherapy-induced nausea and vomiting (CINV) for many years. Current clinical guidelines from the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), and the Multinational Association of Supportive Care in Cancer (MASCC) all recommend the use of olanzapine at 10mg per day for CINV. There has been debate on whether to use the 5mg or 10mg dose, since many patients cannot tolerate the daytime sedation associated with the higher dose. In a recent Phase 3 trial published in *Lancet Oncology*, known as the J-FORCE trial, olanzapine 5mg combined with standard anti-emetic therapy was compared to placebo with standard anti-emetic therapy in 710 patients who were treated with cisplatin for the first time. Standard anti-emetic therapy included aprepitant, palonosetron, and dexamethasone. The results showed that 95% of the patients in the treatment group experienced no CINV during the first 24 hours of chemotherapy, compared to 89% who received placebo (P=0.0021). In the delayed phase (24-120 hours after chemotherapy), 79% of patients in the treatment group were free of CINV, compared to 66% of patients who received placebo (P<0.0001). The severity of daytime sleepiness was similar between both the treatment and placebo groups from day 2 onward. Although the trial did not compare the 5mg dose head-to-head with the 10mg dose, the results from the trial suggest that olanzapine at the lower dose of 5mg is effective at treating CINV with the lower risk of daytime sedation that is associated with higher doses of olanzapine.

**Pipeline:**

- **TAK-951:** Takeda is currently recruiting patients for its Phase 2 trial comparing the efficacy of TAK-951, a peptide agonist, to ondansetron for prevention of PONV.

## Barhemsys® (Amisulpride) Product Summary[5,6,7,8,910]

**Indication(s):** Barhemsys® (amisulpride) is a dopamine $D_2$ and $D_3$ receptor antagonist indicated in adults for the following:

- Prevention of PONV, either alone or in combination with an anti-emetic of a different class
- Treatment of PONV in patients who have received anti-emetic prophylaxis with an agent of a different class or have not received prophylaxis

**How Supplied:** 5mg/2mL (2.5mg/mL) or 10mg/4mL (2.5mg/mL) single-dose vials (SDVs)

**Dosing and Administration:**

- For the prevention of PONV, either alone or in combination with another anti-emetic: 5mg as a single IV dose infused over 1 to 2 minutes at the time of induction of anesthesia
- For the treatment of PONV: 10mg as a single IV dose infused over 1 to 2 minutes in the event of nausea and/or vomiting after a surgical procedure
- Dilution of Barhemsys® is not required before administration
- Barhemsys® is subject to photodegradation and should be protected from light
- Barhemsys® should be administered within 12 hours of removal of the vial from the protective carton

**Mechanism of Action:** Amisulpride is a selective dopamine $D_2$ and $D_3$ receptor antagonist. $D_2$ receptors are located in the chemoreceptor trigger zone (CTZ) and respond to dopamine released from the nerve endings. Activation of the CTZ relays stimuli to the vomiting center which is involved in emesis. $D_3$ receptors are found in the area postrema and also play a role in emesis.

**Contraindication(s):** Known hypersensitivity to amisulpride

**Adverse Reactions:** Common adverse reactions reported in at least 2% of adult patients who received Barhemsys® 5mg and at a higher rate than placebo in Studies 1 and 2 for the prevention of PONV include chills, hypokalemia, procedural hypotension, and abdominal distension.

**Efficacy:** The safety and efficacy of amisulpride were assessed in 4 randomized, double-blind, placebo-controlled, multi-center studies in patients undergoing general anesthesia and elective surgery. Study 1 and 2 assessed the efficacy of amisulpride for the prevention of PONV, while Study 3 and 4 assessed the efficacy of amisulpride for the treatment of PONV.

- Study 1 included 342 patients who received amisulpride monotherapy at the induction of anesthesia.
    - Inclusion Criteria: Male or female patients 18 years of age and older who were undergoing elective surgery under general anesthesia, expected to last at least 1 hour from induction of anesthesia to wound closure and expected to require at least 1 overnight stay in hospital.
    - Primary Endpoint: The primary endpoint was the number of patients with a complete response (CR), which was defined as no emesis (vomiting or retching) and no use of rescue medication in the 24 hours after the end of surgery, between the active group and the placebo group.
    - Results: 78 out of 176 (44%) patients in the treatment group achieved a CR compared to 54 out of 166 patients (33%) who received the placebo. A difference of 12% was seen between the treatment group and placebo (95% Confidence Interval (CI): 2%, 22%).
- Study 2 included 1,147 patients who received amisulpride in combination with 1 other IV administered, non-dopaminergic anti-emetic (ondansetron, dexamethasone, or betamethasone) at the induction of anesthesia.
    - Inclusion Criteria: The inclusion criteria was similar to Study 1, except Study 2 also included patients with at least 3 Apfel risk factors for PONV. Apfel risk factors for PONV include use of post-operative opioids, non-smoker, female gender, and history of PONV or motion sickness.
    - Primary Endpoint: The primary endpoint was the same as in Study 1.
    - Results: 330 out of 572 (58%) patients in the treatment group achieved a CR compared to 268 out of 575 patients (47%) who received the placebo. A difference of 11% was seen between the treatment group and placebo (95% CI: 5%, 17%).
- Study 3 included 369 patients who received amisulpride and did not receive prior PONV prophylaxis. Patients were excluded if they received a $D_2$ receptor antagonist anti-emetic.
    - Inclusion Criteria: Male or female patients 18 years of age and older who were scheduled to undergo elective surgery under general anesthesia expected to last at least 1 hour from induction of anesthesia to extubation. Participants also had to be judged by the investigator to have a low to moderate risk of experiencing PONV based on risk factors that included non-smoking status, gender, and history of motion sickness. For females of child-bearing potential, willingness to use a highly effective form of

contraception between the date of screening and at least 48 hours after administration of the study medication was required.
    - Primary Endpoint: The primary endpoint was the number of patients with a CR 0-2 hours after administration of the study medication. A CR was defined as no emetic episodes (vomiting or retching) from 30 minutes to 2 hours after administration of study medication and no administration of anti-emetic rescue medication at any time in the 2-hour period after administration of study medication.
    - Results: 59 out of 188 (31%) patients in the treatment group achieved a CR compared to 39 out of 181 patients (22%) who received the placebo. A difference of 10% was seen between the treatment group and placebo (95% CI: 1%, 19%).
- Study 4 included 465 patients who received and failed PONV prophylaxis with an anti-emetic of another class. Patients were excluded if they received a $D_2$ receptor antagonist anti-emetic.
    - Inclusion Criteria: The inclusion criteria was similar to Study 3.
    - Primary Endpoint: The primary endpoint was the number of patients with a CR within 0-24 hours after administration of the study medication. Success was defined as no emetic episodes (vomiting or retching) from 30 minutes to 24 hours after administration of study medication and no administration of anti-emetic rescue medication at any time in the 24-hour period after administration of study medication.
    - Results: 96 out of 230 (42%) patients in the treatment group achieved a CR compared to 67 out of 235 patients (29%) who received the placebo. A difference of 13% was seen between the treatment group and placebo (95% CI: 5%, 22%).

**Cost Comparison:**

| Medication | Cost Per Unit* | Cost Per Vial or Patch |
|---|---|---|
| **Barhemsys 10mg/4mL SDV** | **$21.25** | **$85.00** |
| **Barhemsys 5mg/2mL SDV** | **$21.25** | **$42.50** |
| scopolamine 1mg/3 days patch | $14.39 | $14.39 |
| granisetron 1mg/mL SDV | $10.85 | $10.85 |
| dexamethasone 4mg/mL SDV | $0.78 | $0.78 |
| ondansetron 4mg/2mL SDV | $0.27 | $0.55 |

SDV = Single-dose vial
Costs do not reflect rebated prices or net costs.
Cost per unit based on Wholesale Acquisition Cost (WAC), National Average Drug Acquisition Cost (NADAC), or State Maximum Allowable Cost (SMAC).
*Unit = 1mL or 1 patch

## Recommendations

The College of Pharmacy recommends the prior authorization of Barhemsys® (amisulpride) with the following criteria:

**Barhemsys® (Amisulpride) Approval Criteria:**

1. An FDA approved indication of 1 of the following:
   a. Prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an anti-emetic of a different class; or
   b. Treatment of PONV in patients who have received anti-emetic prophylaxis with an agent of a different class or have not received prophylaxis; and
2. Member must be 18 years of age or older; and
3. Member must not receive a preoperative dopamine-2 ($D_2$) antagonist (e.g., metoclopramide); and
4. A patient-specific, clinically significant reason why the member cannot use other cost-effective therapeutic alternatives for the prevention or treatment of PONV (e.g. ondansetron, dexamethasone) must be provided.

## Utilization Details of Anti-Emetic Medications: Calendar Year 2020

**Pharmacy Claims**

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **ONDANSETRON PRODUCTS** | | | | | |
| ONDANSETRON TAB 4MG ODT | 45,724 | 36,091 | $678,587.78 | $14.84 | 1.27 |
| ONDANSETRON TAB 4MG | 14,263 | 9,884 | $174,771.83 | $12.25 | 1.44 |
| ONDANSETRON TAB 8MG ODT | 10,233 | 6,803 | $161,068.19 | $15.74 | 1.5 |
| ONDANSETRON TAB 8MG | 4,575 | 2,786 | $53,697.01 | $11.74 | 1.64 |
| ONDANSETRON SOL 4MG/5ML | 3,406 | 3,073 | $65,637.52 | $19.27 | 1.11 |
| ONDANSETRON INJ 40MG/20ML | 6 | 4 | $65.61 | $10.94 | 1.5 |
| ONDANSETRON INJ 4MG/2ML | 4 | 3 | $163.63 | $40.91 | 1.33 |
| **SUBTOTAL** | **78,211** | **58,644** | **$1,133,991.57** | **$14.50** | **1.33** |
| **DOXYLAMINE/PYRIDOXINE PRODUCTS** | | | | | |
| DICLEGIS TAB 10/10MG | 439 | 302 | $165,177.34 | $376.26 | 1.45 |
| BONJESTA TAB 20/20MG | 1 | 1 | $194.61 | $194.61 | 1 |
| **SUBTOTAL** | **440** | **303** | **$165,371.95** | **$375.85** | **1.45** |
| **DRONABINOL PRODUCTS** | | | | | |
| DRONABINOL CAP 5MG | 96 | 33 | $13,739.90 | $143.12 | 2.91 |
| DRONABINOL CAP 2.5MG | 34 | 21 | $2,719.90 | $80.00 | 1.62 |
| DRONABINOL CAP 10MG | 15 | 3 | $4,112.66 | $274.18 | 5 |
| **SUBTOTAL** | **145** | **57** | **$20,572.46** | **$ 141.88** | **2.54** |
| **GRANISETRON PRODUCTS** | | | | | |
| SANCUSO DIS 3.1MG | 16 | 8 | $21,091.91 | $1,318.24 | 2 |
| GRANISETRON TAB 1MG | 13 | 5 | $1,168.19 | $89.86 | 2.6 |
| GRANISETRON INJ 1MG/ML | 7 | 2 | $519.87 | $74.27 | 3.5 |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER |
|---|---|---|---|---|---|
| **SUBTOTAL** | **36** | **15** | **$22,779.97** | **$632.78** | **2.4** |
| **APREPITANT PRODUCTS** | | | | | |
| APREPITANT PAK 80 & 125MG | 26 | 9 | $12,866.42 | $494.86 | 2.89 |
| EMEND SUS 125MG | 8 | 3 | $1,650.95 | $206.37 | 2.67 |
| APREPITANT CAP 80MG | 2 | 2 | $279.92 | $139.96 | 1 |
| **SUBTOTAL** | **36** | **14** | **$14,797.29** | **$411.04** | **2.57** |
| **TOTAL** | **78,868** | **54,749*** | **$1,357,513.24** | **$17.21** | **1.44** |

CAP = Capsule; DIS = Patches; INJ = Injection; ODT = Orally Disintegrating Tablet; PAK = Pack; SOL = Solution, SUS = Suspension; TAB = Tablet
*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 |
|---|---|---|---|---|---|
| PALONOSETRON INJ (J2469) | 2,332 | 521 | $103,139.58 | $44.23 | 4.48 |
| APREPITANT INJ (J0185) | 792 | 215 | $199,129.31 | $251.43 | 3.68 |
| FOSAPREPITANT INJ (J1453) | 688 | 206 | $118,258.61 | $171.89 | 3.34 |
| GRANISETRON INJ (J1626) | 613 | 96 | $337.77 | $0.55 | 6.39 |
| FOSNETUPITANT/PALONOSETRON INJ (J1454) | 92 | 35 | $33,022.32 | $358.94 | 2.63 |
| APREPITANT CAP (J8501) | 14 | 7 | $1,004.59 | $71.76 | 2.00 |
| **TOTAL** | **4,531†** | **679*** | **$454,892.18** | **$100.40** | **6.67** |

CAP = Capsule; INJ = Injection
†Total number of unduplicated claims.
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

[1] Helsinn Healthcare S.A. Helsinn Group Announces FDA Approval of a New Liquid Formulation of Akynzeo® (fosnetupitant/palonosetron) Injection in the United States. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/06/02/2042225/0/en/Helsinn-Group-announces-FDA-approval-of-a-new-liquid-formulation-of-AKYNZEO-fosnetupitant-palonosetron-injection-in-the-United-States.html. Issued 06/02/2020. Last accessed 02/11/2021.
[2] Leask H. 'Major Impact': Olanzapine for CINV at 5mg, Not 10mg. *Medscape*. Available online at: https://www.medscape.com/viewarticle/923291. Issued 01/02/2020. Last accessed 02/16/2021.
[3] TAK-951 Versus Ondansetron in Prophylaxis for Postoperative Nausea and Vomiting in High-Risk Participants. *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT04557189. Last revised 01/25/2021. Last accessed 02/16/2021.
[4] FDA Approves Acacia Pharma's Barhemsys for PONV. *Biospace*. Available online at: https://www.biospace.com/article/fda-approves-acacia-pharma-s-barhemsys-for-ponv/. Issued 02/27/2020. Last Accessed 02/19/2021.
[5] Barhemsys® Prescribing Information. Acacia Pharma. Available online at: https://bynder.acaciapharma.com/m/5d7c2cd0d58865f7/original/Barhemsys-Prescribing-Information.pdf. Last revised 09/2020. Last accessed 02/20/2021.
[6] US Phase III Study of APD421 in PONV. *ClinicalTrials.gov*. Available online at: https://www.clinicaltrials.gov/ct2/show/results/NCT01991860?view=results. Last revised 02/12/2019. Last accessed 02/20/2021.
[7] Phase IIIb Study of APD421 in Combination as PONV Prophylaxis. *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/record/NCT02337062?view=record. Last revised 03/20/2019. Last accessed 02/20/2021.
[8] Study of APD421 as PONV Treatment (No Prior Prophylaxis). *ClnicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02449291. Last revised 01/22/2019. Last accessed 02/20/2021.
[9] Study of APD421 as PONV Treatment (Prior Prophylaxis). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02646566. Last revised 01/22/2019. Last accessed 02/20/2021.
[10] Gan T, Belani K, Bergese S, et al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. *Anesth Analg* 2020; 131(2):411-448.

# Appendix S

# Calendar Year 2020 Annual Review of Growth Hormone Products and 30-Day Notice to Prior Authorize Sogroya® (Somapacitan-beco)

**Oklahoma Health Care Authority**
**March 2021**

## Current Prior Authorization Criteria

| Growth Hormone Products | |
|---|---|
| **Tier-1*** | **Tier-2** |
| **Genotropin®** (Pfizer) - Cartridge, MiniQuick | **Humatrope®** (Eli Lilly) - Vials, Cartridge Kits |
| | **Norditropin®** (NovoNordisk) - FlexPro® Pens |
| | **Nutropin® and Nutropin AQ®** (Genentech) - Vials, Pen Cartridge, NuSpin® |
| | **Omnitrope®** (Sandoz) - Vials, Cartridge |
| | **Saizen®** (EMD Serono) - Vials, click.easy® |
| | **Serostim®** (EMD Serono) - Vials |
| | **Zomacton® and Zoma-Jet®** (Ferring) - Vials, Injection Device |
| | **Zorbtive®** (EMD Serono) - Vials |

*Supplementally rebated product(s); tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Cost (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC).
All products contain the identical 191 amino acid sequence found in pituitary-derived human growth hormone (hGH).

**Growth Hormone Covered Indications** *(prior to epiphyseal closure)*:

1. Classic human growth hormone (hGH) deficiency as determined by childhood hGH stimulation tests; or
2. Panhypopituitarism with history of pituitary or hypothalamic injury due to tumor, trauma, surgery, whole brain radiation, irradiation, hemorrhage or infarction, or a congenital anomaly, and 1 of the following:
    a. Deficiency of 3 or more pituitary hormones and insulin-like growth factor (IGF)-1 ≥2.5 standard deviations (SD) below the mean for the member's age and gender; or
    b. No deficiency or deficiency in <3 pituitary hormones and IGF-1 <50th percentile and failure of a growth hormone stimulation test; or
    c. Member is 12 months post trauma or surgery and does not have evidence of tumor recurrence and member's growth has not restarted; the member must still meet all the other criteria,

however authorization does not require height to be ≥2.25 SD below the mean for age and gender in these circumstances; or

3. Panhypopituitarism in children with height ≥2.25 SD below the mean for age and gender and MRI evidence of pituitary stalk agenesis, empty sella, or ectopic posterior pituitary "bright spot"; or
4. Short stature associated with Prader-Willi Syndrome; or
5. Short stature associated with Noonan Syndrome; or
6. Short stature associated with chronic renal insufficiency (pre-transplantation); or
7. History of intrauterine growth restriction in children who have not reached a normal height (≥2.25 SD below mean for age and gender) by 2 years of age; or
8. Idiopathic short stature (ISS) in children who are ≥2.25 SD below mean for height (based on age and gender) and are unlikely to catch up in height; or
9. Turner syndrome or 45X, 46XY mosaicism; or
10. Hypoglycemia with evidence for hGH deficiency; or
11. Short-stature homeobox-containing gene (SHOX) deficiency with genetic evidence for SHOX deficiency; or
12. Other evidence for hGH deficiency submitted for panel review and decision.

**Growth Hormone Tier-2 Approval Criteria:**

1. Documented allergic reaction to non-active components of all available Tier-1 products; or
2. A clinical exception applies to members with a diagnosis of acquired immunodeficiency syndrome (AIDS) wasting syndrome, in which case Serostim® can be used, regardless of its current Tier status.

**Requirements for Initiation of Growth Hormone Therapy – All Indications:**

1. Evaluated and prescribed by an endocrinologist, pediatric nephrologist, or infectious disease specialist; and
2. Covered indication; and
3. Member must be 2 years of age or older [*Exceptions*: hypoglycemia related to growth hormone deficiency (GHD): any age; idiopathic short stature (ISS): 8 years of age or older]; and
4. Height ≥2.25 SD below the mean for age (excludes chronic renal failure); and
5. Evidence of delayed bone age (excludes chronic renal failure) and open epiphyses; and
6. The following information must be provided:
    a. Growth chart; and
    b. Parental heights.

**Discontinuation of Therapy or Transition to Adult Therapy Criteria:**

1. Failure to show improvement in height percentile on growth chart after 1 year of treatment; or
2. Growth velocity <2.5cm/year unless associated with another growth-limiting and treatable medical condition (i.e., hypothyroidism); or
3. Epiphyseal closure; or
4. Covered height has been reached:
    a. 152.4cm (60 inches) for girls; or
    b. 165.1cm (65 inches) for boys; or
5. Inadequate compliance; or
6. Significant adverse effects.

**Insulin-Like Growth Factor-1 (IGF-1) Analog Medications: Increlex® and Iplex™ [Mecasermin (rDNA Origin) Injection] Approval Criteria:**

1. Therapy initiated by an endocrinologist; and
2. Diagnosis of primary IGF-1 deficiency with all of the following:
    a. Height >3 standard deviations (SD) below the mean; and
    b. Basal IGF-1 >3 SD below the mean; and
    c. Normal or elevated growth hormone (GH); and
3. Documentation of mutation in GH receptor (GHR) or mutation in post-GHR signaling pathway or IGF-1 gene defects (Laron Syndrome); and
4. IGF-1 analog medications will not be approved for use in secondary IGF-1 deficiencies related to GH deficiency, malnutrition, hypothyroidism, or chronic steroid therapy.

**Serostim® (Somatropin) Approval Criteria:**

1. Initial Approval:
    a. An FDA approved diagnosis of human immunodeficiency virus (HIV)-associated wasting; and
    b. Member must be receiving optimal antiretroviral treatment; and
    c. Member must have an unintentional weight loss of >10% if baseline pre-morbid weight was <120% of ideal body weight (IBW) or unintentional weight loss of >20% if baseline pre-morbid weight was >120% of IBW; and
    d. Member must not have a reversible cause of weight loss such as infection, gastrointestinal (GI) bleed/obstruction, or malnutrition; and
    e. Member is receiving aggressive nutritional intake or supplementation; and
    f. Member must not have an active malignancy (except localized Kaposi's sarcoma); and
    g. Member has failed a trial of megestrol acetate and/or dronabinol; and

    h. Male members must have been evaluated for testosterone deficiency and treated as needed; and
    i. Approvals will be for 4 weeks initially and a quantity limit of 28 vials per 28 days will apply.
2. Continuation Approval:
    a. At 4 weeks, member must be evaluated for response to therapy (weight gain), side effects, and compliance. If member's response and compliance is appropriate, another 4 weeks of therapy will be approved; and
    b. Subsequent follow up evaluations will be required every 4 weeks to assess response and compliance. The member may receive another 4 weeks of therapy for a maximum of 12 weeks continuous therapy.
3. Discontinuation Criteria:
    a. Completion of the FDA approved 12 week duration of therapy; or
    b. Treatment failure measured by no weight gain despite 8 weeks of therapy, or continued/resumed weight loss at any time following 8 weeks of therapy when other potential causes have resolved or ruled out; or
    c. Member noncompliance; or
    d. Adverse effects that are refractory to dose reduction; or
    e. New or progressive Kaposi's Sarcoma; or
    f. Member weight exceeds 110% of pre-morbid weight.

**Zorbtive® (Somatropin) Approval Criteria:**

1. An FDA approved diagnosis of short bowel syndrome (SBS); and
2. Documentation of specialized nutritional support (may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences; nutritional supplements may be added according to the discretion of the treating physician); and
3. Must be used in conjunction with optimal management of SBS (may include dietary adjustments, enteral feedings, parenteral nutrition, fluids, and micronutrient supplements as needed); and
4. Member must be under the care of a gastroenterologist; and
5. Dose does not exceed 8mg/day; and
6. Approvals will be for 4 weeks of treatment.

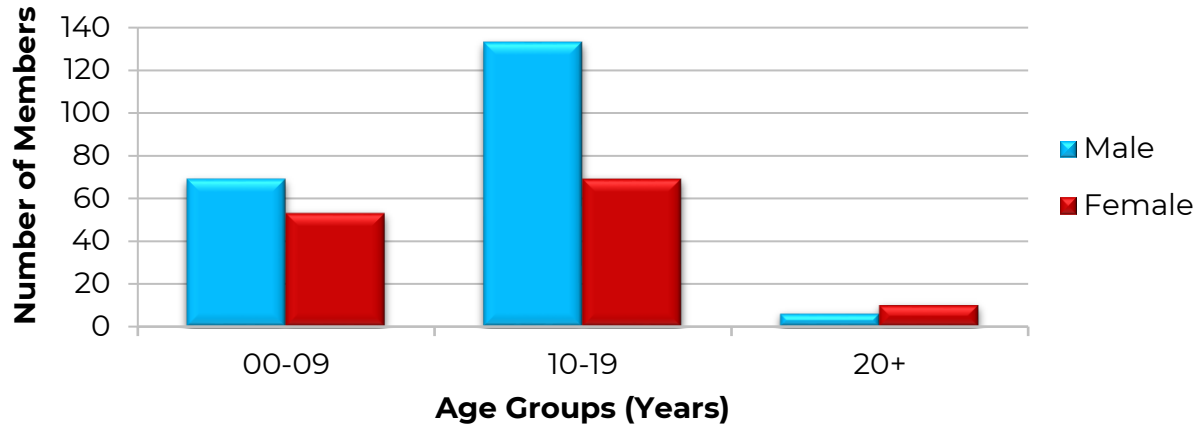
## Utilization of Growth Hormone: Calendar Year 2020

### Comparison of Calendar Years

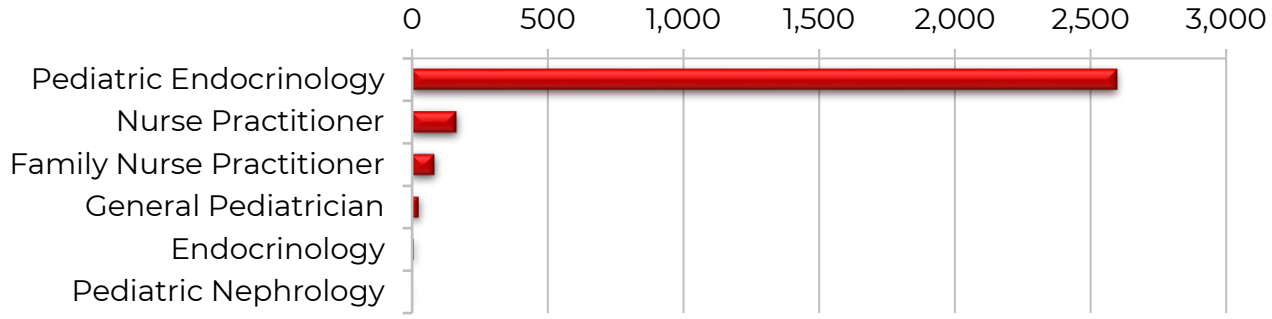
| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2019** | 352 | 3,000 | $10,833,028.55 | $3,611.01 | $125.93 | 48,223 | 86,023 |
| **2020** | 340 | 2,891 | $11,121,066.25 | $3,846.79 | $136.14 | 33,189 | 81,689 |
| **% Change** | **-3.40%** | **-3.60%** | **2.70%** | **6.50%** | **8.10%** | **-31.20%** | **-5.00%** |
| **Change** | **-12** | **-109** | **$288,037.70** | **$235.78** | **$10.21** | **-15,034** | **-4,334** |

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

### Demographics of Members Utilizing Growth Hormone

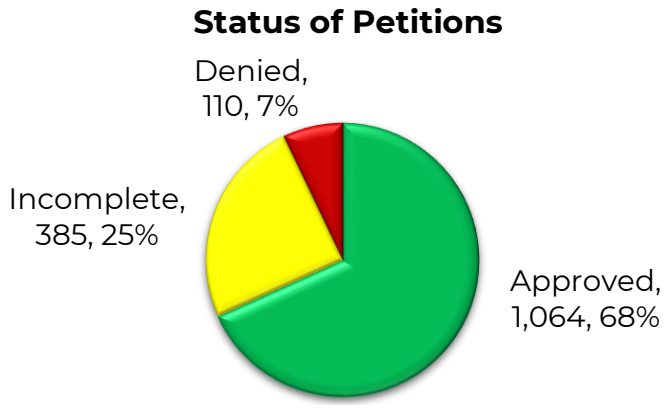



### Top Prescriber Specialties of Growth Hormone by Number of Claims




## Prior Authorization of Growth Hormone

There were 1,559 prior authorization requests submitted for 387 unique members for growth hormone during calendar year 2020. The following chart shows the status of the submitted petitions for calendar year 2020.




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

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

- **August 2020:** The FDA approved Sogroya® (somapacitan-beco) for the replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD). Sogroya® is the first product for GHD to be approved for once-weekly subcutaneous (sub-Q) administration; other FDA approved products are administered daily.

**Pipeline:**

- **Somatrogon:** Pfizer and OPKO are developing somatrogon for the treatment of pediatric patients with GHD. Somatrogon is a glycosylated human growth hormone (hGH) product that also contains multiple copies of the C-terminal peptide (CTP) from the beta chain of human chorionic gonadotropin (hCG). The glycosylation and CTP domains increase the half-life of the molecule and allow for once-weekly dosing. In January 2021, Pfizer and OPKO announced the FDA accepted their Biologics License Application (BLA) for somatrogon for the treatment of pediatric patients with GHD. The BLA submission is supported by data from a Phase 3 study in 224 pediatric patients with GHD. Patients were randomized 1:1 to weekly somatrogon or daily Genotropin® (somatropin). The results of the study demonstrated that once-weekly somatrogon was non-inferior to daily Genotropin® for the primary endpoint of annual height velocity at 12 months. The FDA is expected to make a decision regarding the BLA for somatrogon in October 2021.
- **TransCon hGH (Lonapegsomatropin):** Ascendis is developing TransCon hGH (lonapegsomatropin), a long-acting, once-weekly prodrug of somatropin for adults and pediatric patients with GHD. TransCon hGH is formulated with an inert polyethylene glycol (PEG)-containing carrier molecule designed to extend the half-life and reduce dosing from daily to once-weekly. Ascendis is also developing an auto-injector for use with TransCon hGH which will deliver small volume once-weekly doses with potential Bluetooth® connectivity to enable

patient support and data capture functions. In June 2020, Ascendis announced the submission of a BLA for TransCon hGH for the treatment of pediatric GHD with a Prescription Drug User Fee Act (PDUFA) action date of June 25, 2021.

## Sogroya® (Somapacitan-beco) Product Summary[7,8]

**Indication(s):** Sogroya® (somapacitan-beco) is an hGH analog indicated for the replacement of endogenous growth hormone in adults with GHD.

**How Supplied:** Solution containing 10mg/1.5mL somapacitan in a single-patient-use prefilled pen

**Dosing and Administration:**

- Initial Dosing: 1.5mg sub-Q once weekly for most patients
  - Dose should be titrated every 2 to 4 weeks by approximately 0.5mg to 1.5mg based on clinical response and serum insulin-like growth factor 1 (IGF-1) concentrations.
- Maximum Dose: 8mg once weekly
- Patients 65 Years of Age and Older: Initial dose should be 1mg once weekly and smaller dose increases should be used when titrating.
- Patients with Moderate Hepatic Impairment: Initial dose should be 1mg once weekly and smaller dose increases should be used when titrating.
  - Sogroya® is not recommended in patients with severe hepatic impairment.
- Patients Receiving Oral Estrogen: Initial dose of 2mg once weekly is recommended
- Sogroya® should be administered as a sub-Q injection into the abdomen or thigh.
- Injection sites should be rotated regularly to avoid lipohypertrophy.
- Sogroya® should be stored refrigerated at 2°C to 8°C (36°F to 46°F) before and during use. Sogroya® should not be used if it has been frozen or kept above 30°C (86°F). The total cumulative time allowed at room temperature [up to 25°C (77°F)] is 72 hours regardless of whether the product is in-use (opened) or unopened.

**Mechanism of Action:** Somapacitan is an hGH analog containing a single substitution in the 191 amino acid backbone. Specifically, a leucine at position 101 has been substituted for a cysteine, to which an albumin-binding side chain has been attached. By binding to albumin, the clearance of somapacitan is reduced and the half-life is extended, allowing for once-weekly dosing. Somapacitan binds to a dimeric growth hormone receptor in the cell membrane of target cells, resulting in intracellular signal transduction and a variety of subsequent pharmacodynamic effects, some of which are mediated through IGF-1.

**Contraindication(s):**

- Acute critical illness after open-heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure because of the risk of increased mortality with use of pharmacologic doses of Sogroya®
- Active malignancy
- Hypersensitivity to Sogroya® or any of its excipients
- Active proliferative or severe non-proliferative diabetic retinopathy

**Adverse Reactions:** The most common adverse reactions (occurring in >2% of patients receiving Sogroya® and ≥1% more than in placebo) in clinical trials were back pain, arthralgia, dyspepsia, sleep disorder, dizziness, tonsillitis, peripheral edema, vomiting, adrenal insufficiency, hypertension, blood creatine phosphokinase increase, weight increase, and anemia.

**Efficacy:** The safety and efficacy of Sogroya® were established in a 35-week double-blind, placebo-controlled study in 300 adult patients with GHD. Patients included in the study were all treatment-naïve or had no exposure to hGH therapy for >180 days prior to randomization. Patients were randomized 2:1:2 to receive somapacitan 10mg/1.5mL once weekly, placebo once weekly, or somatropin 10mg/1.5mL once daily for a 34-week treatment period. The primary endpoint was the change from baseline in truncal fat percentage at week 34. Patients receiving once-weekly somapacitan had a 1.06% decrease from baseline in truncal fat. Patients receiving once-weekly placebo had a 0.47% increase from baseline in truncal fat. Patients receiving daily somatropin had a 2.23% decrease from baseline in truncal fat. The absolute treatment difference (comparing once-weekly somapacitan and once-weekly placebo) of -1.53% was statistically significant in favor of somapacitan (P=0.0090). Additionally, the average IGF-1 standard deviation score was normalized in patients receiving somapacitan but not in patients receiving placebo at week 34. There were no formal statistical comparisons performed between weekly somapacitan and daily somatropin in this study.

**Cost:** Cost information is not yet available for Sogroya®, and a launch date for the product has not yet been announced.

## Recommendations

The College of Pharmacy recommends the placement of Sogroya® (somapacitan-beco) into Tier-2 of the growth hormone products Product Based Prior Authorization (PBPA) category with the following criteria in red:

**Sogroya® (Somatropin) Approval Criteria:**

1. Member must have a confirmed diagnosis of adult growth hormone deficiency (GHD) confirmed by 1 of the following:

   a. Insulin tolerance test (ITT) or glucagon test with a peak growth hormone (GH) response <3ng/mL; or
   b. ≥3 pituitary hormone deficiencies and insulin like growth factor-1 (IGF-1) standard deviation score (SDS) <-2.0; and
2. Member must be 18 years of age or older; and
3. Sogroya® must be prescribed by an endocrinologist; and
4. Member's baseline IGF-1 level and SDS must be provided; and
5. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use all Tier-1 product(s) must be provided; and
6. Prescriber must verify the member does not have active malignancy or active proliferative or severe non-proliferative diabetic retinopathy; and
7. Prescriber must verify the member has been counseled on proper administration and storage of Sogroya®; and
8. Approval quantity will be based on the FDA approved dosing in accordance with the Sogroya® *Prescribing Information*; and
9. Initial approvals will be for the duration of 6 months. For additional approval consideration, compliance will be evaluated and the prescriber must verify the member is responding well to treatment as demonstrated by a reduction in truncal fat percentage or normalization of IGF-1 level (IGF-1 SDS of -0.5 to 1.75); and
10. A maximum approved dose of 8mg per week will apply.

| Growth Hormone Products | |
|---|---|
| **Tier-1*** | **Tier-2** |
| **Genotropin®** (Pfizer) - Cartridge, MiniQuick | **Humatrope®** (Eli Lilly) - Vials, Cartridge Kits |
| | **Norditropin®** (NovoNordisk) - FlexPro® Pens |
| | **Nutropin® and Nutropin AQ®** (Genentech) - Vials, Pen Cartridge, NuSpin® |
| | **Omnitrope®** (Sandoz) - Vials, Cartridge |
| | **Saizen®** (EMD Serono) - Vials, click.easy® |
| | **+Serostim®** (EMD Serono) - Vials |
| | **+Sogroya® (somapacitan-beco)** (NovoNordisk) - Pens |
| | **Zomacton® and Zoma-Jet®** (Ferring) - Vials, Injection Device |
| | **+Zorbtive®** (EMD Serono) - Vials |

*Supplementally rebated product(s); tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Cost (NADAC), or Wholesale Acquisition Cost (WAC) if NADAC unavailable.

+Additional approval criteria applies.

All products, other than Sogroya®, contain the identical 191 amino acid sequence found in pituitary-derived human growth hormone (hGH). For Sogroya®, 1 amino acid has been substituted and linked to an albumin-binding side chain.

## Utilization Details of Growth Hormone: Calendar Year 2020

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM | CLAIMS/ MEMBER | % COST |
|---|---|---|---|---|---|---|
| **TIER-1 PRODUCTS** | | | | | | |
| **GENOTROPIN PRODUCTS** | | | | | | |
| GENOTROPIN INJ 12MG | 1,111 | 153 | $5,423,909.70 | $4,882.01 | 7.26 | 48.77% |
| GENOTROPIN INJ 5MG | 534 | 146 | $1,495,934.12 | $2,801.37 | 3.66 | 13.45% |
| GENOTROPIN INJ 0.4MG | 153 | 41 | $233,828.10 | $1,528.29 | 3.73 | 2.10% |
| GENOTROPIN INJ 1MG | 152 | 39 | $607,815.11 | $3,998.78 | 3.9 | 5.47% |
| GENOTROPIN INJ 0.6MG | 116 | 45 | $282,344.34 | $2,434.00 | 2.58 | 2.54% |
| GENOTROPIN INJ 0.2MG | 110 | 28 | $90,516.58 | $822.88 | 3.93 | 0.81% |
| GENOTROPIN INJ 2MG | 79 | 19 | $633,918.91 | $8,024.29 | 4.16 | 5.70% |
| GENOTROPIN INJ 0.8MG | 75 | 28 | $252,335.45 | $3,364.47 | 2.68 | 2.27% |
| GENOTROPIN INJ 1.2MG | 68 | 17 | $369,777.60 | $5,437.91 | 4 | 3.33% |
| GENOTROPIN INJ 1.4MG | 66 | 26 | $368,142.56 | $5,577.92 | 2.54 | 3.31% |
| GENOTROPIN INJ 1.6MG | 63 | 26 | $402,958.88 | $6,396.17 | 2.42 | 3.62% |
| GENOTROPIN INJ 1.8MG | 46 | 12 | $332,263.98 | $7,223.13 | 3.83 | 2.99% |
| **TIER-1 SUBTOTAL** | **2,573** | **316*** | **$10,493,745.33** | **$4,078.41** | **8.14** | **94.36%** |
| **TIER-2 PRODUCTS⁺** | | | | | | |
| **NORDITROPIN PROUCTS** | | | | | | |
| NORDITROPIN INJ 5MG/1.5ML | 148 | 22 | $209,784.02 | $1,417.46 | 6.73 | 1.89% |
| NORDITROPIN INJ 10MG/1.5ML | 86 | 16 | $160,107.83 | $1,861.72 | 5.38 | 1.44% |
| NORDITROPIN INJ 15MG/1.5ML | 52 | 9 | $114,170.02 | $2,195.58 | 5.78 | 1.03% |
| NORDITROPIN INJ 30MG/3ML | 14 | 4 | $132,166.34 | $9,440.45 | 3.5 | 1.19% |
| **SUBTOTAL** | **300** | **51** | **$616,228.21** | **$2,054.09** | **5.88** | **5.54%** |
| **HUMATROPE PRODUCTS** | | | | | | |
| HUMATROPE INJ 12MG | 9 | 2 | $6,870.20 | $763.36 | 4.5 | 0.06% |
| **SUBTOTAL** | **9** | **2** | **$6,870.20** | **$763.36** | **4.5** | **0.06%** |
| **NUTROPIN PRODUCTS** | | | | | | |
| NUTROPIN AQ INJ 10MG/2ML | 5 | 1 | $789.55 | $157.91 | 5 | 0.01% |
| **SUBTOTAL** | **5** | **1** | **$789.55** | **$157.91** | **5** | **0.01%** |
| **OMNITROPE PRODUCTS** | | | | | | |
| OMNITROPE INJ 5MG/1.5ML | 2 | 1 | $734.81 | $367.41 | 2 | 0.01% |
| OMNITROPE INJ 10MG/1.5ML | 2 | 2 | $2,698.15 | $1,349.08 | 1 | 0.02% |
| **SUBTOTAL** | **4** | **3** | **$3,432.96** | **$858.24** | **1.33** | **0.03%** |
| **TIER-2 SUBTOTAL** | **318** | **54*** | **$627,320.92** | **$1,972.71** | **5.89** | **5.64%** |
| **TOTAL** | **2,891** | **340*** | **$11,121,066.25** | **$3,846.79** | **8.5** | **100.00%** |

INJ = injection
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
⁺Claims for Tier-2 products largely consist of claims for which SoonerCare is not the primary payer; therefore, the reimbursed amount included in the above data is not a true reflection of the cost of the medication for SoonerCare.

[1] Park B. FDA Approves Sogroya®, a Once-Weekly Growth Hormone Deficiency Therapy. *MPR*. Available online at: https://www.empr.com/home/news/fda-approves-sogroya-a-once-weekly-growth-hormone-deficiency-therapy/. Issued 09/02/2020. Last accessed 02/11/2021.
[2] U.S. Food and Drug Administration (FDA). FDA Approves Weekly Therapy for Adult Growth Hormone Deficiency. Available online at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-weekly-therapy-adult-growth-hormone-deficiency. Issued 09/01/2020. Last accessed 02/11/2021.
[3] OPKO Biologics. OPKO Pipeline: Somatrogon. Available online at: https://www.opkobiologics.com/pipeline/product-candidates/hgh-ctp/. Last accessed 02/11/2021.
[4] Pfizer, Inc. US FDA Accepts Regulatory Submission from Pfizer and OPKO for Review of Somatrogon to Treat Pediatric Patients with Growth Hormone Deficiency. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/us-fda-accepts-regulatory-submission-pfizer-and-opko-review. Issued 01/04/2021. Last accessed 02/11/2021.
[5] Ascendis Pharma. Ascendis Pipeline: TransCon hGH. Available online at: https://ascendispharma.us/pipeline/endocrinology/transcon-hgh/. Last accessed 02/11/2021.
[6] Ascendis Pharma. Ascendis Pharma A/S Announces Submission of Biologics License Application (BLA) to FDA for TransCon hGH in Pediatric Growth Hormone Deficiency. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2020/06/26/2054042/0/en/Ascendis-Pharma-A-S-Announces-Submission-of-Biologics-License-Application-BLA-to-FDA-for-TransCon-hGH-in-Pediatric-Growth-Hormone-Deficiency.html. Issued 06/26/2020. Last accessed 02/11/2021.
[7] Sogroya® (Somapacitan-beco) Prescribing Information. Novo Nordisk, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761156s000lbl.pdf. Last revised 08/2020. Last accessed 02/11/2021.
[8] Trial to Compare the Efficacy and Safety of NNC0195-0092 (Somapacitan) with Placebo and Norditropin® FlexPro® (Somatropin) in Adults with Growth Hormone Deficiency. (REAL 1). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02229851. Last revised 11/23/2020. Last accessed 02/11/2021.

# Appendix T

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

**FDA NEWS RELEASE**

**For Immediate Release: February 17, 2021**

**FDA Approves First in the World, First-of-Its-Kind Implant for the Treatment of Rare Bone Disease as a Humanitarian Use Device**

The FDA approved the Patient Specific Talus Spacer 3D-printed talus implant for humanitarian use. The Patient Specific Talus Spacer is the first in the world and first-of-its-kind implant to replace the talus for the treatment of avascular necrosis (AVN) of the ankle joint, a serious and progressive condition that causes the death of bone tissue stemming from a lack of blood supply to the area. The implant provides a joint-sparing alternative to other surgical interventions commonly used in late-stage AVN that may disable motion of the ankle joint.

AVN is often caused by a sudden injury such as a broken bone or a dislocated joint or sustained damage to the tissue that develops over time, and it occurs when there is a lack of blood supply to bone tissue, causing it to become necrotic. When the bones of a joint are affected, such as in the case of the ankle, the cartilage that keeps the bones from rubbing together can deteriorate, causing arthritis and pain. Late-stage AVN of the ankle may result in the talus bone partially or fully collapsing. Current available treatments include fusing the joints in the foot and ankle together, a procedure which helps to alleviate pain caused by AVN but eliminates motion in the joint, or below-the-knee amputation.

The Patient Specific Talus Spacer is a 3D printed implant that can be used in talus replacement surgery. The talus spacer is made for each patient individually, modeled from computed tomography (CT) imaging, and is fitted to a patient's specific anatomy. During the replacement surgery, the patient's talus bone is removed and replaced with the implant, which is made from cobalt chromium alloy.

While fusion may become necessary in the future should the condition worsen, talus replacement surgery with the Patient Specific Talus Spacer is intended to be a joint-sparing procedure, as it allows the patient to retain motion in the ankle joint.

The FDA reviewed data for the Patient Specific Talus Spacer through the humanitarian device exemption (HDE) process. A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects not more than 8,000 individuals in the United States per year.

Data supporting the safety and probable benefit of the Patient Specific Talus Spacer include results from 31 patients and 32 talus replacement surgeries (1 patient had operations on both ankles) with the implant. At 3 years post-operation, the average reported pain decreased from “moderate to severe” prior to surgery to “mild” post-surgery, and average range of motion in the ankle joint also improved. These measures were assessed using standard subjective scoring systems for pain and functionality.

By the 3-year mark, out of 32 cases, there were 3 reported additional surgeries. The most common reported adverse events were pain and scar tissue at the surgery site.

**FDA NEWS RELEASE**

**For Immediate Release: February 12, 2021**

**FDA Approves Drug to Reduce Bone Marrow Suppression Caused by Chemotherapy**

The FDA approved Cosela (trilaciclib) as the first therapy in its class to reduce the frequency of chemotherapy-induced bone marrow suppression in adults receiving certain types of chemotherapy for extensive-stage small cell lung cancer. Cosela may help protect bone marrow cells from damage caused by chemotherapy by inhibiting cyclin-dependent kinase 4/6, a type of enzyme.

Chemotherapy drugs are designed to kill cancer cells but can damage normal tissues as well. The bone marrow is particularly susceptible to chemotherapy damage. The bone marrow makes red blood cells, white blood cells, and platelets that transport oxygen, fight infection, and stop bleeding. When damaged, the bone marrow produces fewer of these cells, leading to fatigue, increased risk of infection, and bleeding, among other problems. Cosela may help protect the normal bone marrow cells from the harmful effects of chemotherapy.

The effectiveness of Cosela was evaluated in 3 randomized, double-blind, placebo-controlled studies in patients with extensive-stage small cell lung cancer. Combined, these studies randomly assigned 245 patients to receive either an intravenous (IV) infusion of Cosela or a placebo before chemotherapy. The studies then compared the 2 groups for the proportion of patients with severe neutropenia and the duration of severe neutropenia in the first cycle of chemotherapy. In all 3 studies, patients who received Cosela had a lower chance of having severe neutropenia compared to patients who received a placebo. Among those who had severe neutropenia, patients who received Cosela, on average, had it for a shorter time than patients who received a placebo.

The most common side effects of Cosela include fatigue; low levels of calcium, potassium and phosphate; increased levels of an enzyme called aspartate aminotransferase; headache; and pneumonia. Patients should also

be advised about injection site reactions, acute drug hypersensitivity, interstitial lung disease/pneumonitis and embryo-fetal toxicity.

Cosela received FDA Priority Review and Breakthrough Therapy designations for the indication noted above.

**FDA NEWS RELEASE**

**For Immediate Release: February 9, 2021**

**Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19**

The FDA issued an emergency use authorization (EUA) for bamlanivimab and etesevimab administered together for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients 12 years of age or older weighing at least 40kg who test positive for SARS-CoV-2 and who are at high risk for progressing to severe COVID-19. The authorized use includes treatment for those who are 65 years of age or older or who have certain chronic medical conditions.

In a clinical trial of patients with COVID-19 at high risk for disease progression, a single IV infusion of bamlanivimab and etesevimab administered together significantly reduced COVID-19-related hospitalization and death during 29 days of follow-up compared to placebo. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continue to be evaluated.

Bamlanivimab and etesevimab are not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. Treatment with bamlanivimab and etesevimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses. Bamlanivimab and etesevimab are monoclonal antibodies that are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells. Bamlanivimab and etesevimab bind to different but overlapping sites on the spike protein of the virus.

The issuance of an EUA is different than an FDA approval. In determining whether to issue an EUA, the FDA evaluates the totality of available scientific evidence and carefully balances any known or potential risks with any known or potential benefits of the product for use during an emergency. Based on the FDA's review of the totality of the scientific evidence available, the agency has determined that it is reasonable to believe that bamlanivimab and etesevimab administered together may be effective in treating certain patients with mild or moderate COVID-19. When used to

treat COVID-19 for the authorized population, the known and potential benefits of these antibodies outweigh the known and potential risks. There are no adequate, approved, and available alternative treatments to bamlanivimab and etesevimab administered together for the authorized population.

The data supporting this EUA for bamlanivimab and etesevimab are based on a randomized, double-blind, placebo-controlled clinical trial in 1,035 non-hospitalized adults with mild-to-moderate COVID-19 symptoms who were at high risk for progressing to severe COVID-19. Of these patients, 518 received a single infusion of bamlanivimab 2,800mg and etesevimab 2,800mg together, and 517 received placebo. The primary endpoint was COVID-19 related hospitalizations or death by any cause during 29 days of follow-up. Hospitalization or death occurred in 36 (7%) patients who received placebo compared to 11 (2%) patients treated with bamlanivimab 2,800mg and etesevimab 2,800mg administered together, a 70% reduction. All 10 deaths (2%) deaths occurred in the placebo group. Thus, all-cause death was significantly lower in the bamlanivimab 2,800mg and etesevimab 2,800mg group than the placebo group.

The authorized dosage of 700mg bamlanivimab and 1,400mg etesevimab administered together is based on analyses of available preclinical, clinical, and virologic data, as well as pharmacokinetic and pharmacodynamic modeling, which, in totality, support that the authorized dosage is expected to have a similar clinical and virologic effect to 2,800mg bamlanivimab and 2,800mg etesevimab administered together.

On November 9, 2020, the FDA issued an EUA for a single infusion of 700mg bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and certain pediatric patients. While bamlanivimab and etesevimab administered together resulted in a lower risk of resistant viruses developing during treatment compared with bamlanivimab administered alone, both treatments are expected to benefit patients at high risk of disease progression. At present, both 700mg bamlanivimab alone as well as 700mg bamlanivimab and 1,400mg etesevimab administered together will be available under an EUA.

Under the EUA, fact sheets that provide important information about using bamlanivimab and etesevimab administered together in treating COVID-19 as authorized must be made available to health care providers and to patients and caregivers. These fact sheets include dosing instructions, potential side effects, and drug interactions. Serious and unexpected adverse events including hypersensitivity, anaphylaxis, and infusion-related reactions have been observed with bamlanivimab with and without coadministration of etesevimab. In addition, clinical worsening following bamlanivimab administration has been reported, although it is not known if these events were related to bamlanivimab use or were due to progression of COVID-19.

Possible side effects of bamlanivimab and etesevimab administered together include nausea, dizziness, pruritus, and rash.

**FDA NEWS RELEASE**

**For Immediate Release: February 5, 2021**

**FDA Approves New Treatment for Adults with Relapsed or Refractory Large B-Cell Lymphoma**

The FDA approved Breyanzi (lisocabtagene maraleucel), a cell-based gene therapy to treat adult patients with certain types of large B-cell lymphoma who have not responded to, or who have relapsed after, at least 2 other types of systemic treatment. Breyanzi, a chimeric antigen receptor (CAR) T-cell therapy, is the third gene therapy approved by the FDA for certain types of non-Hodgkin lymphoma, including diffuse large B-cell lymphoma (DLBCL). Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma.

DLBCL is the most common type of non-Hodgkin lymphoma in adults. Non-Hodgkin lymphomas are cancers that begin in certain cells of the immune system and can be either aggressive, fast-growing or slow-growing. Approximately 77,000 new cases of non-Hodgkin lymphoma are diagnosed in the United States each year and DLBCL represents approximately 1 in 3 newly diagnosed cases.

Each dose of Breyanzi is a customized treatment created using a patient's own T-cells to help fight the lymphoma. The patient's T-cells are collected and genetically modified to include a new gene that facilitates targeting and killing of the lymphoma cells. Once the cells are modified, they are infused back into the patient.

The safety and efficacy of Breyanzi were established in a multicenter clinical trial of more than 250 adults with refractory or relapsed large B-cell lymphoma. The complete remission rate after treatment with Breyanzi was 54%.

Treatment with Breyanzi has the potential to cause severe side effects. The labeling carries a *Boxed Warning* for cytokine release syndrome (CRS), which is a systemic response to the activation and proliferation of CAR T-cells, causing high fever and flu-like symptoms and neurologic toxicities. Both CRS and neurological events can be life-threatening. Other side effects include hypersensitivity reactions, serious infections, low blood cell counts, and a weakened immune system. Side effects generally appear within the first 1 to 2 weeks following treatment, but some side effects may occur later.

Because of the risk of CRS and neurologic toxicities, Breyanzi is being approved with a risk evaluation and mitigation strategy (REMS) which includes elements to assure safe use (ETASU). The FDA is requiring, among other things, that health care facilities that dispense Breyanzi be specially certified. As part of that certification, staff involved in the prescribing, dispensing, or administering of Breyanzi are required to be trained to

recognize and manage the risks of CRS and neurologic toxicities. The REMS program specifies that patients be informed of the signs and symptoms of CRS and neurological toxicities following infusion and of the importance of promptly returning to the treatment site if they develop fever or other adverse reactions after receiving treatment with Breyanzi.

To further evaluate the long-term safety, the FDA is also requiring the manufacturer to conduct a post-marketing observational study involving patients treated with Breyanzi.

The FDA granted Breyanzi Orphan Drug, Regenerative Medicine Advanced Therapy (RMAT), and Breakthrough Therapy designations. The RMAT designation program was created under the 21st Century Cures Act to help facilitate the expeditious development of regenerative medicine therapies intended for serious conditions. Breyanzi is the first regenerative medicine therapy with RMAT designation to be licensed by the FDA.

**FDA NEWS RELEASE**

**For Immediate Release: February 5, 2021**

**FDA Authorizes Marketing of Novel Device to Reduce Snoring and Mild Obstructive Sleep Apnea in Patients 18 Years and Older**

The FDA authorized marketing of a new prescription only device intended to reduce snoring and mild obstructive sleep apnea (OSA). Unlike devices used while patients sleep, this is the first device used while awake that is intended to improve tongue muscle function, which in time can help prevent the tongue from collapsing backwards and obstructing the airway during sleep.

OSA is a prevalent sleep-disordered breathing issue with potential serious long-term effects. It can occur when the upper airway becomes blocked repeatedly during sleep, reducing or completely stopping airflow. Untreated OSA can lead to serious complications such as heart attack, glaucoma, diabetes, cancer, and cognitive and behavioral disorders. OSA is categorized by the number of apneas plus the number of hypopneas that occur, on average, each hour. This number, called the Apnea-Hypopnea Index (AHI) measures the severity of OSA. Mild OSA is defined as an AHI score of >5 but <15. The device, the eXciteOSA, is a removable tongue muscle stimulation device that delivers neuromuscular stimulation to the tongue in order to reduce snoring and mild OSA for patients who are 18 years of age or older.

The eXciteOSA device works by delivering electrical muscle stimulation through a mouthpiece that sits around the tongue. The eXciteOSA mouthpiece has 4 electrodes, 2 located above the tongue and 2 located below the tongue. The device provides electrical muscle stimulation action in sessions that consist of a series of electrical pulses with rest periods in between. It is used for 20 minutes once a day during a wakeful state, for a period of 6-weeks, and once a week thereafter.

The FDA assessed the safety and effectiveness of the eXciteOSA device in 115 patients with snoring, including 48 patients with snoring and mild OSA. All patients used the device for 20 minutes, once a day for 6 weeks, then discontinued use for 2 weeks before they were reassessed. Overall, the percent of time spent snoring at levels louder than 40dB was reduced by more than 20% in 87 out of the 115 patients. In a 48-patient subset with snoring and mild OSA, the average AHI reduced by 48%, from 10.21 to 5.27, in 41 out of 48 patients. The most common adverse events observed were excessive salivation, tongue or tooth discomfort, tongue tingling, dental filling sensitivity, metallic taste, gagging, and tight jaw.

Patients should receive a comprehensive dental examination prior to use of the device. The eXciteOSA device is contraindicated for patients with pacemakers or implanted pacing leads (electrodes); patients with temporary or permanent implants, dental braces, intraoral metal prosthesis/ restorations/appliances or dental jewelry in the mouth; patients who are pregnant or may be pregnant; or patients suffering from ulcerations in or around the mouth. The eXciteOSA device is not intended for patients who have or are suspected of having OSA with an AHI of 15 and higher.

The FDA reviewed the device through the De Novo premarket review pathway, a regulatory pathway for low- to moderate-risk devices of a new type. Along with this authorization, the FDA is establishing special controls for devices of this type, including requirements related to labeling and performance testing. This means that subsequent devices of the same type with the same intended use may go through the FDA's 510(k) premarket notification process, whereby devices can obtain marketing authorization by demonstrating substantial equivalence to a predicate device. When met, the special controls, along with general controls, provide reasonable assurance of safety and effectiveness for devices of this type.

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

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

| | |
|---|---|
| Acetazolamide Injection | ***Currently in Shortage*** |
| Amifostine Injection | ***Currently in Shortage*** |
| Amino Acids | ***Currently in Shortage*** |
| Amoxapine Tablets | ***Currently in Shortage*** |
| Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets | ***Currently in Shortage*** |
| 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*** |
| 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*** |
| Calcium Disodium Versenate Injection | ***Currently in Shortage*** |
| Capreomycin Injection, USP | ***Currently in Shortage*** |
| Cefazolin Injection | ***Currently in Shortage*** |
| Cefotaxime Sodium Injection | ***Currently in Shortage*** |
| Cefotetan Disodium Injection | ***Currently in Shortage*** |
| Cefoxitin for Injection, USP | ***Currently in Shortage*** |
| Ceftazidime and Avibactam (AVYCAZ®) for Injection, 2 grams/0.5 grams | ***Currently in Shortage*** |
| Ceftolozane and Tazobactam (Zerbaxa®) Injection | ***Currently in Shortage*** |
| 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*** |
| Diltiazem Hydrochloride Injection | ***Currently in Shortage*** |
| Dimercaprol (Bal in Oil) Injection USP | ***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*** |
| Histreline Acetate Implant | ***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*** |
| Imipenem and Cilastatin for Injection, USP | ***Currently in Shortage*** |
| Isoniazid 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*** |
| Midazolam Injection, USP | ***Currently in Shortage*** |
| Misoprostol Tablets | ***Currently in Shortage*** |
| Morphine Sulfate Injection | ***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*** |
| Rifampin Injection | ***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*** |
| Succimer (Chemet) Capsules | ***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*** |

| | |
|---|---|
| Trimethobenzamide Hydrochloride Capsules | ***Currently in Shortage*** |
| Valproate Sodium Injection, USP | ***Currently in Shortage*** |
| Vecuronium Bromide for Injection | ***Currently in Shortage*** |
| Zinc Acetate Capsules | ***Currently in Shortage*** |