Oklahoma Health Care Authority

# Drug Utilization Review Board

## Wednesday,
## March 13, 2019
## 4:00pm

**Oklahoma Health Care Authority**
**4345 N. Lincoln Blvd.**
**Oklahoma City, OK 73105**

# *The University of Oklahoma*

*Health Sciences Center*

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS


MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – March 13, 2019

DATE: February 28, 2019

Note: The DUR Board will meet at 4:00pm The meeting will be held at 4345 N. Lincoln Blvd.

*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**

**Update on Medication Coverage Authorization Unit/Update: Drug Utilization Review of Prenatal Vitamins (PV) – Appendix B**

**Action Item – Vote to Prior Authorize Inbrija™ (Levodopa Inhalation) and Osmolex ER™ [Amantadine Extended-Release (ER)] – Appendix C**

**Action Item – Vote to Prior Authorize Aimovig™ (Erenumab-aooe), Ajovy™ (Fremanezumab-vfrm), and Emgality® (Galcanezumab-gnlm) – Appendix D**

**Action Item – Vote to Prior Authorize Epidiolex® (Cannabidiol), Diacomit® (Stiripentol), and Sympazan™ (Clobazam Oral Film) – Appendix E**

**Action Item – Vote to Prior Authorize Gamifant® (Emapalumab-lzsg) – Appendix F**

**Action Item – Vote to Prior Authorize Firdapse® (Amifampridine) – Appendix G**

**Action Item – Vote to Prior Authorize Retacrit™ (Epoetin Alfa-epbx) – Appendix H**

**Annual Review of Chronic Lymphocytic Leukemia (CLL) Medications and 30-Day Notice to Prior Authorize Copiktra™ (Duvelisib) – Appendix I**

**Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat) – Appendix J**

**30-Day Notice to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – Appendix K**

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

**Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide) – Appendix M**

**Annual Review of Multiple Sclerosis (MS) Medications – Appendix N**

**Annual Review of Luxturna™ (Voretigene Neparvovec-rzyl) – Appendix O**

**Annual Review of Osteoporosis Medications – Appendix P**

**Industry News and Updates – Appendix Q**

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

**Future Business**

**Adjournment**

# Oklahoma Health Care Authority

**Drug Utilization Review Board**
**(DUR Board)**
**Meeting – March 13, 2019 @ 4:00pm**

Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

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## AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

**1. Call to Order**

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

**2. Public Comment Forum**

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. February 13, 2019 DUR Minutes – Vote
B. February 13, 2019 DUR Recommendations Memorandum
C. Correspondence

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

**4. Update on Medication Coverage Authorization Unit/Update: Drug Utilization Review of Prenatal Vitamins (PV) – See Appendix B**

A. Medication Coverage Activity for February 2019
B. Pharmacy Helpdesk Activity for February 2019
C. Update: Drug Utilization Review of Prenatal Vitamins (PV)

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

**5. Action Item – Vote to Prior Authorize Inbrija™ (Levodopa Inhalation) and Osmolex ER™ [Amantadine Extended-Release (ER)] – See Appendix C**

A. Introduction
B. College of Pharmacy Recommendations

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

**6. Action Item – Vote to Prior Authorize Aimovig™ (Erenumab-aooe), Ajovy™ (Fremanezumab-vfrm), and Emgality® (Galcanezumab-gnlm) – See Appendix D**

A. Introduction
B. Cost Comparison
C. College of Pharmacy Recommendations

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

**7. Action Item – Vote to Prior Authorize Epidiolex® (Cannabidiol), Diacomit® (Stiripentol), and Sympazan™ (Clobazam Oral Film) – See Appendix E**

A. Introduction
B. Market News and Updates
C. College of Pharmacy Recommendations

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

**8. Action Item – Vote to Prior Authorize Gamifant® (Emapalumab-lzsg) – See Appendix F**

A. Introduction
B. College of Pharmacy Recommendations

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

**9. Action Item – Vote to Prior Authorize Firdapse® (Amifampridine) – See Appendix G**

A. Introduction
B. College of Pharmacy Recommendations

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

**10. Action Item – Vote to Prior Authorize Retacrit™ (Epoetin Alfa-epbx) – See Appendix H**

A. Introduction
B. College of Pharmacy Recommendations

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

**11. Annual Review of Chronic Lymphocytic Leukemia (CLL) Medications and 30-Day Notice to Prior Authorize Copiktra™ (Duvelisib) – See Appendix I**

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of CLL Medications
D. Prior Authorization of CLL Medications
E. Market News and Updates
F. Copiktra™ (Duvelisib) Product Summary
G. Recommendations
H. Utilization Details of CLL Medications

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

**12. Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc ), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat) – See Appendix J**

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. Recommendations
H. Utilization Details of Lymphoma Medications

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

**13. 30-Day Notice to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – See Appendix K**

A. Introduction
B. Market News and Updates
C. Product Summaries
D. Recommendations

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

**14. Action Item – Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – See Appendix L**

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

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

**15. Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide) – See Appendix M**

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

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

**16. Annual Review of Multiple Sclerosis (MS) Medications – See Appendix N**

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

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

**17. Annual Review of Luxturna™ (Voretigene Neparvovec-rzyl) – See Appendix O**

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Luxturna™ (Voretigene Neparvovec-rzyl)
D. Prior Authorization of Luxturna™ (Voretigene Neparvovec-rzyl)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

**18. Annual Review of Osteoporosis Medications – See Appendix P**

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

Non-Presentation; Questions Only:

**19. Industry News and Updates – See Appendix Q**

A. Introduction
B. News and Updates

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

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

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

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

A. Annual Review of Pharmacy Benefit
B. Diabetic Medications
C. Antihypertensive Medications
D. Lung Cancer Medications
E. Granulocyte Colony-Stimulating Factors

**Future business subject to change.*

## 22. Adjournment

# Appendix A

**OKLAHOMA HEALTH CARE AUTHORITY**
**DRUG UTILIZATION REVIEW BOARD MEETING**
**MINUTES OF MEETING OF FEBRUARY 13, 2019**

| BOARD MEMBERS: | PRESENT | ABSENT |
|---|---|---|
| Stephen Anderson, Pharm.D. | | x |
| Markita Broyles, D.Ph.; MBA | x | |
| Darlla D. Duniphin, MHS; PA-C | x | |
| Theresa Garton, M.D. | x | |
| Carla Hardzog-Britt, M.D. | x | |
| Ashley Huddleston, Pharm.D.; BCOP | | x |
| John Muchmore, M.D.; Ph.D.; Chairman | x | |
| Lee Munoz, D.Ph. | x | |
| James Osborne, Pharm.D. | x | |
| Paul Louis Preslar, D.O.; MBA; Vice Chairman | x | |

| COLLEGE OF PHARMACY STAFF: | PRESENT | ABSENT |
|---|---|---|
| Terry Cothran, D.Ph.; Pharmacy Director | x | |
| Melissa Abbott, Pharm.D.; Clinical Pharmacist | x | |
| Michyla Adams, Pharm.D.; Clinical Pharmacist | x | |
| Wendi Chandler, Pharm.D.; Clinical Pharmacist | x | |
| Sarai Connell, Pharm.D.; MBA; Resident | x | |
| Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison | x | |
| Thomas Ha, Pharm.D.; Clinical Pharmacist | x | |
| Bethany Holderread, Pharm.D.; Clinical Coordinator | x | |
| Shellie Keast, Ph.D.; Assistant Professor | | x |
| Brandy Nawaz, Pharm.D.; Clinical Pharmacist | x | |
| Regan Smith, Pharm.D.; Clinical Pharmacist | | x |
| Ashley Teel, Pharm.D.; Clinical Pharmacist | x | |
| Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist | x | |
| Graduate Students: Philip Looper, Pharm.D. | | x |
| Michael Nguyen, Pharm.D. | x | |
| Laura Tidmore, Pharm.D. | x | |
| Corby Thompson, Pharm.D. | | x |
| Reagan Williams, Pharm.D. | x | |
| Visiting Pharmacy Student(s): Ebot Taku | x | |

| OKLAHOMA HEALTH CARE AUTHORITY STAFF: | PRESENT | ABSENT |
|---|---|---|
| Melody Anthony, Deputy State Medicaid Director | | x |
| Marlene Asmussen, R.N.; Population Care Management Director | | x |
| Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Sr. Director of Pharmacy | | x |
| Kelli Brodersen, Marketing Coordinator | | x |
| Susan Eads, J.D.; Director of Litigation | | x |
| Robert Evans, M.D.; Sr. Medical Director | | x |
| Michael Herndon, D.O.; Chief Medical Officer | | x |
| Maria Maule, J.D.; Senior Director Legal Services | x | |
| Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director | x | |
| Thomas Nunn, D.O.; Medical Director | | x |
| Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director; CEO | | x |
| Jill Ratterman, D.Ph.; Clinical Pharmacist | x | |
| Kerri Wade, Pharmacy Operations Manager | x | |

| OTHERS PRESENT: | | |
|---|---|---|
| Doug Wood, ViiV HC | Karthik Rajasekaran, Greenwich | Dave Poskey, UCB |
| Tony Salicos, Greenwich | Zachary Henney, Dova | Sumar Bieda, Abbott |
| Don Nopper, Dova | Chris Stanfield, Supernus | Charlie Collins, Sanofi Genzyme |
| Jane Stephen, Amgen | Desi Petree, Pharmacyclics | Frances Bauman, Nov0 Nordisk |
| Matt Forney, Merck | Brent Hildebrand, Gilead | Sandra Manning, Acorda |
| Stacie Cadle, Acorda | Aaron Shaw, BI | Amber Schrantz, Lilly |
| Jim Dunlap, PhRMA | Brian Maves, Pfizer | |

| PRESENT FOR PUBLIC COMMENT: | |
|---|---|
| Karthik Rajasekaran | Greenwich Biosciences |
| Zachary Henney | Dova Pharmaceuticals |

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

**1A: ROLL CALL**

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

**ACTION: NONE REQUIRED**

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

**2A: AGENDA ITEM NO. 10 ZACHARY HENNEY**

**2B: AGENDA ITEM NO. 15 KARTHIK RAJASEKARAN**

**ACTION: NONE REQUIRED**

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

**3A: DECEMBER 12, 2018 DUR MINUTES – VOTE**

**3B: DECEMBER 12, 2018 DUR RECOMMENDATIONS MEMORANDUM**

**3C: JANUARY 9, 2019 DUR RECOMMENDATIONS MEMORANDUM**

Materials included in agenda packet; presented by Dr. Cothran

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

**ACTION: MOTION CARRIED**

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

**4A: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2019**

**4B: PHARMACY HELPDESK ACTIVITY FOR JANUARY 2019**

**4C: ACADEMIC DETAILING PROGRAM UPDATE**

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

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 5:** **NARROW THERAPEUTIC INDEX (NTI) DRUG LIST**

**5A: INTRODUCTION**

**5B: SOONERCARE NTI DRUG LIST**

Materials included in agenda packet; presented by Dr. Holderread

Dr. Garton recommended the addition of desipramine and nortriptyline

Dr. Broyles moved to approve; seconded by Dr. Hardzog-Britt

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 6:** **VOTE TO PRIOR AUTHORIZE ARIKAYCE® (AMIKACIN LIPOSOME INHALATION SUSPENSION)**

**6A: INTRODUCTION**

**6B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Holderread

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 7:** **VOTE TO PRIOR AUTHORIZE REVCOVI™ (ELAPEGADEMASE-LVLR)**

**7A: INTRODUCTION**

**7B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Holderread

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 8:** **VOTE TO PRIOR AUTHORIZE LONHALA® MAGNAIR® (GLYCOPYRROLATE INHALATION SOLUTION), YUPELRI™ (REVEFENACIN INHALATION SOLUTION), AND DUPIXENT® (DUPILUMAB) AND TO UPDATE THE PRIOR AUTHORIZATION CRITERIA FOR ARNUITY® ELLIPTA® (FLUTICASONE FUROATE), ARMONAIR™ RESPICLICK® (FLUTICASONE PROPIONATE), AIRDUO™ RESPICLICK® (FLUTICASONE PROPIONATE/SALMETEROL), BREO® ELLIPTA® (FLUTICASONE FUROATE/ VILANTEROL), TRELEGY™ ELLIPTA® (FLUTICASONE FUROATE/UMECLIDINIUM/VILANTEROL), XOLAIR® (OMALIZUMAB), AND FASENRA™ (BENRALIZUMAB)**

**8A: INTRODUCTION**

**8B: MARKET NEWS AND UPDATES**

**8C: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Nawaz

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 9:** **VOTE TO PRIOR AUTHORIZE LOKELMA™ (SODIUM ZIRCONIUM CYCLOSILICATE) AND TO UPDATE THE VELTASSA® (PATIROMER) PRIOR AUTHORIZATION CRITERIA**

**9A: INTRODUCTION**

**9B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Nawaz

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 10:** **VOTE TO PRIOR AUTHORIZE TAVALISSE™ (FOSTAMATINIB), DOPTELET® (AVATROMBOPAG), AND MULPLETA® (LUSUTROMBOPAG)**

**10A: INTRODUCTION**

**10B: MARKET NEWS AND UPDATES**

**10C: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Abbott

Dr. Broyles moved to approve; seconded by Dr. Hardzog-Britt

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 11:** **VOTE TO PRIOR AUTHORIZE CARBAGLU® (CARGLUMIC ACID)**

**11A: INTRODUCTION**

**11B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Connell

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 12:** **VOTE TO PRIOR AUTHORIZE XELPROS™ (LATANOPROST 0.005% EMULSION)**

**12A: INTRODUCTION**

**12B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 13:** **VOTE TO PRIOR AUTHORIZE MAKENA® [HYDROXYPROGESTERONE CAPROATE SUBCUTANEOUS (SUB-Q) AUTO-INJECTOR]**

**13A: INTRODUCTION**

**13B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Adams

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 14:** **VOTE TO PRIOR AUTHORIZE AKYNZEO® IV [FOSNETUPITANT/ PALONOSETRON INJECTION FOR INTRAVENOUS (IV) USE]**

**14A: INTRODUCTION**

**14B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Adams

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 15:** **ANNUAL REVIEW OF ANTICONVULSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EPIDIOLEX® (CANNABIDIOL), DIACOMIT® (STIRIPENTOL), AND SYMPAZAN™ (CLOBAZAM ORAL FILM)**

**15A: CURRENT PRIOR AUTHORIZATION CRITERIA**

**15B: UTILIZATION OF ANTICONVULSANTS**

**15C: PRIOR AUTHORIZATION OF ANTICONVULSANTS**

**15D: MARKET NEWS AND UPDATES**

**15E: EPIDIOLEX® (CANNABIDIOL ORAL SOLUTION) PRODUCT SUMMARY**

**15F: DIACOMIT® (STIRIPENTOL) PRODUCT SUMMARY**

**15G: COLLEGE OF PHARMACY RECOMMENDATIONS**

**15H: UTILIZATION DETAILS OF ANTICONVULSANTS**

Materials included in agenda packet; presented by Dr. Adams

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 16:** **ANNUAL REVIEW OF ANTI-MIGRAINE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AIMOVIG™ (ERENUMAB-AOOE), AJOVY™ (FREMANEZUMAB-VFRM), AND EMGALITY® (GALCANEZUMAB-GNLM)**

**16A: CURRENT PRIOR AUTHORIZATION CRITERIA**

**16B: UTILIZATION OF ANTI-MIGRAINE MEDICATIONS**

**16C: PRIOR AUTHORIZATION OF ANTI-MIGRAINE MEDICATIONS**

**16D: MARKET NEWS AND UPDATES**

**16E: AIMOVIG™ (ERENUMAB-AOOE) PRODUCT SUMMARY**

**16F: AJOVY™ (FREMANEZUMAB-VFRM) PRODUCT SUMMARY**

**16G: EMGALITY® (GALCANEZUMAB-GNLM) PRODUCT SUMMARY**

**16H: COST COMPARISON**

**16I: COLLEGE OF PHARMACY RECOMMENDATIONS**

**16J: UTILIZATION DETAILS OF ANTI-MIGRAINE MEDICATIONS**

Materials included in agenda packet; presented by Dr. Abbott

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 17:** **30-DAY NOTICE TO PRIOR AUTHORIZE GAMIFANT® (EMAPALUMAB-LZSG)**

**17A: INTRODUCTION**

**17B: GAMIFANT® (EMAPALUMAB-LZSG) PRODUCT SUMMARY**

**17C: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 18:** **30-DAY NOTICE TO PRIOR AUTHORIZE FIRDAPSE® (AMIFAMPRIDINE)**

**18A: INTRODUCTION**
**18B: MARKET NEWS AND UPDATES**
**18C: FIRDAPSE® (AMIFAMPRIDINE) PRODUCT SUMMARY**
**18D: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Connell

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 19:** **ANNUAL REVIEW OF ERYTHROPOIETIN STIMULATING AGENTS (ESAs) AND 30-DAY NOTICE TO PRIOR AUTHORIZE RETACRIT™ (EPOETIN ALFA-EPBX)**

**19A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**19B: UTILIZATION OF ESAs**
**19C: PRIOR AUTHORIZATION OF ESAs**
**19D: MARKET NEWS AND UPDATES**
**19E: COLLEGE OF PHARMACY RECOMMENDATIONS**
**19F: UTILIZATION DETAILS OF ESAs (PHARMACY CLAIMS)**
**19G: UTILIZATION DETAILS OF ESAs (MEDICAL CLAIMS)**

Materials included in agenda packet; presented by Dr. Nawaz

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 20:** **ANNUAL REVIEW OF PARKINSON'S DISEASE (PD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE INBRIJA™ (LEVODOPA INHALATION) AND OSMOLEX ER™ [AMANTADINE EXTENDED-RELEASE (ER)]**

**20A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**20B: UTILIZATION OF PD MEDICATIONS**
**20C: PRIOR AUTHORIZATION OF PD MEDICATIONS**
**20D: MARKET NEWS AND UPDATES**
**20E: INBRIJA™ (LEVODOPA INHALATION) PRODUCT SUMMARY**
**20F: OSMOLEX ER™ (AMANTADINE ER) PRODUCT SUMMARY**
**20G: COLLEGE OF PHARMACY RECOMMENDATIONS**
**20H: UTILIZATION DETAILS OF PD MEDICATIONS**

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 21:** **INDUSTRY NEWS AND UPDATES**

**21A: INTRODUCTION**
**21B: NEWS AND UPDATES**

Materials included in agenda packet; Non-presentation; Questions only

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 22:** **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 23:** **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

**23A: MULTIPLE SCLEROSIS MEDICATIONS**
**23B: LYMPHOMA MEDICATIONS**
**23C: CHRONIC LYMPHOCYTIC LEUKEMIA MEDICATIONS**
**23D: HEREDITARY ANGIOEDEMA MEDICATIONS**
**23E: OSTEOPOROSIS MEDICATIONS**

**Future business subject to change.*

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 24:** **ADJOURNMENT**

The meeting was adjourned at 5:32 pm

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

# Memorandum

**Date:** February 14, 2019

**To:** Nancy Nesser, Pharm.D.; J.D.
Pharmacy Director
Oklahoma Health Care Authority (OHCA)

Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.
Pharmacy Director
OHCA

**From:** Bethany Holderread, Pharm.D.
Clinical Coordinator
Pharmacy Management Consultants

**Subject:** Drug Utilization Review (DUR) Board Recommendations from Meeting of February 13, 2019

## Recommendation 1: Academic Detailing Program Update

NO ACTION REQUIRED.

## Recommendation 2: Narrow Therapeutic Index (NTI) Drug List

MOTION CARRIED by unanimous approval.

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

## Recommendation 3: Vote to Prior Authorize Arikayce® (Amikacin Liposome Inhalation Suspension)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Arikayce® (amikacin liposome inhalation suspension) with the following criteria:

**Arikayce® (Amikacin Liposome Inhalation Suspension) Approval Criteria:**

1. An FDA approved indication for the treatment of *Mycobacterium avium* complex (MAC) lung disease in adults who have limited or no alternative treatment options; and
2. Member must have had a minimum of 6 consecutive months of a multidrug background regimen therapy used compliantly and not achieved negative sputum cultures within the last 12 months. Dates of previous treatments and regimens must be listed on the prior authorization request; and
    a. If claims for a multidrug background regimen are not in the member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the prescriber; and
3. Member must continue a multidrug background regimen therapy while on Arikayce®, unless contraindicated, or provide reasoning why continuation of a multidrug background regimen is not appropriate for the member; and
4. A patient-specific, clinically significant reason why the member requires an inhaled aminoglycoside in place of an intravenous or intramuscular aminoglycoside (e.g., amikacin, streptomycin) must be provided; and
5. Arikayce® will not be approved for patients with non-refractory MAC lung disease; and
6. Arikayce® must be prescribed by, or in consultation with, a pulmonary disease or infectious disease specialist (or be an advanced care practitioner with a supervising physician who is a pulmonary disease or infectious disease specialist); and
7. Initial approvals will be for the duration of 6 months after which time the prescriber must document the member is responding to treatment for continued approval; and
8. A quantity limit of 28 vials per 28 days will apply.

## Recommendation 4: Vote to Prior Authorize Revcovi™ (Elapegademase-lvlr)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Revcovi™ (elapegademase-lvlr) with the following criteria:

**Revcovi™ (Elapegademase-lvlr) Approval Criteria:**

1. An FDA approved diagnosis of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients; and
    a. Diagnosis of ADA deficiency should be confirmed by demonstrating biallelic mutations in the *ADA* gene; and
2. Revcovi™ must be prescribed by, or in consultation with, a physician who specializes in the treatment of immune deficiency disorders; and

3. The member must have failed to respond to a bone marrow transplant or not be a current suitable candidate for a bone marrow transplant; and
4. A patient-specific, clinically significant reason why Adagen® (pegademase bovine) is not appropriate for the member; or
5. Previous failure of Adagen® (pegademase bovine) used compliantly. Failure is defined as the inability to maintain ADA activity or reduce erythrocyte deoxyadenosine nucleotides (dAXP), or the member is experiencing adverse effects associated with Adagen® therapy that are not expected to occur with Revcovi™; and
6. Prescriber must agree to monitor trough plasma ADA activity, trough dAXP levels, and/or total lymphocyte counts to ensure efficacy and compliance and to monitor for neutralizing antibodies when suspected; and
7. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
8. Initial approvals will be for the duration of 6 months at which time the prescriber must confirm improvement or stabilization in ADA activity or dAXP levels or improvement in immune function. Subsequent approvals will require the prescriber to verify the member is still not a current suitable candidate for a bone marrow transplant.

## Recommendation 5: Vote to Prior Authorize Lonhala® Magnair® (Glycopyrrolate Inhalation Solution), Yupelri™ (Revefenacin Inhalation Solution), and Dupixent® (Dupilumab) and to Update the Prior Authorization Criteria for Arnuity® Ellipta® (Fluticasone Furoate), ArmonAir™ RespiClick® (Fluticasone Propionate), AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol), Breo® Ellipta® (Fluticasone Furoate/Vilanterol), Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/ Vilanterol), Xolair® (Omalizumab), and Fasenra™ (Benralizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Lonhala® Magnair® (glycopyrrolate inhalation solution) and Yupelri™ (revefenacin inhalation solution) into Tier-2 of the Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA) Product Based Prior Authorization (PBPA) category with the following criteria:

**Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA) Tier-2 Approval Criteria:**

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), chronic bronchitis, or emphysema; and
3. A 4-week trial of at least 1 LABA and a 4-week trial of 1 LAMA within the past 90 days; or
4. A documented adverse effect, drug interaction, or contraindication to all available Tier-1 products; and
5. A clinical exception may apply for members who are unable to effectively use hand-actuated devices, such as Spiriva® Handihaler®, or who are stable on nebulized therapy.

| Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA) | |
|---|---|
| **Tier-1*** | **Tier-2** |
| **Long-Acting Beta$_2$ Agonists* (LABA)** | |
| salmeterol inhalation powder (Serevent®) | arformoterol nebulizer solution (Brovana®) |
| | formoterol nebulizer solution (Perforomist®) |
| | indacaterol inhalation powder (Arcapta® Neohaler®) |
| | olodaterol inhalation spray (Striverdi® Respimat®) |
| **Long-Acting Muscarinic Antagonists (LAMA)** | |
| tiotropium inhalation powder (Spiriva® HandiHaler®) | aclidinium inhalation powder (Tudorza® PressAir®) |
| | glycopyrrloate inhalation powder (Seebri® Neohaler®) |
| | **glycopyrrolate inhalation solution (Lonhala® Magnair®)** |
| | **revefenacin inhalation solution (Yupelri™)** |
| | tiotropium soft mist inhaler (Spiriva® Respimat®)+ |
| | umeclidinium inhalation powder (Incruse® Ellipta®) |

*Combination agents that contain a long-acting beta$_2$ agonist (LABA) ingredient qualify as Tier-1 agents.
Tier-1 medications do not require prior authorization for members with a COPD diagnosis.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Unique criteria applies for a diagnosis of asthma.

The College of Pharmacy also recommends updating the current prior authorization criteria for Dupixent® (dupilumab), Arnuity® Ellipta® (fluticasone furoate), ArmonAir™ RespiClick® (fluticasone propionate), AirDuo™ RespiClick® (fluticasone propionate/salmeterol), Breo® Ellipta® (fluticasone furoate/vilanterol), Trelegy™ Ellipta® (fluticasone furoate/umeclidinium/ vilanterol), Xolair® (omalizumab), and Fasenra™ (benralizumab). The following criteria would apply (changes noted in red):

**Dupixent® (Dupilumab Injection) Approval Criteria [Eosinophilic Phenotype Asthma Diagnosis]:**

1. An FDA approved indication for add-on maintenance treatment of patients with moderate-to-severe eosinophilic phenotype asthma or oral corticosteroid-dependent asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a baseline blood eosinophil count of ≥150cell/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a high-dose ICS (≥880mcg/day fluticasone propionate or equivalent daily dose or ≥440mcg/day in ages 12 to 17 years) used compliantly for at least the past 12 months (for ICS/LABA combination products, the highest FDA approved dose meets this criteria); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past 3 months; and

7. The prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
8. Dupixent® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Quantities approved must not exceed FDA recommended dosing requirements.

**Arnuity® Ellipta® (Fluticasone Furoate) and ArmonAir™ RespiClick® (Fluticasone Propionate) Approval Criteria:**

1. An FDA approved diagnosis of asthma; and
2. Member must be at or above the minimum age indicated; and
3. ~~Member must be 12 years of age or older; and~~
4. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) is not appropriate for the member must be provided.

**AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol) Approval Criteria:**

1. An FDA approved diagnosis of asthma; and
2. Member must be at or above the minimum age indicated; and
3. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member; 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 the severity of asthma.

**Breo® Ellipta® (Fluticasone Furoate/Vilanterol) Approval Criteria:**

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD) or chronic bronchitis and/or emphysema associated with COPD; and
    a. For a diagnosis of COPD or chronic bronchitis and/or emphysema associated with COPD, trials of Advair® and Symbicort®, consisting of at least 30 days each within the last 90 days that did not adequately control COPD symptoms; or
2. An FDA approved diagnosis of asthma in patients 18 years of age and older; and
    a. For a diagnosis of asthma, trials of Advair®, Dulera®, and Symbicort® consisting of at least 30 days each within the last ~~90~~ 120 days that did not adequately control asthma symptoms.

**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. 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
3. 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 with a LAMA must be provided.

**Xolair® (Omalizumab Injection) Approval Criteria [Chronic Idiopathic Urticaria Diagnosis]:**

1. An FDA approved diagnosis of chronic idiopathic urticaria; and
2. Member must be 12 years of age or older; and
3. Other forms of urticaria must be ruled out; and
4. Other potential causes of urticaria must be ruled out; and
5. Member must have an Urticaria Activity Score (UAS) ≥16; and
6. Prescriber must be an allergist, immunologist, dermatologist, or be an advanced care practitioner with a supervising physician that is an allergist, immunologist, or dermatologist; and
7. ~~Member must have tried and failed to obtain relief from other treatments including the following trials within the last 6 months (member must fail all classes unless contraindicated):~~
   a. ~~At least 2 different $H_1$-antihistamine trials for a minimum duration of 2 weeks each:~~
      i. ~~One~~ A trial ~~must be~~ of a second generation $H_1$ antihistamine dosed 4 times the maximum FDA dose within the last 3 months for at least 4 weeks (or less if symptoms are intolerable); and
      ii. ~~One trial must be tried in combination with an $H_2$-antihistamine; and~~
   b. ~~A 4-week trial of a leukotriene receptor antagonist in combination with a 4-week trial of doxepin 10mg to 50mg daily; and~~
8. Initial dosing will only be approved for 150mg every 4 weeks. If the member has inadequate results at this dose, then the dose may be increased to 300mg every 4 weeks; and
9. Initial approvals will be for the duration of 3 months.

**Fasenra™ (Benralizumab Injection) Approval Criteria:**

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a baseline blood eosinophil count of ~~300~~ ≥150cell/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a high-dose ICS (≥880mcg/day fluticasone propionate or equivalent daily dose or ≥440mcg/day in ages 12 to 17 years) used compliantly for at least the past 12 months (for ICS/LABA combination medications, the highest FDA approved dose meets this criteria); and

6. Member must have failed at least 1 other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past 3 months; and
7. Fasenra™ must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
8. Fasenra™ must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. A quantity limit of 1 prefilled syringe per 56 days will apply.

## Recommendation 6: Vote to Prior Authorize Lokelma™ (Sodium Zirconium Cyclosilicate) and to Update the Veltassa® (Patiromer) Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Lokelma™ (sodium zirconium cyclosilicate) and recommends updating the prior authorization criteria for Veltassa® (patiromer). The following criteria would apply (changes noted in red):

**Lokelma™ (Sodium Zirconium Cyclosilicate) Approval Criteria:**

1. An FDA approved diagnosis of hyperkalemia; and
2. Medications known to cause hyperkalemia [e.g., angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), aldosterone antagonists, nonsteroidal anti-inflammatory drugs (NSAIDs)] have been discontinued or reduced to the lowest effective dose where clinically appropriate; and
3. A trial of a potassium-eliminating diuretic or documentation why a diuretic is not appropriate for the member; and
4. Documentation of a low potassium diet; and
5. A quantity limit of 30 packets per 30 days will apply. Quantity limit overrides will be granted to allow for initial 3 times daily dosing.

**Veltassa® (Patiromer) Approval Criteria:**

1. An FDA approved diagnosis of hyperkalemia; and
2. Medications known to cause hyperkalemia [e.g., angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), aldosterone antagonists, nonsteroidal anti-inflammatory drugs (NSAIDs)] have been discontinued or reduced to the lowest effective dose where clinically appropriate; and
3. A trial of a potassium-eliminating diuretic or documentation why a diuretic is not appropriate for the member; and
4. Documentation of a low potassium diet; and
5. ~~A patient-specific, clinically significant reason why member cannot use sodium polystyrene sulfonate powder which is available without a prior authorization; and~~
6. A quantity limit of 30 packets per 30 days will apply.

## Recommendation 7: Vote to Prior Authorize Tavalisse™ (Fostamatinib), Doptelet® (Avatrombopag), and Mulpleta® (Lusutrombopag)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Tavalisse™ (fostamatinib), Doptelet® (avatrombopag), and Mulpleta® (lusutrombopag) with the following criteria:

**Tavalisse™ (Fostamatinib) Approval Criteria:**

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment; and
2. Member must be 18 years of age or older (Tavalisse™ is not recommended for use in patients younger than 18 years of age because adverse effects on actively growing bones were observed in nonclinical studies); and
3. Member must have a clinical diagnosis of persistent/chronic ITP for at least 3 months; and
4. Previous insufficient response with at least 2 of the following treatments:
    a. Corticosteroids; or
    b. Immunoglobulins; or
    c. Splenectomy; or
    d. Thrombopoietin receptor agonists; and
5. Degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
6. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
7. Prescriber must verify the member's complete blood count (CBC), including platelet counts, will be monitored monthly until a stable platelet count (at least 50 X $10^9$/L) is achieved and will be monitored regularly thereafter; and
8. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored monthly; and
9. Prescriber must verify member's blood pressure will be monitored every 2 weeks until establishment of a stable dose, then monthly thereafter; and
10. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Female members of reproductive potential must be willing to use effective contraception while on therapy and for at least 1 month after therapy completion; and
11. Prescriber must verify member is not breastfeeding; and
12. Member must not be taking strong CYP3A4 inducers (e.g., rifampicin) concurrently with Tavalisse™; and
13. Initial approvals will be for the duration of 12 weeks; and
14. Discontinuation criteria:
    a. Platelet count does not increase to a level sufficient to avoid clinically important bleeding after 12 weeks of therapy; and
15. A quantity limit of 2 tablets daily will apply.

**Doptelet® (Avatrombopag) Approval Criteria:**

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure; and

2. A patient-specific, clinically significant reason why the member cannot use Mulpleta® (lusutrombopag) must be provided; and
3. Date of procedure must be listed on the prior authorization request; and
4. Prescriber must verify the member will have the procedure within 5 to 8 days after the member receives the last dose of Doptelet®; and
5. Member must have a baseline platelet count <50 X $10^9$/L (recent baseline platelet count must be provided); and
6. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and
7. Doptelet® must not be used in an attempt to normalize platelet counts; and
8. A quantity limit of 15 tablets per scheduled procedure will apply.

**Mulpleta® (Lusutrombopag) Approval Criteria:**

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure; and
2. Date of procedure must be listed on the prior authorization request; and
3. Prescriber must verify the member will have the procedure 2 to 8 days after the member receives the last dose of Mulpleta®; and
4. Member must have a baseline platelet count <50 X $10^9$/L (recent baseline platelet count must be provided); and
5. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and
6. Mulpleta® must not be used in an attempt to normalize platelet counts; and
7. A quantity limit of 7 tablets per scheduled procedure will apply.

Additionally, the College of Pharmacy recommends removing the prior authorization for Nplate® (romiplostim) and Promacta® (eltrombopag), based on net cost and appropriate utilization.

## Recommendation 8: Vote to Prior Authorize Carbaglu® (Carglumic Acid)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Carbaglu® (carglumic acid) with the following criteria:

**Carbaglu® (Carglumic Acid) Approval Criteria:**

1. An FDA approved diagnosis of N-acetylglutamate synthase (NAGS) deficiency; and
2. Carbaglu® must be prescribed by, or in consultation with, a geneticist; and
3. Documentation of active management with a low protein diet; and
4. Initial approvals will be for the duration of 1 year. After that time, reauthorization will require the prescriber to verify the member is responding well to therapy.

## Recommendation 9: Vote to Prior Authorize Xelpros™ (Latanoprost 0.005% Emulsion)

MOTION CARRIED by unanimous approval.

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

1. The placement of Xelpros™ (latanoprost 0.005% emulsion) into the Special Prior Authorization (PA) Tier. Current Special PA criteria will apply.
2. Moving methazolamide (Neptazane®) from Tier-1 to the Special PA Tier based on net cost. Current Special PA criteria will apply. Current users will be grandfathered.
3. Removing Travatan® (travoprost 0.004%) based on product discontinuation.

Proposed changes are shown in red in the following Glaucoma Medications Tier Chart.

| Glaucoma Medications* | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Special PA** |
| **Alpha-2 Adrenergic Agonists** | | |
| brimonidine (Alphagan® 0.2%) | apraclonidine (Iopidine® 0.5%, 1%) | brimonidine (Alphagan-P® 0.15%) |
| brimonidine (Alphagan-P® 0.1%) | | |
| brimonidine/timolol (Combigan® 0.2%/0.5%) | | |
| brinzolamide/brimonidine (Simbrinza® 0.2%/1%) | | |
| **Beta-Blockers** | | |
| brimonidine/timolol (Combigan® 0.2%/0.5%) | betaxolol (Betoptic® 0.5%, Betoptic-S® 0.25%) | dorzolamide/timolol (Cosopt® PF 2%/0.5%) |
| carteolol (Ocupress® 1%) | | timolol maleate (Timoptic Ocudose® 0.25%, 0.5%; Timoptic-XE® 0.25%, 0.5%) |
| dorzolamide/timolol (Cosopt® 22.3mg/mL/6.8mg/mL) | | |
| levobunolol (Betagan® 0.25%, 0.5%) | | |
| timolol maleate (Istalol® 0.5%, Timoptic® 0.25%, 0.5%) | | |
| **Carbonic Anhydrase Inhibitors** | | |
| acetazolamide (Diamox® 500mg caps; 125mg, 250mg tabs)+ | | dorzolamide/timolol (Cosopt® PF 2%/0.5%) |
| brinzolamide (Azopt® 1%) | | **methazolamide (Neptazane® 25mg, 50mg tabs)+** |
| brinzolamide/brimonidine (Simbrinza® 0.2%/1%) | | |
| dorzolamide (Trusopt® 2%) | | |
| dorzolamide/timolol (Cosopt® 22.3mg/mL/6.8mg/mL) | | |
| **Cholinergic Agonists/Cholinesterase Inhibitors** | | |
| echothiophate iodide (Phospholine Iodide® 0.125%) | pilocarpine (Isopto® Carpine 1%, 2%, 4%) | |
| **Prostaglandin Analogs** | | |
| latanoprost (Xalatan® 0.005%) | bimatoprost (Lumigan® 0.01%, 0.03%) | **latanoprost (Xelpros™ 0.005%)** |
| travoprost (Travatan-Z® 0.004%) | tafluprost (Zioptan® 0.0015%) | latanoprostene bunod (Vyzulta® 0.024%) |

| Glaucoma Medications* | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Special PA** |
| | ~~travoprost (Travatan® 0.004%)~~ | |
| **Rho Kinase Inhibitors** | | |
| netarsudil (Rhopressa® 0.02%) | | |

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Indicates available oral medications.
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.
caps = capsules; tabs = tablets; PA = prior authorization

## Recommendation 10: Vote to Prior Authorize Makena® [Hydroxyprogesterone Caproate Subcutaneous (Sub-Q) Auto-Injector]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Makena® (hydroxyprogesterone caproate sub-Q auto-injector) with the following criteria (changes noted in red):

**Makena® [Hydroxyprogesterone Caproate Intramuscular (IM) Injection and Subcutaneous (Sub-Q) Auto-Injector] Approval Criteria:**

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and
3. Gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation; and
4. Authorizations will be for once weekly administration by a health care professional through 36 weeks, 6 days of gestation; and
5. For Makena® sub-Q auto-injector:
    a. Initial dose must be administered by a health care professional; and
    b. Member and caregiver must be trained by a health care professional on sub-Q administration and storage of Makena® sub-Q auto-injector; and
    c. A patient-specific, clinically significant reason why Makena® IM injection cannot be used must be provided.* (*The manufacturer of Makena® has currently provided a supplemental rebate to make the net cost per injection of the sub-Q auto-injector equivalent to the IM injection and therefore make the sub-Q auto-injector available with the current Makena® criteria; however, use of Makena® sub-Q auto-injector will require a reason why Makena® IM injection cannot be used if the manufacturer chooses not to participate in supplemental rebates.)

## Recommendation 11: Vote to Prior Authorize Akynzeo® IV [Fosnetupitant/ Palonosetron Injection for Intravenous (IV) Use]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Akynzeo® IV (fosnetupitant/palonosetron IV) with the following criteria (changes noted in red):

**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.

Additionally, the College of Pharmacy recommends updating the approval criteria for Marinol® (dronabinol) based on generic availability and low net cost (changes noted in red):

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

~~1. Approval can be granted for 6 months for the diagnosis of HIV related loss of appetite; or~~
~~2. The diagnosis of chemotherapy-induced nausea and vomiting requires the following:~~
~~a. A recent trial of ondansetron (within the past 6 months) used for at least 3 days or 1 cycle that resulted in inadequate response; and~~

3. An FDA approved diagnosis; and
4. Approval length will be based on duration of need; and
5. For Marinol® (dronabinol) and Cesamet® (nabilone), a quantity limit of 60 capsules per 30 days will apply; and
6. Cesamet® (nabilone) will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used; and
7. For Syndros® (dronabinol) oral solution, the quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging; and
8. 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.

## Recommendation 12: Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Epidiolex® (Cannabidiol), Diacomit® (Stiripentol), and Sympazan™ (Clobazam Oral Film)

NO ACTION REQUIRED.

## Recommendation 13: Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Aimovig™ (Erenumab-aooe), Ajovy™ (Fremanezumab-vfrm), and Emgality™ (Galcanezumab-gnlm)

NO ACTION REQUIRED.

## Recommendation 14: 30-Day Notice to Prior Authorize Gamifant® (Emapalumab-lzsg)

NO ACTION REQUIRED.

## Recommendation 15: 30-Day Notice to Prior Authorize Firdapse® (Amifampridine)

NO ACTION REQUIRED.

## Recommendation 16: Annual Review of Erythropoietin Stimulating Agents (ESAs) and 30-Day Notice to Prior Authorize Retacrit™ (Epoetin Alfa-epbx)

NO ACTION REQUIRED.

## Recommendation 17: Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Inbrija™ (Levodopa Inhalation) and Osmolex ER™ [Amantadine Extended-Release (ER)]

NO ACTION REQUIRED.

## Recommendation 18: Industry News and Updates

NO ACTION REQUIRED.

## Recommendation 19: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

## Recommendation 20: Future Business

NO ACTION REQUIRED.

# *Baha Abu-Esheh, MD. PC*

1001 12th Ave. NW, Suite 100
Ardmore, OK 73401
Phone: 580-223-0447 Fax: 580-223-2989


February 1, 2019

RE: Ajovy

To Whom It May Concern:

Dr. Baha Abu-Esheh, MD is requesting Ajovy as a monthly or quarterly option for treatment of his migraine patients.

Sincerely,

Baha Abu-Esheh, MD


Board Certified Neurologist
Board Certified in Sleep Medicine Board Certified in Headache


(f)

NORMAN
REGIONAL
Health System

Neurology Associates
Oklahoma Headache Center

*Brett Dees, MD* *Smaranda Galis, MD* *Michael Merkey, MD* *Christi Pendergraft, MD* *Saria Refai, MD*

3400 W. Tecumseh Rd., Suite 300
Norman, OK 73072

Tel: 405.307.5700
Fax: 405.307.5704

January 30, 2019

RE: Ajovy

To Whom It May Concern:

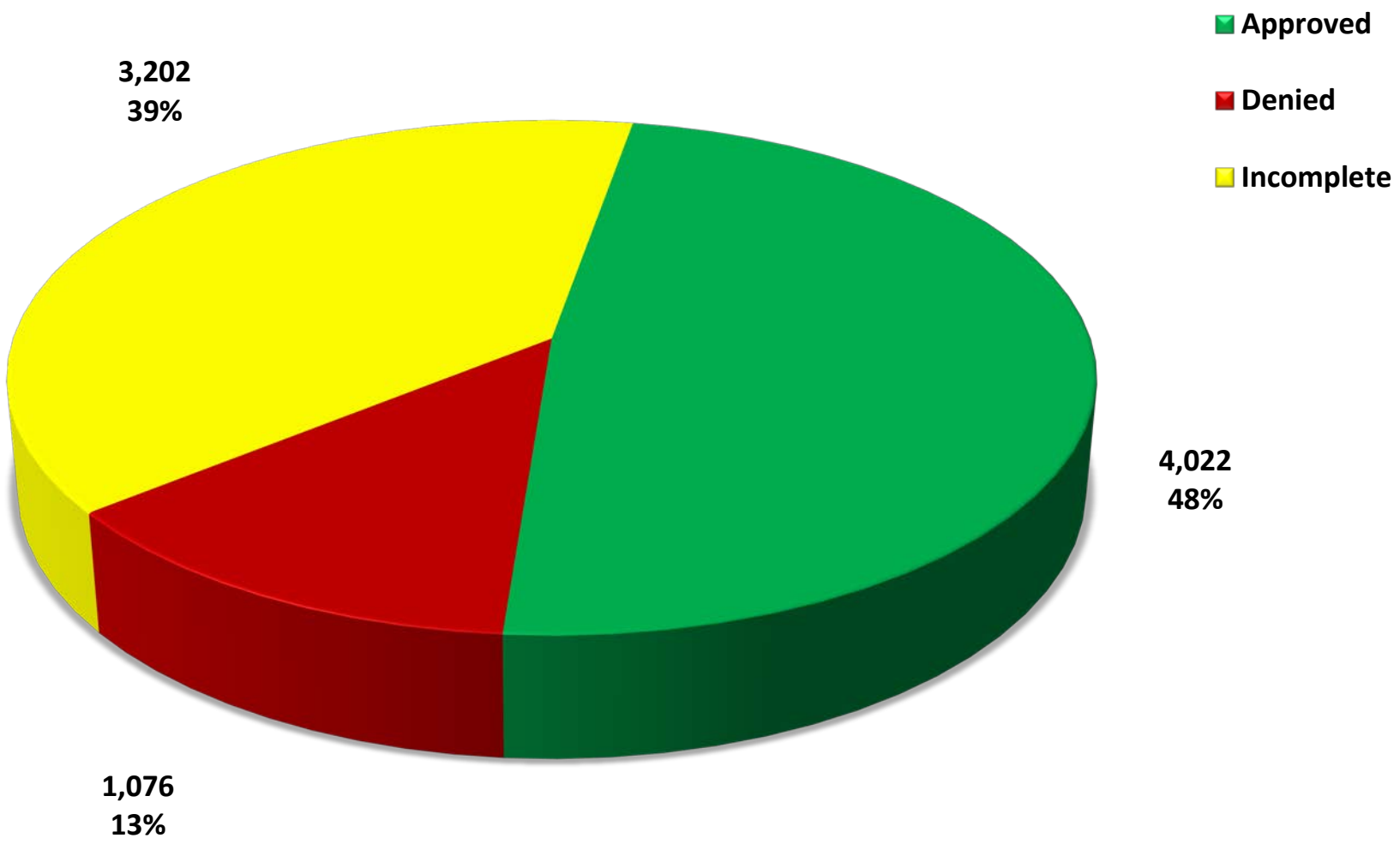
Dr. Christi Pendergraft is requesting Ajovy as a monthly or quarterly option for treatment of her migraine patients.

Sincerely,

Christi Pendergraft, MD

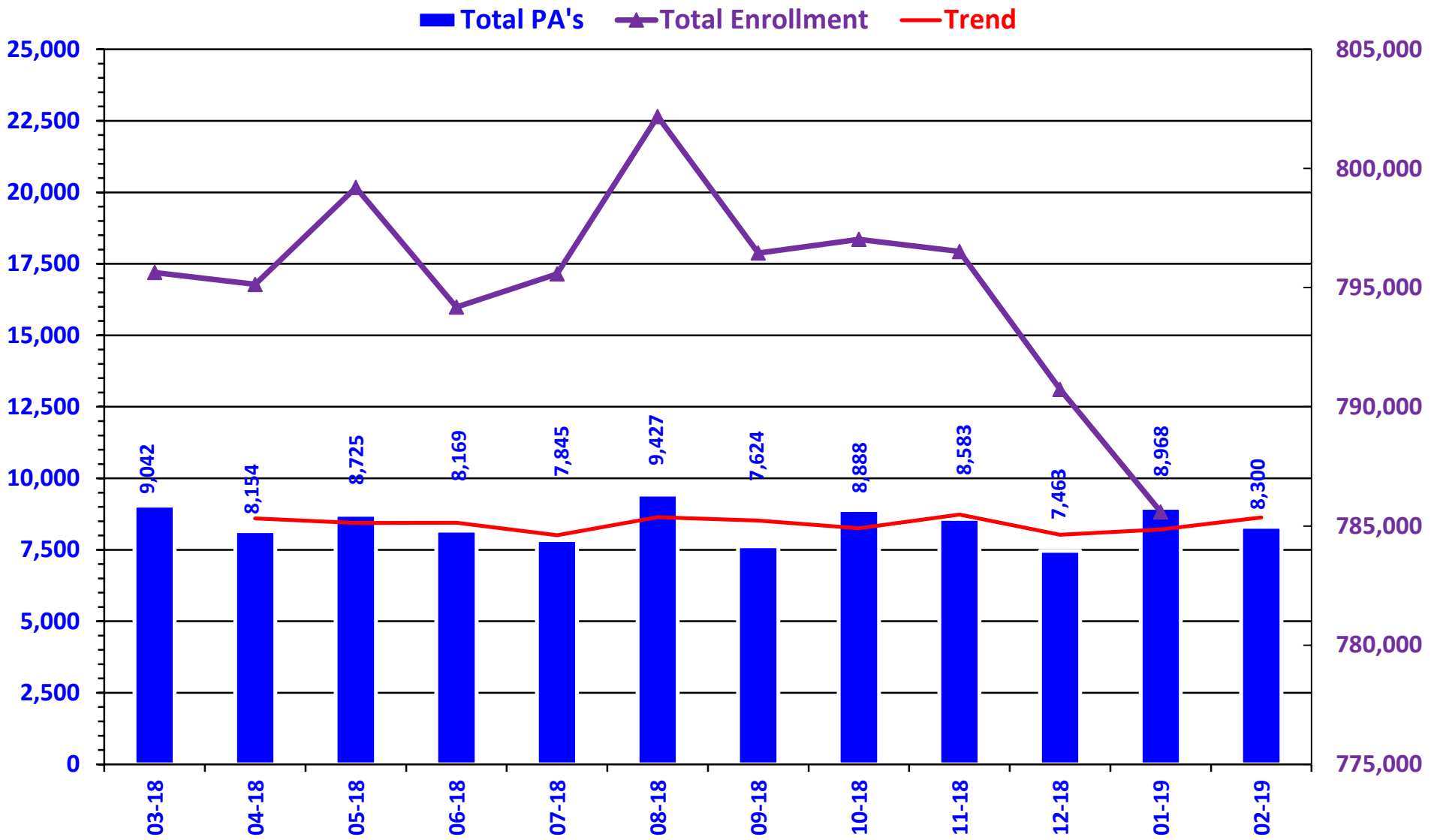
# Appendix B

# PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY 2019



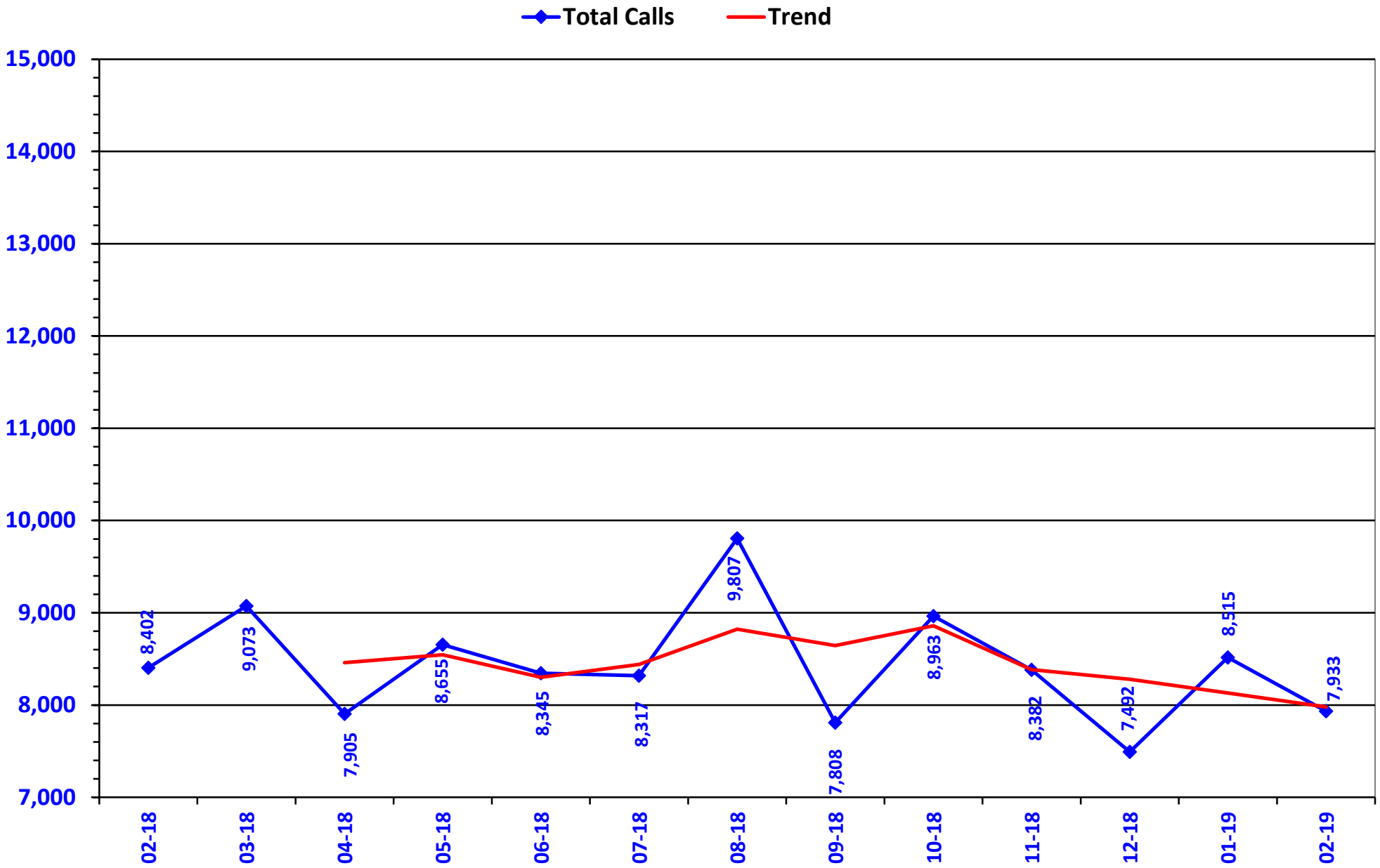

*PA totals include approved/denied/incomplete/overrides*

# PRIOR AUTHORIZATION REPORT: FEBRUARY 2018 – FEBRUARY 2019




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

# CALL VOLUME MONTHLY REPORT:
# FEBRUARY 2018 – FEBRUARY 2019



# Prior Authorization Activity

## 2/1/2019 Through 2/28/2019

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Advair/Symbicort/Dulera/QVAR | 88 | 10 | 27 | 51 | 322 |
| Analgesic - NonNarcotic | 19 | 0 | 5 | 14 | 0 |
| Analgesic - Narcotic | 325 | 153 | 43 | 129 | 155 |
| Angiotensin Receptor Antagonist | 30 | 5 | 6 | 19 | 358 |
| Antiasthma | 90 | 25 | 18 | 47 | 267 |
| Antibiotic | 30 | 13 | 2 | 15 | 287 |
| Anticonvulsant | 194 | 96 | 15 | 83 | 259 |
| Antidepressant | 200 | 49 | 32 | 119 | 322 |
| Antidiabetic | 243 | 94 | 35 | 114 | 352 |
| Antihistamine | 25 | 9 | 8 | 8 | 206 |
| Antimigraine | 137 | 19 | 37 | 81 | 155 |
| Antineoplastic | 109 | 66 | 6 | 37 | 172 |
| Antiparasitic | 54 | 12 | 10 | 32 | 8 |
| Antiulcers | 136 | 36 | 45 | 55 | 128 |
| Anxiolytic | 21 | 3 | 2 | 16 | 215 |
| Atypical Antipsychotics | 207 | 102 | 26 | 79 | 335 |
| Biologics | 157 | 75 | 30 | 52 | 302 |
| Bladder Control | 54 | 8 | 19 | 27 | 391 |
| Blood Thinners | 246 | 152 | 9 | 85 | 343 |
| Botox | 36 | 26 | 5 | 5 | 358 |
| Buprenorphine Medications | 441 | 298 | 10 | 133 | 73 |
| Calcium Channel Blockers | 15 | 1 | 3 | 11 | 32 |
| Cardiovascular | 71 | 30 | 10 | 31 | 259 |
| Chronic Obstructive Pulmonary Disease | 158 | 33 | 32 | 93 | 323 |
| Constipation/Diarrhea Medications | 192 | 43 | 71 | 78 | 255 |
| Contraceptive | 24 | 11 | 3 | 10 | 358 |
| Dermatological | 338 | 103 | 80 | 155 | 76 |
| Diabetic Supplies | 511 | 279 | 18 | 214 | 236 |
| Endocrine & Metabolic Drugs | 150 | 80 | 16 | 54 | 158 |
| Erythropoietin Stimulating Agents | 17 | 9 | 1 | 7 | 109 |
| Fibromyalgia | 15 | 1 | 1 | 13 | 360 |
| Fish Oils | 11 | 0 | 5 | 6 | 0 |
| Gastrointestinal Agents | 119 | 37 | 18 | 64 | 219 |
| Genitourinary Agents | 14 | 2 | 4 | 8 | 357 |
| Growth Hormones | 103 | 68 | 9 | 26 | 151 |
| Hematopoietic Agents | 11 | 2 | 3 | 6 | 223 |
| Hepatitis C | 161 | 107 | 11 | 43 | 8 |
| HFA Rescue Inhalers | 85 | 1 | 15 | 69 | 359 |
| Insomnia | 41 | 2 | 12 | 27 | 174 |
| Insulin | 138 | 54 | 13 | 71 | 329 |
| Miscellaneous Antibiotics | 18 | 1 | 2 | 15 | 12 |
| Multiple Sclerosis | 58 | 30 | 7 | 21 | 160 |
| Muscle Relaxant | 54 | 5 | 18 | 31 | 91 |
| Nasal Allergy | 91 | 18 | 30 | 43 | 129 |
| Neurological Agents | 74 | 25 | 19 | 30 | 224 |
| NSAIDs | 35 | 5 | 10 | 20 | 233 |
| Ocular Allergy | 46 | 8 | 12 | 26 | 117 |
| Ophthalmic | 14 | 1 | 4 | 9 | 25 |
| Ophthalmic Anti-infectives | 16 | 2 | 2 | 12 | 28 |
| Osteoporosis | 4 | 3 | 1 | 0 | 355 |

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

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Otic Antibiotic | 25 | 2 | 3 | 20 | 16 |
| Pediculicide | 13 | 0 | 2 | 11 | 0 |
| Respiratory Agents | 28 | 22 | 0 | 6 | 194 |
| Statins | 20 | 5 | 7 | 8 | 154 |
| Stimulant | 741 | 349 | 77 | 315 | 348 |
| Synagis | 167 | 129 | 7 | 31 | 48 |
| Testosterone | 40 | 16 | 6 | 18 | 335 |
| Topical Antifungal | 35 | 4 | 5 | 26 | 14 |
| Topical Corticosteroids | 74 | 2 | 36 | 36 | 28 |
| Vitamin | 77 | 18 | 35 | 24 | 191 |
| Pharmacotherapy | 60 | 57 | 1 | 2 | 257 |
| Emergency PAs | 0 | 0 | 0 | 0 | |
| **Total** | **6,706** | **2,816** | **999** | **2,891** | |
| | | | | | |
| **Overrides** | | | | | |
| Brand | 15 | 45 | 5 | 17 | 285 |
| Compound | 11 | 10 | 0 | 1 | 52 |
| Cumulative Early Refill | 2 | 2 | 0 | 0 | 170 |
| Diabetic Supplies | 8 | 7 | 0 | 1 | 84 |
| Dosage Change | 330 | 312 | 0 | 18 | 12 |
| High Dose | 7 | 5 | 0 | 2 | 139 |
| Ingredient Duplication | 7 | 7 | 0 | 0 | 20 |
| Lost/Broken Rx | 90 | 88 | 1 | 1 | 14 |
| NDC vs Age | 292 | 189 | 30 | 73 | 258 |
| Nursing Home Issue | 65 | 65 | 0 | 0 | 23 |
| Opioid MME Limit | 28 | 15 | 0 | 13 | 43 |
| Opioid Quantity | 43 | 34 | 3 | 6 | 150 |
| Other* | 44 | 42 | 1 | 1 | 10 |
| Quantity vs. Days Supply | 552 | 353 | 35 | 164 | 239 |
| STBS/STBSM | 14 | 10 | 1 | 3 | 67 |
| Stolen | 6 | 6 | 0 | 0 | 18 |
| Third Brand Request | 28 | 16 | 1 | 11 | 11 |
| **Overrides Total** | **1,594** | **1,206** | **77** | **311** | |
| **Total Regular PAs + Overrides** | **8,300** | **4,022** | **1,076** | **3,202** | |

| **Denial Reasons** | |
|---|---|
| Unable to verify required trials. | 2,753 |
| Does not meet established criteria. | 1,189 |
| Lack required information to process request. | 578 |

| **Other PA Activity** | |
|---|---|
| Duplicate Requests | 611 |
| Letters | 11,004 |
| No Process | 19 |
| Changes to existing PAs | 708 |
| Helpdesk Initiated Prior Authorizations | 578 |
| PAs Missing Information | 27 |

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

# Update: Drug Utilization Review of Prenatal Vitamins (PV)

**Oklahoma Health Care Authority**
**March 2019**

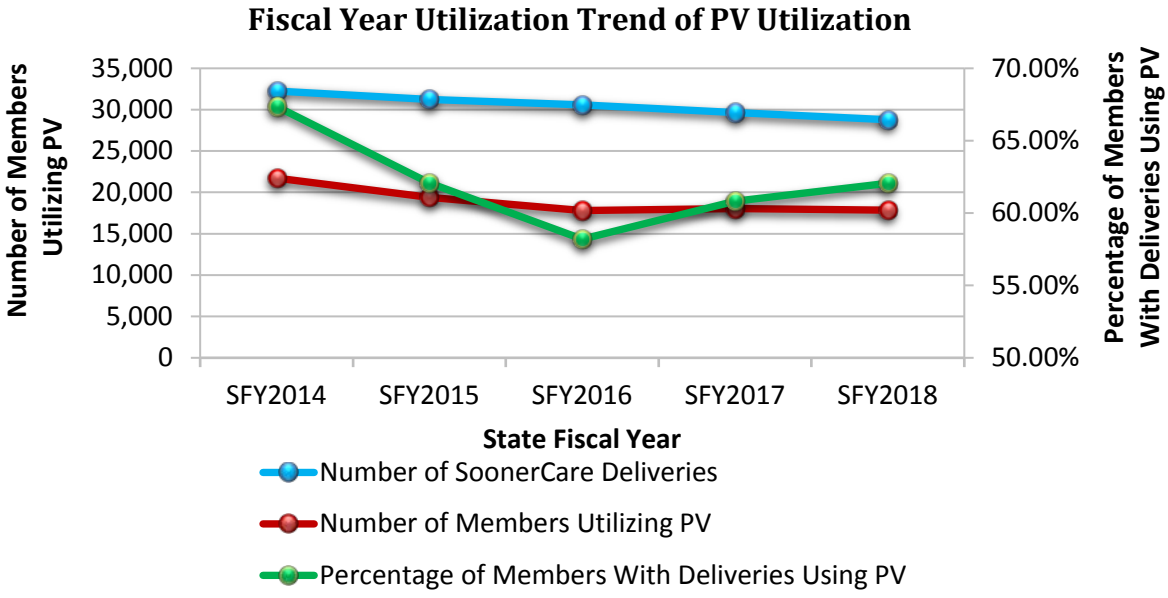
## Introduction

The College of Pharmacy and the Oklahoma Health Care Authority (OHCA) are engaged in an effort to increase utilization of prenatal vitamins (PV) among pregnant SoonerCare members. In May 2018, educational outreach including prescriber letters, pharmacy fax blasts, and articles in the provider newsletter regarding declining utilization of PV among pregnant SoonerCare members were disseminated.

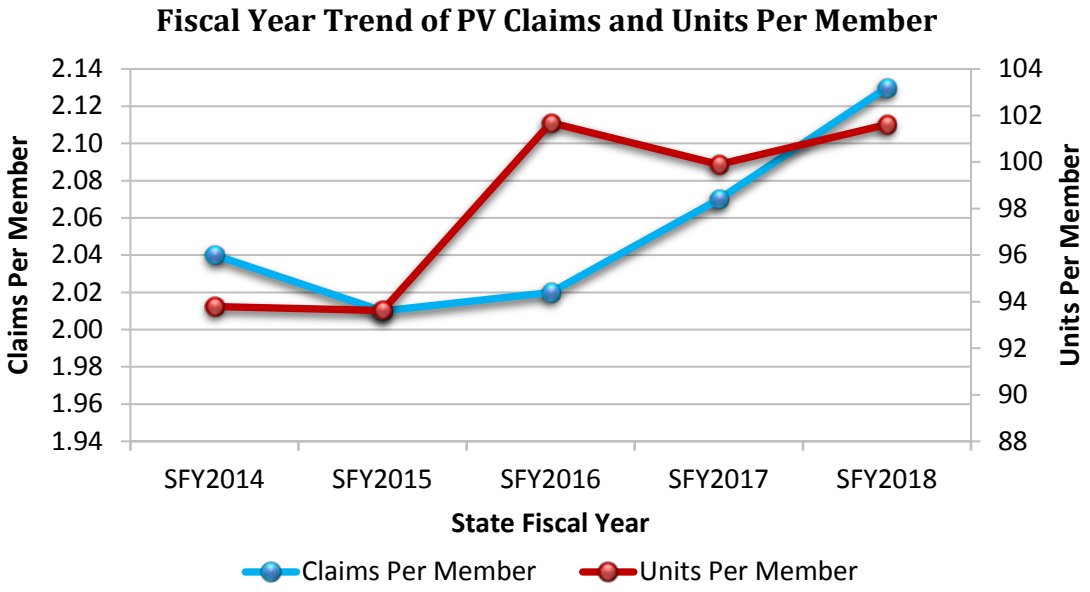
Similar educational efforts have been conducted previously in 2014 and in 2015. In 2014, SoonerCare added reminders regarding PV utilization to the SoonerCare "Text for Baby" program. In November 2016, the College of Pharmacy began incorporating regular prenatal education, based on previous successful interventions, into its workflow to maintain increased utilization of PV. Interventions included reminders to prescribers of pregnant members if no paid claims for PV were found in the member's claims history, and including a list of preferred PV available without prior authorization in response to each prior authorization received for a non-preferred PV. The preferred PV list is also available on the SoonerCare website.

## Utilization of PV: Fiscal Year Trends[1]

The following graph shows the fiscal year utilization of PV for the last 5 years. The number of members utilizing PV is compared to the number of SoonerCare deliveries. Prior to state fiscal year (SFY) 2016 a concerning decline was seen in the percentage of members utilizing PV compared to the number of deliveries. While the percentage has improved in SFY 2017 and SFY 2018, a large percentage of deliveries are not associated with a member utilizing PV.



The following graph outlines the number of claims and units of PV each member received by SFY. While the claims per member has increased from SFY 2016, the number of claims per member still remains slightly >2. Since many PV formulations are packaged in 90 and 100-day supply bottles, the number of units per member was also assessed. In SFY 2018, members averaged 101.62 units equating to a little more than 3 months of therapy.




## Discussion[2]

While deliveries have declined in the last several fiscal years, utilization of PV has also declined. The number of members utilizing PV compared to the number of SoonerCare deliveries shows <65% of members with deliveries utilize PV. While there was a slight increase in recent years (6.63% increase from SFY 2016 to SFY 2018), the percentage of members utilizing PV compared to the number of deliveries remains a concern.

Another concern revealed by the claims analysis is the number of claims per member. Most members received only 2 paid claims for PV during a given fiscal year. This number has remained steady over the last 5 fiscal years, and was not accounted for by an increase in units implying a larger quantity per claim (e.g., 3 month supply for 1 claim). The maximum benefit of PV requires continued use throughout pregnancy and ideally starts before the member becomes pregnant.

Utilization of PV is difficult to assess and may be falsely low due to the large number of over-the-counter (OTC) products available that members may be using. Data for use of OTC products for SoonerCare members are not obtainable and are therefore not included in this analysis.

## Recommendations

Based on the decline in the percentage of members utilizing PV compared to the number of deliveries, further educational efforts are warranted. Efforts in the prenatal class appear to have an initial increase with a waning effect over time. The College of Pharmacy will continue

incorporating regular prenatal education, based on previous successful interventions, into its workflow to maintain increased utilization of PV. Opportunities for new interventions will be sought wherever possible.

Previous successful interventions included a letter sent to more than 3,000 SoonerCare prescribers emphasizing PV utilization. The mailing included a list of PV covered without prior authorization as well as a sample prescription detailing how a physician could write for the desired ingredients in a PV and the pharmacist could substitute to a covered product. Similarly, a fax blast was sent to SoonerCare pharmacies which included a list of the PV that do not require prior authorization along with the National Drug Codes (NDCs) so the pharmacy could easily order a product from the list. The pharmacies and prescribers also received directions for accessing the SoonerCare website and locating the updated PV list of non-prior authorized products. Articles regarding the importance of PV have also been included in the SoonerCare member and provider newsletters. Members enrolled in the SoonerCare "Text for Baby" program receive reminders regarding PV as well.

[1] Oklahoma Health Care Authority (OHCA). Annual Deliveries. Available online at: http://www.okhca.org/research.aspx?id=87. Last revised 11/27/2018. Last accessed 02/06/2019.

[2] March of Dimes. Fewer than half of U.S. women take recommended vitamins prior to pregnancy, according to March of Dimes new Prenatal Health & Nutrition Survey. Available online at: https://www.marchofdimes.org/news/fewer-than-half-of-u-s-women-take-recommended-vitamins-prior-to-pregnancy-according-to-march-of-dimes-new-prenatal-health-nutrition-survey.aspx. Issued 09/19/2017. Last accessed 03/04/2019.

# Appendix C

# Vote to Prior Authorize Inbrija™ (Levodopa Inhalation) and Osmolex ER™ [Amantadine Extended-Release (ER)]

**Oklahoma Health Care Authority**
**March 2019**

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

**Osmolex ER™ [amantadine extended-release (ER) tablets]:** In February 2018, the U.S. Food and Drug Administration (FDA) approved Osmolex ER™ for the treatment of Parkinson's disease (PD) and drug-induced extrapyramidal symptoms in adults. Osmolex ER™ is available as 129mg, 193mg, and 258mg ER oral tablets. The recommended initial dosage of Osmolex ER™ is 129mg administered by mouth once daily in the morning. The dosage may be increased in weekly intervals to a maximum daily dose of 322mg (administered as a 129mg and 193mg tablet), taken in the morning. Osmolex ER™ is not interchangeable with other amantadine immediate-release (IR) or ER products. For patients unable to tolerate more than 100mg per day of IR amantadine, there is no equivalent dose or dosing regimen of Osmolex ER™. Osmolex ER™ is contraindicated in patients with end-stage renal disease (ESRD) [i.e., creatinine clearance (CrCl) <15mL/min/1.73m$^2$]. The efficacy of Osmolex ER™ is based upon bioavailability studies comparing Osmolex ER™ to amantadine IR.

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per Month* | Cost Per Year* |
|---|---|---|---|
| **Osmolex ER™ (amantadine ER) 129mg, 193mg, and 258mg tablet** | **$15.00** | **$900.00** | **$10,800.00** |
| amantadine 100mg capsule | $0.49 | $29.40 | $352.80 |
| amantadine 100mg tablet | $1.00 | $60.00 | $720.00 |
| amantadine 50mg/5mL oral syrup | $0.21 | $126.00 | $1,512.00 |
| Gocovri™ (amantadine ER) 68.5mg and 137mg capsule | $39.58 | $2,374.80 | $28,497.60 |

Unit = capsule, tablet, or mL; ER = extended-release
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Dosing based on adjunctive therapy in patients taking concomitant levodopa.

**Inbrija™ (levodopa inhalation):** In December 2018, the FDA approved Inbrija™ for the intermittent treatment of "off" episodes in patients with PD who are being treated with carbidopa/levodopa. "Off" episodes are periods when PD symptoms return as a result of low levels of dopamine, often occurring between doses of oral carbidopa/levodopa. Inbrija™ is available as a carton containing (60) or (92) 42mg levodopa capsules for oral inhalation and 1 Inbrija™ inhaler. The recommended dosage of Inbrija™ is oral inhalation of the contents of (2) 42mg capsules (84mg) as needed, up to 5 times daily. The maximum dose per "off" period is 84mg, and the maximum daily dosage is 420mg. Inbrija™ has been shown to be effective only in combination with carbidopa/levodopa. Inbrija™ is contraindicated in patients currently taking a nonselective monoamine oxidase inhibitor (MAOI) (e.g., phenelzine, tranylcypromine) or who

have recently (within 2 weeks) taken a nonselective MAOI. Hypertension (HTN) can occur if these drugs are used concurrently.

**Cost Comparison:**

| Medication | Cost Per Unit | Cost Per Month | Cost Per Year |
|---|---|---|---|
| **Inbrija™ (levodopa) 42mg capsule** | **$15.83** | **$4,749.00^** | **$56,988.00^** |
| selegiline 5mg tablet | $1.09 | $65.40* | $784.80* |
| Apokyn® (apomorphine) 30mg/3mL injection | $331.67 | $5,970.06+ | $71,640.72+ |

Unit = capsule, tablet, or mL
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
^Dosing based on FDA maximum recommended dose of 84mg 5 times daily.
*Dosing based on adjunctive therapy in patients taking concomitant levodopa (5mg twice daily).
+Dosing based on FDA recommended starting dose of 2mg three times daily.

**Nuplazid® (pimavanserin):** A September 2018 communication released by the FDA indicated that after a completed review of all postmarketing reports of death reported with the use of pimavanserin, the FDA did not identify any new or unexpected safety findings and that the safety findings were consistent with what is described in the drug label. The FDA did identify "concerning prescribing patterns" of pimavanserin, particularly the concomitant use with other antipsychotic drugs or drugs that can cause potential QT prolongation. QT prolongation is noted in the *Warnings and Precautions* section of the pimavanserin product labeling, and using pimavanserin with other drugs that prolong the QT interval can increase the risk of arrhythmias. The FDA reminded health care providers to be aware of the risks described in the pimavanserin prescribing information, and that none of the other antipsychotic medications are approved for the treatment of PD psychosis.

## Recommendations

The College of Pharmacy recommends the prior authorization of Inbrija™ (levodopa inhalation) and Osmolex ER™ (amantadine ER) with the following criteria:

**Inbrija™ (Levodopa Inhalation) Approval Criteria:**

1. An FDA approved indication for the treatment of "off" episodes in patients with Parkinson's disease (PD) treated with carbidopa/levodopa; and
2. Member must be taking levodopa/carbidopa in combination with Inbrija™. Inbrija™ has been shown to be effective only in combination with carbidopa/levodopa; and
3. The member must be experiencing motor fluctuations with a minimum of 2 hours of "off" time and demonstrate levodopa responsiveness; and
4. Member must not be taking nonselective monoamine oxidase inhibitors (MAOIs) concomitantly with Inbrija™ or within 2 weeks prior to initiating Inbrija™; and
5. A previous failed trial of immediate-release (IR) carbidopa/levodopa formulations alone or in combination with long-acting carbidopa/levodopa formulations or a reason why supplementation with IR carbidopa/levodopa formulations is not appropriate for the member must be provided; and
6. A quantity limit of 10 capsules for inhalation per day will apply.

**Osmolex ER™ [Amantadine Extended-Release (ER)] Approval Criteria:**

1. An FDA approved indication for the treatment of Parkinson's disease (PD) or drug-induced extrapyramidal reactions in adults patients; and
2. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m$^2$]; and
3. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
4. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
5. A quantity limit will apply based on FDA approved dosing regimen(s).

Additionally, the College of Pharmacy recommends updating the Nuplazid® (pimavanserin) prior authorization criteria based on recent FDA safety warnings regarding concomitant therapy. The following criteria would apply (changes noted in red):

**Nuplazid® (Pimavanserin) Approval Criteria:**

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease (PD) psychosis; and
2. Member must have a concomitant diagnosis of PD; and
3. Member must not be taking concomitant medications known to prolong the QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin); and
4. The member must not have a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia, hypomagnesemia, and the presence of congenital prolongation of the QT interval; and
5. Nuplazid® will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD psychosis; and
6. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
7. A quantity limit of 2 tablets daily will apply.

Lastly, the College of Pharmacy recommends updating the Gocovri™ (amantadine ER) criteria based on net cost compared to other amantadine ER products. The following criteria would apply (changes noted in red):

**Gocovri™ [Amantadine Extended-Release (ER)] Approval Criteria:**

1. An FDA approved indication for the treatment of dyskinesia in patients with Parkinson's disease (PD) receiving levodopa-based therapy; and
2. Member must use Gocovri™ concomitantly with levodopa therapy; and

3. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m$^2$]; and
4. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
5. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
6. A patient-specific, clinically significant reason why Osmolex ER™ (amantadine ER) cannot be used must be provided; and
7. A quantity limit of (1) 68.5mg capsule or (2) 137mg capsules per day will apply.

[1] Brooks M. FDA OKs Extended-Release Amantadine (Osmolex ER) for Parkinson's. *Medscape*. Available online at: https://www.medscape.com/viewarticle/892873. Issued 02/20/2018. Last accessed 03/04/2019.
[2] Acorda Therapeutics, Inc. Acorda Therapeutics Announces FDA Approval of INBRIJA™ (levodopa inhalation powder). *Business Wire*. Available online at: http://ir.acorda.com/investors/investor-news/investor-news-details/2018/Acorda-Therapeutics-Announces-FDA-Approval-of-INBRIJA-levodopa-inhalation-powder/default.aspx. Issued 12/21/2018. Last accessed 03/04/2019.
[3] Inbrija™ Prescribing Information. Acorda Therapeutics. Available online at: https://www.inbrija-hcp.com/?webSyncID=cc75ec2b-2167-2149-82bd-0331cec50041&sessionGUID=79982075-a417-8900-6b9d-b4547b41248a. Last revised 12/2018. Last accessed 03/04/2019.
[4] Osmolex ER™ Prescribing Information. Vertical Pharmaceuticals, LLC. Available online at: https://www.osmolex.com/images/pdf/Prescribing_Information.pdf. Last revised 07/2018. Last accessed 03/04/2019.
[5] Ellis B, Hicken M. FDA worried drug was risky; now reports of deaths spark concern. *CNN*. Available online at: https://www.cnn.com/2018/04/09/health/parkinsons-drug-nuplazid-invs/index.html. Issued 04/09/2018. Last accessed 03/04/2019.
[6] Institute for Safe Medication Practices (ISMP). Safety Signals For Two Novel Drugs. *Quarter Watch*. Available online at: https://www.ismp.org/sites/default/files/attachments/2018-01/2017Q1_0.pdf. Issued 11/01/2017. Last accessed 03/04/2019.
[7] FDA. FDA analysis finds no new or unexpected safety risks associated with Nuplazid (pimavanserin), a medication to treat the hallucinations and delusions of Parkinson's disease psychosis. Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm621160.htm. Issued 09/20/2018. Last accessed 03/04/2019.

# Appendix D

# Vote to Prior Authorize Aimovig™ (Erenumab-aooe), Ajovy™ (Fremanezumab-vfrm), and Emgality® (Galcanezumab-gnlm)

**Oklahoma Health Care Authority**
**March 2019**

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

**Aimovig™ (erenumab)** is a calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine in adults. It is supplied as a SureClick® autoinjector in packs of 1 or 2 autoinjectors and as a single-dose prefilled syringe in packs of 1 or 2 syringes. The recommended dosage is 70mg subcutaneously (sub-Q) once monthly (QM); some patients may benefit from a dosage of 140mg QM. The 140mg dose is administered QM as 2 consecutive injections of 70mg each. The effectiveness of Aimovig™ for the preventive treatment of migraine was evaluated in 3 clinical trials, comparing erenumab to placebo. Study 1 enrolled 955 patients with a history of episodic migraine; erenumab-treated patients experienced, on average, 1 to 2 fewer monthly migraine days (MMD) than those on placebo over the course of 6 months. Study 2 enrolled 577 patients with a history of episodic migraine; erenumab-treated patients experienced, on average, 1 fewer MMD than those on placebo over the course of 3 months. Study 3 evaluated 667 patients with a history of chronic migraine; erenumab-treated patients experienced, on average, 2.5 fewer MMDs versus those receiving placebo over the course of 3 months.

**Ajovy™ (fremanezumab)** is a CGRP antagonist indicated for the preventive treatment of migraine in adults. It is supplied as a 225mg/1.5mL single-dose pre-filled syringe. The recommended dosage is 225mg sub-Q QM or 675mg sub-Q every 3 months (quarterly). The 675mg quarterly dosage is administered as 3 consecutive injections of 225mg each. The efficacy of Ajovy™ for the preventive treatment of migraine was evaluated in 2 randomized, 3-month studies. The first study enrolled 875 patients with episodic migraine; patients treated with fremanezumab with quarterly or monthly dosing regimens experienced 1.2 and 1.5 fewer MMDs, respectively, compared to those receiving placebo. Study 2 enrolled 1,130 patients with chronic migraine; patients treated with quarterly or monthly dosing regimens experienced 1.8 and 2.1 fewer monthly headache days of at least moderate severity, respectively, compared to those receiving placebo.

**Emgality® (galcanezumab)** is a CGRP antagonist indicated for the preventive treatment of migraine in adults. It is supplied in 120mg/mL single-dose prefilled pens and prefilled syringes. The recommended dose is 240mg as a loading dose (administered as 2 consecutive sub-Q injections of 120mg each), followed by monthly doses of 120mg sub-Q. The efficacy of Emgality® was evaluated in 3 studies. Study 1 and 2 were 6-month studies evaluating the efficacy of galcanezumab in patients with episodic migraine; in Study 1 and 2, patients treated with galcanezumab 120mg experienced, on average, 1.9 and 2.0 fewer monthly migraine headache days, respectively versus those receiving placebo. Study 3 was a 3-month study evaluating the efficacy of galcanezumab in patients with chronic migraine; patients treated with

galcanezumab 120mg experienced, on average, 2.1 fewer monthly migraine headache days versus those receiving placebo. In all 3 studies, treatment with galcanezumab 240mg demonstrated no additional benefit over the 120mg dose.

## Cost Comparison

| Medication | Cost Per mL | Cost Per Month | Cost Per Year |
|---|---|---|---|
| Aimovig™ (erenumab) 70mg/mL | $278.37 - $557.26^ | $278.37 - $557.26^ | $3,340.44 - $6,687.12^ |
| Ajovy™ (fremanezumab) 225mg/1.5mL | $369.90 | $554.85 | $6,658.20 |
| Emgality® (galcanezumab) 120mg/mL | $575.00 | $575.00* | $6,900.00* |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
^Aimovig™ cost based on 70mg monthly dosing; some patients may benefit from 140mg QM (as 2 consecutive injections of 70mg each). Aimovig™ is currently supplied in 1 and 2 packs.
*Emgality® cost based on maintenance dosing of 120mg QM. For initiation of therapy, a loading dose of 240mg (as 2 consecutive 120mg doses) is required.

## Recommendations

The College of Pharmacy recommends the following changes to the Anti-Migraine Medications Product Based Prior Authorization (PBPA) category:

1. Moving Treximet® (sumatriptan/naproxen) from the Special Prior Authorization (PA) Tier to Tier-1 based on net cost.
2. Updating the Onzetra® Xsail® (sumatriptan nasal powder) PA criteria as shown in red in the following criteria.
3. Removing Sumavel® DosePro® (sumatriptan 6mg/0.5mL injection) from the Tier Chart based on product discontinuation.
4. The prior authorization of Aimovig™ (erenumab-aooe), Ajovy™ (fremanezumab-vfrm), and Emgality® (galcanezumab-gnlm) with the following criteria. Please note, criteria may change based on supplemental rebate participation.

Proposed changes are shown in red in the following Anti-Migraine Medications Tier Chart:

| Anti-Migraine Medications | | | |
|---|---|---|---|
| **Tier-1** | **Tier-2** | **Tier-3** | **Special PA** |
| eletriptan (Relpax®) – **brand only** | 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 (Relpax®) – **generic** |
| **sumatriptan/naproxen (Treximet®)** | | | sumatriptan injection (Imitrex®) |
| | | | ~~**sumatriptan injection (Sumavel® DosePro®)**~~ |

| Anti-Migraine Medications | | | |
|---|---|---|---|
| **Tier-1** | **Tier-2** | **Tier-3** | **Special PA** |
| | | | sumatriptan injection (Zembrace™ SymTouch™) |
| | | | sumatriptan nasal powder (Onzetra® Xsail®) |
| | | | sumatriptan nasal spray (Imitrex®) |

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

**Anti-Migraine Medications Tier-2 Approval Criteria:**

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

**Anti-Migraine Medications Tier-3 Approval Criteria:**

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

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

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of ~~Onzetra® Xsail® or~~ Zembrace™ SymTouch™ 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 Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual components separately or lower-tiered triptan medications.~~
4. 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.
5. 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®).

6. 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 CYP 3A4 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.
7. 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).

**Aimovig™ (Erenumab-aooe) and Ajovy™ (Fremanezumab-vfrm) Approval Criteria:**

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:
    a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
    b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months; and
        i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and
4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 3 agents with different mechanisms of action. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:

a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
c. Opioids (≥10 days/month for >3 months); and
d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
e. Ergotamine-containing medications (≥10 days/month for >3 months); and
f. Triptans (≥10 days/month for >3 months); and

8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Aimovig™, Ajovy™) recommended as treatment (not necessarily prescribed by a neurologist); and
10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. ~~Members who smoke or use tobacco products will not be approved~~ Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. A patient-specific, clinically significant reason why member cannot use Emgality® (galcanezumab-gnlm) must be provided; and*
14. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
15. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig™, a quantity limit of 2 syringes or autoinjectors per 30 days will apply. The autoinjector 2-pack [(2) 70mg autoinjectors] will be preferred in place of the individual autoinjector. Claims for members receiving the 70mg dose should be submitted for a 60-day supply; 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.
    [*The manufacturer of Emgality® has currently provided a supplemental rebate to be the preferred calcitonin gene-related peptide (CGRP) inhibitor; however, Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.]

**Emgality® (Galcanezumab-gnlm) 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 2* agents with different mechanisms of action. (*The manufacturer of Emgality® has currently provided a supplemental rebate to require a trial with 2 other migraine preventative therapies; however, Emgality® will follow the original criteria and require trials with 3 other migraine preventative therapies if the manufacturer chooses not to participate in supplemental rebates.) This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and
8. Member is not taking any medications that are likely to be the cause of the headaches; and

9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and
10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. ~~Members who smoke or use tobacco products will not be approved~~ Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
14. A quantity limit of 1 syringe or pen per 30 days will apply. Requests for an initial loading dose (240mg administered as 2 consecutive 120mg injections) will be approved for a quantity limit override upon meeting Emgality® approval criteria.
    [*The manufacturer of Emgality® has currently provided a supplemental rebate to be the preferred calcitonin gene-related peptide (CGRP) inhibitor; however, Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.]

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[1] Aimovig™ (erenumab-aooe) Prescribing Information. Amgen. Available online at: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/aimovig/aimovig_pi_hcp_english.ashx. Last revised 05/2018. Last accessed 02/19/2019.
[2] Aimovig™ (erenumab-aooe) – New drug approval. OptumRx. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_aimovig_2018-0517.pdf. Last accessed 02/25/2019.
[3] Ajovy™ (fremanezumab-vfrm) Prescribing Information. Teva. Available online at: https://www.ajovy.com/globalassets/ajovy/ajovy-pi.pdf. Last revised 01/2019. Last accessed 02/19/2019.
[4] Ajovy™ (fremanezumab-vfrm) – New drug approval. OptumRx. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_ajovy_2018-0917.pdf. Last accessed 02/25/2019.
[5] Emgality® (galcanezumab-gnlm) Prescribing Information. Lilly. Available online at: http://uspl.lilly.com/emgality/emgality.html#pi. Last revised 09/2018. Last accessed 02/25/2019.
[6] Emgality™ (galcanezumab-gnlm) – New drug approval. OptumRx. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_emgality_2018_1001.pdf. Last accessed 02/25/2019.

# Appendix E

# Vote to Prior Authorize Epidiolex® (Cannabidiol), Diacomit® (Stiripentol), and Sympazan™ (Clobazam Oral Film)

**Oklahoma Health Care Authority**
**March 2019**

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

**Epidiolex® [cannabidiol (CBD) oral solution]** was approved by the U.S. Food and Drug Administration (FDA) in June 2018 for the treatment of seizures associated with 2 rare and severe forms of epilepsy, Lennox-Gastaut syndrome (LGS) and Dravet syndrome, in patients 2 years of age and older. This is the first FDA-approved drug that contains a purified drug substance from marijuana; CBD is a chemical component of the marijuana plant, but does not cause intoxication or euphoria that comes from tetrahydrocannabinol (THC), which is the primary psychoactive component of marijuana. In September 2018, the Drug Enforcement Administration (DEA) placed Epidiolex® in schedule V of the Controlled Substances Act (CSA), the least restrictive schedule of the CSA. The DEA limited the rescheduling of CBD to a specific formulation of an FDA-approved drug product (FDA-approved drugs that contain CBD derived from cannabis and no more than 0.1% THC) and re-emphasized that except for this specific formulation, CBD remains a schedule I substance. Epidiolex® is supplied as a 100mg/mL oral solution, and the maximum recommended maintenance dosage is 10mg/kg by mouth twice daily (20mg/kg/day). Because of the risk of hepatocellular injury, serum transaminases (ALT and AST) and total bilirubin levels should be obtained in all patients prior to starting treatment with Epidiolex®. The Wholesale Acquisition Cost (WAC) of Epidiolex® is $12.35 per mL, resulting in a monthly cost of $1,852.50 for a patient weighing 25kg at the maximum dosage of 20mg/kg/day.

**Diacomit® (stiripentol)** was approved by the FDA in August 2018 for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam. Stiripentol was previously approved for adjunctive treatment with clobazam and valproate for Dravet syndrome in 27 countries in the European Union (2007), Canada (2012), and Japan (2012). There are no clinical data to support the use of stiripentol as monotherapy in Dravet syndrome. To enroll in clinical trials for stiripentol, patients were required to be inadequately controlled on clobazam and valproate, and patients were then randomized to receive either stiripentol or placebo, added to their treatment with clobazam and valproate. Diacomit® is supplied as 250mg and 500mg oral capsules and as a powder for oral suspension, and the recommended dosage of stiripentol is 50mg/kg/day, administered by mouth in 2 or 3 divided doses, with a maximum total dosage of 3,000mg/day. Diacomit® was expected to be available in early January 2019; however, it is not yet available on the market and cost information is also not yet available.

**Sympazan™ (clobazam oral film)** was approved by the FDA in November 2018 for the adjunctive treatment of seizures associated with LGS in patients 2 years of age and older. Sympazan™ is the first and only oral film FDA-approved to treat seizures associated with LGS.

Sympazan™ oral film is available in 5mg, 10mg, and 20mg strengths. The FDA previously approved clobazam as brand name Onfi® in 2011, which is available as oral tablets (10mg and 20mg) and oral suspension (2.5mg/mL), with both formulations recently becoming available generically. The WAC of Sympazan™ 20mg is $52.00 per film. At the maximum dose of 40mg per day, this results in a monthly cost of $3,120.00 for Sympazan™ 20mg films, compared to $72.60 for clobazam 20mg tablets or $321.60 for clobazam 2.5mg/mL oral suspension.

- As a result of increased generic availability and resulting lower net cost for clobazam tablets and oral suspension (generic Onfi®), the prior authorization was removed from clobazam tablets and oral suspension in December 2018.

## Market News and Updates[8,9,10]

**Pipeline:**

- **Fintepla® (Fenfluramine; ZX008):** Zogenix submitted a New Drug Application (NDA) to the FDA in February 2019 for Fintepla®, a low-dose fenfluramine oral solution, for the treatment of seizures associated with Dravet syndrome. Fenfluramine is an amphetamine derivative that was initially developed as an appetite suppressant (as 20mg and 60mg oral tablets and capsules) but was withdrawn from the market by the FDA in the 1990s due to cardiovascular safety concerns. Clinical trials with Fintepla® (dosed at 0.5mg/kg/day) have shown no safety signal of cardiovascular toxicity. Fintepla® was previously granted Orphan Drug, Fast Track, and Breakthrough Therapy designations by the FDA. Zogenix is also currently evaluating Fintepla® for the treatment of seizures associated with LGS in an ongoing Phase 3 trial.
- **Valtoco™ (Diazepam Nasal Spray; NRL-1):** Neuralis submitted an NDA to the FDA in September 2018 for Valtoco™ nasal spray as a treatment for epilepsy patients 6 years of age and older who experience increased bouts of seizure activity, also known as cluster or acute repetitive seizures. Valtoco™ is a proprietary formulation of diazepam, incorporating the unique combination of vitamin E-based solution and Intravail® absorption enhancement, delivered via a nasal spray formulation that is designed to be administered by a family member or caregiver. In clinical trials, Valtoco™ was well tolerated and demonstrated high bioavailability, as well as low variability from dose to dose. The FDA previously granted Valtoco™ Orphan Drug and Fast Track designations. If approved by the FDA, Valtoco™ nasal spray would provide an alternative to rectal diazepam and would be the first new therapy approved for the treatment of cluster or acute seizures in over 20 years.
- **Midazolam Nasal Spray:** UCB submitted an NDA to the FDA in August 2018 for midazolam nasal spray as an acute treatment of seizures in patients who require control of intermittent bouts of increased seizure activity (e.g., seizure clusters, acute repetitive seizures). Midazolam nasal spray is intended to be delivered intranasally without active inhalation by the patient. Midazolam nasal spray was previously granted Orphan Drug and Fast Track designations by the FDA. Similar to Valtoco™, if approved by the FDA, midazolam nasal spray would provide an alternative to rectal diazepam and would be the first new therapy approved for the treatment of cluster or acute seizures in over 20 years.

## Recommendations

The College of Pharmacy recommends the prior authorization of Epidiolex® (CBD oral solution), Diacomit® (stiripentol), and Sympazan™ (clobazam oral film) with the following criteria:

**Epidiolex® (Cannabidiol Oral Solution) Approval Criteria:**

1. An FDA approved diagnosis of 1 of the following:
    a. Lennox-Gastaut syndrome (LGS); or
    b. Dravet syndrome; and
2. Member must be 2 years 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 or be inadequately controlled with at least 1 anticonvulsant; or
5. For a diagnosis of LGS, the member must have failed therapy with at least 3 other anticonvulsants; and
6. Members currently stable on Epidiolex® and who have a seizure diagnosis will be grandfathered; and
7. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

**Diacomit® (Stiripentol) Approval Criteria:**

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

**Sympazan™ (Clobazam Oral Film) Approval Criteria:**

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

Additionally, the College of Pharmacy recommends updating the approval criteria for Trokendi XR® (topiramate ER) to require a reason why the member cannot use Qudexy® XR (topiramate ER) based on net cost (changes noted in red):

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

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

Lastly, the College of Pharmacy recommends updating the approval criteria for Briviact® (brivaracetam) to add an age restriction on the oral solution to be consistent with other anticonvulsants with special formulations (changes noted in red):

**Briviact® (Brivaracetam) Approval Criteria:**

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

[1] FDA News Release. FDA Approves First Drug Comprised of an Active Ingredient Derived from Marijuana to Treat Rare, Severe Forms of Epilepsy. Available online at: https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm611046.htm. Issued 06/25/2018. Last accessed 02/15/2019.

[2] Drug Enforcement Administration (DEA) News Release. FDA-Approved Drug Epidiolex® Placed in Schedule V of Controlled Substances Act. Available online at: https://www.dea.gov/press-releases/2018/09/27/fda-approved-drug-epidiolex-placed-schedule-v-controlled-substance-act. Issued 09/27/2018. Last accessed 02/15/2019.

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[6] Epidiolex® (Cannabidiol) Prescribing Information. Greenwich Biosciences, Inc. Available online at: https://www.epidiolex.com/sites/default/files/EPIDIOLEX_Full_Prescribing_Information.pdf. Last revised 12/2018. Last accessed 02/15/2019.

[7] Diacomit® (Stiripentol) Prescribing Information. Biocodex. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206709s000,207223s000lbl.pdf. Last revised 08/2018. Last accessed 02/15/2019.

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# Appendix F

# Vote to Prior Authorize Gamifant® (Emapalumab-lzsg)

**Oklahoma Health Care Authority**
**March 2019**

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

Hemophagocytic lymphohistiocytosis (HLH) is an aggressive and life-threatening syndrome of excessive immune activation that causes inflammation and tissue destruction. It most frequently affects infants from birth to 18 months of age, but the disease is also observed in children and adults of all ages. When HLH occurs as a genetic disorder, it is known as primary HLH. Excessive cytokine production by macrophages, natural killer (NK) cells, and cytotoxic lymphocytes (CTLs) is thought to be a primary mediator of tissue damage that is responsible for multiorgan failure and the high mortality rate of HLH. One of the underlying gene defects involves mutations in the gene encoding perforin (*PRF*). Perforin is secreted from CTLs and NK cells. Mutations in *PRF* account for 20 to 40% of all affected primary HLH patients.

The most typical findings of HLH are fever, hepatosplenomegaly, and cytopenias. Other common findings include hypertriglyceridemia, hypofibrinogenemia, hyperferritinemia, and neurological symptoms. Patients with HLH can have a single episode of the disease or relapsing episodes, with relapses occurring most often in patients with primary HLH.

The incidence of primary HLH is estimated to be around 1 in 50,000 live-born children with approximately 100 patients diagnosed each year in the United States. All forms of HLH, including cases treated adequately, may have a high mortality rate. The long-term prognosis of primary forms without treatment is poor, with a median survival of <2 months to 6 months after diagnosis. Even with treatment, only 21 to 26% are expected to survive 5 years.

**Gamifant® (emapalumab-lzsg)** was approved by the U.S. Food and Drug Administration (FDA) in November 2018 for the treatment of adult and pediatric (newborn and older) patients with primary HLH with refractory, recurrent, or progressive disease or who are intolerant to conventional HLH therapy. Emapalumab is a monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ), which is suggested to play a role in HLH by being hypersecreted. Gamifant® is available as a 5mg/mL solution for intravenous (IV) infusion, supplied as 10mg/2mL and 50mg/10mL single-dose vials (SDV). The recommended starting dose of emapalumab is 1mg/kg twice per week (every 3 to 4 days). Subsequent doses may be increased based on clinical and laboratory criteria to a maximum of 10mg/kg. After the patient's clinical condition is stabilized, the dose should be decreased to the previous level to maintain clinical response. Dexamethasone should be started at a daily dose of at least 5 to 10mg/$m^2$ the day before emapalumab treatment begins and continued throughout treatment. During treatment with emapalumab, patients should be monitored for tuberculosis (TB), adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated. Emapalumab should be continued until hematopoietic stem cell transplantation (HSCT) is performed or unacceptable toxicity occurs. The Wholesale Acquisition Cost (WAC) of Gamifant® is $3,711 per

milliliter (mL). This results in a cost per dose of $7,422 and a yearly cost of $712,512 for the minimum dose of 1mg/kg twice weekly in a 10kg child. At a maximum dose of 10mg/kg in a 10kg child, the cost per dose is $74,220 and the annual cost is $7,125,120. Dosing is weight-based and may be adjusted based on patient response; therefore, pricing will vary.

## Recommendations

The College of Pharmacy recommends the prior authorization of Gamifant® (emapalumab-lzsg) with the following criteria:

**Gamifant® (Emapalumab-lzsg) Approval Criteria:**

1. An FDA approved indication for the treatment of adult and pediatric patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or who are intolerant to conventional HLH therapy; and
2. Diagnosis of primary HLH must be confirmed by 1 of the following:
    a. Genetic testing confirming mutation of a gene known to cause primary HLH (e.g., *PRF*, *UNC13D*, *STX11*); or
    b. Family history consistent with primary HLH; or
    c. Member meets 5 of the following 8 diagnostic criteria:
        i. Fever; or
        ii. Splenomegaly; or
        iii. Cytopenias affecting at least 2 of 3 lineages in the peripheral blood (hemoglobin <9, platelets <100 x $10^9$/L, neutrophils <1 x $10^9$/L); or
        iv. Hypertriglyceridemia (fasting triglycerides >3mmol/L or ≥265mg/dL) and/or hypofibrinogenemia (≤1.5g/L); or
        v. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy; or
        vi. Low or absent natural killer (NK)-cell activity; or
        vii. Hyperferritinemia (ferritin ≥500mcg/L); or
        viii. High levels of soluble interleukin-2 receptor (soluble CD25 ≥2,400U/mL); and
3. Gamifant® must be prescribed by, or in consultation with, a physician who specializes in the treatment of immune deficiency disorders; and
4. Member must have at least 1 of the following:
    a. Failure of at least 1 conventional HLH treatment (e.g., etoposide, dexamethasone, cyclosporine); or
    b. Documentation of progressive disease despite conventional HLH treatment; or
    c. A patient-specific, clinically significant reason why conventional HLH treatment is not appropriate for the member must be provided; and
5. Prescriber must verify dexamethasone dosed at least 5mg/$m^2$/day will be used concomitantly with Gamifant®; and
6. Prescriber must verify member has received or will receive prophylaxis for herpes zoster, *Pneumocystis jirovecii,* and fungal infection(s); and

7. Prescriber must verify member will be monitored for tuberculosis (TB), adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated; and
8. 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
9. Approvals will be for the duration of 6 months with reauthorization granted if the prescriber documents the member is responding well to treatment, no unacceptable toxicity has occurred, and the member has not received hematopoietic stem cell transplantation (HSCT).

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[1] McClain KL, Eckstein O. Clinical features and diagnosis of hemophagocytic lymphohistiocytosis. *UpToDate*. Available online at: https://www.uptodate.com/contents/clinical-features-and-diagnosis-of-hemophagocytic-lymphohistiocytosis?search=primary%20hemophagocytic%20lymphohistiocytosis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Last revised 10/29/2018. Last accessed 02/18/2019.

[2] Henter JI, Horne AC, Arico M, et al. HLH-2004: Diagnostic and Therapeutic Guidelines for Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer* 2007; 48(2):124-131.

[3] National Institute of Health (NIH) National Center for Advancing Translational Sciences. Hemophagocytic lymphohistiocytosis. *Genetic Rare Diseases Information Center*. Available online at: https://rarediseases.info.nih.gov/diseases/6589/hemophagocytic-lymphohistiocytosis. Last revised 09/11/2017. Last accessed 02/18/2019.

[4] McClain K. Treatment and prognosis of hemophagocytic lymphohistiocytosis. *UpToDate*. Available online at: https://www.uptodate.com/contents/treatment-and-prognosis-of-hemophagocytic-lymphohistiocytosis?search=primary%20hemophagocytic%20lymphohistiocytosis&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Last revised 12/14/2018. Last accessed 02/18/2019.

[5] Gamifant® Prescribing Information. Sobi, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761107lbl.pdf. Last revised 11/2018. Last accessed 02/18/2019.

# Appendix G

# Vote to Prior Authorize Firdapse® (Amifampridine)

**Oklahoma Health Care Authority**
**March 2019**

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

Lambert-Eaton myasthenic syndrome (LEMS) is a syndrome of weakness and fatigue due to an autoimmune process. LEMS is caused by antibodies produced by the body that destroy the voltage-gated calcium channels on the motor neuron at neuromuscular junctions. These channels help regulate the amount of acetylcholine that is released. When there is not enough acetylcholine released, the muscles do not contract. Nearly 40 to 60% of patients with LEMS also are diagnosed with cancer, typically lung cancer. Symptoms of LEMS may present prior to a diagnosis of cancer and once a diagnosis of LEMS has been made, the patient should be followed for the development of cancer.

Symptoms of LEMS are related to muscle weakness, primarily in the proximal legs and arms. Weakness may also occur in the neck and can affect swallowing, breathing, or speaking. Onset of symptoms is gradual, typically occurring over several weeks to months. The most effective treatment of LEMS associated with cancer is eradication of the cancer. Symptomatic treatment is an option for patients with more severe symptoms, which includes medications that increase the release or abundance of neurotransmitters for muscles to respond (e.g., amifampridine, pyridostigmine). Immunosuppressants can be used to reduce the production of antibodies. Other treatment options include plasmapheresis and intravenous immunoglobulin (IVIG) therapy.

In November 2018, the U.S. Food and Drug Administration (FDA) approved **Firdapse® (amifampridine)** tablets, the first FDA approved treatment for LEMS. Amifampridine is a potassium channel blocker indicated for the treatment LEMS in adults. Firdapse® is supplied as off-white 10mg scored tablets with a recommended starting dose of 15 to 30mg by mouth dailu in 3 to 4 divided doses. The dose can be increased based on symptoms and tolerability up to a maximum single dose of 20mg and a maximum daily dose of 80mg. For patients with renal impairment [creatinine clearance (CrCL) 15 to 90mL/min], hepatic impairment, or who are known N-acetyltransferase 2 (NAT2) poor metabolizers, it is recommended to start at lower doses. Amifampridine is contraindicated in patients with a history of seizures and should be used cautiously in patients that are taking medications that lower the seizure threshold.

**Cost:**

| Medication | Cost Per Tablet | Cost Per 30 Days* | Cost Per Year* |
|---|---|---|---|
| **Firdapse® (amifampridine phosphate) 10mg tablet** | **$171.23** | **$15,410.70** | **$184,928.40** |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Cost based on a dose of 30mg per day.

## Recommendations

The College of Pharmacy recommends the prior authorization of Firdapse® (amifampridine) with the following criteria:

**Firdapse® (Amifampridine) Approval Criteria:**

1. A diagnosis of Lambert-Eaton myasthenic syndrome (LEMS); and
2. Diagnosis must be confirmed by 1 of the following:
   a. A high titer anti-P/Q-type voltage-gated calcium channel (VGCC) antibody assay; or
   b. A confirmatory electrodiagnostic study [e.g., repetitive nerve stimulation (RNS), needle electromyography (EMG), single-fiber electromyography (SFEMG)]; and
3. Firdapse® must be prescribed by, or in consultation with, a neurologist or oncologist; and
4. Member must not have a history of seizures or be taking medications that lower the seizure threshold (e.g., bupropion, tramadol, amphetamines, theophylline); and
5. A quantity limit of 240 tablets per 30 days will apply; and
6. Initial approvals will be for 6 months. Continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with Firdapse®.

[1] Lambert-Eaton Myasthenic Syndrome. National Organization for Rare Disorders. Available online at: https://rarediseases.org/rare-diseases/lambert-eaton-myasthenic-syndrome/. Last accessed 03/04/2019.
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[3] Lindquist S, Stangel M. Update on treatment options for Lambert-Eaton myasthenic syndrome: focus on use of amifampridine. *Neuropsychiatr Dis Treat* 2011; 7:341-349.
[4] U.S. Food and Drug Administration (FDA). FDA approves first treatment for Lambert-Eaton myasthenic syndrome, a rare autoimmune disorder. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm627093.htm. Issued 11/28/2018. Last accessed 03/04/2019.

# Appendix H

# Vote to Prior Authorize Retacrit™ (Epoetin Alfa-epbx)

**Oklahoma Health Care Authority**
**March 2019**

## Introduction[1,2]

In May 2018, the U.S. Food and Drug Administration (FDA) approved **Retacrit™ (epoetin alfa-epbx)**, a biosimilar of Epogen®/Procrit® (epoetin alfa) for the treatment of anemia due to chronic kidney disease (CKD) in patients on dialysis and not on dialysis, anemia due to use of zidovudine in patients with Human Immunodeficiency Virus (HIV) infection, and anemia due to the effects of concomitant myelosuppressive chemotherapy. It is also approved for the reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery. The approval was based on comparisons of extensive structural and functional product characterization, animal data, human pharmacokinetic and pharmacodynamic data, and clinical immunogenicity between Retacrit™ and Epogen®/Procrit®, demonstrating that Retacrit™ is highly similar to Epogen®/Procrit® and that there are no clinically meaningful differences between the products. Retacrit™ has not been shown to be interchangeable with Epogen®/Procrit®. Like Epogen®/Procrit®, the labeling for Retacrit™ contains a *Boxed Warning* to alert health care professionals and patients about an increased risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access, and tumor progression or recurrence.

**Cost Comparison:**

| Medication | Cost Per Vial |
|---|---|
| **Retacrit™ (epoetin alfa-epbx) 10,000/mL vial** | **$110.30** |
| Epogen® (epoetin alfa) 10,000/mL vial | $165.80 |
| Procrit® (epoetin alfa) 10,000/mL vial | $258.97 |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

**Medicaid Drug Rebate Program:** Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any payer. If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices and now applies to both brand and generic medications. As wholesale acquisition cost (WAC) or list price increases, the rebated amount per unit (RAPU) increases as well, resulting in minimal effect on Medicaid net cost. Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. Please note that costs listed in the cost comparison chart do not reflect rebated prices or net costs for Medicaid reimbursement.

## Recommendations

The College of Pharmacy recommends the prior authorization of Retacrit™ (epoetin alfa-epbx). The following criteria would apply (changes noted in red):

**Procrit® (Epoetin Alfa), Epogen® (Epoetin Alfa), and Retacrit™ (Epoetin Alfa-epbx) Approval Criteria:**

1. An FDA approved diagnosis of 1 of the following:
    a. Anemia due to chemotherapy in patients with non-myeloid malignancies; or
    b. Anemia in zidovudine-treated Human Immunodeficiency Virus (HIV)-infected patients; or
    c. The reduction of allogeneic blood transfusion(s) in surgery patients; or
    d. An FDA approved diagnosis of anemia associated with chronic renal failure; and
        i. For the diagnosis of anemia associated with chronic renal failure: member must not be receiving dialysis [erythropoietin stimulating agents (ESAs) are included in the bundled dialysis payment if member is on any form of dialysis and cannot be billed separately]; and
2. Authorization of Retacrit™ requires a patient-specific, clinically significant reason why the member cannot use Procrit® or Epogen®; and
3. Recent hemoglobin levels must be provided; and
4. Approvals will be for the duration of 16 weeks of therapy. Recent hemoglobin levels must be provided with continuation requests, and further approval may be granted if the member's recent hemoglobin level is <11g/dL.

[1] U.S. Food and Drug Administration (FDA). FDA Approves Retacrit as a Biosimilar to Epogen/Procrit. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm607723.htm. Issued 05/15/2018. Last accessed 02/18/2019.

[2] Retacrit™ (epoetin alfa-epbx) Prescribing Information. Pfizer Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125545s000lbl.pdf. Last revised 05/2018. Last accessed 02/20/2019.

# Appendix I

# Calendar Year 2018 Annual Review of Chronic Lymphocytic Leukemia (CLL) Medications and 30-Day Notice to Prior Authorize Copiktra™ (Duvelisib)

**Oklahoma Health Care Authority**
**March 2019**

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

Leukemia is an abnormal and autonomous proliferation of 1 or more blood-forming elements with infiltrations of the bone marrow and other organs. Leukemia is a heterogeneous group of neoplasms arising from the malignant transformation of hematopoietic cells that eventually replaces the normal marrow, leading to the signs and symptoms of leukemia. Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are indolent diseases, as patients may survive many years without therapy. The major difference between CLL and SLL is that in CLL, a significant number of abnormal lymphocytes are found in the blood in addition to bone marrow and lymphoid tissue versus SLL where there are few circulating abnormal lymphocytes and disease is mostly found in the lymph nodes, bone marrow, and other lymphoid tissues. CLL/SLL is primarily a disease of the elderly; the median age at diagnosis is 72 years. CLL/SLL is the most prevalent adult leukemia in western countries. In 2018, there were an estimated 20,940 new diagnoses and 4,510 deaths due to CLL. Treatment has evolved significantly over the past several decades. Immunotherapy and small molecule inhibitors targeting critical signaling pathways [e.g., Bruton's tyrosine kinase (BTK), phosphatidylinositol 3-kinase (PI3K)] have improved efficacy in therapies for CLL/SLL.

## Current Prior Authorization Criteria

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

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

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

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

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

1. In combination with chlorambucil or bendamustine for first-line therapy; or
2. As a single-agent for relapsed or refractory disease.

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

1. A 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.

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

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

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

1. A diagnosis of cGVHD after failure of 1 or more lines of therapy.

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

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

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

1. As second-line or subsequent therapy; and
2. Used 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. A 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 [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.

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

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

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

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

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

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

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

1. For relapsed/refractory disease; and
2. In combination with rituximab or as a single-agent.

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

1. A 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.

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

1. For relapsed or refractory disease; and
2. In combination with rituximab or rituximab/bendamustine; or
3. As a single-agent.

## Utilization of CLL Medications: Calendar Year 2018

### Comparison of Calendar Years: Pharmacy Claims

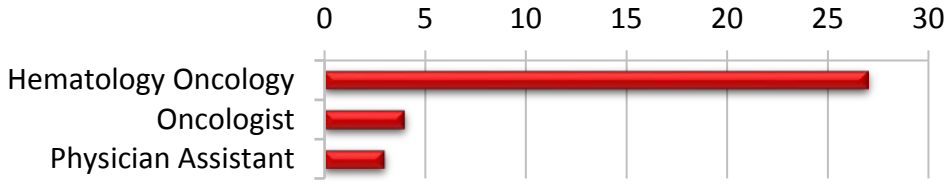
| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 7 | 38 | $453,509.97 | $11,934.47 | $397.82 | 3,690 | 1,140 |
| **2018** | 7 | 34 | $350,302.46 | $10,303.01 | $356.72 | 1,522 | 982 |
| **% Change** | **0.00%** | **-10.50%** | **-22.80%** | **-13.70%** | **-10.30%** | **-58.80%** | **-13.90%** |
| **Change** | **0** | **-4** | **-$103,207.51** | **-$1,631.46** | **-$41.10** | **-2,168** | **-158** |

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

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

- Due to the limited number of members utilizing CLL medications during calendar year 2018, detailed demographic information could not be provided.

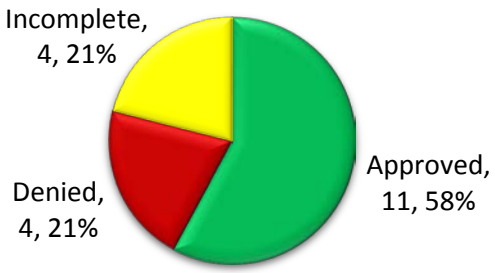
### Top Prescriber Specialties of CLL Medications By Number of Claims: Pharmacy Claims




## Prior Authorization of CLL Medications

There were 19 prior authorization requests submitted for CLL medications during calendar year 2018. The following chart shows the status of the submitted petitions for calendar year 2018.

### Status of Petitions




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

**Anticipated Patent Expiration(s):**

- Venclexta® (venetoclax): June 2031
- Copiktra™ (duvelisib): May 2032

- Zydelig® (idelalisib): September 2033
- Imbruvica® (ibrutinib): October 2034

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

- **September 2018:** The FDA approved Copiktra™ (duvelisib) for the treatment of adults with relapsed or refractory CLL or SLL after at least 2 prior therapies. The FDA also granted accelerated approval to duvelisib for patients with follicular lymphoma (FL) after at least 2 systemic therapies.

**New Indication(s) and Label Update(s):**

- **June 2018:** The FDA approved Venclexta® (venetoclax) for the treatment of patients with CLL or SLL, with or without 17p deletion, who have received at least 1 prior therapy. The FDA granted venetoclax in combination with rituximab Breakthrough Therapy designation and granted the application priority review.
- **August 2018:** The FDA approved Imbruvica® (ibrutinib) in combination with rituximab for the treatment of Waldenström's macroglobulinemia (WM). The approval expanded the label for ibrutinib in WM beyond its previously approved use as monotherapy to include combination use with rituximab. This approval is the first approved non-chemotherapy combination option for the treatment of WM.
- **November 2018:** The FDA granted accelerated approval to Venclexta® (venetoclax) in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC) for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are 75 years of age or older, or who have comorbidities that preclude use of intensive induction chemotherapy. This indication was approved under accelerated approval based on response rates and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- **January 2019:** The FDA approved Imbruvica® (ibrutinib) in combination with Gazyva® (obinutuzumab) for use in untreated patients with CLL/SLL. This is the first approval for a non-chemotherapy combination regimen for treatment-naïve patients with CLL/SLL.

**Pipeline:**

- **JCAR017:** Chimeric antigen receptor (CAR) T-cell therapy targeted at CD19 (JCAR017) is being studied in relapsed/refractory CLL or SLL
- **Acalabrutinib:** Acalabrutinib received an accelerated FDA approval for patients with relapsed/refractory mantle cell lymphoma (MCL) in 2017 and is currently being evaluated in patients with CLL. Results of Phase 1/2 trials demonstrated overall response rates (ORR) of 96% in treatment-naïve patients, 93% in relapsed/refractory patients, and 76% in ibrutinib-intolerant patients with CLL.

## Copiktra™ (Duvelisib) Product Summary[13]

**Copiktra™ (Duvelisib):**

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For the treatment of adult patients with:
    - Relapsed or refractory CLL or SLL after at least 2 prior therapies; or

- Relapsed or refractory FL after at least 2 prior systemic therapies
    - This indication is approved under accelerated approval based on ORR; continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 15mg and 25mg capsules
- **Dose:** 25mg orally twice daily; dosage should be modified for toxicity
- **Cost:** Wholesale Acquisition Cost (WAC) of $210.71 per capsule, resulting in a cost per 28-day treatment cycle of $11,799.76

## Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations; changes can be seen in the following criteria listed in red (only criteria with updates listed)
- The prior authorization of Copiktra™ (duvelisib) with the following criteria listed in red

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

1. In combination with chlorambucil, bendamustine, or ibrutinib for first-line therapy; or
2. As a single-agent for relapsed or refractory disease.

**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 [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.

**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; and
3. Must be used in combination with azacitidine, or decitabine, or low-dose cytarabine.

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

1. Diagnosis of relapsed or refractory FL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. Must be used as a single-agent.

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

1. Diagnosis of relapsed or refractory CLL or SLL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. Must be used as a single-agent.

## Utilization Details of CLL Medications: Calendar Year 2018

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBERS | COST/ CLAIM |
|---|---|---|---|---|---|
| IMBRUVICA CAP 140MG | 15 | 4 | $134,109.80 | 3.75 | $8,940.65 |
| IMBRUVICA TAB 420MG | 12 | 4 | $136,542.80 | 3 | $11,378.57 |
| IMBRUVICA TAB 140MG | 4 | 1 | $45,513.84 | 4 | $11,378.46 |
| IMBRUVICA TAB 560MG | 3 | 1 | $34,136.02 | 3 | $11,378.67 |
| **TOTAL** | **34** | **7*** | **$350,302.46** | **4.9** | **$10,303.01** |

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

### Medical Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBERS | COST/ CLAIM |
|---|---|---|---|---|---|
| OBINUTUZUMAB J9301 | 13 | 2 | $73,687.00 | 6.50 | $5,668.23 |
| **TOTAL** | **13^** | **2*** | **$73,687.00** | **6.50** | **$5,668.23** |

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

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# Appendix J

# Calendar Year 2018 Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc ), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat)

**Oklahoma Health Care Authority**
**March 2019**

## 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 nation and is slightly more common in Caucasian men. In 2018, there were an estimated 74,680 new diagnoses of NHL and 19,910 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 cell 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 2018, there were an estimated 8,500 new diagnoses of HL and 1,050 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 tiredness. 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 type 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

Criteria for Gazyva® (obinutuzumab), Imbruvica® (ibrutinib), and Zydelig® (idelalisib) for indications other than lymphoma can be found in the March 2019 Drug Utilization Review (DUR) Board packet. These medications are reviewed annually with the chronic lymphocytic leukemia (CLL) 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 [Follicular Lymphoma (FL) Diagnosis]:**

1. A 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. A 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.

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

1. A 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 criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) includes only criteria for indications of lymphoma or with recent changes based on recent U.S. Food and Drug Administration (FDA) approved indications or updates. Complete prior authorization criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) can be found in the October 2018 DUR Board packet. These medications are reviewed annually with the skin cancer medications.

**Keytruda® (Pembrolizumab) Approval Criteria [Hodgkin Lymphoma (HL) Diagnosis]:**

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

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

1. Diagnosis of metastatic NSCLC; and
2. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for PD-L1 expression as follows:
    a. As a single-agent, first-line: ≥50%; or
    b. First-line in combination with carboplatin and pemetrexed: no expression required; or
    c. As a single-agent, second-line: ≥1%; and
4. Member meets 1 of the following:
    a. Previously untreated metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    b. New diagnosis as first-line therapy (patient has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; or
    c. Single-agent for disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin):
        i. Members with EGFR-mutation-positive should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
            1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*
        ii. Members with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to

receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and

1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*

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

1. Diagnosis of unresectable or metastatic melanoma; and
2. Pembrolizumab must be used as a single-agent; and
3. Member meets 1 of the following:
   a. Pembrolizumab is being used as first-line therapy; or
   b. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used; and
4. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

**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 patients 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 [Hodgkin Lymphoma (HL) Diagnosis]:**

1. Diagnosis of relapsed or refractory classical HL; 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 2018

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

### Comparison of Calendar Years: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 9 | 43 | $518,415.92 | $12,056.18 | $401.87 | 4,260 | 1,290 |
| **2018** | 8 | 45 | $515,486.25 | $11,455.25 | $392.90 | 2,842 | 1,312 |
| **% Change** | **-11.10%** | **4.70%** | **-0.60%** | **-5.00%** | **-2.20%** | **-33.30%** | **1.70%** |
| **Change** | **-1** | **2** | **-$2,929.67** | **-$600.93** | **-$8.97** | **-1,418** | **22** |

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

### Calendar Year 2018 Utilization: Medical Claims

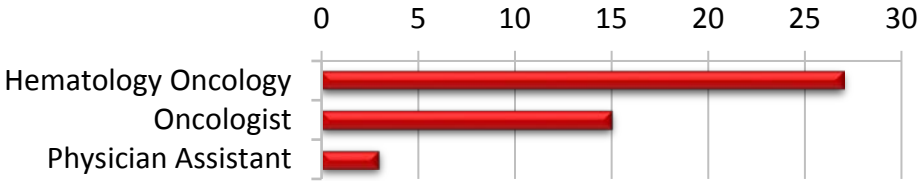
| *Total Members | +Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|
| 128 | 609 | $4,949,109.57 | $8,126.62 | 4.76 |

*Total number of unduplicated 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.

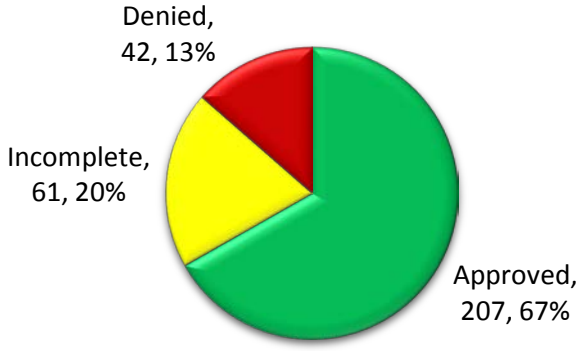
### Top Prescriber Specialties of Lymphoma Medications By Number of Claims: Pharmacy Claims




## Prior Authorization of Lymphoma Medications

There were 310 prior authorization requests submitted for lymphoma medications during calendar year 2018. The following chart shows the status of the submitted petitions for calendar year 2018.

### Status of Petitions




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

**Anticipated Patent Expiration(s):**

- Istodax® (romidepsin): August 2021
- Folotyn® (pralatrexate): May 2025
- Beleodaq® (belinostat): October 2027
- Zolinza® (vorinostat): March 2028
- Zydelig® (idelalisib): September 2033

- Imbruvica® (ibrutinib): October 2033
- Calquence® (acalabrutinib): July 2036

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

- **August 2018:** The FDA approved Poteligeo® (mogamulizumab-kpkc) for adult patients with relapsed or refractory MF or Sézary syndrome (SS) after at least 1 prior systemic therapy.
- **November 2018:** The FDA approved Truxima® (rituximab-abbs) as the first biosimilar to Rituxan® (rituximab) for the treatment of adult patients with CD20-positive, B-cell NHL to be used as a single-agent or in combination with chemotherapy. Truxima® is the first biosimilar to be approved in the United States for the treatment of NHL.

**New Indication(s) and Label Update(s):**

- **March 2018:** The FDA approved Adcetris® (brentuximab vedotin) to treat adult patients with previously untreated Stage 3 or 4 cHL in combination with chemotherapy.
- **October 2018:** The FDA approved Keytruda® (pembrolizumab) in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC).
- **November 2018:** The FDA approved Adcetris® (brentuximab vedotin) in combination with chemotherapy for previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing PTCLs, including AITL and PTCL, NOS. This is the first FDA approval for previously untreated PTCL including sALCL.
- **November 2018:** The FDA approved Keytruda® (pembrolizumab) for the treatment of patients with hepatocellular carcinoma (HCC) who have previously been treated with sorafenib.
- **December 2018:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) for adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).
- **February 2019:** The FDA approved Keytruda® (pembrolizumab) for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.

**Pipeline:**

- **Chimeric Antigen Receptor (CAR) T-cell Therapy:** According to data presented at the National Comprehensive Cancer Network (NCCN) Annual Congress: Hematologic Malignancies in 2018, CAR T-cell therapy appears to be a promising approach to HL. The data set is small and not yet mature, but based on available data it suggests this approach may play a role by targeting CD30 or Epstein Barr virus. In addition, Kymriah® (tisagenlecleucel) is in Phase 3 development for treatment of MCL, a subtype of NHL.
- **Lymphoma Vaccines:** Lymphoma vaccines are currently being investigated as a way to treat, not prevent, lymphomas. The goal of the lymphoma vaccine is to create an immune reaction against lymphoma cells in patients who have very early disease or in patients who are in remission. A potential advantage of this type of treatment is that it seems to have very limited side effects. There have been a few successes so far with this approach, and it is a major area of research in lymphoma treatment.

## Product Summaries[20,21,22,23,24,25,26,27,28]

**Adcetris® (Brentuximab Vedotin):**

- **Therapeutic Class:** CD30-directed antibody-drug conjugate
- **Indication(s):** For the treatment of adult patients with:
  - Previously untreated Stage III or IV cHL, in combination with doxorubicin, vinblastine, and dacarbazine
  - cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
  - cHL after failure of auto-HSCT or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
  - Previously untreated, systemic ALCL (sALCL) or other CD30-expressing PTCL, including AITL and PTCL, NOS, in combination with cyclophosphamide, doxorubicin, and prednisone
  - sALCL after failure of at least 1 prior multi-agent chemotherapy regimen
  - Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing MF who have received prior systemic therapy
- **How Supplied:** 50mg lyophilized powder in a single-dose vial (SDV)
- **Dose:**
  - Recommended dose as monotherapy is 1.8mg/kg via intravenous (IV) infusion up to a maximum of 180mg every 3 weeks
  - Recommended dose in combination with chemotherapy for previously untreated Stage III or IV cHL is 1.2mg/kg via IV infusion up to a maximum of 120mg every 2 weeks for a maximum of 12 doses
- **Cost:** Wholesale Acquisition Cost (WAC) of $7,662.00 per vial, resulting in a cost of $22,986.00 per dose for an 80kg patient receiving Adcetris® as monotherapy

**Beleodaq® (Belinostat):**

- **Therapeutic Class:** Histone deacetylase (HDAC) inhibitor
- **Indication(s):** For the treatment of patients with relapsed or refractory PTCL
  - This indication is approved under accelerated approval based on tumor response rate and duration of response; an improvement in survival or disease-related symptoms has not been established (continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial)
- **How Supplied:** 500mg lyophilized powder in SDV for reconstitution
- **Dose:** Recommended dose is 1,000mg/$m^2$ administered over 30 minutes by IV infusion once daily on days 1 to 5 of a 21-day cycle
  - Cycles can be repeated until disease progression or unacceptable toxicity
  - Treatment discontinuation or interruption with or without dosage reductions by 25% may be needed to manage adverse reactions
- **Cost:** WAC of $1,885.30 per vial, resulting in a cost of $28,279.50 per treatment cycle for a patient with a body surface area (BSA) of 1.5$m^2$

**Calquence® (Acalabrutinib):**

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For the treatment of adult patients with MCL who have received at least 1 prior therapy
  - This indication is approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 100mg capsule
- **Dose:** 100mg orally approximately every 12 hours
- **Cost:** WAC of $234.40 per capsule, resulting in a cost of $14,064.00 per month

**Folotyn® (Pralatrexate):**

- **Therapeutic Class:** Folate analog metabolic inhibitor
- **Indication(s):** For the treatment of patients with relapsed or refractory PTCL
  - This indication is based on ORR; clinical benefit such as improvement in progession-free survival or overall survival has not been demonstrated
- **How Supplied:** 20mg/mL and 40mg/2mL SDVs
- **Dose:** Recommended dose is 30mg/$m^2$ administered as an IV push over 3 to 5 minutes once weekly for 6 weeks in 7-week cycles; dose omissions and/or dose reductions may be needed to manage adverse drug reactions
- **Cost:** WAC of $5,442.69 per mL, resulting in a cost of $65,312.28 per treatment cycle for a patient with a BSA of 1.3$m^2$

**Istodax® (Romidepsin):**

- **Therapeutic Class:** HDAC inhibitor
- **Indication(s):**
  - Treatment of CTCL in adult patients who have received at least 1 prior systemic therapy
  - Treatment of PTCL in adult patients who have received at least 1 prior therapy
    - This indication is approved under accelerated approval based on response rate; continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 10mg SDV for reconstitution
- **Dose:**
  - 14mg/$m^2$ administered via IV infusion over a 4-hour period on days 1, 8, and 15 of a 28-day cycle
  - Cycles should be repeated every 28 days provided that the patient continues to benefit from and tolerates the drug
  - Discontinuation or interruption of treatment (with or without dose reduction to 10mg/$m^2$) may be needed to manage drug toxicity
- **Cost:** Specialty Pharmaceutical Acquisition Cost (SPAC) of $1,583.92 per vial, resulting in a cost per treatment cycle of $9,503.52 for a patient with a BSA of 1.4$m^2$

**Poteligeo® (Mogamulizumab-kpkc):**

- **Therapeutic Class:** CC chemokine receptor type 4 (CCR4)-directed monoclonal antibody
- **Indication(s):** For the treatment of adult patients with relapsed or refractory MF or SS after at least 1 prior systemic therapy
- **How Supplied:** 20mg/5mL (4mg/mL) solution in a SDV
- **Dose:** 1mg/kg as an IV infusion over at least 60 minutes on days 1, 8, 15, and 22 of the first 28-day cycle and on days 1 and 15 of each subsequent cycle
- **Cost:** WAC of $3,790.00 per vial, resulting in a cost of $30,320.00 per treatment cycle (for subsequent cycles) for an 80kg patient

**Zevalin® (Ibritumomab Tiuxetan):**

- **Therapeutic Class:** CD20-directed radiotherapeutic antibody
- **Indication(s):** For the treatment of patients with:
  - Relapsed or refractory, low-grade or follicular B-cell NHL
  - Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy
- **How Supplied:** A kit is used for preparing Y-90 radiolabeled Zevalin®; kit includes:
  - 1 Zevalin® vial containing 3.2mg ibritumomab tiuxetan in 2mL 0.9% sodium chloride
  - (1) 50mM sodium acetate vial
  - 1 formulation buffer vial
  - 1 empty reaction vial
- **Dose:**
  - Day 1: Administer rituximab 250mg/$m^2$ via IV infusion
  - Day 7, 8, or 9: Administer rituximab 250mg/$m^2$ IV infusion
    - If platelets ≥150,000/$mm^3$: Within 4 hours after rituximab infusion, administer 0.4mCi/kg Y-90 Zevalin® via IV infusion
    - If platelets ≥100,000 but ≤149,000/$mm^3$ in relapsed or refractory patients: Within 4 hours after rituximab infusion, administer 0.3mCi/kg Y-90 Zevalin® via IV infusion
- **Cost:** Approximately $52,155 for 1 kit

**Zolinza® (Vorinostat):**

- **Therapeutic Class:** HDAC inhibitor
- **Indication(s):** For the treatment of cutaneous manifestations in patients with CTCL who have progressive, persistent, or recurrent disease on or following 2 systemic therapies
- **How Supplied:** 100mg capsule
- **Dose:** 400mg orally once daily with food; dosage reduction may be required for patients intolerant to therapy and in patients with mild or moderate hepatic impairment
- **Cost:** WAC of $125.08 per capsule, resulting in a cost of $15,009.60 per month

## Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations; changes can be seen in the following criteria listed in red (only criteria with updates listed)
- The prior authorization of Adcetris® (brentuximab vedotin), Beleodaq® (belinostat), Calquence® (acalabrutinib), Folotyn® (pralatrexate), Istodax® (romidepsin), Poteligeo® (mogamulizumab-kpkc), Truxima® (rituximab-abbs), Zevalin® (ibritumomab tiuxetan), and Zolinza® (vorinostat) with the following criteria listed in red

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

1. Diagnosis of metastatic NSCLC; and
2. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for PD-L1 expression as follows:
    a. As a single-agent, first-line: ≥50%; or
    b. First-line in combination: no expression required; or
    c. As a single-agent, second-line: ≥1%; and
4. Member meets 1 of the following:
    a. Previously untreated, metastatic squamous NSCLC in combination with carboplatin and either paclitaxel or nab-paclitaxel; or
    b. Previously untreated metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    c. New diagnosis as first-line therapy (patient has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; or
    d. Single-agent for disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin):
        i. Members with EGFR-mutation-positive should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
            1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*
        ii. Members with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
            1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*

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

1. Member meets 1 of the following:

    a. Adjuvant treatment of members with melanoma with involvement of lymph node(s) following complete resection; or
    b. Diagnosis of unresectable or metastatic melanoma; and
2. Pembrolizumab must be used as a single-agent; and
3. Member meets 1 of the following:
    a. Pembrolizumab is being used as first-line therapy; or
    b. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used; and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].
5. For adjuvant treatment of melanoma, dose as follows:
    a. 200mg every 3 weeks; and
    b. Maximum duration of 1 year.

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

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

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

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

**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 Lymphoma 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. For DLBCL relapsed/refractory disease in non-autologous stem cell transplant (SCT) candidates; or
4. For 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; 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.

**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.

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

1. As a single-agent in members who have received ≥1 prior therapy.

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

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

**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 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 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.

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

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

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

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

**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.

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

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

## Utilization Details of Lymphoma Medications: Calendar Year 2018

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **IBRUTINIB PRODUCTS** | | | | | |
| IMBRUVICA CAP 140MG | 15 | 4 | $134,109.80 | 3.75 | $8,940.65 |
| IMBRUVICA TAB 420MG | 12 | 4 | $136,542.80 | 3 | $11,378.57 |
| IMBRUVICA TAB 140MG | 4 | 1 | $45,513.84 | 4 | $11,378.46 |
| IMBRUVICA TAB 560MG | 3 | 1 | $34,136.02 | 3 | $11,378.67 |
| **SUBTOTAL** | **34** | **10** | **$350,302.46** | **3.4** | **$10,303.01** |
| **VORINOSTAT PRODUCTS** | | | | | |
| ZOLINZA CAP 100MG | 11 | 1 | $165,183.79 | 11 | $15,016.71 |
| **SUBTOTAL** | **11** | **1** | **$165,183.79** | **11** | **$15,016.71** |
| **TOTAL** | **45** | **8*** | **$515,486.25** | **5.63** | **$11,455.25** |

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

### Medical Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBERS | COST/ CLAIM |
|---|---|---|---|---|---|
| BRENTUXIMAB J9042 | 25 | 7 | $478,876.00 | 3.57 | $19,155.04 |
| NIVOLUMAB J9299 | 381 | 75 | $2,603,745.15 | 5.08 | $6,833.98 |
| OBINUTUZUMAB J9301 | 13 | 2 | $73,687.00 | 6.50 | $5,668.23 |
| PEMBROLIZUMAB J9271 | 190 | 46 | $1,792,801.42 | 4.13 | $9,435.80 |
| **TOTAL** | **609^** | **128*** | **$4,949,109.57** | **4.76** | **$8,126.62** |

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

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# Appendix K

# 30-Day Notice to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib)

**Oklahoma Health Care Authority**
**March 2019**

## 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 U.S. 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 cancer drug to be approved based on a DNA test, instead of based on a tissue of origin.

## Market News and Updates[5,6,7]

**Anticipated Patent Expiration(s):**

- Vitrakvi® (larotrectinib): November 2035

**New FDA Approval(s):**

- **January 2018:** The FDA approved Lutathera® (lutetium Lu 177 dotatate) for the treatment of a type of cancer that affects the pancreas or GI tract called GEP-NETs. It is indicated for adult patients with somatostatin receptor-positive GEP-NETs. This is the first time a radiopharmaceutical has been approved for the treatment of GEP-NETs.
- **November 2018:** The FDA granted accelerated approval to Vitrakvi® (larotrectinib), a treatment for adult and pediatric patients whose cancers have a specific genetic feature (biomarker). Larotrectinib is indicated for the treatment of adult and pediatric patients with solid tumors that have a *NTRK* gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have no satisfactory alternative treatments or that have progressed following treatment.

## Product Summaries[8,9]

**Lutathera® (Lutetium Lu 177 Dotatate):**

- **Therapeutic Class:** Radiolabeled somatostatin analog
- **Indication(s):** For the treatment of somatostatin receptor-positive GEP-NETs, including foregut, midgut, and hindgut neuroendocrine tumors in adults
- **How Supplied:** 370MBq/mL (10mCi/mL) in single-dose vials
- **Dose:** 7.4GBq (200mCi) via intravenous (IV) infusion every 8 weeks for a total of 4 doses; please refer to prescribing information for further details regarding appropriate administration of premedication and concomitant medications with lutetium Lu 177 dotatate
- **Cost:** Wholesale Acquisition Cost (WAC) of $48,900 per vial; resulting in a cost of $195,600 for 4 total doses

**Vitrakvi® (Larotrectinib):**

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For the treatment of adult and pediatric patients with solid tumors that:
  - Have an *NTRK* gene fusion without a known acquired resistance mutation; and
  - Are metastatic or where surgical resection is likely to result in severe morbidity; and
  - Have no satisfactory alternative treatments or that have progressed following treatment
    - This indication is approved under accelerated approval based on overall response rate and duration of response; continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 25mg and 100mg capsules; 20mg/mL oral solution
- **Dose:**
  - Recommended dose in adult and pediatric patients with body surface area (BSA) $\geq 1.0 m^2$ is 100mg orally twice daily

- Recommended dose in pediatric patients with BSA <1.0$m^2$ is 100mg/$m^2$ orally twice daily

- **Cost:** WAC of $546.67 per 100mg capsule; resulting in a cost of $32,800.20 per month for adult patients

## Recommendations

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

1. Diagnosis of progressive locoregional advanced disease or metastatic disease; and
2. Positive imaging of somatostatin receptor; and
3. Must be 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.

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# Appendix L

# Calendar Year 2018 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

**Oklahoma Health Care Authority**
**March 2019**

## Current Prior Authorization Criteria

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

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

**Brilinta® (Ticagrelor) Approval Criteria:**

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

**Plavix® 300mg (Clopidogrel) Approval Criteria:**

1. An FDA approved diagnosis of non-ST-segment elevated acute coronary syndrome or ST-segment elevated acute myocardial infarction; and
2. Approvals will be for 1 dose only of 300mg.

**Zontivity® (Vorapaxar) Approval Criteria:**

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

**Eliquis® (Apixaban) Approval Criteria:**

1. An FDA approved diagnosis of 1 of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) or for the reduction in the risk of recurrent DVT and PE following initial therapy; or
    c. PE or DVT prophylaxis in patients who have had hip or knee replacement surgery.

**Pradaxa® (Dabigatran) Approval Criteria:**

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

**Savaysa® (Edoxaban) Approval Criteria:**

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

**Xarelto® (Rivaroxaban) Approval Criteria:**

1. An FDA approved diagnosis of 1 of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; or
    c. Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery; and
2. Xarelto® (rivaroxaban) 15mg and 20mg:
    a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. Xarelto® (rivaroxaban) 10mg:
    a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use in patients following hip or knee replacement surgery.

## Utilization of Anticoagulants and Platelet Aggregation Inhibitors: Calendar Year 2018

### Comparison of Calendar Years: Anticoagulants

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 2,347 | 12,819 | $2,427,024.49 | $189.33 | $5.75 | 550,512 | 422,000 |
| **2018** | 2,416 | 13,327 | $3,138,722.34 | $235.52 | $7.23 | 594,598 | 434,420 |
| **% Change** | **2.90%** | **4.00%** | **29.30%** | **24.40%** | **25.70%** | **8.00%** | **2.90%** |
| **Change** | **69** | **508** | **$711,697.85** | **$46.19** | **$1.48** | **44,086** | **12,420** |

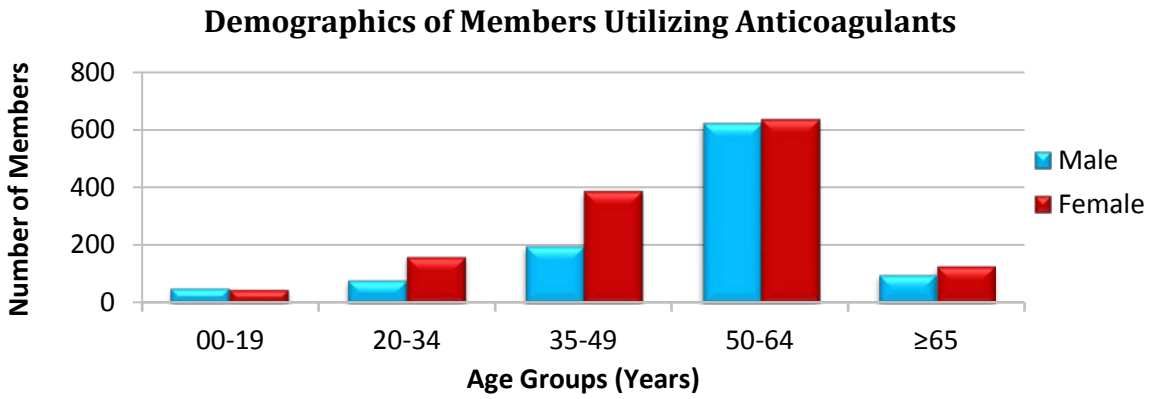
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

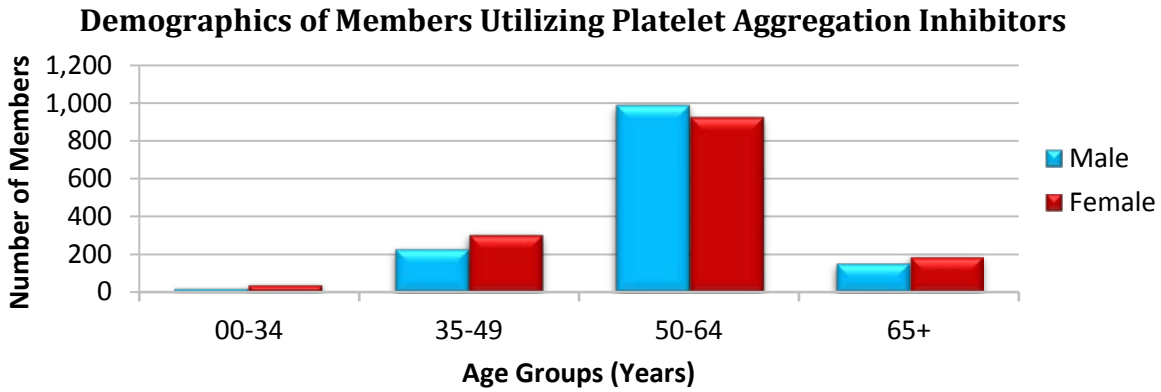
### Comparison of Calendar Years: Platelet Aggregation Inhibitors

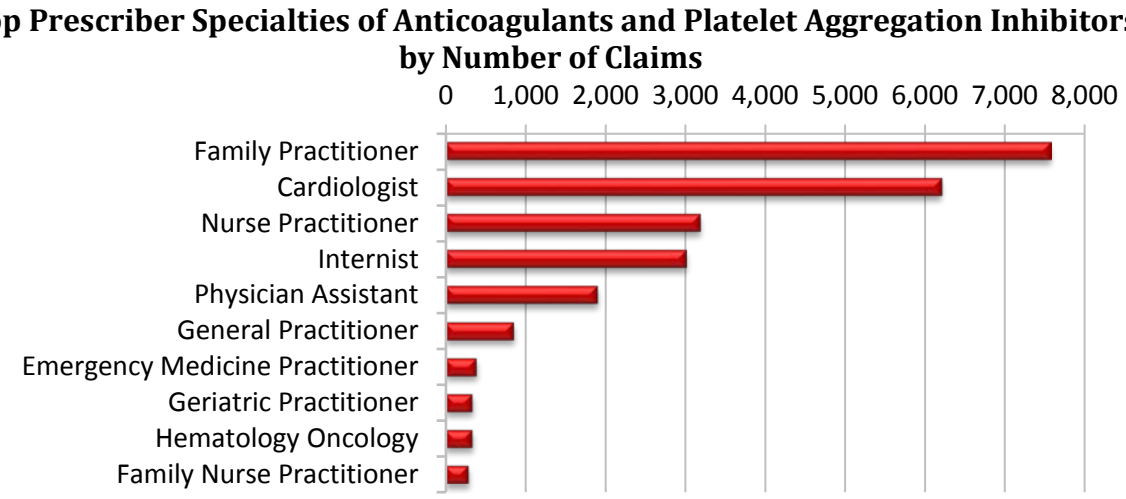
| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 2,812 | 12,248 | $721,022.98 | $58.87 | $1.33 | 570,365 | 541,692 |
| **2018** | 2,835 | 12,168 | $614,390.01 | $50.49 | $1.11 | 594,351 | 554,715 |
| **% Change** | **0.80%** | **-0.65%** | **-14.79%** | **-14.20%** | **-16.50%** | **4.20%** | **2.40%** |
| **Change** | **23** | **-80** | **-$106,632.97** | **-$8.38** | **-$0.22** | **23,986** | **13,023** |

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

- Please note, due to new federal regulations, a new pricing methodology for pharmacy claims reimbursement was implemented by SoonerCare on January 3, 2017. Ingredient reimbursement changed from an estimated acquisition cost (EAC) to an actual acquisition cost (AAC). In addition, the professional dispensing fee increased from $3.60 in 2016 to $10.55 effective January 2017; professional dispensing fees are included in the reimbursement totals in the following report. The impact of the pricing methodology and dispensing fee change are estimated to be budget neutral. This change in reimbursement should be considered when evaluating reimbursement changes from year to year. Medications with a very low cost per claim and large volume of claims will appear to increase in price due to the increase in dispensing fee; however, these increases will be neutralized by changes in ingredient reimbursement for higher cost medications.



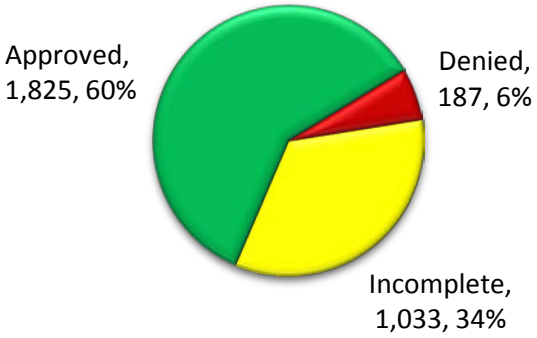




## Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

There were 3,045 prior authorization requests submitted for anticoagulants and platelet aggregation inhibitors during calendar year 2018. The following chart shows the status of the submitted petitions for calendar year 2018.

**Status of Petitions**




## Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19]

**Anticipated Patent Expiration(s):**

- Zontivity® (vorapaxar): May 2024
- Xarelto® (rivaroxaban): November 2024
- Savaysa® (edoxaban): March 2028
- Brilinta® (ticagrelor): April 2030
- Pradaxa® (dabigatran): January 2031
- Eliquis® (apixaban): February 2031

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

- **April 2018:** The FDA approved of Praxbind® (idarucizumab), the specific reversal agent for Pradaxa® (dabigatran). Idarucizumab is indicated for patients treated with dabigatran when reversal of the anticoagulant effects of dabigatran is needed for emergency surgery/urgent procedures or in life-threatening or uncontrolled bleeding. The FDA granted accelerated approval to idarucizumab in October 2015, with continued approval contingent upon results from the Phase 3 RE-VERSE AD™ trial, the largest study to investigate a reversal agent for a non-vitamin K oral anticoagulant (NOAC). The final results of RE-VERSE AD™ were published in *The New England Journal of Medicine (NEJM)* in July 2017, and showed that idarucizumab immediately reversed the anticoagulant effect of dabigatran. The majority of patients had complete reversal of anticoagulation within 4 hours as measured by ecarin clotting time (ECT, 82%) or diluted thrombin time (dTT, 99%). In the RE-VERSE AD™ study, no adverse safety signals were observed and there was a low rate of thrombotic events.
- **May 2018:** The FDA approved Andexxa® [coagulation factor Xa (recombinant), inactived-zhzo], the first and only antidote indicated for patients treated with Xarelto® (rivaroxaban) and Eliquis® (apixaban), when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Andexxa® received both Orphan Drug and Breakthrough Therapy designations by the FDA and was approved under the FDA's Accelerated Approval pathway based on the change from baseline in anti-factor Xa activity in healthy volunteers. Continued approval for this indication may be contingent upon post-marketing study results to demonstrate an improvement in hemostasis in patients receiving the antidote.

**New Indication(s):**

- **October 2018:** The FDA approved Xarelto® (rivaroxaban) for an expanded indication to reduce the risk of major cardiovascular (CV) events in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD). This new indication is based on results from the COMPASS trial, which showed a significant 24% reduction of the risk of major CV events in patients with chronic CAD and/or PAD with rivaroxaban 2.5mg twice daily plus aspirin 100mg once daily, compared to aspirin alone. This finding was driven by a 42% reduction in stroke, 22% reduction in CV death, and 14% reduction in heart attack. The risk of major bleeding was significantly higher in patients taking the rivaroxaban/aspirin regimen compared to aspirin alone, with no significant increase in fatal or intracranial bleeds. This label expansion adds to 6 existing rivaroxaban indications granted since initial launch in 2011, including the FDA approval in October 2017 for the 10mg once daily dose for reducing the continued risk for recurrent venous thromboembolism (VTE) after completing at least 6 months of initial anticoagulation therapy. Approval was based on data from the EINSTEIN CHOICE clinical study.

**Generic [Abbreviated New Drug Application (ANDA)] Approval(s):**

- **July 2017:** The FDA approved the first generic version of Effient® (prasugrel) manufactured by Mylan Pharmaceuticals. In August 2017, Mylan's A-B rated generic and Prasco Laboratories' authorized generic of brand Effient® launched. After Mylan's 60 days of market exclusivity, several other manufacturers' generic versions were approved and are currently available.
- **September 2018:** The FDA approved the first generic version of Brilinta® (ticagrelor) 60mg and 90mg strength tablets for post-acute coronary syndrome management. This generic is manufactured by Watson Laboratories, Inc., a subsidiary of Teva Pharmaceuticals.

**News:**

- **March 2018:** Results of the Management of Myocardial Injury After Noncardiac Surgery (MANAGE) study were presented at the American College of Cardiology (ACC) 2018 Scientific Sessions. In the international, double-blind, placebo-controlled trial, 1,754 patients with ischemic myocardial injury after noncardiac surgery (MINS) were randomized to receive Pradaxa® (dabigatran) 110mg twice daily or matching placebo. The patients received dabigatran for a minimum of 4 months and a maximum of 2 years. The primary efficacy endpoint was a major vascular complication including a composite of vascular mortality and myocardial infarction (MI), nonhemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic VTE. The primary safety endpoint was a composite of life-threatening bleeding, major bleeding, and critical organ bleeding. After an average follow-up of 16 months, 11.1% of patients receiving dabigatran experienced 1 or more primary efficacy endpoint event(s) compared with 15.2% of patients on placebo, for a 28% reduction in risk for patients on dabigatran. Although the absolute event rates were low (2 vs. 10 strokes), analysis of the individual efficacy endpoints showed that patients on dabigatran had a statistically significant 80% reduced risk of nonhemorrhagic stroke than those receiving placebo. Patients receiving

dabigatran were 20% less likely to die from a CV cause, 20% less likely to have an MI, 30% less likely to have an amputation, and 53% less likely to have a VTE. However, none of these individual differences were statistically significant. There were no statistically significant differences between the 2 groups in the primary safety endpoint. More patients receiving dabigatran experienced lower gastrointestinal (GI) tract bleeding and minor bleeding compared with patients receiving placebo.

- **June 2018:** Real-world data of patients with atrial fibrillation (AF) found a reduced risk of MI with direct oral anticoagulants (DOACs or NOACs) compared with vitamin K antagonist (VKA) therapy according to a Danish cohort study published in the *Journal of the American College of Cardiology (JACC)*. From 2013 to 2016, data on over 30,000 AF patients who were treated with NOACs for preventing stroke were reviewed. The standardized 1-year absolute risk for MI in the nationwide cohort was 1.56% with a VKA (i.e., warfarin), 1.16% with Eliquis® (apixaban), 1.20% with Pradaxa® (dabigatran), and 1.07% with Xarelto® (rivaroxaban). The risk differences were significant for all NOACs compared with VKA therapy; however, the risk for MI was not significantly different between NOACs.
- **July 2018:** A post hoc analysis of the RE-LY study published in *JACC* found that concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) with any anticoagulants in patients with AF increases the risk of major bleeding and stroke, particularly extracranial risk. Results of the parent study in 18,113 patients with AF showed that Pradaxa® (dabigatran) dosed 110mg or 150mg twice daily was noninferior to warfarin for stroke or systemic embolism, although MI risk was significantly increased with the 150mg dose. The new analysis involved 2,279 of the participants, who used NSAIDs at least once during the study period. Patients taking NSAIDs with an oral anticoagulant (OAC) had significantly higher rates of major bleeding than those who did not use NSAIDs [5.4% vs. 3.2%; hazard ratio (HR): 1.68; 95% confidence interval (CI): 1.40 to 2.02]. The finding was present across all OAC treatment groups. NSAID use was also associated with significantly more major GI bleeding (HR: 1.81; 95% CI: 1.35 to 2.43) and more frequent hospitalizations (HR: 1.64; 95% CI: 1.51 to 1.77).
- **August 2018:** The results of the Phase 3 MARINER and COMMANDER HF (heart failure) studies were presented at the European Society of Cardiology (ESC) Congress 2018 and simultaneously published in *NEJM*. In both studies, there were no significant differences found between Xarleto® (rivaroxaban) and placebo for the primary efficacy endpoints. MARINER demonstrated that rivaroxaban did not reduce the composite endpoint of symptomatic VTE, or blood clots, and VTE-related death in acute medically ill patients following hospital discharge. In COMMANDER HF, rivaroxaban did not impact overall mortality outcomes compared to standard of care. However, there were numerically fewer heart attacks and strokes with rivaroxaban in sick patients with significant CAD and reduced left ventricular ejection fraction (LVEF) who experienced a recent episode of acute decompensated HF. These results suggest that the high death rate in these patients is primarily driven by poor heart function, and not by thrombotic events. The MARINER and COMMANDER HF studies are part of rivaroxaban's clinical development program EXPLORER, which evaluates the potential role of rivaroxaban in treating a wide range of critical medical needs.

- **October 2018:** A population-based cohort study examining the association of AF with cognitive decline and dementia in old age was published in *Neurology*. The study included 2,685 dementia-free participants from the Swedish National Study on Aging and Care in Kungsholmen, who were regularly examined from 2001 to 2004 and from 2010 to 2013. A total of 243 participants (9.1%) with AF were identified at baseline. During the 9-year follow-up period, 279 participants (11.4%) developed AF and 399 (14.9%) developed dementia. As a time-dependent variable, AF was significantly associated with a faster annual Mini-Mental State Examination decline (β coefficient: -0.24, 95% CI: -0.31 to -0.16) and an increased HR of all-cause dementia (HR: 1.40, 95% CI: 1.11 to 1.77) and vascular and mixed dementia (HR: 1.88, 95% CI: 1.09 to 3.23), but not Alzheimer's disease (HR: 1.33, 95% CI: 0.92 to 1.94). Among participants with either prevalent or incident AF, use of anticoagulant drugs, but not antiplatelet treatment, was associated with a 60% decreased risk of dementia (HR: 0.40, 95% CI: 0.18 to 0.92). The study concluded the use of anticoagulant drugs may reduce dementia risk in patients with AF.

**Guideline Update(s):**

- **November 2018:** The American Society of Hematology (ASH) released new clinical practice guidelines for VTE. In partnership with the McMaster University GRADE Centre, a world leader in guideline development and an authority on thrombosis, ASH brought together more than 100 experts including hematologists, other clinicians, guideline development specialists, and patient representatives. ASH announced the release of the *2018 ASH Clinical Practice Guidelines on Venous Thromboembolism* in a press event timed to the publication of the first 6 chapters in the Society's peer-reviewed journal *Blood Advances*. Four more chapters are in development. The 10 evidence-based clinical guidelines chapters cover VTE through a number of areas in which there is currently uncertainty and variation in clinical practice and include: prophylaxis for hospitalized and non-hospitalized medical patients; diagnosis of VTE; optimal management of anticoagulation therapy; heparin-induced thrombocytopenia; VTE in the context of pregnancy; treatment of pediatric VTE; treatment of DVT and PE (anticipated in 2019); VTE in patients with cancer (anticipated in 2019); thrombophilia (anticipated in 2019); and prevention of VTE in surgical patients (anticipated in 2019).
- **December 2018:** A new clinical-practice guideline titled *Dual Antiplatelet Therapy with Aspirin and Clopidogrel for Acute High Risk Transient Ischaemic Attack and Minor Ischaemic Stroke: A Clinical Practice Guideline* provides recommendations on dual antiplatelet therapy as part of *The British Medical Journal's* (*BMJ*) Rapid Recommendations Project, a collaboration with the MAGIC research and innovation program. After analyzing results from the CHANCE, POINT, and FASTER trials, including more than 10,000 participants in total, results revealed that patients given clopidogrel and aspirin within 24 hours of a transient ischemic attack (TIA) or minor stroke were 30% less likely than those who received aspirin only to have another stroke over the next 30 to 90 days, reducing absolute risk by 1.9 percentage points, a significant finding. Dual antiplatelet therapy appeared to have little effect on all-cause mortality. The recommendations state patients with a minor ischemic stroke or high-risk TIA should

start dual antiplatelet therapy with aspirin plus clopidogrel as soon as possible after the event, preferably within 24 hours. The guidelines make a strong recommendation that dual therapy is preferred over aspirin alone given that there is a lower risk for recurrent stroke and functional disability with dual therapy. The guideline committee also makes a strong recommendation in favor of a shorter duration of dual therapy (10 to 21 days, as opposed to 22 to 90 days). However, most patients should probably continue to take a single antiplatelet, often aspirin, indefinitely. If a patient's stroke work-up reveals an indication for anticoagulation (e.g., AF), patients should switch from antiplatelet therapy to anticoagulation. Dual therapy shouldn't be used in patients with a major stroke because of increased risk for intracranial bleeding.

## Recommendations

The College of Pharmacy recommends updating the Xarelto® (rivaroxaban) prior authorization approval criteria based on the FDA approved expanded indication. The following criteria would apply (changes noted in red):

**Xarelto® (Rivaroxaban) Approval Criteria:**

1. An FDA approved diagnosis of one of the following:
   a. Non-valvular atrial fibrillation; or
   b. Treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; or
   c. Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery; ~~and~~ or
   d. In combination with aspirin, to reduce the risk of major cardiovascular events [cardiovascular (CV) death, myocardial infarction (MI), and stroke] in members with chronic coronary artery disease (CAD) or peripheral artery disease (PAD); and
2. Xarelto® (rivaroxaban) 15mg and 20mg:
   a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. Xarelto® (rivaroxaban) 10mg:
   a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use in patients following hip or knee replacement surgery; or
4. Xarelto® (rivaroxaban) 2.5mg:
   a. Must be used in combination with aspirin 75 to 100mg to reduce the risk of major CV events in members with chronic CAD or PAD.

## Utilization Details of Anticoagulants: Calendar Year 2018

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| **WARFARIN PRODUCTS** | | | | | | |
| WARFARIN TAB 5MG | 1,790 | 483 | $20,666.43 | $0.29 | $11.55 | 0.66% |
| WARFARIN TAB 1MG | 718 | 183 | $9,446.23 | $0.41 | $13.16 | 0.30% |
| WARFARIN TAB 4MG | 619 | 165 | $7,538.10 | $0.34 | $12.18 | 0.24% |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| WARFARIN TAB 2MG | 489 | 134 | $5,790.37 | $0.36 | $11.84 | 0.18% |
| WARFARIN TAB 3MG | 471 | 140 | $5,836.84 | $0.35 | $12.39 | 0.19% |
| WARFARIN TAB 6MG | 364 | 95 | $5,214.99 | $0.38 | $14.33 | 0.17% |
| WARFARIN TAB 7.5MG | 349 | 123 | $4,513.98 | $0.27 | $12.93 | 0.14% |
| WARFARIN TAB 2.5MG | 299 | 95 | $3,659.74 | $0.36 | $12.24 | 0.12% |
| WARFARIN TAB 10MG | 269 | 99 | $3,414.84 | $0.26 | $12.69 | 0.11% |
| JANTOVEN TAB 5MG | 36 | 12 | $511.80 | $0.38 | $14.22 | 0.02% |
| JANTOVEN TAB 4MG | 16 | 3 | $184.79 | $0.34 | $11.55 | 0.01% |
| COUMADIN TAB 1MG | 13 | 1 | $2,800.23 | $7.29 | $215.40 | 0.09% |
| JANTOVEN TAB 1MG | 12 | 2 | $189.80 | $0.53 | $15.82 | 0.01% |
| COUMADIN TAB 5MG | 8 | 3 | $998.20 | $4.16 | $124.78 | 0.03% |
| JANTOVEN TAB 2MG | 7 | 1 | $118.64 | $0.33 | $16.95 | 0.00% |
| JANTOVEN TAB 2.5MG | 7 | 1 | $121.29 | $0.34 | $17.33 | 0.00% |
| COUMADIN TAB 6MG | 5 | 2 | $1,148.73 | $2.95 | $229.75 | 0.04% |
| JANTOVEN TAB 3MG | 4 | 1 | $42.00 | $0.35 | $10.50 | 0.00% |
| JANTOVEN TAB 6MG | 3 | 2 | $45.13 | $0.50 | $15.04 | 0.00% |
| JANTOVEN TAB 7.5MG | 3 | 3 | $46.71 | $0.31 | $15.57 | 0.00% |
| COUMADIN TAB 10MG | 2 | 1 | $230.99 | $3.85 | $115.50 | 0.01% |
| COUMADIN TAB 7.5MG | 1 | 1 | $276.08 | $3.07 | $276.08 | 0.01% |
| **SUBTOTAL** | **5,485** | **1,550** | **$72,795.91** | **$0.01** | **$13.27** | **2.33%** |
| **DABIGATRAN PRODUCTS** | | | | | | |
| PRADAXA CAP 150MG | 187 | 27 | $72,052.58 | $12.56 | $385.31 | 2.30% |
| PRADAXA CAP 75MG | 21 | 4 | $7,849.18 | $13.08 | $373.77 | 0.25% |
| PRADAXA CAP 110MG | 1 | 1 | $388.20 | $12.94 | $388.20 | 0.01% |
| **SUBTOTAL** | **209** | **32** | **$80,289.96** | **$12.61** | **$384.16** | **2.56%** |
| **RIVAROXABAN PRODUCTS** | | | | | | |
| XARELTO TAB 20MG | 2,582 | 452 | $1,040,908.67 | $13.60 | $403.14 | 33.16% |
| XARELTO TAB 10MG | 283 | 138 | $94,671.75 | $13.46 | $334.53 | 3.02% |
| XARELTO TAB 15MG | 263 | 59 | $106,376.90 | $14.99 | $404.47 | 3.39% |
| XARELTO STAR TAB 15/20MG | 8 | 8 | $5,574.92 | $20.65 | $696.87 | 0.18% |
| XARELTO TAB 2.5MG | 1 | 1 | $425.94 | $14.20 | $425.94 | 0.01% |
| **SUBTOTAL** | **3,137** | **658** | **$1,247,958.18** | **$0.01** | **$397.82** | **39.76%** |
| **APIXABAN PRODUCTS** | | | | | | |
| ELIQUIS TAB 5MG | 3,950 | 825 | $1,534,342.87 | $13.41 | $388.44 | 48.88% |
| ELIQUIS TAB 2.5MG | 534 | 132 | $199,143.40 | $13.40 | $372.93 | 6.34% |
| ELIQUIS ST P TAB 5MG | 1 | 1 | $525.86 | $14.21 | $525.86 | 0.02% |
| **SUBTOTAL** | **4,485** | **958** | **$1,734,012.13** | **$13.41** | **$386.62** | **55.24%** |
| **EDOXABAN PRODUCTS** | | | | | | |
| SAVAYSA TAB 60MG | 11 | 2 | $3,666.16 | $11.11 | $333.29 | 0.12% |
| **SUBTOTAL** | **11** | **2** | **$3,666.16** | **$11.11** | **$333.29** | **0.12%** |
| **TOTAL** | **13,327** | **2,416*** | **$3,138,722.34** | **$7.23** | **$235.52** | **100%** |

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

## Utilization Details of Platelet Aggregation Inhibitors: Calendar Year 2018

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| **CLOPIDOGREL PRODUCTS** | | | | | | |
| CLOPIDOGREL TAB 75MG | 10,048 | 2,496 | $115,374.76 | $0.23 | $11.48 | 18.78% |
| **SUBTOTAL** | **10,048** | **2,496** | **$115,374.76** | **$0.23** | **$11.48** | **18.78%** |
| **PRASUGREL PRODUCTS** | | | | | | |
| PRASUGREL TAB 10MG | 635 | 108 | $18,721.18 | $0.97 | $29.48 | 3.05% |
| PRASUGREL TAB 5MG | 34 | 6 | $1,277.96 | $1.25 | $37.59 | 0.21% |
| **SUBTOTAL** | **669** | **114** | **$19,999.14** | **$0.99** | **$29.89** | **3.26%** |
| **TICAGRELOR PRODUCTS** | | | | | | |
| BRILINTA TAB 90MG | 1,274 | 276 | $420,255.32 | $11.41 | $329.87 | 68.40% |
| BRILINTA TAB 60MG | 131 | 23 | $44,992.82 | $11.53 | $343.46 | 7.32% |
| **SUBTOTAL** | **1,405** | **299** | **$465,248.14** | **$11.42** | **$331.14** | **75.72%** |
| **VORAPAXAR PRODUCTS** | | | | | | |
| ZONTIVITY TAB 2.08MG | 34 | 7 | $10,587.98 | $10.40 | $311.41 | 1.72% |
| **SUBTOTAL** | **34** | **7** | **$10,587.98** | **$10.40** | **$311.41** | **1.72%** |
| **ASPIRIN-DIPYRIDAMOLE PRODUCTS** | | | | | | |
| ASA/DIPYRIDA CAP 25-200MG | 12 | 1 | $3,179.99 | $8.83 | $265.00 | 0.52% |
| **SUBTOTAL** | **12** | **1** | **$3,179.99** | **$8.83** | **$265.00** | **0.52%** |
| **TOTAL** | **12,168** | **2,835*** | **$614,390.01** | **$1.11** | **$50.49** | **100%** |

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

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# Appendix M

# Fiscal Year 2018 Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide)

**Oklahoma Health Care Authority**
**March 2019**

## Current Prior Authorization Criteria

**Cinryze® (C1 Esterase Inhibitor) and Haegarda® (C1 Esterase Inhibitor) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. History of at least 1 or more abdominal or respiratory HAE attack(s) per month, or history of laryngeal attacks, or 3 or more emergency medical treatments per year; and
4. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
5. Member meets the following:
    a. Documented intolerance, insufficient response, or contraindication to attenuated androgens (e.g., danazol, stanozolol, oxandrolone, methyltestosterone); and
    b. Documented intolerance, insufficient response, or contraindication to antifibrinolytic agents (e.g., ε – aminocaproic acid, tranexamic acid); or
    c. Recent hospitalization for severe episode of angioedema; and
6. 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. Patients 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
7. Haegarda® Dosing:
    a. 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
    b. A quantity limit of 2 treatments per week or 8 treatments per 28 days will apply.

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

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Berinert®, Kalbitor®, or Firazyr® must be used for the *treatment* of acute attacks of HAE.

**Ruconest® (C1 Esterase Inhibitor) Approval Criteria:**

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Ruconest® must be used for *treatment* of acute attacks of HAE; and
3. A patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor) must be provided.

## Utilization of HAE Medications: Fiscal Year 2018

### Comparison of Fiscal Years

| Fiscal Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 2 | 37 | $1,238,526.45 | $33,473.69 | $2,497.03 | 451 | 496 |
| **2018** | 3 | 8 | $199,993.07 | $24,999.13 | $2,020.13 | 100 | 99 |
| **% Change** | **50.00%** | **-78.40%** | **-83.90%** | **-25.30%** | **-19.10%** | **-77.80%** | **-80.00%** |
| **Change** | **1** | **-29** | **-$1,038,533.38** | **-$8,474.56** | **-$476.90** | **-351** | **-397** |

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

- There were no paid medical claims for HAE medications during fiscal year 2018.

### Demographics of Members Utilizing HAE Medications

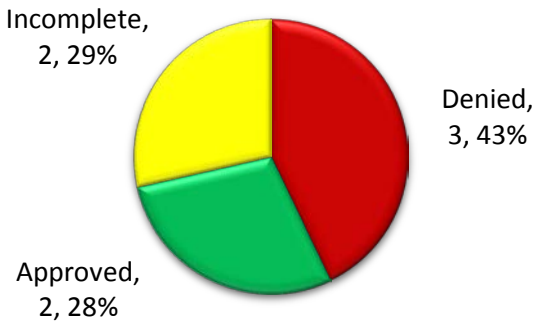
- Due to the limited number of members utilizing HAE medications, detailed demographic information could not be provided.

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

- The only prescriber specialty listed on paid claims for HAE medications during fiscal year 2018 was allergist.

## Prior Authorization of HAE Medications

There were 7 prior authorization requests submitted for HAE medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



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

**Anticipated Patent Expiration(s):**

- Firazyr® [icatibant acetate subcutaneous (sub-Q) injection]: July 2019

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

- **June 2018:** Shire announced the FDA approved a label expansion for Cinryze® [C1 esterase inhibitor (human)]. The approved label expansion includes an indication for prophylactic treatment of HAE in children 6 years of age and older. The approval was based on data from a dedicated Phase 3 multicenter, single-blind study that evaluated the use of Cinryze® in 12 patients, 7 to 11 years of age with HAE. Compared to the baseline observational period, the mean reduction in the number of attacks for Cinryze® dosed at 500 units and 1,000 units every 3 to 4 days for 12 weeks was 71.1% and 84.5%, respectively. Both doses lessened the severity of attacks and reduced the use of acute treatment compared to baseline. Cinryze® was originally approved by the FDA in October 2008 for routine HAE prophylaxis in adolescents and adults.
- **August 2018:** Shire announced that, following priority review, the FDA approved Takhzyro™ (lanadelumab-flyo) injection. Takhzyro™ is indicated for prophylaxis of HAE in patients 12 years of age and older. It is the only monoclonal antibody (mAb) that provides targeted inhibition of plasma kallikrein, an enzyme which is chronically uncontrolled in people with HAE.

**Guideline Update(s):**

- **February 2018:** The first revision and update of the global guideline for the diagnosis and management of HAE was published in the *World Allergy Organization Journal*. The World Allergy Organization (WAO) developed the update in collaboration with the European Academy of Allergy and Clinical Immunology (EAACI). While several of the recommendations have remained the same, first-line and second-line treatment for long-term prophylaxis have changed. The following recommendations are included in the update:
    - For first-line treatment, the guidelines recommend the use of plasma-derived C1 inhibitor (C1-INH) for long-term prophylaxis for the prevention of HAE attacks in adults. Consistent with the previous guideline, C1-INH continues to be the first-line recommendation for long-term prophylaxis in children and, if needed, in pregnant or breastfeeding women.
    - Due to the adverse androgenic and anabolic effects, drug interactions, and contraindications, the current guidelines now recommend the use of androgens as second-line for long-term prophylaxis in adults.
    - Antifibrinolytics are not recommended for long-term prophylaxis. Data for their efficacy are largely lacking; antifibrinolytics are primarily used when C1-INH concentrate is not available and androgens are contraindicated.
    - The current guidelines now recommend testing children from HAE-affected families as soon as possible, and that all offspring of an affected parent should be tested. Previously, the guideline recommendation was to defer screening in children from HAE-affected families until the age of 12 months.

**News:**

- **November 2018:** The Institute for Clinical and Economic Review (ICER) released a Final Evidence Report and Report-at-a-Glance assessing the comparative clinical effectiveness and value of therapies for long-term prophylaxis against HAE attacks. In its report, ICER assessed 3 therapies for the prevention of HAE attacks: lanadelumab (Takhzyro™) and 2 C1-INHs (Haegarda® and Cinryze®). ICER's report was reviewed at a public meeting of the California Technology Assessment Forum (CTAF) in October 2018. CTAF found that the evidence demonstrated a net health benefit for using the C1-INHs as long-term prophylaxis, but that the evidence was insufficient to distinguish between Cinryze® and Haegarda®. Because of concerns about risks with a new therapy, the committee also found that current evidence was not adequate to determine whether long-term prophylaxis with lanadelumab is superior to on-demand therapy alone. CTAF voted that both Cinryze® and lanadelumab represent a low long-term value for the money when compared to on-demand therapy. When evaluating the long-term value for the money of Haegarda®, the panel's majority vote was split evenly between low and intermediate value. All 3 prophylactic treatments, at current pricing, exceed commonly cited thresholds for cost-effectiveness of $50,000 to $150,000 per quality-adjusted life year (QALY) gained. Since this calculation is highly dependent on the baseline frequency of HAE attacks, the overall cost-effectiveness of these treatments is less certain. The FDA label for lanadelumab suggests that patients who remain attack-free for 6 months may be considered for less-frequent dosing. However, the real-world proportion of patients who will switch to (and remain on) the less frequent dose is unknown. Lanadelumab would meet commonly-cited cost-effectiveness thresholds if approximately 75% of eligible patients switch to the less-frequent dosing. Key policy recommendations included that payers seeking to negotiate better prices may consider giving all market share to the 2 sub-Q treatments, Haegarda® and lanadelumab, due to these therapies' simpler administration compared to intravenous (IV) drugs. Additionally, it was recommended that prior authorization criteria should be based on clinical evidence with input from clinical experts and patient groups. Insurers creating coverage policy may seek to confirm HAE through lab tests or physician attestation, determine the appropriateness of long-term prophylaxis based on the frequency and severity of attacks, and use a patient's weight to more precisely manage dosing of weight-based treatments.

**Pipeline:**

- **BCX7353:** BioCryst Pharmaceuticals, Inc. announced in August 2018 that they have been granted Fast Track designation by the FDA for their medication BCX7353. BCX7353 is a novel, oral, once-daily, selective inhibitor of plasma kallikrein currently in development for the prevention and treatment of angioedema attacks in patients with HAE. It was generally safe and well tolerated in the Phase 2 APeX-1 clinical trial. BioCryst is currently conducting a Phase 3 clinical trial and a long-term safety clinical trial, both evaluating 2 strengths of BCX7353. They are also conducting the ZENITH-1 clinical trial, a proof-of-concept Phase 2 clinical trial, to test an oral liquid formulation of BCX7353 for the acute

treatment of HAE. BioCryst is planning to submit a New Drug Application (NDA) for BCX7353 to the FDA in the second half of 2019.

## Takhzyro™ (Lanadelumab-flyo) Product Summary[8]

**Indication(s):** Takhzyro™ (lanadelumab-flyo) is a plasma kallikrein inhibitor indicated for prophylaxis to prevent HAE attacks in patients 12 years of age and older.

**Dosing:**

- Takhzyro™ is supplied as a 300mg/2mL ready-to-use solution in a single-dose glass vial.
- The vials should be refrigerated at 36 to 46°F (2 to 8°C) until 15 minutes before use.
- Takhzyro™ is intended for self-administration or administration by a caregiver. The patient or caregiver should be trained by a health care professional prior to use.
- The recommended starting dose is 300mg given sub-Q every 2 weeks.
- A dosing interval of 300mg every 4 weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months.

**Mechanism of Action:** Lanadelumab is a fully human mAb that binds plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high-molecular-weight-kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with HAE. In patients with HAE due to C1-INH deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Lanadelumab decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE.

**Warnings and Precautions:**

- Hypersensitivity Reactions: Hypersensitivity reactions have been observed with lanadelumab. In cases of severe hypersensitivity reaction, it is recommended to discontinue lanadelumab administration and institute appropriate treatment.

**Contraindication(s):** None

**Adverse Reactions:**

- In clinical trials, adverse reactions occurring in ≥10% of patients treated with lanadelumab and at a higher rate than placebo included injection site reactions, upper respiratory infection, headache, rash, myalgia, dizziness, and diarrhea.
- As with all therapeutic proteins, there is a potential for immunogenicity. In clinical trials, 10 (12%) lanadelumab-treated and 2 (5%) placebo-treated patients had at least 1 anti-drug antibody (ADA)-positive sample during the treatment period. The development of ADA including neutralizing antibodies against lanadelumab did not appear to adversely affect pharmacokinetics, pharmacodynamics, safety, or clinical response.

**Use in Specific Populations:**

- Pregnancy: There are no available data on lanadelumab use in pregnant women to inform any drug-associated risks. Lanadelumab, like other mAbs, is transported across

the placenta during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy. An enhanced pre- and postnatal development study conducted in pregnant monkeys at doses resulting in exposures of up to 33 times the exposure at the maximum recommended human dose revealed no evidence of harm to the developing fetus.

- Lactation: There are no data on the presence of lanadelumab in human milk, its effects on the breastfed infant, or its effects on milk production. Lanadelumab was detected in the milk of lactating cynomolgus monkeys at approximately 0.2% of the maternal plasma concentration.
- Pediatric Use: The safety and efficacy of lanadelumab were evaluated in a subgroup of patients (N=10) 12 to younger than 18 years of age in Trial 1. Results of the subgroup analysis by age were consistent with overall study results. An additional 13 adolescent patients 12 to younger than 18 years of age were enrolled in the open-label extension study. The safety and efficacy of lanadelumab in pediatric patients younger than 12 years of age have not been established.
- Geriatric Use: The safety and efficacy of lanadelumab were evaluated in a subgroup of patients (N=5) 65 years of age or older in Trial 1. Results of the subgroup analysis by age were consistent with overall study results.

**Efficacy:**

- Trial 1: In this trial, the efficacy of lanadelumab for the prevention of angioedema attacks in patients 12 years of age and older with Type I or II HAE was demonstrated in a multicenter, randomized, double-blind, placebo-controlled, parallel-group study. The study included 125 adult and adolescent patients with Type I or II HAE who experienced at least 1 investigator-confirmed attack per 4 weeks during the run-in period. Patients were randomized into 1 of 4 parallel treatment arms, stratified by baseline attack rate, in a 3:2:2:2 ratio [placebo, lanadelumab 150mg every 4 weeks (q4wks), lanadelumab 300mg q4wks, or lanadelumab 300mg q2wks by sub-Q injection] for the 26-week treatment period. Patients 18 years of age or older were required to discontinue other prophylactic HAE medications prior to entering the study; however, all patients were allowed to use rescue medications for treatment of breakthrough HAE attacks. The primary efficacy endpoint of this trial was the rate of HAE attacks from day 0 to day 182 (the treatment period). All lanadelumab treatment arms met the primary endpoint and produced clinically meaningful and statistically significant reductions in the mean HAE attack rate compared to placebo ($P<0.001$) in the Intent-to-Treat (ITT) population. Additionally, secondary endpoints, including number of HAE attacks requiring acute treatment from day 0 to 182 and number of moderate or severe HAE attacks from day 0 to 182, achieved clinically meaningful and statistically significant reductions in the mean HAE attack rate compared to placebo ($P<0.001$).
- Trial 2: Patients who completed Trial 1 were eligible to rollover into Trial 2, an open-label extension study. Regardless of randomization group in Trial 1, patients in Trial 2 received a single dose of lanadelumab 300mg at study entry and were followed until the first HAE attack occurred. At week 4 post-dose, approximately 80% of patients who had been in the 300mg q2wks treatment group (N=25) in Trial 1 remained attack-free. After

the first HAE attack, all patients received open-label treatment with lanadelumab 300mg q2wks.

**Cost Comparison:**

| Medication | Cost Per Vial | Cost Per 28 Days* |
|---|---|---|
| **Takhzyro™ (lanadelumab-flyo)** | **$22,070.00** | **$44,140.00** |
| Cinryze® [C1 esterase inhibitor (human)] | $2,758.79 | $44,140.64 |
| Haegarda® [C1 esterase inhibitor (human)] | $1,880.00 – $2,820.00 | $37,600.00[Δ] |

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per 28 days based on FDA recommended dosing.
[Δ]Cost 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 Takhzyro™ (lanadelumab-flyo) with criteria similar to Cinryze® and Haegarda® (C1 esterase inhibitors) and to update the current Cinryze® and Haegarda® criteria to be consistent with guideline recommendations (changes shown in red):

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

1. An FDA diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. 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; and
4. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
5. ~~Member meets the following:~~ Approval consideration will be given if the member has a recent hospitalization for a severe episode of angioedema; and
   a. ~~Documented intolerance, insufficient response, or contraindication to attenuated androgens (e.g., danazol, stanozolol, oxandrolone, methyltestosterone); and~~
   b. ~~Documented intolerance, insufficient response, or contraindication to antifibrinolytic agents (e.g., ε – aminocaproic acid, tranexamic acid); or~~
   c. ~~Recent hospitalization for 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).
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; patients 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 dosing is 60 IU/kg 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 28 days will apply; or
9. Takhzyro™ Dosing:
    a. The recommended dose of Takhzyro™ is 300mg subcutaneous (sub-Q) every 2 weeks (dosing every 4 weeks may be considered in some patients); 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 current Kalbitor® (ecallantide) criteria based on net cost (changes shown in red):

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

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

## Utilization Details of HAE Medications: Fiscal Year 2018

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| FIRAZYR INJ 30MG/3ML | 4 | 2 | $30,932.87 | $937.36 | $7,733.22 | 15.47% |
| CINRYZE SOL 500 UNIT | 2 | 1 | $110,364.70 | $1,839.41 | $55,182.35 | 55.18% |
| BERINERT INJ 500 UNIT | 2 | 1 | $58,695.50 | $9,782.58 | $29,347.75 | 29.35% |
| **TOTAL** | **8** | **3*** | **$199,993.07** | **$2,020.13** | **$24,999.13** | **100.00%** |

*Total number of unduplicated 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 12/2018. Last accessed 02/12/2019.
[2] Shire PLc. Shire Announces FDA Approval for Label Expansion of CINRYZE® for Prevention of Attacks in Pediatric HAE. *Globe Newswire*. Available online at: https://globenewswire.com/news-release/2018/06/21/1527592/0/en/Shire-Announces-FDA-Approval-for-Label-Expansion-of-CINRYZE-for-Prevention-of-Attacks-in-Pediatric-HAE.html. Issued 06/21/2018. Last accessed 02/18/2019.
[3] Shire PLc. Shire Announces FDA Approval of TAKHZYRO™ (lanadelumab-flyo), a First-of-its-Kind mAb Preventive Treatment for Hereditary Angioedema. *Globe Newswire*. Available online at: https://globenewswire.com/news-release/2018/08/23/1556201/0/en/Shire-Announces-FDA-Approval-of-TAKHZYRO-lanadelumab-flyo-a-First-of-its-Kind-mAb-Preventive-Treatment-for-Hereditary-Angioedema.html. Issued 08/23/2018. Last accessed 02/18/2019.
[4] Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema– the 2017 revision and update. *World Allergy Organ J* 2018; 11:5.
[5] Craig T, Pursun EA, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. *World Allergy Organ J* 2012; 5(12):182-199.
[6] The Institute for Clinical and Economic Review (ICER). Institute for Clinical and Economic Review Issues Final Report on Long-Term Prophylaxis for Hereditary Angioedema, Provides Policy Recommendations to Improve Cost-Effectiveness. Available online at: https://icer-review.org/announcements/institute-for-clinical-and-economic-review-issues-final-report-on-long-term-prophylaxis-for-hereditary-angioedema-provides-policy-recommendations-to-improve-cost-effectiveness/. Issued 11/15/2018. Last accessed 02/18/2019.
[7] BioCryst Pharmaceuticals, Inc. U.S. FDA Grants Fast Track Designation for BioCryst's BCX7353. *Globe Newswire*. Available online at: http://ir.biocryst.com/news-releases/news-release-details/us-fda-grants-fast-track-designation-biocrysts-bcx7353. Issued 08/06/2018. Last accessed 02/18/2019.
[8] Takhzyro™ (lanadelumab-flyo). Shire PLc. Prescribing Information. Available online at: https://www.shirecontent.com/PI/PDFs/TAKHZYRO_USA_ENG.pdf. Last revised 08/2018. Last accessed 02/18/2019.

# Appendix N

# Calendar Year 2018 Annual Review of Multiple Sclerosis (MS) Medications

**Oklahoma Health Care Authority**
**March 2019**

## Current Prior Authorization Criteria

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

1. An FDA approved diagnosis of relapsing 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 (Rebif®) |
| Interferon β - 1b (Betaseron®) | Interferon β - 1a (Plegridy®) |
| | 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) if NADAC unavailable.

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

1. An FDA approved diagnosis of 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 that 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.
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); 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 and verification that levels are acceptable to the prescriber; and
    e. Blood pressure measurement and verification that blood pressure is being monitored; and
    f. Verification that the member does not have tuberculosis, or completion of standard medical treatment for members with tuberculosis; 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 liver function tests 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 blood pressure 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); and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
4. 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
5. 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)* (*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 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); 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.

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

1. An FDA approved diagnosis of relapsing or primary progressive forms of multiple sclerosis (MS); 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 relapsing forms of multiple sclerosis (MS); 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 multiple sclerosis (MS) or Crohn's disease; 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.

## Utilization of MS Medications: Calendar Year 2018

### MS Medications Calendar Year Comparison: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 189 | 1,350 | $7,911,212.78 | $5,860.16 | $202.97 | 189 | 1,350 |
| **2018** | 193 | 1,412 | $8,533,740.43 | $6,043.73 | $208.69 | 193 | 1,412 |
| **% Change** | **2.10%** | **4.60%** | **7.90%** | **3.10%** | **2.80%** | **2.10%** | **4.60%** |
| **Change** | **4** | **62** | **$622,527.65** | **$183.57** | **$5.72** | **4** | **62** |

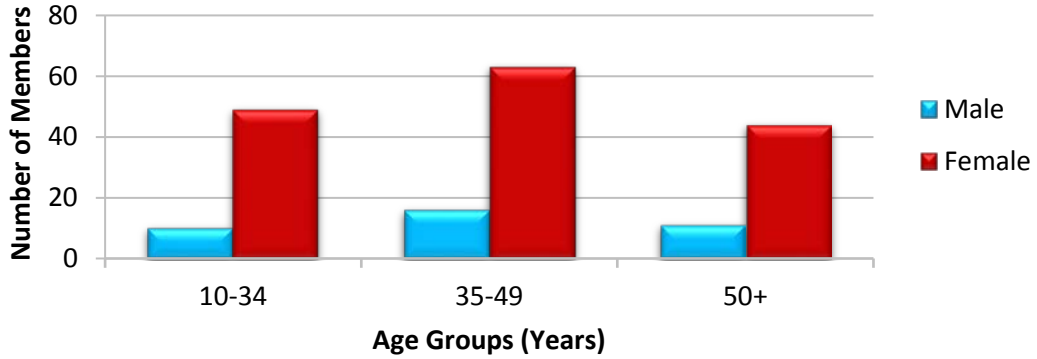
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

### MS Medications Calendar Year Comparison: Medical Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Claims/ Member |
|---|---|---|---|---|---|
| **2017** | 20 | 114 | $804,959.46 | $7,061.05 | 5.7 |
| **2018** | 46 | 198 | $2,159,987.12 | $10,909.03 | 4.3 |
| **% Change** | **130.00%** | **73.68%** | **168.33%** | **54.50%** | **-24.56%** |
| **Change** | **26** | **84** | **$1,355,027.66** | **$3,847.98** | **-1.4** |

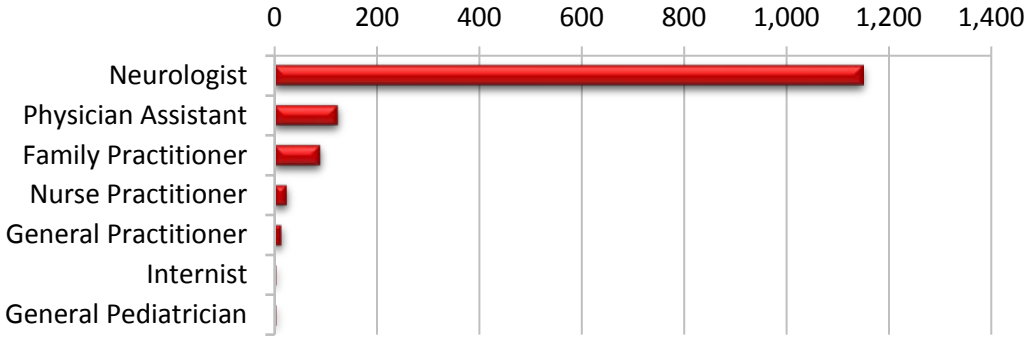
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

**Demographics of Members Utilizing MS Medications: Pharmacy Claims**




- All members younger than 21 years of age were verified to have a diagnosis of MS in their diagnosis history, and their MS therapies were prescribed by a specialist in neurology.

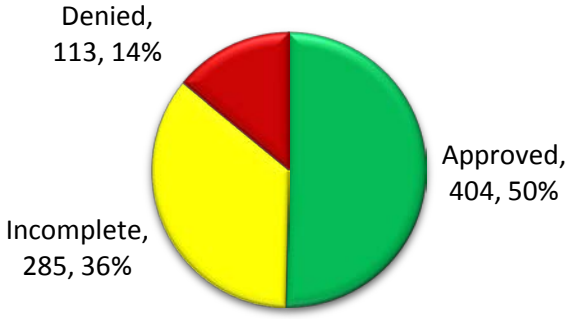
**Top Prescriber Specialties of MS Medications by Number of Claims: Pharmacy Claims**




## Prior Authorization of MS Medications

There were 802 prior authorization requests submitted for 223 unique members for MS medications during calendar year 2018. The following chart shows the status of the submitted petitions for calendar year 2018.

**Status of Petitions**




## Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21]

**Anticipated Patent Expiration(s):**

- Tecfidera® (dimethyl fumarate): February 2028
- Gilenya® (fingolimod): September 2032
- Aubagio® (teriflunomide): February 2034

**Generic Formulation Update(s):**

- **September 2018:** An authorized generic formulation of Ampyra® (dalfampridine) extended-release (ER) tablets was launched by Mylan Pharmaceuticals. Several other companies received subsequent U.S. Food and Drug Administration (FDA) approval for generic marketing of dalfampridine and are currently available.
- **November 2018:** The FDA approved Glenmark Pharmaceuticals' generic version of Aubagio® (teriflunomide) oral tablets. Glenmark is eligible for 180 days of shared generic drug exclusivity, a press release reports. Shared exclusivity can be granted for 180 days to "multiple generic firms that are first to challenge different patents on the same drug," the FDA notes. Launch information for the generic teriflunomide formulation was not provided and there are currently no generic teriflunomide formulations available through SoonerCare.
- **December 2018:** The FDA granted Lupin tentative approval for a generic formulation of Tecfidera® (dimethyl fumarate). This is the first FDA approval of a generic formulation of dimethyl fumarate. Full approval would not be expected until after patent expiration of Tecfidera® in June 2020.

**New FDA Approval(s):**

- **May 2018:** The FDA approved Gilenya® (fingolimod) to treat relapsing MS in children and adolescents 10 years of age and older. This is the first FDA approval of a drug to treat MS in pediatric patients. Fingolimod was first approved by the FDA in 2010 to treat adults with relapsing MS.
- **January 2019:** Banner Life Sciences announced that Bafiertam™ (monomethyl fumarate), a prodrug to Tecfidera® (dimethyl fumarate), received tentative FDA approval for the treatment of relapsing forms of MS. Bafiertam™ is expected to be available as delayed-release 95mg oral capsules. According to the FDA, Bafiertam™ met the required safety, efficacy, quality, and bioequivalence standards for tentative approval. Full approval, however, is expected after patent expiration of Tecfidera® in June 2020 or sooner depending on the outcome of pending litigation with Biogen, the manufacturer of Tecfidera®. Bafiertam™ will be brought to the Drug Utilization Review (DUR) Board for review after full approval has been granted by the FDA.

**Safety Update(s):**

- **April 2018:** Publications in the March issue of *Neurology* highlighted potentially life-threatening adverse events associated with the use of Lemtrada® (alemtuzumab) for MS. Three separate articles outline 8 cases of acute acalculous cholecystitis (AAC), 2 cases of hemophagocytic lymphohistiocytosis (HLH), and 1 occurrence of acute coronary syndrome (ACS), all thought to be linked to alemtuzumab use. A separate editorial discussed other rare adverse reactions to alemtuzumab that have emerged in postmarketing reports including uncommon infections such as listeriosis and meningitis. As a result of the AAC cases outlined in the aforementioned publication and a small number of cases in alemtuzumab clinical trials, AAC was added to the *Warnings and Precautions* section of the product labeling.
- **November 2018:** The FDA issued a safety announcement regarding worsening of MS symptoms and disability upon discontinuation of Gilenya® (fingolimod), potentially

resulting in permanent disability. The FDA required a new warning regarding this risk be added to the fingolimod prescribing information. Prescribers are advised to carefully observe patients who discontinue fingolimod for evidence of an exacerbation of MS.

- **November 2018:** The FDA issued a safety announcement regarding rare but serious cases of stroke and tears in the lining of the arteries in the head and neck that have occurred in MS patients receiving Lemtrada® (alemtuzumab). The FDA has added a warning about these risks to the prescribing information in the product label in addition to adding a *Boxed Warning* regarding the risk of stroke.

**Guideline Update(s):**

- **April 2018:** The American Academy of Neurology (AAN) released updated guidelines for the use of disease-modifying therapies (DMTs) in adults with relapsing-remitting MS (RRMS) and progressive forms of MS. The last update to the MS guidelines was published in 2002. The guidelines recommended starting treatment with DMTs for MS as early as possible to allow for the greatest chance to alter the disease course. Other recommendations included taking into account patient preferences regarding DMT safety, adverse effects, and efficacy when initiating DMTs. Recommendations were also provided regarding monitoring DMT therapy effectiveness, adherence, and when to consider switching DMTs.

**Pipeline Update(s):**

- **Cladribine:** In July 2018, EMD Serono, the biopharmaceutical business of Merck KGaA, announced a resubmission of a New Drug Application (NDA) for cladribine tablets as a potential treatment for RRMS. The NDA follows global approvals of cladribine tablets under the trade name Mavenclad® in 38 countries since August 2017. Cladribine is an investigational agent that has been studied as a short-course (a maximum of 20 days of treatment over 2 years) oral therapy that is thought to selectively target lymphocytes, which may be integral to the pathological process of relapsing MS. Rather than regular dosing, cladribine tablets would be dosed in infrequent treatment cycles. The NDA acceptance includes close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of safety data in some patients.
- **Diroximel Fumarate:** In February 2019, the FDA accepted an NDA for Alkermes' diroximel fumarate, an oral prodrug of monomethyl fumarate being studied for the treatment of relapsing forms of MS. Diroximel fumarate is anticipated to have fewer gastrointestinal side effects than Tecfidera® (dimethyl fumarate). The final decision by the FDA is expected in the fourth quarter of 2019.
- **EHP-101:** Emerald Health Pharmaceuticals announced that it has begun enrolling healthy participants for a Phase 1 trial evaluating the safety and tolerability of EHP-101, an investigational cannabidiol treatment for MS and scleroderma. The initial study will evaluate the safety and pharmacokinetics as well as assessing various ascending doses. Previous studies of cannabinoid receptors have found the pathway may reduce neuroinflammation and fibrosis.
- **Evobrutinib:** In March 2018, Merck KgaA announced positive results from its Phase 2b study of evobrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, in RRMS. The study has met its primary endpoint, demonstrating that evobrutinib resulted in a clinically

meaningful reduction of gadolinium-enhancing T1 lesions measured at weeks 12, 16, 20, and 24 in comparison to patients receiving placebo.

- **Ibudilast:** In October 2017, results of a Phase 2 trial of ibudilast, an investigational phosphodiesterase type 4 and 10 enzyme (PDE-4 and PDE-10) inhibitor, revealed that ibudilast may slow the loss of brain tissue in progressive MS patients. The Phase 2 SPRINT-MS trial evaluated the efficacy of ibudilast in 255 adult patients with primary or secondary progressive MS (SPMS). Patients must have shown clear signs of disability progression in the 2 years before enrollment and were randomly assigned to ibudilast or placebo. Patients were followed for 96 weeks, with doctor's evaluations and imaging assessments of patients' brains performed every 24 weeks. Brain shrinkage, was evaluated using a measure known as brain parenchymal fraction (BPF). Compared to placebo, ibudilast treatment was associated with a 48% slowing in the rate of atrophy progression. Approximately 92% of the ibudilast-treated participants experienced adverse events, versus 88% in the placebo group, with the most common being nausea, diarrhea, abdominal pain, and vomiting.
- **Ozanimod:** In October 2018, Celgene Corporation announced results from 2 post hoc analyses of data from the Phase 3 SUNBEAM and RADIANCE Part B trials, which evaluated the efficacy of ozanimod, an oral sphingosine 1-phosphate 1 and 5 (S1PR1 and S1PR5) receptor modulator, versus Avonex® [interferon (IFN) β-1a] in patients with RRMS. A post hoc analysis of 12-month data from SUNBEAM examined the effect of ozanimod on cognitive processing speed, based on performance on the Symbol Digit Modalities Test (SDMT). More patients exhibited clinically meaningful (≥4-point) improvements in processing speed at month 12 with ozanimod 1mg [rate ratio: 1.3; 95% confidence interval (CI): 1.05, 1.55] and 0.5mg (1.2; 95% CI: 0.94, 1.40) versus IFN. A second post hoc analysis regarding annualized relapse rates (ARR) and MRI lesions examined the effect of ozanimod in patients with early RRMS compared with patients with more advanced disease. Early RRMS was defined based on a composite baseline profile, including 3 years or less since diagnosis, an Expanded Disability Status Scale (EDSS) of ≤3.5, and the use of 1 or no disease-modifying treatments. ARR was lower at 12 months for both early and more advanced RRMS with ozanimod 1mg (early ARR=0.149; advanced ARR=0.217) and ozanimod 0.5mg (early ARR=0.200; advanced ARR=0.277) compared with IFN (early ARR=0.285; advanced ARR=0.363). In the SUNBEAM and RADIANCE clinical trials, the most common adverse reactions (≥5%) experienced that were higher with ozanimod than with IFN were upper respiratory tract infections, urinary tract infections, increases of alanine aminotransferase, and increases of gamma-glutamyl transferase. Celgene previously received a refuse to file letter for an NDA for ozanimod regarding insufficient data in February 2018, but has said it will file a second NDA in the first quarter of 2019.
- **Siponimod:** In October 2018, Novartis announced FDA acceptance of an NDA for siponimod, an oral S1PR1 and S1PR5 receptor modulator under investigation for the treatment of SPMS in adults. Novartis used a priority review voucher to expedite the review of siponimod by the FDA and a response is expected in March 2019. Siponimod demonstrated efficacy in the EXPAND study, a randomized, double-blind, placebo-controlled, Phase 3 study, comparing the efficacy and safety of siponimod versus placebo in SPMS patients. At study initiation, more than 50% of patients in the EXPAND

study relied on a walking aid. Results showed that siponimod significantly reduced the risk of 3-month confirmed disability progression versus placebo (primary endpoint; 21% vs. placebo, P=0.013). Siponimod also meaningfully delayed the risk of 6-month confirmed disability progression (26% vs. placebo, P=0.0058). In addition, Novartis conducted the BOLD study, a randomized, double-blind, placebo-controlled, adaptive dose-ranging, Phase 2 study in patients with RRMS. The study showed that siponimod significantly reduced the ARR over 6 months compared to placebo (siponimod ARR 2mg: 0.20 vs. placebo ARR: 0.58; P=0.041).

- **Ublituximab:** In June 2018, TG Therapeutics announced positive results from a Phase 2 trial of ublituximab, an investigational B-cell targeting therapy, in relapsing MS patients. Treatment with intravenous (IV) ublituximab 450mg resulted in massive depletion (99% depletion at week 4 and maintained at week 24 in 44 of 46 patients) of immune B-cells believed to be involved in MS development; in addition, ublituximab led to a reduction in lesions in the brain and spinal cord (44 of 46 patients free of gadolinium-enhancing lesions 6 months after treatment). Of note, 98% of the ublituximab-treated patients were relapse-free by week 24, and 83% showed no disability progression during this period.

**Other News:**

- **August 2018:** Researchers reported a potential new subtype of MS, myelocortical MS, in *The Lancet Neurology*. Myelocortical MS supports the concept that neurodegeneration and demyelination can occur independently in MS. The subtype is characterized by demyelination only in the spinal cord and cerebral cortex but not in cerebral white matter. In a postmortem study of 100 MS patients, 12 individuals had MS lesions in the spinal cord and cerebral cortex but not in brain white matter. While the cortical demyelinated lesion area was similar between these myelocortical MS patients and traditional MS patients, the spinal cord demyelinated area was greater in typical MS patients. Despite having no cerebral white matter demyelination, myelocortical MS brains had reduced neuronal density and cortical thickness. This is the first study to provide pathological evidence that neuronal degeneration can occur without white matter myelin loss in the brains of patients with MS.
- **January 2019:** Biogen announced the initiation of a Phase 3b trial to evaluate the safety and efficacy of extended-interval dosing with Tysabri® (natalizumab) in patients with RRMS. Results of the 6-week dosing interval will be compared with the approved standard-interval dosing regimen, which consists of IV infusions (300mg) every 4 weeks.

## Recommendations

The College of Pharmacy does not recommend any changes to the current MS medications prior authorization criteria at this time.

## Utilization Details of MS Medications: Calendar Year 2018

### Pharmacy Claims: Calendar Year 2018

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **INTERFERON BETA-1A PRODUCTS** | | | | | |
| AVONEX PEN KIT 30MCG/0.5ML | 49 | 10 | $319,557.62 | 4.9 | $6,521.58 |
| REBIF REBIDO INJ 44MCG/0.5ML | 42 | 5 | $303,605.16 | 8.4 | $7,228.69 |
| REBIF INJ 22MCG/0.5ML | 26 | 2 | $71,405.05 | 13 | $2,746.35 |
| REBIF INJ 44MCG/0.5ML | 22 | 2 | $153,799.67 | 11 | $6,990.89 |
| REBIF REBIDO INJ 22MCG/0.5ML | 9 | 1 | $65,210.36 | 9 | $7,245.60 |
| AVONEX SYR KIT 30MCG/0.5ML | 4 | 2 | $25,834.98 | 2 | $6,458.75 |
| **SUBTOTAL** | **152** | **20** | **$939,412.84** | **7.6** | **$6,180.35** |
| **INTERFERON BETA-1B PRODUCTS** | | | | | |
| BETASERON INJ 0.3MG | 82 | 9 | $562,825.62 | 9.11 | $6,863.73 |
| **SUBTOTAL** | **82** | **9** | **$562,825.62** | **9.11** | **$6,863.73** |
| **PEGINTERFERON BETA-1A PRODUCTS** | | | | | |
| PLEGRIDY INJ 125MCG/0.5ML | 14 | 2 | $94,651.51 | 7 | $6,760.82 |
| PLEGRIDY INJ STARTER | 1 | 1 | $6,796.50 | 1 | $6,796.50 |
| **SUBTOTAL** | **15** | **2** | **$101,448.01** | **7.5** | **$6,763.20** |
| **DALFAMPRIDINE PRODUCTS** | | | | | |
| AMPYRA TAB 10MG | 179 | 27 | $451,493.08 | 6.63 | $2,522.31 |
| DALFAMPRIDIN TAB 10MG ER | 18 | 8 | $18,551.40 | 2.25 | $1,030.63 |
| **SUBTOTAL** | **197** | **28** | **$470,044.48** | **7.04** | **$2,386.01** |
| **TERIFLUNOMIDE PRODUCTS** | | | | | |
| AUBAGIO TAB 14MG | 117 | 22 | $739,857.13 | 5.32 | $6,323.57 |
| AUBAGIO TAB 7MG | 25 | 3 | $161,961.39 | 8.33 | $6,478.46 |
| **SUBTOTAL** | **142** | **25** | **$901,818.52** | **5.68** | **$6,350.83** |
| **GLATIRAMER ACETATE PRODUCTS** | | | | | |
| COPAXONE INJ 40MG/ML | 204 | 31 | $1,153,117.23 | 6.58 | $5,652.54 |
| COPAXONE INJ 20MG/ML | 173 | 34 | $1,195,035.64 | 5.09 | $6,907.72 |
| GLATIRAMER INJ 40MG/ML | 19 | 6 | $74,796.97 | 3.17 | $3,936.68 |
| **SUBTOTAL** | **396** | **65** | **$2,422,949.84** | **6.09** | **$6,118.56** |
| **FINGOLIMOD PRODUCTS** | | | | | |
| GILENYA CAP 0.5MG | 209 | 24 | $1,552,800.00 | 8.71 | $7,429.67 |
| **SUBTOTAL** | **209** | **24** | **$1,552,800.00** | **8.71** | **$7,429.67** |
| **DIMETHYL FUMARATE PRODUCTS** | | | | | |
| TECFIDERA CAP 240MG | 183 | 31 | $1,347,248.74 | 5.9 | $7,362.01 |
| TECFIDERA MIS STARTER | 15 | 15 | $110,606.82 | 1 | $7,373.79 |
| **SUBTOTAL** | **198** | **35** | **$1,457,855.56** | **5.66** | **$7,362.91** |
| **NATALIZUMAB PRODUCTS** | | | | | |
| TYSABRI INJ 300/15ML | 16 | 3 | $88,370.31 | 5.33 | $5,523.14 |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **SUBTOTAL** | **16** | **3** | **$88,370.31** | **5.33** | **$5,523.14** |
| **DACLIZUMAB PRODUCTS** | | | | | |
| ZINBRYTA INJ 150MG/ML | 5 | 2 | $36,215.25 | 2.5 | $7,243.05 |
| **SUBTOTAL** | **5** | **2** | **$36,215.25** | **2.5** | **$7,243.05** |
| **TOTAL** | **1,412** | **193*** | **$8,533,740.43** | **7.32** | **$6,043.73** |

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

## Medical Claims: Calendar Year 2018

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **ALEMTUZUMAB PRODUCTS** | | | | | |
| LEMTRADA 10MG/1ML (J0202) | 14 | 4 | $397,969.08 | 3.5 | $28,426.36 |
| **NATALIZUMAB PRODUCTS** | | | | | |
| TYSABRI INJ 300MG/15ML (J2323) | 136 | 21 | $789,423.00 | 6.5 | $5,804.58 |
| **OCRELIZUMAB PRODUCTS** | | | | | |
| OCREVUS INJ 300MG/10ML (J2350) | 48 | 24 | $972,595.04 | 2 | $20,262.40 |
| **TOTAL** | **198+** | **46*** | **$2,159,987.12** | **4.3** | **$10,909.03** |

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

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# Appendix O

# Calendar Year 2018 Annual Review of Luxturna™ (Voretigene Neparvovec-rzyl)

**Oklahoma Health Care Authority**
**March 2019**

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

Luxturna™ (voretigene neparvovec-rzyl) is a live, non-replicating adeno-associated virus serotype 2 (AAV2) vector-based gene therapy, designed to deliver a normal copy of the gene encoding the human retinal pigment epithelial 65 kDa protein (*RPE65*) to cells of the retina in patients with reduced or absent levels of biologically active *RPE65*. The U.S. Food and Drug Administration (FDA) approved Luxturna™, a 1-time gene therapy product, in December 2017 for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy that leads to vision loss and may cause complete blindness in certain patients. Patients must have viable retinal cells as determined by the treating physician(s). Mutations in the *RPE65* gene lead to reduced or absent levels of *RPE65* isomerohydrolase activity, blocking the visual cycle and resulting in impairment of vision. The absence of *RPE65* eventually leads to the accumulation of toxic precursors and damage to the RPE cells, which, over time, results in damage to the photoreceptors due to their dependence on the RPE cells for cellular metabolism. Patients with untreated *RPE65*-mediated inherited retinal dystrophy eventually lose the ability to detect light of any intensity. Biallelic *RPE65* mutation-associated retinal dystrophy affects approximately 1,000 to 2,000 patients in the United States. Retinal diseases caused by biallelic *RPE65* mutations include some forms of Leber's congenital amaurosis (LCA) and retinitis pigmentosa (RP), among other disorders, with mutations in *RPE65* estimated to be responsible for 7 to 9% of LCA cases and 1 to 2% of RP cases. The hallmark of biallelic *RPE65* mutation-associated retinal dystrophy is nyctalopia, which is the inability to see or perceive in dim light, and it manifests in both reduced visual function and functional vision, accompanied by impairment in visual field and visual acuity.

Injection of Luxturna™ into the subretinal space results in transduction of some RPE cells with complementary DNA (cDNA) encoding normal human *RPE65* protein, thus providing the potential to restore the visual cycle. This does not repair or eliminate the defective gene, but rather introduces a normal copy of the gene into the cell. While Luxturna™ is a 1-time therapy, long-term efficacy remains a question for this treatment. Individuals with an *RPE65* mutation have significant retinal degeneration leading to worse functional vision over time. The therapeutic effects of gene therapy may not be permanent. Visual improvements past 3 years have been described by clinical experts, but no published data exist beyond 1 year. Even if improvements persist in treated cells, it remains unclear whether long-term retinal degeneration is impacted by gene therapy.

Luxturna™ is supplied as a single-dose vial (SDV) containing an intraocular suspension for subretinal injection that must be diluted prior to use and should be prepared within 4 hours of

administration using sterile technique; Luxturna™ and diluent should be stored frozen at ≤-65°C prior to dilution and administration. Luxturna™ should be administered by subretinal injection to each eye on separate days within a close interval, but no fewer than 6 days apart, and is to be administered at selected Ocular Gene Therapy Treatment Centers in the United States by leading retinal surgeons, who will receive surgical training provided by the pharmaceutical company on the administration procedure. Systemic oral corticosteroids equivalent to prednisone 1mg/kg/day (maximum of 40mg/day) are recommended for a total of 7 days (starting 3 days before administration of Luxturna™ to the first eye), and followed by tapering the dose during the following 10 days. The same corticosteroid regimen applies for the administration of Luxturna™ to the second eye. The wholesale acquisition cost (WAC) of Luxturna™ is $425,000 per SDV, resulting in a cost of $850,000 per patient.

## Current Prior Authorization Criteria

**Luxturna™ (Voretigene Neparvovec-rzyl) Approval Criteria:**

1. An FDA approved diagnosis of biallelic *RPE65* mutation-associated retinal dystrophy; and
    a. Diagnosis must be confirmed by genetic testing; and
2. Member must have sufficient viable retinal cells in both eyes as determined by the treating physician(s); and
3. Member must have best corrected visual acuity of 20/60 or worse in both eyes and/or visual field less than 20 degrees in any meridian in both eyes; and
4. Member must be 4 years of age or older; and
5. Member must not have participated in a previous *RPE65* gene therapy study or have previously received treatment with Luxturna™; and
6. Member must not have had intraocular surgery in the past 6 months; and
7. Female members of child bearing age must not be pregnant and must have a negative pregnancy test immediately prior to administration of Luxturna™; and
8. Male and female members of child bearing age must be willing to use effective contraception during treatment with Luxturna™ and for at least 4 months after administration of Luxturna™; and
9. Member must take the recommended systemic oral corticosteroid regimen, starting 3 days prior to administration of Luxturna™ to each eye, and continuing after administration of Luxturna™, as per package labeling of Luxturna™; and
10. Luxturna™ must be prescribed and administered by a retinal surgeon with expertise in the treatment of biallelic *RPE65* mutation-associated retinal dystrophy and in the administration of Luxturna™ at an Ocular Gene Therapy Treatment Center; and
    a. Luxturna™ must be shipped via cold chain supply shipping and delivery to the Ocular Gene Therapy Treatment Center where the member is scheduled to receive treatment; and
    b. Luxturna™ must be stored frozen prior to preparation for administration (Luxturna™ should be administered within 4 hours of preparation); and
    c. The receiving facility must have in place a mechanism to track patient-specific Luxturna™ from receipt to storage to administration; and

11. Luxturna™ must be administered subretinally to each eye on separate days within a close interval, but no fewer than 6 days apart; and
    a. The scheduled procedure date for each eye must be provided; and
12. Only 1 single-dose vial per eye will be approved per member per lifetime; and
    a. Each single-dose vial of Luxturna™ is to be dispensed immediately prior to the scheduled procedure for the specific eye; or
13. A prior authorization request with patient-specific information may be submitted for consideration of Luxturna™ for members not meeting all of the current prior authorization criteria requirements.

## Utilization of Luxturna™ (Voretigene Neparvovec-rzyl): Calendar Year 2018

There was no SoonerCare utilization of Luxturna™ (voretigene neparvovec-rzyl) during calendar year 2018.

## Prior Authorization of Luxturna™ (Voretigene Neparvovec-rzyl)

There were no prior authorization requests submitted for Luxturna™ (voretigene neparvovec-rzyl) during calendar year 2018.

## Market News and Updates[8,9,10,11,12,13,14,15]

**News:**

- **October 2018:** Spark Therapeutics presented 3 post-hoc analyses from the Phase 3 clinical trial of Luxturna™ (voretigene neparvovec-rzyl) at the American Academy of Ophthalmology annual meeting including the use of a different measurement for best-corrected visual acuity, mutation subtype analysis, and analysis of full-field light sensitivity threshold (FST) testing data.
- **November 2018:** Luxturna™ (voretigene neparvovec-rzyl) received regulatory approval from the European Commission, making it the first gene therapy to be approved in both the United States and the European Union.

**Pipeline:**

- **QR-110 (Sepofarsen):** ProQR Therapeutics is developing QR-110 for the treatment of Leber's congenital amaurosis 10 (LCA10). LCA10 is a severe and the most frequent form of LCA, leading to early loss of vision and causing most people to lose their sight in the first few years of life. LCA10 is caused by mutations in the *CEP290* gene, of which the p.Cys998X mutation is the most common. QR-110 is a first-in-class investigational RNA-based oligonucleotide designed to address the underlying cause of LCA10 due to the p.Cys998X mutation in the *CEP290* gene. QR-110 is designed to repair the genetic defect in the RNA, such that it leads to a normal "wild-type" mRNA, leading to the production of normal *CEP290* protein. QR-110 is intended to be administered through intravitreal injections and has been granted Orphan Drug and Fast Track designations by the FDA. An ongoing Phase 1/2 study of QR-110 will be completed and in parallel, a Phase 2/3 study (ILLUMINATE) of QR-110 is expected to be initiated in the first half of 2019. Additionally, ProQR plans to start an open-label extension study (INSIGHT) where

eligible patients that complete the Phase 1/2 study will be given the opportunity to continue treatment with QR-110.

- **QR-1123:** ProQR Therapeutics is also developing QR-1123 for the treatment of autosomal dominant retinitis pigmentosa (adRP). Symptoms of adRP usually start with night blindness during childhood and progress with loss of peripheral vision leading to tunnel vision; loss of central vision appears during adulthood and blindness is frequent in mid-adulthood. There are over 20 known genes that can cause adRP when they are mutated but most often the disease is caused by a mutation in the rhodopsin (*RHO*) gene; in the United States, the P23H mutation is the most common. QR-1123 aims to block the formation of the mutated toxic version of the rhodopsin protein by specifically binding to the mutated *RHO* mRNA, with the goal of stopping the progression or reversing the effects of the disease. The preclinical phase of testing has been completed for QR-1123; ProQR plans to initiate the first clinical study in humans as soon as possible.
- **GS010:** GenSight Biologics is developing GS010, an AAV2 gene therapy vector that encodes the human wild-type ND4 protein, for the treatment of Leber's hereditary optic neuropathy (LHON) caused by mutation of the *ND4* gene. LHON is a rare, maternally inherited mitochondrial genetic disease that causes irreversible and severe vision loss, eventually leading to blindness and disability, mostly in teens and young adults. Vision loss is typically the only symptom of LHON. Phase 3 trials (RESCUE and REVERSE) are underway in Europe and the United States to evaluate GS010 in LHON patients with a recent onset of disease (i.e., less than 1 year), with 2 additional studies being initiated: 1 clinical trial (REFLECT) pursuant to a special protocol assessment with the FDA to evaluate the efficacy and safety of bilateral intravitreal injections of GS010 for the treatment of vision loss up to 1 year and 1 LHON registry study (REALITY) to understand the evolution of visual function and structural changes and other associated symptoms in patients with LHON.
- **GS030:** GenSight is also developing GS030 for the treatment of RP. GS030 uses optogenetics, a biologic technique that involves the transfer of a gene that encodes for a light-sensitive protein, which in turn causes neuronal cells to respond to light stimulation. GS030 is an innovative combination of 2 complementary components, a gene therapy product encoding a photoactivatable channelrhodopsin protein (delivered via a modified AAV2 vector known as AAV2 7m8) and biomimetic goggles that stimulate the engineered retinal cells (images are projected onto the retina by a light source that uses a specific wavelength). Preclinical proof-of-concept studies demonstrated that GS030 can restore light sensitivity in the retina of blind mice and non-human primates. GenSight has initiated the PIONEER study, a Phase 1/2 dose-escalation study to evaluate the safety and tolerability of GS030 in patients with RP. GS030 has been granted Orphan Drug designation by the FDA for the treatment of RP.

## Recommendations

The College of Pharmacy does not recommend any changes to the current Luxturna™ (voretigene neparvovec-rzyl) prior authorization criteria at this time.

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[10] ProQR Therapeutics N.V. News Release. ProQR Announces Publication in Nature Medicine of QR-110 Data for Leber's Congenital Amaurosis 10. *Globe Newswire*. Available online at: https://globenewswire.com/news-release/2018/12/17/1668180/0/en/ProQR-Announces-Publication-in-Nature-Medicine-of-QR-110-Data-for-Leber-s-Congenital-Amaurosis-10.html. Issued 12/17/2018. Last accessed 02/18/2019.

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# Appendix P

# Calendar Year 2018 Annual Review of Osteoporosis Medications

**Oklahoma Health Care Authority**
**March 2019**

## Current Prior Authorization Criteria

| Osteoporosis Medications | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Special PA** |
| alendronate tabs (Fosamax®) | alendronate + vitamin D tabs (Fosamax® + D) | Abaloparatide inj (Tymlos®) |
| calcium + vitamin D* | risedronate tabs (Actonel®) | alendronate effervescent tabs (Binosto®) |
| Ibandronate tabs (Boniva®) | | alendronate soln (Fosamax®) |
| Raloxifene tabs (Evista®) | | alendronate 40mg tabs (Fosamax®) |
| zoledronic acid inj (Reclast®) | | denosumab inj (Prolia®) |
| | | ibandronate inj (Boniva® IV) |
| | | risedronate 30mg tabs (Actonel®) |
| | | risedronate DR tabs (Atelvia®) |
| | | teriparatide inj (Forteo®) |

*Must be used in combination with a bisphosphonate to count as a Tier-1 trial.
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) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

**Osteoporosis Medications Tier-2 Approval Criteria:**

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

**Osteoporosis Medications Special Prior Authorization (PA) Approval Criteria:**

1. **Forteo® (Teriparatide):**
    a. A diagnosis of 1 of the following:
        i. Treatment of postmenopausal women with osteoporosis at high risk for fracture; or
        ii. To increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture; or
        iii. Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture; or
        iv. Treatment of non-healing fracture; and
    b. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D or a patient-specific, clinically significant reason the member cannot use a bisphosphonate; and

c. The diagnosis of non-healing fracture may be approved for 6 months; and
d. Treatment duration, including other parathyroid hormone analogs, must not exceed a total of 24 months during the patient's lifetime; and
e. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy.

2. **Prolia® (Denosumab) and Boniva® IV (Ibandronate Injection):**
   a. A minimum of a 12-month trial with a Tier-1 or Tier-2 bisphosphonate plus adequate calcium and vitamin D; or
   b. Contraindication(s) to or intolerable adverse effect(s) with Tier-1 and Tier-2 bisphosphonate medications.
3. **Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets), and Actonel® (Risedronate 30mg Tablets):**
   a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 bisphosphonate medications must be provided; or
   b. Members with the diagnosis of Paget's disease in history will not require prior authorization.
4. **Fosamax® (Alendronate Oral Solution):**
   a. An FDA approved diagnosis of osteoporosis or Paget's disease; and
   b. A patient-specific, clinically significant reason the member cannot use the oral tablet formulation must be provided.
5. **Fosamax® (Alendronate 40mg Tablets):**
   a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 bisphosphonate products, including a 35mg alendronate tablet in combination with a 5mg alendronate tablet to achieve a 40mg dose must be provided; or
   b. Members with the diagnosis of Paget's disease in history will not require prior authorization.
6. **Tymlos® (Abaloparatide):**
   a. A diagnosis of postmenopausal osteoporosis confirmed by the following:
      i. History of vertebral fracture(s) or low trauma or fragility fracture(s) (e.g., prior fracture from minor trauma such as falling from standing height or less) within the past 5 years; or
      ii. A bone mineral density test (T-score at or below -2.5) within the last month in the spine, femoral neck, total hip, or 33% radius; or
      iii. Those with a T-score between -1.0 and -2.5 in the spine, femoral neck, total hip, or 33% radius, if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3%; and
   b. Member must have 1 of the following [if a 12-month bisphosphonate trial is inappropriate for the member, the member must have a trial of Prolia® or a selective estrogen receptor modulator (SERM) or a patient-specific, clinically significant reason why Prolia® or a SERM is not appropriate]:
      i. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D; or
      ii. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or
      iii. A 12-month trial of a SERM, unless contraindicated, intolerant, or allergic, that did not yield adequate results; and

c. A patient-specific, clinically significant reason why the member cannot use Forteo® (teriparatide) must be provided; and
d. Treatment duration, including other parathyroid hormone analogs, must not exceed a total of 24 months during the patient's lifetime; and
e. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy; and
f. A quantity limit of 1 pen per 30 days will apply.

7. **Quantity limits apply based on U.S. Food and Drug Administration (FDA) approved maximum doses.**

## Utilization of Osteoporosis Medications: Calendar Year 2018

### Comparison of Calendar Years: Pharmacy Claims

| Calendar Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2017** | 611 | 3,244 | $180,563.82 | $55.66 | $1.78 | 25,557 | 101,207 |
| **2018** | 608 | 2,877 | $278,409.56 | $96.77 | $2.71 | 23,930 | 102,851 |
| **% Change** | **-0.50%** | **-11.30%** | **54.20%** | **73.90%** | **52.20%** | **-6.40%** | **1.60%** |
| **Change** | **-3** | **-367** | **$97,845.74** | **$41.11** | **$0.93** | **-1,627** | **1,644** |

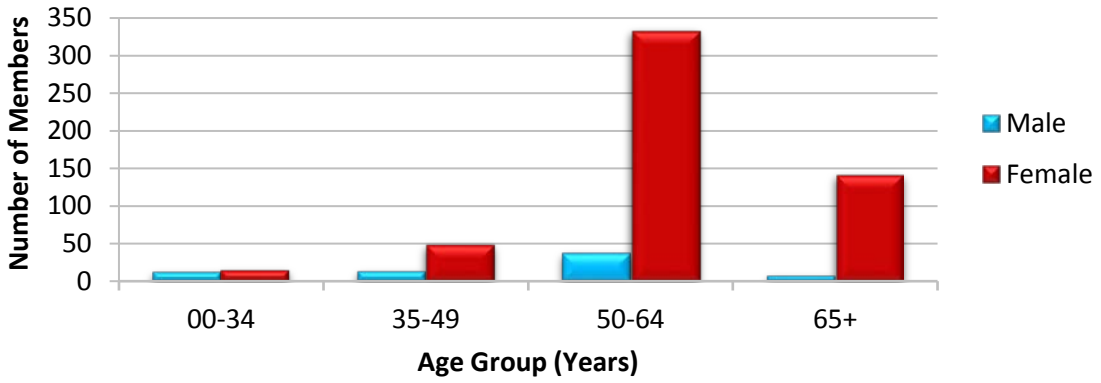
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

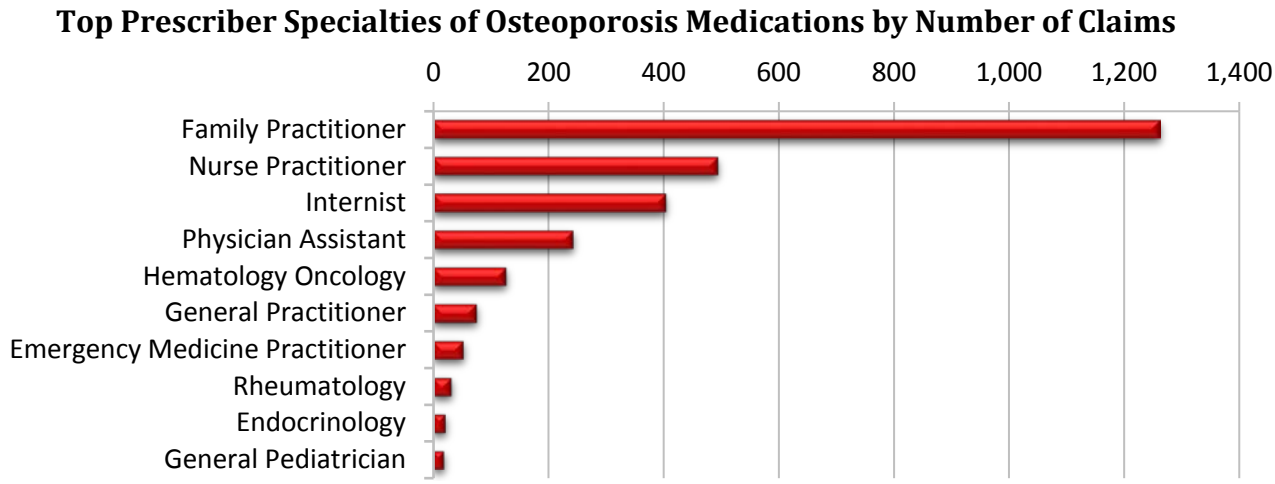
### Calendar Year 2018 Utilization: Medical Claims

| *Total Members | ⁺Total Claims | Total Cost | Cost/Claim | Claims/Member |
|---|---|---|---|---|
| 30 | 39 | $35,329.97 | $905.90 | 1.3 |

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

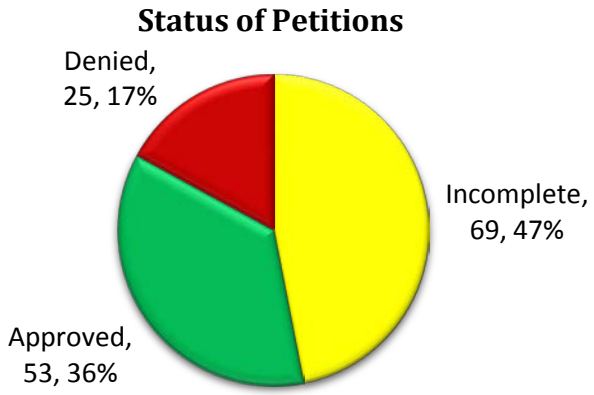
### Demographics of Members Utilizing Osteoporosis Medications






## Prior Authorization of Osteoporosis Medications

There were 147 prior authorization requests submitted for osteoporosis medications during calendar year 2018. Computer edits are in place to detect lower tiered medications or diagnosis information in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for calendar year 2018.




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

**Anticipated Patent Expiration(s):**

- Binosto® (alendronate effervescent tablets): August 2023
- Forteo® (teriparatide injection): March 2025
- Tymlos® (abaloparatide injection): March 2028
- Reclast® (zoledronic acid injection): August 2028

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

- **May 2018:** The FDA expanded the approved indication of Prolia® (denosumab) to include the treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fractures. Data from the Phase 3 study showed that patients on

glucocorticoid therapy who have received Prolia® had greater gains in bone mineral density (BMD) in the lumbar spine compared to those who received risedronate at 1 year (4.4% vs. 2.3%, respectively).

**News:**

- **April 2018:** The United States Preventive Services Task Force (USPSTF) released recommendations on vitamin D supplementation, with or without calcium, to prevent fractures. The USPSTF found inadequate evidence to estimate the benefits of vitamin D, calcium, or combined supplementation to prevent fractures in community-dwelling men and premenopausal women. The USPSTF also concluded that current evidence is insufficient to assess the balance of benefits and harms of daily supplementation with doses >400 IU of vitamin D and >1,000mg of calcium for the primary prevention of fractures in community-dwelling, postmenopausal women. The USPSTF recommended against daily supplementation with ≤400 IU of vitamin D and ≤1,000mg of calcium for the primary prevention of fractures in community-dwelling, postmenopausal women. These recommendations do not apply to people living in nursing homes or other institutional settings. The recommendations also do not apply to persons with a history of osteoporotic fractures, increased risk of falls, or a diagnosis of osteoporosis or vitamin D deficiency.
- **May 2018:** A retrospective study published in the *Journal of Bone and Mineral Research* showed that alendronate use in patients with hip fracture was associated with a decrease in the risk of cardiovascular events. The study looked at 34,991 patients in Hong Kong with a newly diagnosed hip fracture. In the study, alendronate treatment was associated with a significantly lower risk for 1-year cardiovascular mortality [hazard ratio (HR) 0.33] and incidence of myocardial infarction (HR 0.55), and a marginally lower reduction in the risk of strokes at 5 years (HR 0.82) and 10 years (HR 0.83).
- **September 2018:** The American Society for Bone and Mineral Research (ASBMR) Secondary Fracture Prevention Initiative Coalition presented recommendations for patients 65 years of age or older with a hip or vertebral fracture. The coalition made several recommendations centering around the need for a multi-disciplinary clinical system, the evaluation and treatment of osteoporosis, and the risk of future fractures. Some of their recommendations included informing the primary care provider of the occurrence of a fracture and regularly assessing the risk of falls. The coalition also included a recommendation to offer pharmacological therapy for osteoporosis in men and women older than 65 years of age with a hip or vertebral fracture, regardless of BMD levels.

**Pipeline:**

- **Evenity™ (romosozumab):** Amgen and UCB announced in January 2019 that they received strong support from the FDA Bone, Reproductive, and Urologic Drugs Advisory Committee (BRUDAC) for the approval of Evenity™ (romosozumab) for the treatment of postmenopausal women with osteoporosis at high risk for fracture. The committee voted 18 to 1 in favor of approval of Evenity™, but emphasized the need for post-marketing follow-up. Romosozumab is an investigational humanized monoclonal

antibody that inhibits sclerosin, giving it a unique mechanism of action. Evenity™ is still awaiting final approval from the FDA, but received approval for marketing in Japan on January 8, 2019.

## Recommendations

The College of Pharmacy does not recommend any changes to the current osteoporosis medications prior authorization criteria at this time.

## Utilization Details of Osteoporosis Medications: Calendar Year 2018

### Pharmacy Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM |
|---|---|---|---|---|---|
| **TIER-1 PRODUCTS** | | | | | |
| **ALENDRONATE PRODUCTS** | | | | | |
| ALENDRONATE TAB 70MG | 2,176 | 464 | $20,541.21 | $0.29 | $9.44 |
| ALENDRONATE TAB 35MG | 200 | 41 | $2,158.99 | $0.34 | $10.79 |
| ALENDRONATE TAB 10MG | 96 | 19 | $1,257.73 | $0.38 | $13.10 |
| ALENDRONATE TAB 5MG | 31 | 7 | $403.97 | $0.38 | $13.03 |
| **SUBTOTAL** | **2,503** | **531** | **$24,361.90** | **$0.30** | **$9.73** |
| **RALOXIFENE PRODUCTS** | | | | | |
| RALOXIFENE TAB 60MG | 114 | 21 | $5,027.71 | $0.94 | $44.10 |
| **SUBTOTAL** | **114** | **21** | **$5,027.71** | **$0.94** | **$44.10** |
| **ZOLEDRONIC ACID PRODUCTS** | | | | | |
| ZOLEDRONIC INJ 5MG/100ML | 1 | 1 | $80.13 | $0.22 | $80.13 |
| **SUBTOTAL** | **1** | **1** | **$80.13** | **$0.22** | **$80.13** |
| **IBANDRONATE PRODUCTS** | | | | | |
| IBANDRONATE TAB 150MG | 83 | 32 | $2,205.03 | $0.40 | $26.57 |
| **SUBTOTAL** | **83** | **32** | **$2,205.03** | **$0.40** | **$26.57** |
| **TIER-1 SUBTOTAL** | **2,701** | **585** | **$31,674.77** | **$0.34** | **$11.73** |
| **TIER-2 PRODUCTS** | | | | | |
| **RISEDRONATE PRODUCTS** | | | | | |
| RISEDRONATE TAB 35MG | 38 | 4 | $1,531.13 | $1.43 | $40.29 |
| RISEDRONATE TAB 150MG | 13 | 2 | $754.70 | $1.94 | $58.05 |
| RISEDRONATE TAB 5MG | 11 | 1 | $1,159.81 | $3.72 | $105.44 |
| **SUBTOTAL** | **62** | **7** | **$3,445.64** | **$1.94** | **$55.57** |
| **TIER-2 SUBTOTAL** | **62** | **7** | **$3,445.64** | **$1.94** | **$55.57** |
| **SPECIAL PA PRODUCTS** | | | | | |
| **TERIPARATIDE PRODUCTS** | | | | | |
| FORTEO SOL 600MCG/2.4ML | 64 | 11 | $204,457.90 | $112.34 | $3,194.65 |
| **SUBTOTAL** | **64** | **11** | **$204,457.90** | **$112.34** | **$3,194.65** |
| **DENOSUMAB PRODUCTS** | | | | | |
| PROLIA SOL 60MG/ML | 33 | 22 | $36,032.03 | $6.08 | $1,091.88 |
| **SUBTOTAL** | **33** | **22** | **$36,032.03** | **$6.08** | **$1,091.88** |
| **ALENDRONATE PRODUCTS** | | | | | |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM |
|---|---|---|---|---|---|
| ALENDRONATE SOL 70MG/75ML | 8 | 2 | $1,618.24 | $6.86 | $202.28 |
| ALENDRONATE TAB 40MG | 7 | 1 | $953.94 | $4.54 | $136.28 |
| BINOSTO TAB 70MG | 2 | 1 | $227.04 | $4.05 | $113.52 |
| **SUBTOTAL** | **17** | **4** | **$2,799.22** | **$5.58** | **$164.66** |
| **SPECIAL PA SUBTOTAL** | **114** | **37** | **$243,289.15** | **$29.49** | **$2,134.12** |
| **TOTAL** | **2,877** | **608*** | **$278,409.56** | **$2.71** | **$96.77** |

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

## Medical Claims

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ CLAIM |
|---|---|---|---|---|
| PROLIA J0897 | 38 | 29 | $35,314.99 | $929.34 |
| RECLAST J3489 | 1 | 1 | $14.98 | $14.98 |
| **TOTAL** | **39⁺** | **30*** | **$35,329.97** | **$905.90** |

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

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[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 01/2019. Last accessed 02/18/2019.
[2] Amgen. FDA Approves Prolia® (denosumab) For Glucocorticoid-Induced Osteoporosis. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-prolia-denosumab-for-glucocorticoid-induced-osteoporosis-300652126.html. Issued 05/25/2018. Last accessed 02/18/2019.
[3] US Preventive Services Task Force. Vitamin D, Calcium, or Combined Supplementation for the Primary Prevention of Fractures in Community-Dwelling Adults: US Preventive Services Task Force Recommendation Statement. *JAMA* 2018; 319(15):1592-1599.
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[5] The American Society for Bone and Mineral Research. Patients 65 Years of Age or Older Who Experience a Hip or Spine Fracture Should be Treated for Osteoporosis, Says Global Coalition of Bone Health Experts and Patient Advocacy Organizations. ASBMR.org. Available online at: http://www.asbmr.org/about/pressreleases/detail.aspx?cid=8281a027-f61f-446f-ba1f-77b4a2222d8e. Issued 09/27/2018. Last accessed 02/19/2019.
[6] Amgen. Amgen And UCB Receive Positive Vote From FDA Advisory Committee In Favor Of Approval For EVENITY™ (romosozumab). *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/amgen-and-ucb-receive-positive-vote-from-fda-advisory-committee-in-favor-of-approval-for-evenity-romosozumab-300779812.html. Issued 01/16/2019. Last accessed 02/18/2019.

# Appendix Q

# Industry News and Updates

**Oklahoma Health Care Authority**
**March 2019**

## Introduction

The following report is an overview of recent issues, important literature, and select guideline updates impacting pharmacy and health care. Information that is expected to have a particular impact in the SoonerCare population has been included for review.

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

**News:**

- **Gene Therapies:** The U.S. Food and Drug Administration (FDA) is witnessing a large increase in the number of cell and gene therapy products entering early development. It is anticipated that the number of product approvals for cell and gene therapies will grow in the coming years. By 2020, it is anticipated that the FDA will be receiving more than 200 Investigational New Drug (IND) applications, building on the more than 800 INDs currently on file for active cell-based or directly administered gene therapies. It is anticipated that the FDA will be approving 10 to 20 cell and gene therapy products annually based on an assessment of the current pipeline and the clinical success rates of these products.
- **Rare Disease Therapies:** The FDA is updating its 2015 draft guidelines for drug discovery in rare diseases. Public comments are being accepted through mid-March regarding the "Rare Diseases: Common Issues in Drug Development" draft. The draft guidance was released in January 2019 and aims to help pharmaceutical companies and other sponsors of clinical trials testing medicines and biological products for rare diseases be more efficient and successful in their development programs. The draft guidelines offer new guidance on natural history, the choice of "efficacy endpoints" in clinical trials, and how disease biomarkers might be identified and used.
- **Birth Control:** Researchers at the Georgia Institute of Technology created a low-cost contraceptive patch for women using microneedles, which allows the user to wear it for seconds and get a dose that lasts for a month. According to a study published in the journal *Nature Biomedical Engineering*, after the patch is applied for several seconds, microscopic needles break off on the surface of the skin and administer levonorgestrel over a period of time. Researchers report that the patches are still several years from being available to consumers, but they could be mass-produced for $1 each.
- **High-Tech Pill:** Biomacromolecules have effectively transformed our ability to treat certain diseases; however, they are generally limited to parenteral administration due to their poor absorption in the gastrointestinal (GI) tract and rapid degradation. An oral biologic delivery system would need to aid in both permeation and localization to achieve systemic drug uptake. A team of scientists developed an ingestible self-orienting millimeter-scale applicator (SOMA), inspired by the leopard tortoise's ability to passively

reorient, that autonomously positions itself to engage with GI tissue. The applicator then deploys milliposts fabricated from active pharmaceutical ingredients directly through the gastric mucosa while avoiding perforation. The researchers have conducted *in vivo* studies in rats and swine that support the applicator's safety, and using insulin as a model drug, demonstrated that the applicator delivers active pharmaceutical ingredient plasma levels comparable to those achieved with subcutaneous millipost administration.

[1] U.S. Food and Drug Administration (FDA). Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm629493.htm. Issued 01/15/2019. Last accessed 02/01/2019.

[2] Chapman M. FDA Revising 'Draft Guidance' on Developing Treatments for Rare Diseases. *SMA News Today*. Available online at: https://smanewstoday.com/2019/01/30/fda-revising-draft-guidance-on-developing-treatments-for-rare-diseases/. Issued 01/30/2019. Last accessed 02/01/2019.

[3] Molina B. New $1 birth control patch works in seconds, lasts for a month, researchers claim. *USA Today*. Available online at: https://www.usatoday.com/story/news/health/2019/01/16/birth-control-patch-worn-seconds-costs-1-study-suggests/2590888002/. Issued 01/16/2019. Last accessed 02/01/2019.

[4] Abramson A, Caffarel-Salvador E, Khang M, et al. An ingestible self-orienting system for oral delivery of macromolecules. *Science* 2019; 363(6427)611-615. DOI: 10.1126/science.aau2277.

# Appendix R

# 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 6, 2019**

**FDA approves first therapy for the treatment of adult patients with a rare blood clotting disorder**

The FDA approved Cablivi® (caplacizumab-yhdp) injection, the first therapy specifically indicated, in combination with plasma exchange and immunosuppressive therapy, for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), a rare and life-threatening disorder that causes blood clotting.

Patients with aTTP develop extensive blood clots in the small blood vessels throughout the body. These clots can cut off oxygen and blood supply to the major organs and cause strokes and heart attacks that may lead to brain damage or death. Patients can develop aTTP because of conditions such as cancer, HIV, pregnancy, lupus, or infections, or after having surgery, bone marrow transplantation, or chemotherapy.

The efficacy of Cablivi® was studied in a clinical trial of 145 patients who were randomized to receive either Cablivi® or a placebo. Patients in both groups received the current standard of care of plasma exchange and immunosuppressive therapy. The results of the trial demonstrated that platelet counts improved faster among patients treated with Cablivi®, compared to placebo. Treatment with Cablivi® also resulted in a lower total number of patients with either aTTP-related death and recurrence of aTTP during the treatment period, or at least 1 treatment-emergent major thrombotic event (where blood clots form inside a blood vessel and may then break free to travel throughout the body).The proportion of patients with a recurrence of aTTP in the overall study period (the drug treatment period plus a 28-day follow-up period after discontinuation of drug treatment) was lower in the Cablivi® group (13%) compared to the placebo group (38%), a finding that was statistically significant.

Common side effects of Cablivi® reported by patients in clinical trials were bleeding of the nose or gums and headache. The prescribing information for Cablivi® includes a warning to advise health care providers and patients about the risk of severe bleeding.

Health care providers are advised to monitor patients closely for bleeding when administering Cablivi® to patients who currently take anticoagulants.

The FDA granted this application Priority Review designation. Cablivi® also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Cablivi® to Ablynx.

## Safety Announcements

**FDA adds Boxed Warning for increased risk of death with gout medicine Uloric® (febuxostat)**

**[02-21-2019]** The FDA has concluded there is an increased risk of death with Uloric® (febuxostat) compared to another gout medicine, allopurinol. This conclusion is based on an in-depth review of results from a safety clinical trial that found an increased risk of heart-related death and death from all causes with Uloric®.

As a result, the FDA is updating the Uloric® prescribing information to require a *Boxed Warning*, the FDA's most prominent warning, and a new patient Medication Guide. The FDA is also limiting the approved use of Uloric® to certain patients who are not treated effectively or experience severe side effects with allopurinol.

Uloric® was FDA-approved in 2009 to treat gout in adults. Gout happens when a naturally occurring substance in the body called uric acid builds up and causes sudden attacks of redness, swelling, and pain in 1 or more joints. Uloric® works by lowering uric acid levels in the blood. Gout is a chronic disease that affects approximately 8.3 million adults in the United states. The number of medicines to treat gout is limited and there is an unmet need for treatments for this disease.

**Patients** should tell their health care professional if they have a history of heart problems or stroke and discuss the benefits and risks of using Uloric® to treat their gout. Patients should seek emergency medical attention right away if they experience the following symptoms while taking Uloric®:

- Chest pain
- Shortness of breath

- Rapid or irregular heartbeat
- Numbness or weakness on one side of their body
- Dizziness
- Trouble talking
- Sudden severe headache

Patients should not stop taking Uloric® without first talking to their health care professional, as doing so can worsen their gout.

**Health care professionals** should reserve Uloric® for use only in patients who have failed or do not tolerate allopurinol. Patients should be counseled about the cardiovascular risk with Uloric® and be advised to seek medical attention immediately if they experience the symptoms listed previously. When the FDA approved Uloric® in 2009, the FDA included a *Warning and Precaution* regarding possible cardiovascular events in patients treated with Uloric® in the current prescribing information and required the drug manufacturer, Takeda Pharmaceuticals, to conduct a large postmarket safety clinical trial. The trial was conducted in more than 6,000 patients with gout treated with either Uloric® or allopurinol. The primary outcome was a combination of heart-related death, non-deadly heart attack, non-deadly stroke, and a condition of inadequate blood supply to the heart requiring intervention, called unstable angina. The results showed that overall, Uloric® did not increase the risk of these combined events compared to allopurinol. However, when the outcomes were evaluated separately, Uloric® showed an increased risk of heart-related deaths and death from all causes. In patients treated with Uloric®, 15 deaths from heart-related causes were observed for every 1,000 patients treated for a year compared to 11 deaths from heart-related causes per 1,000 patients treated with allopurinol for a year. In addition, there were 26 deaths from any cause per 1,000 patients treated for a year with Uloric® compared to 22 deaths per 1,000 patients treated for a year with allopurinol. This safety trial was also discussed at a public Advisory Committee meeting of outside experts on January 11, 2019. To help the FDA track safety issues with medicines, the FDA urges patients and health care professionals to report side effects involving Uloric® or other medicines to the FDA MedWatch program.

## Safety Announcements

### Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz®, Xeljanz XR®) in rheumatoid arthritis patients; FDA to investigate

**[02-25-2019]** The FDA is alerting the public that a safety clinical trial found an increased risk of blood clots in the lungs and death when a 10mg twice daily dose of tofacitinib (Xeljanz®, Xeljanz XR®) was used in patients with rheumatoid arthritis (RA). The FDA has not approved this 10mg twice-daily dose for RA; this dose is only approved in the dosing regimen for patients with ulcerative colitis.

In this ongoing safety trial required by FDA when it approved tofacitinib for RA, the drug manufacturer, Pfizer, is transitioning patients who were on the high 10mg twice-daily dose to the lower, currently approved dose of 5mg twice daily. This trial will continue and is expected to be completed by the end of 2019. The FDA is working with the manufacturer to evaluate other currently available safety information for tofacitinib and will update the public with any new information based on their ongoing review.

**Health care professionals** should follow the recommendations in the tofacitinib prescribing information for the specific condition they are treating. Patients should be monitored for the signs and symptoms of pulmonary embolism, and advised to seek medical attention immediately if they experience them.

**Patients** should not stop or change their dose of tofacitinib without first talking to their health care professional, as doing so may worsen their condition. Patients taking tofacitinib should seek medical attention immediately if they experience symptoms of a blood clot in their lungs or other unusual symptoms such as:

- Sudden shortness of breath or difficulty breathing
- Chest pain or pain in their back
- Coughing up blood
- Excessive sweating
- Clammy or bluish colored skin

Tofacitinib works by decreasing the activity of the immune system. It was first approved in 2012 to treat adult patients with RA who did not respond well to the medicine methotrexate. In RA, the body attacks its own joints, causing pain, swelling, and loss of function. In 2017, the FDA approved the medicine to treat patients with a second condition, psoriatic arthritis, who did not respond well to methotrexate or other similar medicines called nonbiologic disease-modifying antirheumatic drugs (DMARDs). Psoriatic arthritis is a condition that also

causes joint pain and swelling. In 2018, the FDA approved tofacitinib to treat a condition called ulcerative colitis, which is a chronic, inflammatory bowel disease affecting the colon.
When the FDA first approved tofacitinib, they required a clinical trial among patients with RA to evaluate the risk of heart-related events, cancer, and opportunistic infections with the medicine at 2 doses (10mg twice daily and 5mg twice daily) in combination with methotrexate in comparison to another drug called a tumor necrosis factor (TNF) inhibitor. RA patients in the trial were required to be at least 50 years of age and have at least 1 cardiovascular risk factor. During the most recent analysis of the trial, an external data safety monitoring committee found an increased occurrence of blood clots in the lungs and death in patients treated with tofacitinib 10mg twice daily compared to patients treated with tofacitinib 5mg twice daily or a TNF inhibitor.
To help the FDA track safety issues with medicines, the FDA urges health care professionals and patients to report side effects involving tofacitinib or other medicines to the FDA MedWatch program.

## Current Drug Shortages Index (as of March 4, 2019):

The information provided in this section is provided voluntarily by manufacturers.

| | |
|---|---|
| Abciximab (ReoPro) Injection | ***Currently in Shortage*** |
| Amino Acids | ***Currently in Shortage*** |
| Aminophylline Injection, USP | ***Currently in Shortage*** |
| Asparaginase Erwinia Chrysanthemi (Erwinaze) | ***Currently in Shortage*** |
| Atropine Sulfate Injection | ***Currently in Shortage*** |
| Azithromycin (Azasite) Ophthalmic Solution 1% | ***Currently in Shortage*** |
| Belatacept (Nulojix) Lyophilized Powder for Injection | ***Currently in Shortage*** |
| Bisoprolol Fumarate Tablets | ***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*** |
| Buspirone HCl Tablets | ***Currently in Shortage*** |
| Calcitriol Injection USP 1MCG /ML | ***Currently in Shortage*** |
| Calcium Chloride Injection, USP | ***Currently in Shortage*** |
| Calcium Gluconate Injection | ***Currently in Shortage*** |
| Carbidopa and Levodopa Extended Release Tablets | ***Currently in Shortage*** |
| Cefazolin Injection | ***Currently in Shortage*** |
| Cefepime Injection | ***Currently in Shortage*** |
| Cefotaxime Sodium (Claforan) Injection | ***Currently in Shortage*** |
| Cefotetan Disodium Injection | ***Currently in Shortage*** |
| Cycloserine Capsules, USP | ***Currently in Shortage*** |
| Deferoxamine Mesylate for Injection, USP | ***Currently in Shortage*** |
| Dexamethasone Sodium Phosphate Injection | ***Currently in Shortage*** |
| Dexrazoxane Injection | ***Currently in Shortage*** |
| Dextrose 5% Injection Bags | ***Currently in Shortage*** |
| Dextrose 50% Injection | ***Currently in Shortage*** |
| Diazepam Injection, USP | ***Currently in Shortage*** |
| Diltiazem Hydrochloride | ***Currently in Shortage*** |
| Diltiazem Hydrochloride ER (Twice-a-Day) Capsules | ***Currently in Shortage*** |
| Diphenhydramine Injection | ***Currently in Shortage*** |
| Dobutamine Hydrochloride Injection | ***Currently in Shortage*** |
| Dopamine Hydrochloride Injection | ***Currently in Shortage*** |
| Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution | ***Currently in Shortage*** |
| Dorzolamide Hydrochloride Ophthalmic Solution | ***Currently in Shortage*** |
| Eflornithine Hydrochloride (Vaniqa) Cream | ***Currently in Shortage*** |
| Epinephrine Injection, 0.1 mg/mL | ***Currently in Shortage*** |
| Epinephrine Injection, Auto-Injector | ***Currently in Shortage*** |
| Erythromycin Lactobionate for Injection, USP | ***Currently in Shortage*** |

| | |
|---|---|
| Ethiodized Oil (Lipiodol) Injection | ***Currently in Shortage*** |
| Etoposide Injection | ***Currently in Shortage*** |
| Etoposide Phosphate (Etopophos) Injection | ***Currently in Shortage*** |
| Fentanyl Citrate (Sublimaze) Injection | ***Currently in Shortage*** |
| Fludrocortisone Acetate Tablets | ***Currently in Shortage*** |
| Fluorescein Injection | ***Currently in Shortage*** |
| Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution | ***Currently in Shortage*** |
| Fluorescein Strips | ***Currently in Shortage*** |
| Fluvoxamine ER Capsules | ***Currently in Shortage*** |
| Gemifloxacin Mesylate (Factive) Tablets | ***Currently in Shortage*** |
| Guanfacine Hydrochloride Tablets | ***Currently in Shortage*** |
| Haloperidol Tablets | ***Currently in Shortage*** |
| Heparin Sodium and Sodium Chloride 0.9% Injection | ***Currently in Shortage*** |
| Hydromorphone Hydrochloride Injection, USP | ***Currently in Shortage*** |
| Hydroxyprogesterone Caproate Injection | ***Currently in Shortage*** |
| Imipenem and Cilastatin for Injection, USP | ***Currently in Shortage*** |
| Isocarboxazid Tablets | ***Currently in Shortage*** |
| Ketamine Injection | ***Currently in Shortage*** |
| Ketoprofen Capsules | ***Currently in Shortage*** |
| Ketorolac Tromethamine Injection | ***Currently in Shortage*** |
| L-Cysteine Hydrochloride Injection | ***Currently in Shortage*** |
| Labetalol Hydrochloride 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*** |
| 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*** |
| Lorazepam Injection, USP | ***Currently in Shortage*** |
| Magnesium Sulfate Injection | ***Currently in Shortage*** |
| Methadone Hydrochloride Injection | ***Currently in Shortage*** |
| Methocarbamol Tablets | ***Currently in Shortage*** |
| Methotrexate Sodium Injection | ***Currently in Shortage*** |
| Methyldopa Tablets | ***Currently in Shortage*** |
| Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets | ***Currently in Shortage*** |
| Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension | ***Currently in Shortage*** |
| Metoclopramide Injection, USP | ***Currently in Shortage*** |
| Metronidazole Injection, USP | ***Currently in Shortage*** |
| Morphine Sulfate Injection, USP | ***Currently in Shortage*** |
| Multi-Vitamin Infusion (Adult and Pediatric) | ***Currently in Shortage*** |
| Mupirocin Calcium Nasal Ointment | ***Currently in Shortage*** |
| Nelarabine (Arranon) Injection | ***Currently in Shortage*** |
| Nystatin Oral Suspension | ***Currently in Shortage*** |
| Ondansetron Hydrochloride Injection | ***Currently in Shortage*** |
| Penicillamine (Depen) Titratable Tablets | ***Currently in Shortage*** |
| Penicillin G Procaine Injection | ***Currently in Shortage*** |
| Peritoneal Dialysis Solutions | ***Currently in Shortage*** |
| Phenytoin Sodium Injection, USP | ***Currently in Shortage*** |
| Phosphate Injection Products | ***Currently in Shortage*** |
| Physostigmine Salicylate Injection, USP | ***Currently in Shortage*** |
| Piperacillin and Tazobactam (Zosyn) Injection | ***Currently in Shortage*** |

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|---|---|
| Potassium Chloride Injection | ***Currently in Shortage*** |
| Potassium Phosphate Injection | ***Currently in Shortage*** |
| Procainamide Hydrochloride Injection, USP | ***Currently in Shortage*** |
| Progesterone Injection, USP | ***Currently in Shortage*** |
| Promethazine (Phenergan) Injection | ***Currently in Shortage*** |
| Ranitidine Injection, USP | ***Currently in Shortage*** |
| Remifentanil (Ultiva) Lyophilized Powder for Solution Injection | ***Currently in Shortage*** |
| Ropivacaine Hydrochloride Injection | ***Currently in Shortage*** |
| Sacrosidase (Sucraid) Oral Solution | ***Currently in Shortage*** |
| Sclerosol Intrapleural Aerosol | ***Currently in Shortage*** |
| Scopolamine Transdermal System | ***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 0.9% Injection Bags | ***Currently in Shortage*** |
| Sodium Chloride 23.4% Injection | ***Currently in Shortage*** |
| Sodium Chloride Injection USP, 0.9% Vials and Syringes | ***Currently in Shortage*** |
| Sodium Phosphate Injection | ***Currently in Shortage*** |
| Sterile Talc Powder | ***Currently in Shortage*** |
| Sterile Water | ***Currently in Shortage*** |
| Technetium Tc99m Succimer Injection (DMSA) | ***Currently in Shortage*** |
| Thioridazine Hydrochloride Tablets | ***Currently in Shortage*** |
| Thiothixene Capsules | ***Currently in Shortage*** |
| Timolol Maleate Tablets | ***Currently in Shortage*** |
| Trifluoperazine Hydrochloride Tablets | ***Currently in Shortage*** |
| Valsartan Tablets | ***Currently in Shortage*** |