Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
February 12, 2020
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 – February 12, 2020

DATE: January 30, 2020

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 February meeting.
Material is arranged in order of the agenda.

Call to Order

Public Comment Forum – Appendix A

Action Item – Approval of DUR Board Meeting Minutes – Appendix B

Narrow Therapeutic Index (NTI) Drug List – Appendix C

Update on Medication Coverage Authorization Unit/ADHD Prescription Use in Reproductive-Aged Women – Appendix D

Action Item – Vote to Prior Authorize Ultomiris® (Ravulizumab-cwvz) – Appendix E

Action Item – Vote to Prior Authorize Korlym® (Mifepristone) – Appendix F

Action Item – Vote to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) and to Update the Prior Authorization Criteria for Fasenra® (Benralizumab) and Nucala® (Mepolizumab) – Appendix G

Action Item – Vote to Prior Authorize Rocklatan™ (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution) – Appendix H

Action Item – Vote to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran) – Appendix I

Action Item – Vote to Prior Authorize Ruzurgi® (Amifampridine) – Appendix J

Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti™ (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib) – Appendix K

30-Day Notice to Prior Authorize Azedra® (Iobenguane I-131) – Appendix L

Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] – Appendix M

Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant) – Appendix N

Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Xcopri® (Cenobamate) – Appendix O

Annual Review of Osteoporosis Medications 30-Day Notice to Prior Authorize Evenity® (Romosozumab-aqqg) – Appendix P

Annual Review of Inhaled Short-Acting Beta$_2$ Agonists and 30-Day Notice to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) – 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 – February 12, 2020 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Skrepnek

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum – See Appendix A

A. Acknowledgment of Speakers for Public Comment
B. Changes to Public Comment Procedure

Items to be presented by Dr. Muchmore, Chairman:

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

A. December 11, 2019 DUR Minutes – Vote
B. December 11, 2019 DUR Recommendations Memorandum
C. January 8, 2020 DUR Recommendations Memorandum

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

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

A. NTI Drug List

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

5. Update on Medication Coverage Authorization Unit/ADHD Prescription Use in Reproductive-Aged Women – See Appendix D

A. Pharmacy Helpdesk Activity for January 2020
B. Medication Coverage Activity for January 2020
C. ADHD Prescription Use in Reproductive-Aged Women

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

6. Action Item – Vote to Prior Authorize Ultomiris® (Ravulizumab-cwvz) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Korlym® (Mifepristone) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) and to Update the Prior Authorization Criteria for Fasenra® (Benralizumab) and Nucala® (Mepolizumab) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution) – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran) – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Ruzurgi® (Amifampridine) – See Appendix J

A. Introduction
B. College of Pharmacy Recommendations

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

12. Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti™ (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib) – See Appendix K

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

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

13. 30-Day Notice to Prior Authorize Azedra® (Iobenguane I-131) – See Appendix L

A. Introduction
B. Market News and Updates
C. Azedra® (Iobenguane I-131) Product Summary
D. Recommendations

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

14. Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Factor Replacement Products
C. Prior Authorization of Factor Replacement Products
D. Market News and Updates
E. Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] Product Summary
F. Recommendations
G. Utilization Details of Factor Replacement Products

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

15. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Tosymra™ (Sumatriptan Nasal Spray) Product Summary
F. Reyvow™ (Lasmiditan Tablets) Product Summary
G. Ubrelvy™ (Ubrogepant Tablets) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Anti-Migraine Medications

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

16. Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Xcopri® (Cenobamate) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Anticonvulsants
C. Prior Authorization of Anticonvulsants
D. Market News and Updates
E. Xcopri® (Cenobamate) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anticonvulsants

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

17. Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Evenity® (Romosozumab-aqqg) – 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. Evenity® (Romosozumab-aqqg) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Osteoporosis Medications

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

18. Annual Review of Inhaled Short-Acting Beta$_2$ Agonists and 30-Day Notice to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) – See Appendix Q

A. Current Prior Authorization Criteria
B. Utilization of Inhaled Short-Acting Beta$_2$ Agonists
C. Prior Authorization of Inhaled Short-Acting Beta$_2$ Agonists
D. Market News and Updates
E. ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Inhaled Short-Acting Beta$_2$ Agonists

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

19. 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:

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

A. Multiple Sclerosis Medications
B. Lymphoma Medications
C. Anti-parasitic Medications
D. Anti-emetic Medications

**Future business subject to change.*

21. Adjournment

Appendix A

Changes to Public Comment Procedure

Oklahoma Health Care Authority
February 2020

Public Comment Procedure

Effective January 2020 the following procedures were applied for those who wish to provide public comment at the Oklahoma Health Care Authority (OHCA) Drug Utilization Review (DUR) Board meetings:

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing once the DUR Board agenda has been posted and no later than 24 hours before the meeting. This allows for a 4-day window to sign up.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.
- To sign up for public comment, email DURPublicComment@okhca.org and complete the required testimony registration form PHARM-138 which can be found on the SoonerCare pharmacy forms website (www.okhca.org/rxforms).

Appendix B

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF DECEMBER 11, 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	
Megan A. Hanner, D.O.	x	
Lynn Mitchell, M.D.; Vice Chairwoman	x	
John Muchmore, M.D.; Ph.D.; Chairman	x	
Lee Munoz, D.Ph.		x
James Osborne, Pharm.D.	x	

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	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	
Amy Miller, Operations Coordinator	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Grant H. Skrepnek, Ph.D.; Associate Professor; Interim Director	x	
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Tri Van, Pharm.D.; Pharmacy Resident	x	
Graduate Students: Matthew Dickson, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): Justin Wilson	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		x
Marlene Asmussen, R.N.; Population Care Management Director		x
Ellen Buettner, Chief of Staff		x
Kevin Corbett, C.P.A.; Chief Executive Officer		x
Terry Cothran, D.Ph.; Pharmacy Director	x	
Susan Eads, J.D.; Director of Litigation	x	
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director		x
Thomas Nunn, D.O.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Medical Director	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Don Nopper, Dova	Lee Stout, Chiesi	Burl Beasley, EGID-HealthChoice
Jim Dunlap, PhRMA	Frances Bauman, Novo Nordisk	Gina, Heinen, Novo Nordisk
Dave Poskey, UCB	Cris Valladares, BMS	Brian Maves, Pfizer
Marc Parker, Sunovion	Aaron Shaw, Boehringer Ingelheim	Rick Dabner, Alnylon
Aileen Chi, Dova		

PRESENT FOR PUBLIC COMMENT:	
Aileen Chi	Dova

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA ITEM NO. 12 AILEEN CHI

ACTION: NONE REQUIRED

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

3A: NOVEMBER 13, 2019 DUR MINUTES – VOTE

3B: NOVEMBER 13, 2019 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: MAINTENANCE DRUG LIST

4A: MAINTENANCE DRUG LIST – VOTE

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ATOPIC DERMATITIS PRESCRIBER SPECIALTY ANALYSIS

5A: PHARMACY HELPDESK ACTIVITY FOR NOVEMBER 2019

5B: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2019

5C: ATOPIC DERMATITIS PRESCRIBER SPECIALTY ANALYSIS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE ETICOVO™ (ETANERCEPT-YKRO), HADLIMA™ (ADALIMUMAB-BWWD), HYRIMOZ™ (ADALIMUMAB-ADAZ), RINVOQ™ (UPADACITINIB), AND SKYRIZI™ (RISANKIZUMAB-RZAA)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ELZONRIS® (TAGRAXOFUSP-ERZS) AND INREBIC® (FEDRATINIB)

7A: INTRODUCTION

7B: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE AEMCOLO™ (RIFAMYCIN), MOTEGRITY™ (PRUCALOPRIDE), ZELNORM™ (TEGASEROD), AND IBSRELA® (TENAPANOR)

8A: INTRODUCTION

8B: 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. 9: VOTE TO PRIOR AUTHORIZE DRIZALMA SPRINKLE™ [DULOXETINE DELAYED-RELEASE (DR) CAPSULES], SPRAVATO™ (ESKETAMINE NASAL SPRAY), AND CITALOPRAM 20MG/10ML, ESCITALOPRAM 10MG/10ML, AND FLUOXETINE 20MG/5ML (UNIT DOSE CUPS)

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE BEVYXXA® (BETRIXABAN) AND TO UPDATE THE CURRENT XARELTO® (RIVAROXABAN) PRIOR AUTHORIZATION CRITERIA

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE AVACLYR™ (ACYCLOVIR 3% OPHTHALMIC OINTMENT)

11A: INTRODUCTION

11B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Van

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF THROMBOCYTOPENIA MEDICATIONS

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF THROMBOCYTOPENIA MEDICATIONS

12C: PRIOR AUTHORIZATION OF THROMBOCYTOPENIA MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: COLLEGE OF PHARMACY RECOMMENDATIONS

12F: UTILIZATION DETAILS OF THROMBOCYTOPENIA MEDICATIONS

Materials included in agenda packet; presented by Dr. Abbott

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DUAKLIR® PRESSAIR® (ACLIDINIUM BROMIDE/FORMOTEROL FUMARATE)

13A: CURRENT PRIOR AUTHORIZATION CRITERIA

13B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

13C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

13D: MARKET NEWS AND UPDATES

13E: DUAKLIR® PRESSAIR® (ACLIDINIUM/FORMOTEROL FUMARATE) PRODUCT SUMMARY

13F: COLLEGE OF PHARMACY RECOMMENDATIONS

13G: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
13H: UTILIZATION DETAILS OF INHALED CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: 30-DAY NOTICE TO PRIOR AUTHORIZE SCENESSE® (AFAMELANOTIDE) AND GIVLAARI™ (GIVOSIRAN)
14A: INTRODUCTION
14B: MARKET NEWS AND UPDATES
14C: SCENESSE® (AFAMELANOTIDE) PRODUCT SUMMARY
14D: GIVLAARI™ (GIVOSIRAN) PRODUCT SUMMARY
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF SOLIRIS® (ECULIZUMAB) AND 30-DAY NOTICE TO PRIOR AUTHORIZE ULTOMIRIS® (RAVULIZUMAB-CWVZ)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF SOLIRIS® (ECULIZUMAB)
15C: PRIOR AUTHORIZATION OF SOLIRIS® (ECULIZUMAB)
15D: MARKET NEWS AND UPDATES
15E: ULTOMIRIS® (RAVULIZUMAB-CWVZ) PRODUCT SUMMARY
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF MUSCULAR DYSTROPHY MEDICATIONS
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF MUSCULAR DYSTROPHY MEDICATIONS
16C: PRIOR AUTHORIZATION OF MUSCULAR DYSTROPHY MEDICATIONS
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Mitchell moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF CARBAGLU® (CARGLUMIC ACID)
17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF CARBAGLU® (CARGLUMIC ACID)
17D: PRIOR AUTHORIZATION OF CARBAGLU® (CARGLUMIC ACID)
17E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: INDUSTRY NEWS AND UPDATES
18A: INTRODUCTION
18B: NEWS AND UPDATES
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

NO LIVE MEETING SCHEDULED FOR JANUARY. JANUARY 2020 WILL BE A PACKET ONLY MEETING.

20A: REVCOVI® (ELAPEGADEMASE-LVLR)

20B: GAMIFANT® (EMAPALUMAB-LZSG)

20C: GLAUCOMA MEDICATIONS

20D: INSOMNIA MEDICATIONS

20E: FIRDAPSE® (AMIFAMPRIDINE)

20F: KORLYM® (MIFEPRISTONE)

**Future business subject to change.*

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: **ADJOURNMENT**

The meeting was adjourned at 4:59pm.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: December 12, 2019

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

Terry Cothran, D.Ph.
Pharmacy Director
OHCA

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of December 11, 2019

Recommendation 1: Maintenance Drug List

MOTION CARRIED by unanimous approval.

The College of Pharmacy, in partnership with the OHCA, recommends the addition of the following categories of medications to the maintenance drug list:

- Alzheimer's Medications
- Anticonvulsants
- Antidepressants
- Antihypertensive Medications
- Antipsychotic Medications
- Anti-Ulcer Medications
- Cardiovascular Medications
- Chronic Obstructive Pulmonary Disease (COPD) Medications
- Diabetes Medications
- Glaucoma Medications
- Hyperlipidemia Medications
- Immunosuppressant/Transplant Medications
- Parkinson's Disease Medications

Recommendation 2: Atopic Dermatitis Prescriber Specialty Analysis

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Eticovo™ (Etanercept-ykro), Hadlima™ (Adalimumab-bwwd), Hyrimoz™ (Adalimumab-adaz), Rinvoq™ (Upadacitinib), and Skyrizi™ (Risankizumab-rzaa)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Eticovo™ (etanercept-ykro), Hadlima™ (adalimumab-bwwd), Hyrimoz™ (adalimumab-adaz), Rinvoq™ (upadacitinib), and Skyrizi™ (risankizumab-rzza) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply.

Targeted Immunomodulator Agents Tier-2 Approval Criteria:

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

Targeted Immunomodulator Agents Tier-3 Approval Criteria:

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

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	**adalimumab-adaz (Hyrimoz™)**
hydroxychloroquine		adalimumab-adbm (Cyltezo™)
leflunomide		adalimumab-atto (Amjevita™)
mesalamine		**adalimumab-bwwd (Hadlima™)**
methotrexate		alefacept (Amevive®)
minocycline		anakinra (Kineret®)
NSAIDs		apremilast (Otezla®)β
oral corticosteroids		baricitinib (Olumiant®)
		brodalumab (Siliq™)
		canakinumab (Ilaris®)¥
		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi™)

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
		etanercept-ykro (Eticovo™)
		golimumab (Simponi® & Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-abda (Renflexis™)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		risankizumab-rzza (Skyrizi™)
		rituximab (Rituxan®)~
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®)Ω
		tildrakizumab-asmn (Ilumya™)
		tocilizumab (Actemra®)π
		tofacitinib (Xeljanz® & Xeljanz® XR)
		upadacitinib (Rinvoq™)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

DMARDs = disease modifying anti-rheumatic drugs; NSAIDs = nonsteroidal anti-inflammatory drugs

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC) if NADAC unavailable. Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

±Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.

+Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) and noninfectious intermediate and posterior uveitis and panuveitis.

βUnique criteria applies for a diagnosis of Behçet's disease (BD).

¥Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF).

~Unique criteria applies for a diagnosis of pemphigus vulgaris (PV), granulomatosis with polyangiitis (GPA), and microscopic polyangiitis (MPA).

ΩFor Cosentyx® (secukinumab) only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).

πUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome (CRS).

Additionally, the College of Pharmacy recommends the following criteria for Otezla® (apremilast) for the treatment of ulcers associated with Behçet's Disease (BD) and Rituxan® (rituximab) for the treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA):

Otezla® (Apremilast) Approval Criteria [Behçet's Disease (BD) Diagnosis]:

1. An FDA approved indication for the treatment of oral ulcers associated with BD; and
2. Member must have had oral ulcers at least 3 times in the last 12 month period; and
3. Member must have had a 2 week trial of the following that resulted in inadequate efficacy or intolerable adverse effects (or be contraindicated for the member):
   a. Topical corticosteroids (applied topically to the mouth); and
   b. Colchicine; and
4. Quantity limits according to package labeling will apply.

Rituxan® (Rituximab) Approval Criteria [Granulomatosis With Polyangiitis (GPA, Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) Diagnosis]:

1. An FDA approved diagnosis of GPA or MPA in adult and pediatric members 2 years of age and older; and
2. Rituxan® must be used in combination with corticosteroids; and
3. Approval quantity will be based on Rituxan® prescribing information and FDA approved dosing regimen(s).

Lastly, the College of Pharmacy recommends updating the prior authorization criteria for Humira® (adalimumab) when used for uveitis and Benlysta® (belimumab) based on new FDA approvals. The following criteria will apply (changes and additions noted in red):

Benlysta® (Belimumab) Approval Criteria:

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

Humira® (Adalimumab) Approval Criteria [Noninfectious Intermediate and Posterior Uveitis or Panuveitis Diagnosis]:

1. A diagnosis of noninfectious intermediate uveitis, posterior uveitis, or panuveitis in ~~adults~~ members 2 years of age and older; and
2. A failed trial with a corticosteroid injection or systemic corticosteroid in which member has had an inadequate response; or
3. A patient-specific, clinically significant reason a trial of corticosteroid treatment is inappropriate for the member must be provided.

Recommendation 4: Vote to Prior Authorize Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)

MOTION CARRIED by unanimous approval.

Elzonris® (Tagraxofusp-erzs) Approval Criteria [Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) Diagnosis]:

1. Diagnosis of BPDCN; and
2. Member must be 2 years of age or older; and

3. Must be used as a single-agent.

Inrebic® (Fedratinib) Approval Criteria [Myelofibrosis Diagnosis]:

1. Diagnosis of myelofibrosis in adult members; and
2. Intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia).

Recommendation 5: Vote to Prior Authorize Aemcolo™ (Rifamycin), Motegrity™ (Prucalopride), Zelnorm™ (Tegaserod), and Ibsrela® (Tenapanor)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Aemcolo™ (rifamycin), Motegrity™ (prucalopride), Zelnorm™ (tegaserod), and Ibsrela® (tenapanor) with the following criteria:

Aemcolo™ (Rifamycin) Approval Criteria:

1. An FDA approved diagnosis of travelers' diarrhea; and
2. Member must be 18 years of age or older; and
3. Travelers' diarrhea must be due to non-invasive strains of *Escherichia coli*; and
4. A patient-specific, clinically significant reason why the member cannot use Xifaxan® (rifaximin) oral tablets must be provided; and
5. A quantity limit of 12 tablets per 3 days will apply.

Motegrity™ (Prucalopride) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. A patient-specific, clinically significant reason why member cannot use Linzess® (linaclotide), Amitiza® (lubiprostone), or Trulance® (plecanatide) must be provided; and
6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
7. A quantity limit of 30 tablets per 30 days will apply.

Zelnorm™ (Tegaserod) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with constipation (IBS-C) in female members 18 to 64 years of age; and

2. Member must be female for authorization of Zelnorm™ (the safety and effectiveness of Zelnorm™ in men with IBS-C have not been established); and
3. Member must not have any of the contraindications for use of Zelnorm™ [i.e., history of myocardial infarction (MI), stroke, transient ischemic attack (TIA), or angina; history of ischemic colitis or other forms of intestinal ischemia; severe renal impairment (estimated glomerular filtration rate {eGFR} <15mL/min/1.73m^2) or end-stage renal disease (ESRD); moderate or severe hepatic impairment (Child-Pugh B or C); history of bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions; hypersensitivity to tegaserod]; and
4. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
5. Documented and updated colon screening for members older than 50 years of age; and
6. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
8. Approval will initially be for 6 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment. Zelnorm™ should be discontinued in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment; and
9. A quantity limit of 60 tablets per 30 days will apply.

Ibsrela® (Tenapanor) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
7. A quantity limit of 60 tablets per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the current approval criteria for Symproic® (naldemedine) based on net costs (changes noted in red):

Symproic® (Naldemedine) Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
8. Symproic® must be discontinued if treatment with the opioid pain medication is also discontinued; and
9. A quantity limit of 30 tablets per 30 days will apply.

Recommendation 6: Vote to Prior Authorize Drizalma Sprinkle™ [Duloxetine Delayed-Release (DR) Capsules], Spravato™ (Esketamine Nasal Spray), and Citalopram 20mg/10mL, Escitalopram 10mg/10mL, and Fluoxetine 20mg/5mL (Unit Dose Cups)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Drizalma Sprinkle™ [duloxetine delayed-release (DR) capsules] into the Special Prior Authorization (PA) Tier of the Antidepressants Product Based Prior Authorization (PBPA) category. Current Special PA criteria will apply. When Drizalma Sprinkle™ (duloxetine DR capsule) is being requested for non-depression/anxiety-related diagnoses, the criteria below will apply:

Drizalma Sprinkle™ (Duloxetine Delayed-Release Capsule) Approval Criteria [Diabetic Peripheral Neuropathy/Chronic Musculoskeletal Pain Diagnosis]:

1. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and

2. A patient-specific, clinically significant reason why the member cannot use generic duloxetine 20mg, 30mg, or 60mg capsules, which are available without prior authorization, in place of Drizalma Sprinkle™ must be provided; and
3. A quantity limit of 30 capsules per 30 days will apply.

Additionally, the College of Pharmacy recommends the placement of Spravato™ (esketamine nasal spray) into the Special PA Tier of the Antidepressants PBPA category with the following criteria:

Spravato™ (Esketamine Nasal Spray) Approval Criteria:

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

Finally, the College of Pharmacy recommends the placement of citalopram 20mg/10mL, escitalopram 10mg/10mL, and fluoxetine 20mg/5mL unit dose cups into the Special PA Tier of the Antidepressants PBPA category based on Wholesale Acquisition Cost (WAC) with the following criteria:

Citalopram 20mg/10mL, Escitalopram 10mg/10mL, and Fluoxetine 20mg/5mL Unit Dose Cups Approval Criteria:

1. An FDA approved indication; and
2. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			**citalopram 20mg/10mL soln (UDC)**
escitalopram (Lexapro®)			**escitalopram 10mg/10mL soln (UDC)**
fluoxetine caps (Prozac®)			**fluoxetine 20mg/5mL soln (UDC)**
fluvoxamine (Luvox®)			fluoxetine tabs
paroxetine (Paxil®)			fluoxetine DR (Prozac® Weekly™)
sertraline (Zoloft®)			fluvoxamine CR (Luvox CR®)
			paroxetine CR (Paxil CR®)
			paroxetine (Pexeva®)
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	desvenlafaxine (Pristiq®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron® SolTab™)		nefazodone (Serzone®)	duloxetine 40mg (Irenka™)
trazodone 50mg, 100mg, & 150mg tabs (Desyrel®)		vilazodone (Viibryd®)	**duloxetine (Drizalma Sprinkle™)**
venlafaxine (Effexor®, Effexor XR® caps)			trazodone 300mg tabs (Desyrel®)
			venlafaxine ER tabs (Effexor XR® tabs)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	isocarboxazid (Marplan®)
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	**esketamine nasal spray (Spravato™)**

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

Recommendation 7: Vote to Prior Authorize Bevyxxa® (Betrixaban) and to Update the Current Xarelto® (Rivaroxaban) Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Bevyxxa® (betrixaban) with the following criteria:

Bevyxxa® (Betrixaban) Approval Criteria:

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

Additionally, the College of Pharmacy recommends updating the Xarelto® (rivaroxaban) prior authorization criteria based on the new FDA approved indication, with the following changes noted in red:

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; or
    d. In combination with aspirin, to reduce the risk of major cardiovascular (CV) events [CV death, myocardial infarction (MI), and stroke] in members with chronic coronary artery disease (CAD) or peripheral artery disease (PAD); or
    e. Prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding; and
2. For 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. For Xarelto® (rivaroxaban) 10mg:
    a. One prescription for up to ~~35~~ 39 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis in patients following hip or knee replacement surgery or for prophylaxis of VTE in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding; or
4. For 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.

Recommendation 8: Vote to Prior Authorize Avaclyr™ (Acyclovir 3% Ophthalmic Ointment)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Avaclyr™ (acyclovir 3% ophthalmic ointment) with the following criteria:

Avaclyr™ (Acyclovir 3% Ophthalmic Ointment) Approval Criteria:

1. An FDA approved diagnosis of acute herpetic keratitis (dendritic ulcers) in patients with herpes simplex virus (HSV); and
2. A patient-specific, clinically significant reason why the member cannot use trifluridine 1% ophthalmic solution must be provided; and
3. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir must be provided.

Recommendation 9: Annual Review of Thrombocytopenia Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the current prior authorization criteria for Doptelet® (avatrombopag) based on changes in net cost and a new FDA approved indication with the following criteria (changes and additions noted in red):

Doptelet® (Avatrombopag) Approval Criteria [Chronic Liver Disease (CLD) Scheduled to Undergo a Procedure]:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with CLD who are scheduled to undergo a procedure; and
2. ~~A patient-specific, clinically significant reason why the member cannot use Mulpleta® (lusutrombopag); 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; 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. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
9. Prescriber must verify member is not breastfeeding; and
10. A quantity limit of 15 tablets per scheduled procedure will apply.

Doptelet® (Avatrombopag) Approval Criteria [Chronic Immune Thrombocytopenia Diagnosis]:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment; and
2. Member must be 18 years of age or older; and
3. Previous insufficient response with at least 1 of the following treatments:

a. Corticosteroids; or
b. Immunoglobulins; or
c. Splenectomy; and

4. A patient-specific, clinically significant reason why the member cannot use an alternative thrombopoietin (TPO) receptor agonist available without a prior authorization must be provided; and
5. Prescriber must verify the degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
6. Prescriber must verify platelet counts will be assessed weekly until a stable platelet count greater than 50 x 10^9/L has been achieved, and then obtained monthly thereafter; and
7. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
8. Doptelet® must not be used in an attempt to normalize platelet counts; and
9. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
10. Prescriber must verify member is not breastfeeding; and
11. A quantity limit of 60 tablets per 30 days will apply.

Recommendation 10: Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate)

NO ACTION REQUIRED.

Recommendation 11: 30-Day Notice to Prior Authorization Scenesse® (Afamelanotide) and Givlaari™ (Givosiran)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Soliris® (Eculizumab) and 30-Day Notice to Prior Authorize Ultomiris® (Ravulizumab-cwvz)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Muscular Dystrophy Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the current prior authorization criteria for Emflaza® (deflazacort) with the following change noted in red:

Emflaza® (Deflazacort) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD); and
2. Member must be 2 ~~5~~ years of age or older; and
3. Emflaza® must be prescribed by or in consultation with a prescriber who specializes in the treatment of DMD; and
4. Member must have a minimum 6-month trial of prednisone that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with Emflaza®; and

5. A patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed must be provided; and
6. Patients already established on deflazacort via the ACCESS DMD Program must also document a patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed; and
7. For Emflaza® suspension, a patient-specific, clinically significant reason why the member cannot use the tablet formulation in the place of oral suspension even when the tablets are crushed must be provided; and
8. Prescriber must verify the member has had a baseline eye examination; and
9. The member's recent weight must be provided in order to authorize the appropriate amount of drug required according to package labeling; and
10. For the tablets, a quantity limit of 30 tablets per 30 days will apply and for the suspension, a quantity limit of 39mL (3 bottles) per 30 days will apply. Quantity limit requests will be based on the member's recent weight taken within the last 30 days.

Recommendation 14: Annual Review of Carbaglu® (Carglumic Acid)

NO ACTION REQUIRED.

Recommendation 15: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 16: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 17: Future Business

NO ACTION REQUIRED.

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

Memorandum

Date: January 09, 2020

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

Terry Cothran, D.Ph.
Pharmacy Director
OHCA

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Packet Meeting of January 08, 2020

Recommendation 1: SoonerCare Opioid Initiative Update

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Revcovi™ (Elapegademase-lvlr)

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Gamifant® (Emapalumab-lzsg)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Firdapse® (Amifampridine) and 30-Day Notice to Prior Authorize Ruzurgi® (Amifampridine)

NO ACTION REQUIRED.

Recommendation 6: 30-Day Notice to Prior Authorize Korlym® (Mifepristone)

NO ACTION REQUIRED.

Recommendation 7: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 8: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 9: Future Business

NO ACTION REQUIRED.

Appendix C

Narrow Therapeutic Index (NTI) Drug List

Oklahoma Health Care Authority
February 2020

Introduction[1,2,3]

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

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

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

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

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

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

SoonerCare NTI Drug List

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

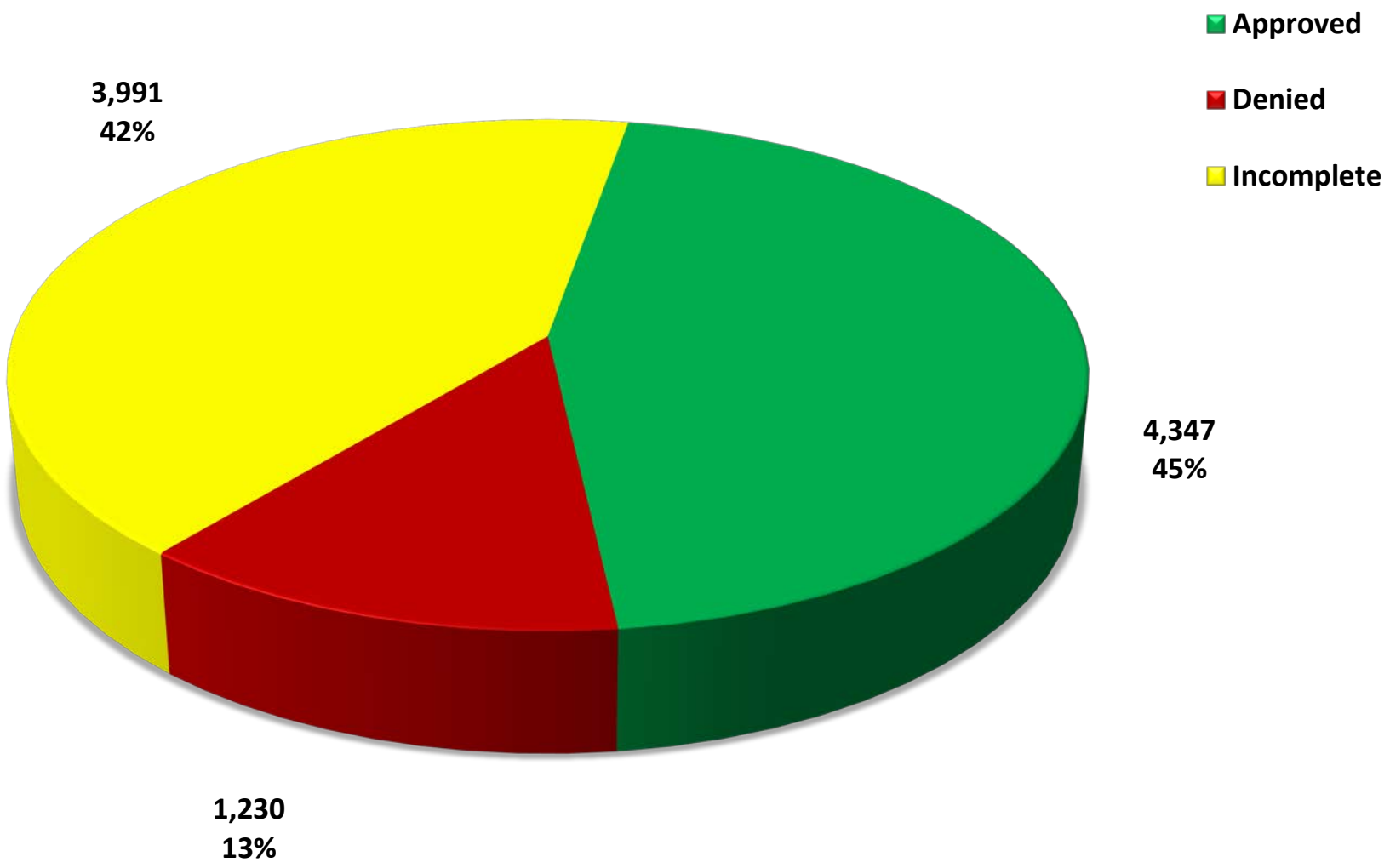
[1] U.S. Food and Drug Administration (FDA). FY2015 Regulatory Science Research Report: Narrow Therapeutic Index Drugs. Available online at: https://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm500577.htm. Last revised 05/09/2017. Last accessed 01/14/2020.

[2] Yu LX. Quality and Bioequivalence Standards for Narrow Therapeutic Index Drugs. FDA. Available online at: https://www.fda.gov/downloads/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/ucm292676.pdf. Issued 2011. Last accessed 01/14/2020.

[3] Jiang W. Building Confidence in Generic Narrow Therapeutic Index (NTI) Drugs. FDA. Available online at: https://www.fda.gov/about-fda/fda-pharmacy-student-experiential-program/building-confidence-generic-narrow-therapeutic-index-nti-drugs. Last revised 09/21/2018. Last accessed 01/14/2020.

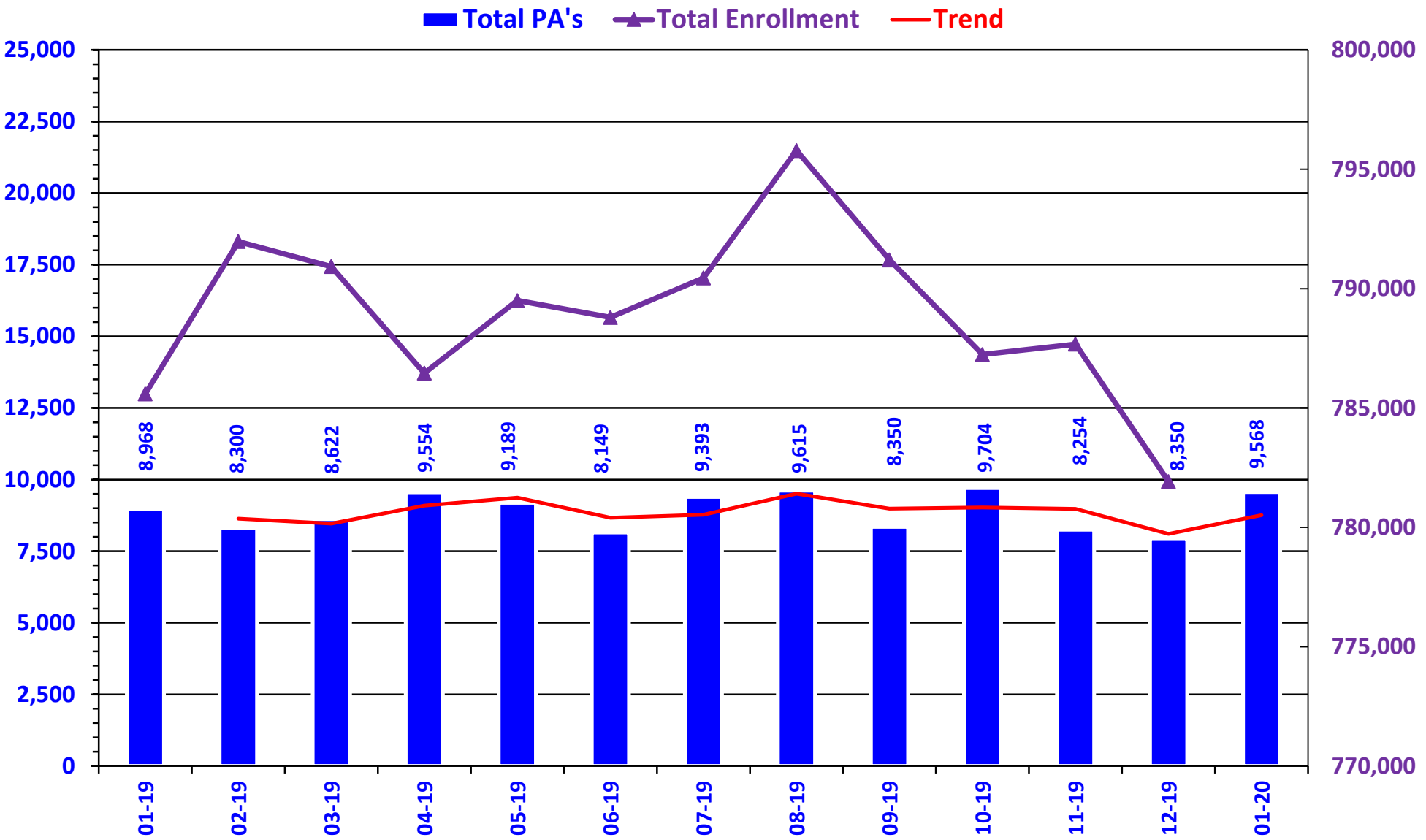
Appendix D

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY 2020



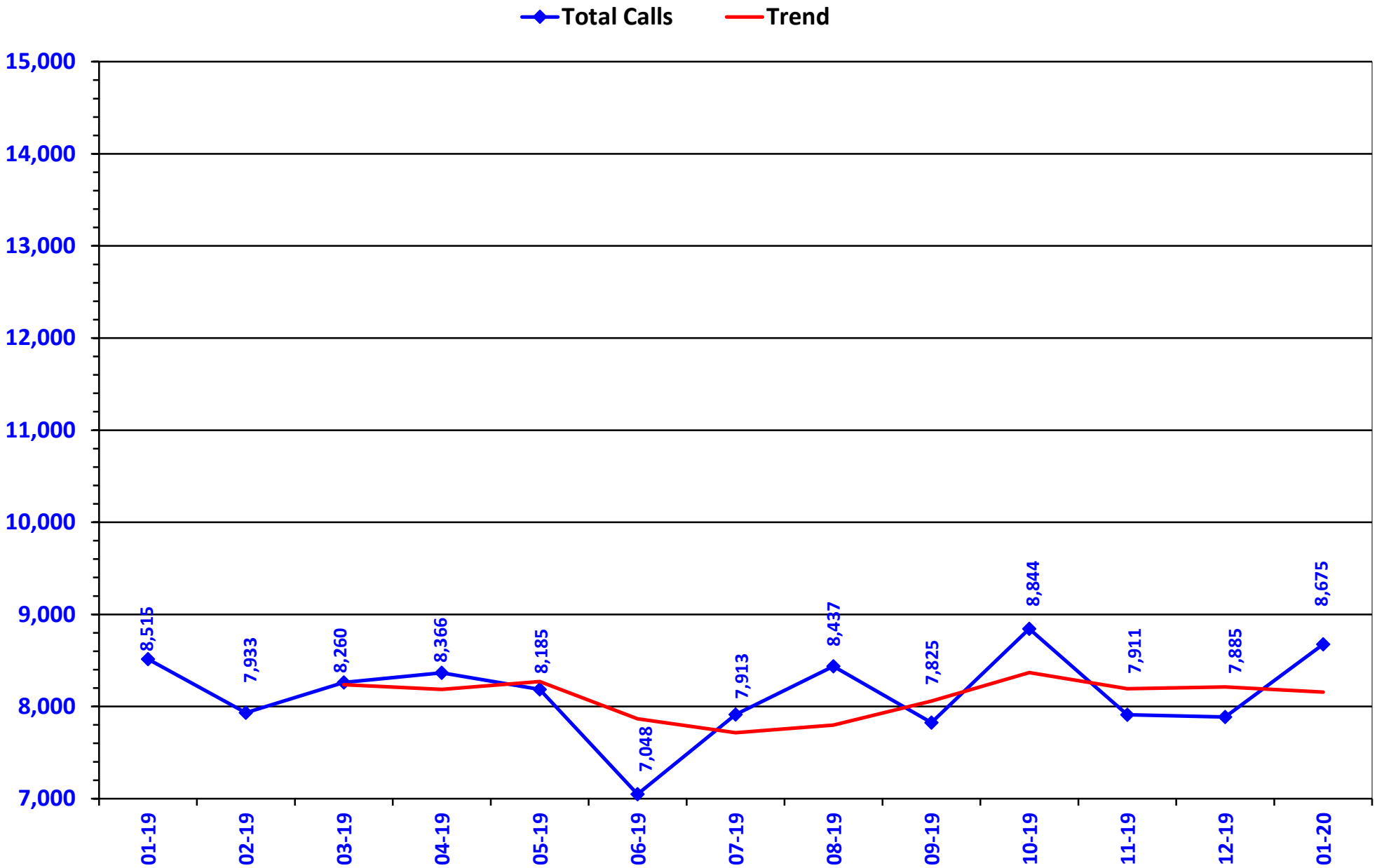
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2019 – JANUARY 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JANUARY 2019 – JANUARY 2020



Prior Authorization Activity

1/1/2020 Through 1/31/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	75	19	13	43	334
Analgesic - NonNarcotic	20	0	3	17	0
Analgesic, Narcotic	450	174	31	245	159
Antiasthma	120	33	24	63	269
Antibiotic	35	15	3	17	282
Anticonvulsant	211	89	23	99	293
Antidepressant	169	38	36	95	344
Antidiabetic	292	98	49	145	347
Antihemophilic Factor	15	11	0	4	244
Antihistamine	16	3	4	9	360
Antimigraine	151	35	48	68	138
Antineoplastic	114	63	11	40	173
Antiparasitic	13	0	5	8	0
Antiulcers	146	36	40	70	127
Anxiolytic	32	3	7	22	237
Atypical Antipsychotics	311	145	34	132	351
Benign Prostatic Hypertrophy	13	1	3	9	359
Biologics	196	101	22	73	257
Bladder Control	44	9	16	19	286
Blood Thinners	361	214	19	128	337
Botox	61	33	19	9	318
Buprenorphine Medications	105	14	4	87	67
Calcium Channel Blockers	14	3	4	7	271
Cardiovascular	71	33	12	26	315
Chronic Obstructive Pulmonary Disease	159	26	36	97	169
Constipation/Diarrhea Medications	184	35	60	89	218
Contraceptive	29	11	7	11	270
Corticosteroid	12	1	4	7	359
Dermatological	335	93	81	161	146
Diabetic Supplies	774	459	67	248	271
Diuretic	10	5	0	5	210
Endocrine & Metabolic Drugs	102	59	5	38	195
Erythropoietin Stimulating Agents	13	9	2	2	95
Fibromyalgia	77	18	0	59	82
Gastrointestinal Agents	135	39	21	75	221
Genitourinary Agents	12	2	4	6	359
Glaucoma	13	3	1	9	156
Growth Hormones	123	83	9	31	149
Hematopoietic Agents	13	4	2	7	198
Hepatitis C	128	79	16	33	8
HFA Rescue Inhalers	79	2	7	70	258
Insomnia	40	3	11	26	145
Insulin	161	55	17	89	324
Miscellaneous Antibiotics	17	2	3	12	16
Multiple Sclerosis	36	13	6	17	133
Muscle Relaxant	62	7	19	36	226
Nasal Allergy	47	6	17	24	177
Neurological Agents	92	26	22	44	263
NSAIDs	56	6	12	38	140
Ocular Allergy	26	1	8	17	84

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	34	7	7	20	360
Other*	278	68	39	171	262
Otic Antibiotic	19	1	2	16	14
Pediculicide	22	6	0	16	9
Respiratory Agents	61	33	5	23	122
Statins	13	1	4	8	359
Stimulant	779	383	71	325	348
Synagis	124	46	19	59	70
Testosterone	83	14	21	48	333
Topical Antifungal	24	5	5	14	91
Topical Corticosteroids	97	1	60	36	26
Vitamin	78	23	34	21	195
Pharmacotherapy	94	80	0	14	271
Emergency PAs	0	0	0	0	
Total	**7,476**	**2,885**	**1,134**	**3,457**	
Overrides					
Brand	53	27	5	21	310
Compound	27	22	0	5	120
Cumulative Early Refill	1	1	0	0	14
Diabetic Supplies	7	6	0	1	74
Dosage Change	360	331	0	29	12
High Dose	2	2	0	0	44
Ingredient Duplication	6	2	0	4	89
Lost/Broken Rx	93	86	1	6	14
MAT Override	223	178	1	44	67
NDC vs Age	338	209	36	93	228
NDC vs Sex	13	10	0	3	105
Nursing Home Issue	42	34	1	7	12
Opioid MME Limit	140	62	8	70	97
Opioid Quantity	29	17	4	8	146
Other	44	37	1	6	14
Quantity vs. Days Supply	638	394	35	209	247
STBS/STBSM	22	10	3	9	69
Step Therapy Exception	2	2	0	0	361
Stolen	1	1	0	0	36
Third Brand Request	51	31	1	19	38
Overrides Total	**2,092**	**1,462**	**96**	**534**	
Total Regular PAs + Overrides	**9,568**	**4,347**	**1,230**	**3,991**	

Denial Reasons	
Unable to verify required trials.	3,147
Does not meet established criteria.	1,262
Lack required information to process request.	794
Other PA Activity	
Duplicate Requests	661
Letters	15,106
No Process	7
Changes to existing PAs	802
Helpdesk Initiated Prior Authorizations	830
PAs Missing Information	17

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

ADHD Prescription Use in Reproductive-Aged Women

Oklahoma Health Care Authority
February 2020

Introduction[1,2,3]

Medication use for the treatment of attention-deficit/hyperactivity disorder (ADHD) is on the rise and the safety of ADHD medication use during pregnancy remains unclear. It has been reported that half of the pregnancies in the United States are unintended, and ADHD medication use in these women could result in unnecessary risk to the fetus. In a study done by the Centers for Disease Control and Prevention (CDC), pharmacy claims data for privately insured women 15 to 44 years of age were analyzed to look at trends of ADHD prescriptions filled from 2003 to 2015. From 2003 to 2015, the number of women who filled at least 1 ADHD medication increased by 344%. A majority of the increase was due to stimulant medications. Use of non-stimulant medications, such as atomoxetine, was stable over the study time frame. The largest increase of ADHD medications occurred in the 25 to 29 year old age group, which rose 700% from 2003 to 2015. It is important to note that the data used did not include what indication the medication was used for, if the women were pregnant, or the incidence of pregnancy.

In August 2019, the College of Pharmacy in partnership with the Oklahoma Health Care Authority (OHCA) sent an education letter to 355 prescribers accounting for 3,296 patients with at least 2 claims for an ADHD medication from June 2019 through August 2019. The letter highlighted details of the aforementioned CDC study and recommended creating a treatment plan for a patient's medical conditions prior to pregnancy in order to minimize risks to the patient and the baby. In addition, the letter recommended consulting the CDC's *Treating for Two* initiative as an important reference in managing health conditions in women of reproductive potential.

SoonerCare Claims Analysis

The following claims analysis for calendar year (CY) 2015 to CY 2019 was conducted by the University of Oklahoma College of Pharmacy. The results were compiled by loosely following the methodology of the CDC study discussed in the introduction section of this report. Female members 15 to 44 years of age were included in the analysis.

ADHD Medication Usage in Women of Reproductive Age: CY 2015 to CY 2019[1]

The CDC analyzed pharmacy claims data from the Truven Health MarketScan Commercial Database from 2003 to 2015. The data was a collection of private, employer-sponsored insurance, including dependents, across the United States. Analysis was restricted to women 15 to 44 years of age, resulting in a sample size of 2.3 to 6.8 million each year (median = 4.6 million). SoonerCare pharmacy claims were analyzed from CY 2015 to CY 2019. Similar to the

CDC study, the SoonerCare claims analysis was restricted to female members 15 to 44 years of age, resulting in a sample size of 165,865 to 224,144 (median = 216,048).

Results of the CDC analysis found a 344% increase from 2003 (0.9% of women) to 2015 (4.0% of women) in the percentage of reproductive-aged women (15 to 44 years of age) who filled at least 1 ADHD prescription. While SoonerCare data did show an increase in the same population from 2015 to 2019, the total percentage of reproductive-aged women who filled at least 1 ADHD prescription peaked at 2.6% in CY 2016 and declined to 2.1% in CY 2019. The percentage change from 2015 to 2019 was 13.7%, and did not consistently increase from year to year as the CDC trend results revealed.

The following is a table of the percentage of female SoonerCare members 15 to 44 years of age with a paid claim for an ADHD medication by age group and calendar year. All age groups in the SoonerCare analysis had a lower percentage of women with ADHD medication paid claims as compared to the CDC analysis during the overlapping year of 2015.

Percentage of Women 15 to 44 Years of Age With ADHD Medication Paid Claim(s)						
Age Group (Years)	**CDC 2015**	**SC 2015**	**SC 2016**	**SC 2017**	**SC 2018**	**SC 2019**
15 to 19	5.4%	3.8%	5.1%	4.2%	4.3%	4.2%
20 to 24	5.5%	0.8%	1.0%	0.7%	0.8%	0.8%
25 to 29	4.0%	0.9%	1.4%	1.0%	1.0%	1.0%
30 to 34	3.3%	1.2%	1.9%	1.4%	1.4%	1.4%
35 to 39	3.0%	1.3%	2.0%	1.4%	1.6%	1.5%
40 to 44	2.9%	1.1%	1.7%	1.4%	1.4%	1.9%
Number of Women Included	**CDC 2015**	**SC 2015**	**SC 2016**	**SC 2017**	**SC 2018**	**SC 2019**
Number of Women Included	4,580,924	223,998	165,865	224,144	216,048	215,756

ADHD = attention-deficit/hyperactivity disorder; CDC = Centers for Disease Control and Prevention; SC = SoonerCare

The following table contains the number of women of reproductive age with at least 1 paid claim for an ADHD medication per year and the average number of ADHD medication paid claims per member per year. The CDC analysis found an average of 7.2 paid claims per member per year while the SoonerCare analysis revealed 6.2 paid claims per member per year during the overlapping year of 2015. Despite an increase from CY 2015 to CY 2019, the CY 2019 SoonerCare average number of ADHD medication paid claims per member per year still remained less than the CDC average for 2015.

Number of Women with ≥1 ADHD Medication Paid Claim(s) Per Year and Average Number of ADHD Medication Paid Claim(s) Per Member Per Year						
Parameter	**CDC 2015**	**SC 2015**	**SC 2016**	**SC 2017**	**SC 2018**	**SC 2019**
# of Women* with ≥1 Paid Claim(s)	183,053	4,067	4,323	4,481	4,545	4,464
Average # of Paid Claims PMPY	7.2	6.2	6.4	6.5	6.4	6.5

ADHD = attention-deficit/hyperactivity disorder; CDC = Centers for Disease Control and Prevention; SC = SoonerCare
# = number; PMPY = per member per year
*Includes women of reproductive age (15 to 44 years of age)

Conclusions[1]

While stimulant use has increased in female SoonerCare members of reproductive age over the last 5 years, it does not appear to have increased at the rate of a large national study. Comparison is limited as the study time frames are different; however, the overlapping year of 2015 allows for some assessment. During 2015, the SoonerCare percentage (1.8%) of female members of reproductive age with a claim for an ADHD medication was less than half of the CDC percentage (4.0%). A lower percentage of ADHD medication claims in female members of reproductive age was consistent across all age groups. Additionally, the average number of paid claims per member per year was lower in the SoonerCare population (CDC: 7.2 vs. SoonerCare: 6.2). Numbers were consistent despite the inclusion of additional medications in the SoonerCare analysis that were not included in the CDC analysis [non-stimulant medications (clonidine extended-release {ER} and guanfacine ER) and narcolepsy medications (modafinil, armodafinil, and sodium oxybate)]. These results may be indicative of appropriate management of ADHD medications in the SoonerCare population. The College of Pharmacy will continue to monitor appropriate stimulant use in this population and make recommendations to the Drug Utilization Review (DUR) Board where appropriate.

[1] Anderson KN, Ailes EC, Danielson M, et al. Attention-Deficit/Hyperactivity Disorder Medication Prescription Claims Among Privately Insured Women Aged 15–44 Years — United States, 2003–2015. *MMWR* 2018; 67:66-70.
[2] National Institute of Mental Health. Attention Deficit Hyperactivity Disorder. Available online at: https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml. Issued 09/2019. Last accessed 01/16/2020.
[3] Brooks M. ADHD Prescriptions Skyrocket Among Young Women. *Medscape*. Available online at: https://www.medscape.com/viewarticle/891501?nlid=120168_745&src=WNL_mdplsfeat_180123_mscpedit_phar&uac=163910MN&spon=30&impID=1540890&faf=1. Issued 01/18/2018. Last accessed 01/16/2020.

Appendix E

Vote to Prior Authorize Ultomiris® (Ravulizumab-cwvz)

Oklahoma Health Care Authority
February 2020

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

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

- **Ultomiris® (ravulizumab-cwvz) for Paroxysmal Nocturnal Hemoglobinuria (PNH):** In December 2018, the FDA approved Ultomiris® (ravulizumab), the first long-acting complement inhibitor administered every 8 weeks, for the treatment of adult patients with PNH. PNH is a chronic, progressive, debilitating, and life-threatening ultra-rare blood disorder characterized by hemolysis that is mediated by an uncontrolled activation of the complement system. PNH has an average age of onset in the early 30s and occurs in both men and women. Patients with PNH may experience a wide range of signs and symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine, and anemia. Hallmark symptoms of PNH include thrombosis, which can occur in blood vessels throughout the body, damage vital organs, and cause premature death. Despite historical supportive care, including transfusion and anticoagulation management, 20 to 35% of patients with PNH die within 5 to 10 years of diagnosis. Prior to FDA approval of ravulizumab, Soliris® (eculizumab) was the primary treatment for PNH. Eculizumab treatment requires biweekly infusions in contrast to ravulizumab which is dosed every 8 weeks.
- **Soliris® (eculizumab) for Neuromyelitis Optica Spectrum Disorder (NMOSD):** In June 2019, the FDA approved Soliris® (eculizumab), a complement inhibitor, for the treatment of adults with NMOSD who are anti-aquaporin-4 (AQP4) antibody positive. Eculizumab is the first FDA-approved treatment for the treatment of NMOSD. NMOSD is an inflammatory disorder of the central nervous system (CNS) characterized by demyelination and axonal damage predominately targeting the optic nerves and spinal cord. Typical presentation of NMOSD includes attacks of optic neuritis, which result in ocular pain and vision loss; patients also commonly have attacks resulting in transverse myelitis and subsequent numbness, weakness, or paralysis of the arms and legs. Attacks can occur in groupings, followed by partial recovery during periods of remission. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. NMOSD can be associated with antibodies that bind to the AQP4 protein; this binding appears to activate other components of the immune system, causing inflammation and damage to the CNS. NMOSD is believed to affect 4,000 to 8,000 patients in the United States. The effectiveness of eculizumab for the treatment of NMOSD was demonstrated in a study of 143 patients with NMOSD who had AQP4 antibodies who were randomized to receive either eculizumab or placebo. Compared with placebo, treatment with eculizumab reduced the number of NMOSD relapses by 94% over 48 weeks [annualized relapse rates for the eculizumab and placebo groups were 0.02 and 0.35, respectively; absolute risk reduction 33%; rate ratio 0.04; 95% confidence interval (CI) 0.01 to 0.15]. Eculizumab also reduced the need for hospitalizations and the need for treatment of acute attacks with corticosteroids and

plasma exchange. Eculizumab was previously FDA approved for the treatment of patients with PNH to reduce hemolysis, for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA), and for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive.

- **Ultomiris® (ravulizumab-cwvz) for aHUS:** In October 2019, the FDA approved Ultomiris® (ravulizumab), a complement inhibitor, for the treatment of aHUS to inhibit complement-mediated TMA for patients 1 month of age and older. aHUS is a rare disease that can affect both children and adults and can lead to potentially irreversible damage to the kidneys and other vital organs, resulting in kidney failure (requiring dialysis or transplant) and premature death. aHUS is characterized by inflammation and the formation of blood clots in small blood vessels throughout the body (TMA) mediated by chronic, uncontrolled activation of the complement system. TMA consists of thrombocytopenia, hemolytic anemia, and acute kidney injury (AKI). If left untreated, significant proportions of adults (46%) and children (16%) can progress to end-stage renal disease (ESRD) or death. Ravulizumab was previously FDA approved for the treatment of adults with PNH.

Cost Comparison:

Medication	Cost Per Vial	Cost for 8 Weeks of Therapy
Ultomiris® (ravulizumab) 300mg/30mL vial	**$6,404.10**	**$70,445.10**
Soliris® (eculizumab) 300mg/30mL vial	$6,522.90	$104,366.40

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC) if NADAC unavailable.
Dosing based on recommended maintenance treatment doses for atypical hemolytic uremic syndrome (aHUS) in a 75kg adult patient.
Cost for 8 weeks of therapy based on maintenance treatment dosing after initial dosing is complete.

Recommendations

The College of Pharmacy recommends the following criteria for Soliris® (eculizumab) for the treatment of neuromyelitis optica spectrum disorder:

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

1. An FDA approved diagnosis of NMOSD; and
2. Member is anti-aquaporin-4 (AQP4) antibody positive; and
3. Member must be 18 years of age or older.

Additionally, the College of Pharmacy recommends the prior authorization of Ultomiris® (ravulizumab) with the following criteria:

Ultomiris® (Ravulizumab) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria Diagnosis]:

1. Member must have an established diagnosis of paroxysmal nocturnal hemoglobinuria via international classification of disease (ICD) coding in member's medical claims history; and

2. An age restriction of 18 years and older will apply.

Ultomiris® (Ravulizumab) Approval Criteria [Atypical Hemolytic Uremic Syndrome (aHUS) Diagnosis]:

1. Member must have a documented diagnosis of aHUS.

---

[1] Alexion Pharmacueticals, Inc. Alexion Receives Early FDA Approval for ULTOMIRIS™ (Ravulizumab-cwvz) in Adults with Paroxysmal Nocturnal Hemoglobinuria (PNH). *Business Wire*. Available online at: https://news.alexion.com/press-release/product-news/alexion-receives-early-fda-approval-ultomiris-ravulizumab-cwvz-adults-par. Issued 12/21/2018. Last accessed 01/14/2020.

[2] Inserro A. Soliris Gains FDA Approval for Neuromyelitis Optica Spectrum Disorder. *American Journal of Managed Care*. Available online at: https://www.ajmc.com/newsroom/soliris-gains-fda-approval-for-neuromyelitis-optica-spectrum-disorder. Issued 06/27/2019. Last accessed 01/14/2020.

[3] Soliris® Prescribing Information. Alexion Pharmaceuticals, Inc. Available online at: https://alexion.com/Documents/Soliris_USPI.pdf. Last revised 06/2019. Last accessed 01/14/2020.

[4] Glisson CC. Neuromyelitis optica spectrum disorders. *UpToDate*. Available online at: https://www.uptodate.com/contents/neuromyelitis-optica-spectrum-disorders?search=neuromyelitis%20optica%20spectrum%20disorders&source=search_result&selectedTitle=1~33&usage_type=default&display_rank=1. Last revised 10/11/2019. Last accessed 01/14/2020.

[5] Alexion Pharmacueticals, Inc. Alexion Receives FDA Approval for ULTOMIRIS® (ravulizumab-cwvz) for Atypical Hemolytic Uremic Syndrome (aHUS). *Business Wire*. Available online at: https://news.alexionpharma.com/press-release/product-news/alexion-receives-fda-approval-ultomiris-ravulizumab-cwvz-atypical-hemolyt. Issued 10/18/2019. Last accessed 01/14/2020.

Appendix F

Vote to Prior Authorize Korlym® (Mifepristone)

Oklahoma Health Care Authority
February 2020

Introduction[1]

Korlym® (mifepristone) is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus (T2DM) or glucose intolerance and have failed surgery or are not candidates for surgery. Korlym® (mifepristone) should not be used for the treatment of T2DM unrelated to endogenous Cushing's syndrome. Mifepristone is a selective antagonist of the progesterone receptor at low doses and blocks the glucocorticoid receptor (GR-II) at higher doses. Mifepristone has high affinity for the GR-II receptor but little affinity for the GR-I (MR, mineralcorticoid) receptor. In addition, mifepristone appears to have little or no affinity for estrogen, muscarinic, histaminic, or monoamine receptors. Korlym® is supplied as 300mg oral tablets and the recommended starting dose of mifepristone is 300mg once daily with a meal. The dose may be increased in 300mg increments to a maximum of 1,200mg once daily based on clinical response and tolerability. The dose should not exceed 20mg/kg/day. Korlym® prescribing information contains a *Boxed Warning* regarding termination of pregnancy as mifepristone has potent antiprogestational effects and will result in the termination of pregnancy. According to the prescribing information, pregnancy should be excluded before the initiation of treatment with mifepristone or if treatment is interrupted for more than 14 days in females of reproductive potential. The Wholesale Acquisition Cost (WAC) of Korlym® (mifepristone) is $524 per 300mg tablet resulting in a cost of $62,880 per 30-day supply based on the maximum dose of 1,200mg per day.

Recommendations

The College of Pharmacy recommends the prior authorization of Korlym® (mifepristone) with the following criteria:

Korlym® (Mifepristone) Approval Criteria:

1. An FDA approved indication to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus (T2DM) or glucose intolerance; and
2. Member must have failed surgery intended to correct the cause of endogenous Cushing's syndrome or not be a candidate for surgery that is expected to correct the cause of endogenous Cushing's syndrome; and
3. Member must be 18 years of age or older; and
4. Korlym® must be prescribed by, or in consultation with, an endocrinologist (or be an advanced care practitioner with a supervising physician who is an endocrinologist); and
5. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and

6. Female members of reproductive potential must use a non-hormonal, medically acceptable method of contraception (unless member has undergone surgical sterilization) during treatment with Korlym® and for at least 1 month after discontinuing treatment; and
7. Member must not have any contraindications to taking Korlym® including the following:
    a. Taking drugs metabolized by CYP3A such as simvastatin, lovastatin, and CYP3A substrates with narrow therapeutic ranges, such as cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus; and
    b. Receiving systemic corticosteroids for lifesaving purposes (e.g., immunosuppression after organ transplantation); and
    c. Female members must not have a history of unexplained vaginal bleeding or endometrial hyperplasia with atypia or endometrial carcinoma; and
    d. Known hypersensitivity to mifepristone or to any of the product components; and
8. Authorizations will be for the duration of 12 months; and
9. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

[1] Korlym® (mifepristone) Prescribing Information. Corcept Therapeutics, Inc. Available online at: http://www.korlym.com/wp-content/uploads/2019/11/K-00017-NOV-2019_electronic-PI_r8_FINAL.pdf. Last revised 11/2019. Last accessed 01/15/2020.

Appendix G

Vote to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) and to Update the Prior Authorization Criteria for Fasenra® (Benralizumab) and Nucala® (Mepolizumab)

Oklahoma Health Care Authority
February 2020

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

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

- **Duaklir® Pressair® (aclidinium/formoterol inhalation powder):** In April 2019, the FDA approved Duaklir® Pressair® (aclidinium/formoterol inhalation powder), a combination of aclidinium bromide, an anticholinergic, and formoterol fumarate, a long-acting beta$_2$-agonist (LABA) indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Duaklir® Pressair® is supplied as a breath-actuated, multi-dose dry powder inhaler that provides 400mcg of aclidinium bromide and 12mcg of formoterol fumarate per actuation. The recommended dose of Duaklir® Pressair® is 1 oral inhalation twice daily (once in the morning and once in the evening).

New FDA Expanded Indication(s)/New Formulation(s):

- **Fasenra® (benralizumab):** In October 2019, the FDA approved Fasenra® (benralizumab) as a prefilled, single-use autoinjector (Fasenra® Pen™) for self-administration. The approval is supported by data from the Phase 3 GRECO trial and the Phase 1 AMES trial, which achieved their primary objective of usability and pharmacokinetic (PK) exposure. The safety and tolerability of Fasenra® Pen™ in these trials were consistent with the established profile of benralizumab.
- **Nucala® (mepolizumab):** In June 2019, the FDA approved 2 new methods for administering Nucala® (mepolizumab), an autoinjector and a prefilled safety syringe, for patients or caregivers to administer once every 4 weeks after a health care professional determines at-home administration is appropriate. The original lyophilised powder version remains available for administration by a health care professional. The approval is supported by positive patient experience data from 2 open-label, single-arm, Phase 3a studies evaluating the real-world use of Nucala® administered via the new options in-clinic and at-home by patients with severe eosinophilic asthma (SEA), or by their caregivers. Both studies showed patients were able to successfully self-administer treatment with both the autoinjector and prefilled syringe after appropriate training. In September 2019, the FDA also approved Nucala® (mepolizumab) for use in children as young as 6 years of age who have SEA. Nucala® was first FDA approved in 2015 as an add-on maintenance treatment for patients 12 years of age and older with SEA. The expanded FDA approval is supported by an open-label PK study conducted in children 6 to 11 years of age who were suffering from SEA. The 52-week study showed that

the safety profile in pediatric patients 6 to 11 years of age was similar to the known safety profile in patients 12 years of age and older.

Recommendations

The College of Pharmacy recommends the prior authorization of Duaklir® Pressair® (aclidinium bromide/formoterol fumarate) with the following criteria (changes and additions noted in red):

Anoro® Ellipta® (Umeclidinium/Vilanterol), Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate), Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate), Stiolto® Respimat® (Tiotropium/Olodaterol), and Utibron® Neohaler® (Indacaterol/Glycopyrrolate) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components must be provided.

Additionally, the College of Pharmacy recommends updating the Fasenra® (benralizumab) and Nucala® (mepolizumab) prior authorization criteria with the following changes noted in red:

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 blood eosinophil count of ≥150cells/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 medium-to-high dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Fasenra® prefilled syringe, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Fasenra® prefilled autoinjector pen, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Fasenra®; and
9. 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

10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 prefilled syringe or prefilled autoinjector pen per 56 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Severe Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have a blood eosinophil count of ≥150 cells/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 medium-to-high dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
9. Nucala® 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
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 vial, prefilled autoinjector, or prefilled syringe per 28 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Eosinophilic Granulomatosis with Polyangiitis (EGPA) Diagnosis]:

1. An FDA approved diagnosis of EGPA; and
2. Member meets 1 of the following:
    a. Member must have a past history of at least 1 confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] within the past 12 months; or

   b. Member must have refractory disease within the last 6 months following induction of a standard treatment regimen administered compliantly for at least 3 months; and
3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
7. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
8. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by a Birmingham Vasculitis Activity Score (BVAS) of 0 (zero), fewer EGPA relapses from baseline, or a decrease in daily OCS dosing from baseline.

---

[1] Circassia Pharmaceuticals. Circassia Announces FDA Approval of Duaklir® for Maintenance Treatment of Chronic Obstructive Pulmonary Disease. Available online at: https://www.circassia.com/media/press-releases/circassia-announces-fda-approval-of-duaklir-for-maintenance-treatment-of-chronic-obstructive-pulmonary-disease/. Issued 04/01/2019. Last accessed 01/08/2020.
[2] Duaklir® Pressair® Prescribing Information. Circassia Pharmaceuticals, Inc. Available online at: https://www.duaklir.com/pdf/duaklir-pressair-prescribing-information.pdf. Last revised 03/2019. Last accessed 01/08/2020.
[3] GlaxoSmithKline. Nucala® (mepolizumab) gains FDA approval for two new self-administration options. Available online at: https://www.gsk.com/en-gb/media/press-releases/nucala-mepolizumab-gains-fda-approval-for-two-new-self-administration-options/. Issued 06/06/2019. Last accessed 01/08/2020.
[4] GlaxoSmithKline. Nucala® is the first biologic approved in the US for six to 11-year-old children with severe eosinophilic asthma. Available online at: https://www.gsk.com/en-gb/media/press-releases/nucala-is-the-first-biologic-approved-in-the-us-for-six-to-11-year-old-children-with-severe-eosinophilic-asthma/. Issued 09/12/2019. Last accessed 01/08/2020.
[5] AstraZeneca. Fasenra® (benralizumab) approved in the US for self-administration in a new pre-filled auto-injector, the Fasenra® Pen™. Available online at: https://www.astrazeneca-us.com/content/az-us/media/press-releases/2019/fasenra-benralizumab-approved-in-the-us-for-self-administration-in-a-new-pre-filled-auto-injector-the-fasenra-pen-10042019.html/. Issued 10/04/2019. Last accessed 01/08/2020.

Appendix H

Vote to Prior Authorize Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution)

Oklahoma Health Care Authority
February 2020

Introduction[1,2]

Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution): In March 2019, the U.S. Food and Drug Administration (FDA) approved Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution), a fixed-dose combination of a Rho kinase (ROCK) inhibitor and a prostaglandin F2α analog, for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension (HTN). Rocklatan® is supplied as an ophthalmic solution containing netarsudil 0.2mg/mL and lantanoprost 0.05mg/mL. The recommended dosage is 1 drop in the affected eye(s) once daily in the evening. The dosage of Rocklatan® should not exceed once daily. Rocklatan® may be used concomitantly with other topical ophthalmic drug products to lower IOP. The efficacy of Rocklatan® was established in 2 clinical studies (Study 301 and 302) in patients with open-angle glaucoma and ocular HTN. Patients were randomized to Rocklatan®, netarsudil 0.02%, or latanoprost 0.005% once daily. The primary endpoint was IOP lowering effect. The average IOP lowering effect of Rocklatan® was 1 to 3mmHg greater than monotherapy with either netarsudil or latanoprost throughout 3 months. In Study 301, IOP reductions were maintained throughout 12 months.

Cost Comparison:

Medication	Cost Per Milliliter (mL)	Cost Per 2.5mL Bottle
Rocklatan® (netarsudil/latanoprost 0.02%/0.005%)	**$109.65**	**$274.13**
latanoprost 0.005% (generic Xalatan®)	$2.22	$5.55
Rhopressa® (netarsudil 0.02%)	$104.55	$261.38

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.

Recommendations

The College of Pharmacy recommends the placement of Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution) into Tier-1 of the Glaucoma Medications Product Based Prior Authorization (PBPA) category based on manufacturer supplemental rebate participation. If the manufacturer chooses not to provide a supplemental rebate, Rocklatan® will be placed into the Special Prior Authorization (PA) Tier and current Special PA criteria would apply. Tier placement is shown in blue in the following chart to reflect current supplemental rebate status.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and

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

Glaucoma Medications Special Prior Authorization (PA) Approval Criteria:

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

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® 22.3/6.8mg/mL)		
levobunolol (Betagan® 0.25%, 0.5%)		
timolol maleate (Istalol® 0.5%, Timoptic® 0.25%, 0.5%)		
Carbonic Anhydrase Inhibitors		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
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® 22.3/6.8mg/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%)
netarsudil/latanoprost (Rocklatan® 0.02%/0.005%)	tafluprost (Zioptan® 0.0015%)	latanoprostene bunod (Vyzulta® 0.024%)
travoprost (Travatan-Z® 0.004%)		
Rho Kinase Inhibitors		
netarsudil (Rhopressa® 0.02%)		
netarsudil/latanoprost (Rocklatan® 0.02%/0.005%)		

*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; PF = preservative free

[1] Rocklatan® Prescribing Information. Aerie Pharmaceuticals, Inc. Available online at: https://rocklatan.com/hcp/assets/pdf/Rocklatan_Prescribing_Information.pdf. Last revised 03/2019. Last accessed 01/08/2020.
[2] Rocklatan® (netarsudil and latanoprost) – New Drug Approval. OptumRx. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_rocklatan_2019-0314.pdf. Issued 2019. Last accessed 01/08/2020.

Appendix I

Vote to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran)

Oklahoma Health Care Authority
February 2020

Introduction[1,2,3,4,5,6,7,8,9]

- **Scenesse® (afamelanotide)** was approved by the U.S. Food and Drug Administration (FDA) in October 2019 to increase pain-free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP). EPP is a very rare, inherited metabolic disorder caused by a deficiency of the enzyme ferrochelatase (FECH), which results in the accumulation of excessive amounts of protoporphyrin in the bone marrow, blood plasma, red blood cells (RBCs), and superficial blood vessels under the skin, which are highly sensitive to sunlight. The major symptoms of EPP are related to phototoxicity, which results in severe pain on exposure to sunlight; standard treatment for EPP consists of avoidance of sunlight and sun protective clothing and measures. The diagnosis of EPP is made by a thorough clinical evaluation (of characteristic symptoms) and specialized laboratory tests (to detect increased levels of protoporphyrin in the plasma or RBCs); genetic testing is useful to confirm the diagnosis. Afamelanotide is an α-melanocyte stimulating hormone (α-MSH) analog that functions as a melanocortin-1 receptor (MC1-R) agonist, resulting in increased production of eumelanin in the skin independent of exposure to sunlight or artificial ultraviolet (UV) light sources. Scenesse® is supplied as a subcutaneous (subQ) implant containing 16mg of afamelanotide, and the recommended dosage is to insert a single implant above the anterior supra-iliac crest every 2 months. Patients should maintain sun and light protection measures during treatment with afamelanotide to prevent phototoxic reactions related to EPP. Cost information for Scenesse® (afamelanotide) is not yet available.
- **Givlaari™ (givosiran)** was approved by the FDA in November 2019 for treatment of adult patients with acute hepatic porphyria (AHP). Porphyrias are a group of disorders characterized by abnormally high levels of porphyrins in the body due to deficiencies of certain enzymes essential to the synthesis of hemoglobin; AHP refers to a set of inherited metabolic disorders in which the enzyme deficiency occurs in the liver, including acute intermittent porphyria (AIP), variegate porphyria (VP), aminolevulinic acid (ALA) dehydratase deficiency porphyria (ALAD), and hereditary coproporphyria (HCP). Acute and chronic symptoms due to the effects on the central nervous system (CNS) and peripheral nervous system (PNS) characterize AHPs; 3 groups of symptoms (abdominal pain, CNS abnormalities, and peripheral neuropathy) are described as a "classic triad" that should suggest AHP. The diagnosis of AHP is made through a thorough clinical evaluation (of characteristic symptoms) and specialized laboratory tests. Urine porphobilinogen (PBG) is the most important first-line screening test, which is both highly sensitive and highly specific and is significantly elevated in almost all cases

of AHPs. The goal of treatment for an acute attack of AHP is to abate the attack as quickly as possible and to provide supportive and symptomatic care until the acute attack resolves. For patients with an acute attack severe enough to require hospitalization, opioid analgesia, or other intravenous (IV) medication, or that is accompanied by nausea and vomiting, motor neuropathy, paresis, seizures, agitation, delirium, psychosis, ileus that prevents oral intake, or hyponatremia, IV administration of hemin is recommended to prevent progression of symptoms based on the high risk of life-threatening sequelae from a severe acute attack of AHP. Liver transplantation is reserved for patients with life-threatening acute attacks or progression of symptoms despite IV hemin therapy. Givosiran is a small interfering RNA (siRNA) therapeutic targeting ALA synthase 1 (ALAS1), which works by specifically reducing elevated levels of ALAS1 messenger RNA (mRNA), leading to reduction of toxins associated with attacks and other disease manifestations of AHP. Givlaari™ is supplied as a 189mg/mL solution for injection in a 1mL single-dose vial (SDV); the recommended dosage of givosiran is 2.5mg/kg via subQ injection once monthly. Givosiran is intended for subQ administration by a health care professional only; medical support to appropriately manage anaphylactic reactions should be available when administering givosiran. The wholesale acquisition cost (WAC) of Givlaari™ is $39,000 per 1mL SDV.

Recommendations

The College of Pharmacy recommends the prior authorization of Scenesse® (afamelanotide) and Givlaari™ (givosiran) with the following criteria:

Scenesse® (Afamelanotide) Approval Criteria:

1. An FDA approved indication to increase pain-free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP); and
    a. The diagnosis of EPP must be confirmed by genetic testing; and
2. Member must be 18 years of age or older; and
3. Scenesse® must be administered by a health care professional who is proficient in the subcutaneous (subQ) implantation procedure and has completed the training program provided by the manufacturer prior to administration of the Scenesse® implant; and
    a. Scenesse® must be shipped via cold chain supply shipping and delivery to the health care setting where the member is scheduled to receive the implant administration; and
    b. Scenesse® must be stored under refrigeration (36 to 46°F) and protected from light prior to implantation; and
4. The Scenesse® implant should be inserted using an SFM Implantation Cannula or other implantation device that has been determined by the manufacturer to be suitable for implantation of Scenesse®; and
5. The prescriber must agree that the member will be monitored by a health care provider for at least 30 minutes after the implant administration; and
6. The prescriber must agree that the member will have a full body skin examination performed at least twice yearly while the member is being treated with Scenesse® to monitor pre-existing and new skin pigmentary lesions; and

7. Documentation that member will maintain sun and light protection measures during treatment with Scenesse® to prevent phototoxic reactions related to EPP; and
8. A quantity limit of 1 implant per 60 days will apply. Initial approvals will be for 2 implants for the duration of 4 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by increased tolerance of sunlight (i.e., less phototoxic reactions).

Givlaari™ (Givosiran) Approval Criteria:

1. An FDA approved diagnosis of acute hepatic porphyria (AHP) confirmed by:
    a. Genetic testing; or
    b. Elevated urinary porphobilinogen (PBG) and signs/symptoms of AHP; and
2. Member must be 18 years of age or older; and
3. Givlaari™ must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
    a. Givlaari™ must be shipped to the health care setting where the member is scheduled to receive treatment; and
4. The prescriber must agree to monitor liver function tests prior to initiating treatment with Givlaari™, every month during the first 6 months of treatment, and as clinically indicated thereafter; and
5. The prescriber must agree to monitor renal function during treatment with Givlaari™ as clinically indicated; and
6. Member must not be taking sensitive CYP1A2 or CYP2D6 substrates (e.g., caffeine, dextromethorphan, duloxetine, amitriptyline, olanzapine, fluoxetine, paroxetine, hydrocodone, tramadol) concomitantly with Givlaari™; 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. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by less porphyria attacks and that the member does not have elevated transaminase levels.

[1] Clinuvel. FDA Grants Marketing Approval for Scenesse®. Available online at: https://www.clinuvel.com/fda-grants-marketing-approval-for-scenesse. Issued 10/09/2019. Last accessed 01/21/2020.
[2] Scenesse® (Afamelanotide) Prescribing Information. Clinuvel. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210797s000lbl.pdf. Last revised 10/2019. Last accessed 01/21/2020.
[3] National Organization for Rare Disorders. Rare Disease Database: Erythropoietic Protoporphyria and X-Linked Protoporphyria. Available online at: https://rarediseases.org/rare-diseases/erythropoietic-protoporphyria/. Last revised 2018. Last accessed 01/21/2020.
[4] Mittal S, Anderson KE. Erythropoietic Protoporphyria and X-Linked Protoporphyria. *UpToDate*. Available online at: https://www.uptodate.com/contents/erythropoietic-protoporphyria-and-x-linked-protoporphyria. Last revised 10/21/2019. Last accessed 01/21/2020.
[5] Anderson KE. Porphyrias: An Overview. *UpToDate*. Available online at: https://www.uptodate.com/contents/porphyrias-an-overview. Last revised 01/13/2020. Last accessed 01/21/2020.
[6] Alnylam. Alnylam Announces Approval of Givlaari™ (Givosiran) by the U.S. Food and Drug Administration (FDA). *Business Wire.* Available online at: https://www.businesswire.com/news/home/20191120005849/en/Alnylam-Announces-Approval-GIVLAARI%E2%84%A2-givosiran-U.S.-Food. Issued 11/20/2019. Last accessed 01/21/2020.
[7] Givlaari™ (Givosiran) Prescribing Information. Alnylam. Available online at: https://www.alnylam.com/wp-content/uploads/pdfs/GIVLAARI-Prescribing-Information.pdf. Last revised 11/2019. Last accessed 01/21/2020.
[8] Kothadia JP, LaFreniere K, Shah JM. Acute Hepatic Porphyria. *StatPearls*. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK537178/. Last revised 09/30/2019. Last accessed 01/21/2020.
[9] Sood GK, Anderson KE. Acute Intermittent Porphyria: Management. *UpToDate*. Available online at: https://www.uptodate.com/contents/acute-intermittent-porphyria-management. Last revised 12/05/2019. Last accessed 01/21/2020.

Appendix J

Vote to Prior Authorize Ruzurgi® (Amifampridine)

Oklahoma Health Care Authority
February 2020

Introduction[1,2]

Ruzurgi® (amifampridine) is a potassium channel blocker indicated for the treatment of Lambert-Eaton Myasthenic Syndrome (LEMS) in patients 6 years to younger than 17 years of age. Ruzurgi® is supplied as 10mg oral tablets. In patients weighing ≥45kg, the initial recommended dosage is 15mg to 30mg daily in divided doses with a maximum recommended single dose of 30mg and a maximum daily dose of 100mg. In patients weighing <45kg, the initial recommended dosage is 7.5mg to 15mg daily, in divided doses with a maximum recommended single dose of 15mg and a maximum daily dose of 50mg. When patients require <5mg dosage increments, have difficulty swallowing, or require feeding tubes, a 1mg/mL suspension can be prepared. For patients with renal or hepatic impairment or who are known N-acetyltransferase 2 (NAT2) poor metabolizers, the lowest recommended initial dosage should be used.

Products Comparison:

Medication	Ruzurgi®	Firdapse®
Generic Name	amifampridine	amifampridine **phosphate**
Date of FDA Approval	May 6, 2019	November 28, 2018
Manufacturer	Jacobus Pharmaceutical Company	Catalyst Pharmaceuticals
Indication	LEMS in **pediatric patients** 6 years to younger than 17 years of age	LEMS in **adult patients**
How Supplied	10mg tablets (functionally scored)	10mg tablets (functionally scored)
Administration	Can be taken without regard to food	Can be taken without regard to food
Dosing	Tablets may be halved or prepared as a 1mg/mL **suspension**; maximum daily dose: 100mg	Tablets may be halved; maximum daily dose: 80mg
Storage and Handling	Prior to Dispensing: Store **refrigerated** between 2°C to 8°C (36°F to 46°F); keep container tightly closed with desiccant canister inside after opening and protect from moisture and light After Dispensing: Store at **20°C to 25°C** (68°F to 77°F) for **up to 3 months**; excursions permitted between 15°C to 30°C (59°F to 86°F)	Store at **20°C to 25°C** (68°F to 77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F)
Cost Per Unit	$80	$171

LEMS = Lambert-Eaton Myasthenic Syndrome; FDA = U.S. Food and Drug Administration
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.

Recommendations

The College of Pharmacy recommends the prior authorization of Ruzurgi® (amifampridine) and recommends updating the current Firdapse® (amifampridine) prior authorization criteria (changes and additions noted in red):

Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine) Approval Criteria:

1. An FDA approved diagnosis of Lambert-Eaton myasthenic syndrome (LEMS); and
2. LEMS 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. The requested medication 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. For Firdapse®, a patient-specific, clinically significant reason why the member cannot use Ruzurgi® must be provided; and
6. For Firdapse®, a quantity limit of 240 tablets per 30 days will apply. For Ruzurgi®, a quantity limit of 300 tablets per 30 days will apply; and
7. Initial approvals will be for 6 months. Consideration for continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with the requested medication.

[1] U.S. Food and Drug Administration (FDA). Drugs@FDA: FDA Approved Drug Products. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/209321s000lbl.pdf. Last revised 05/2019. Last accessed 12/16/2019.

[2] FDA. Drugs@FDA: FDA Approved Drug Products. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208078s000lbl.pdf. Last revised 11/2018. Last accessed 01/17/2020.

Appendix K

Fiscal Year 2019 Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Idhifa® (Enasidenib), Daurismo™ (Glasdegib), Lumoxiti™ (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib)

Oklahoma Health Care Authority
February 2020

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

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

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are indolent diseases, as patients may survive many years without therapy. The major difference between CLL and SLL is that in CLL a significant number of abnormal lymphocytes are found in the blood in addition to bone marrow and lymphoid tissue versus SLL, where there are few circulating abnormal lymphocytes and disease is mostly found in the lymph nodes, bone marrow, and other lymphoid tissues. CLL/SLL is primarily a disease of the elderly; the median age at diagnosis is 72 years. CLL/SLL is the most prevalent adult leukemia in western countries. In 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

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

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

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

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

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

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

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

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

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

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

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

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

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

1. CD30+ disease; and
2. Member meets 1 of the following:
    a. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) in nonresponders to first-line therapy for chronic/smoldering subtype; or
    b. In combination with CHP for first-line therapy for acute or lymphoma subtype; or

c. In combination with CHP for continued treatment in responders to first-line therapy for acute or lymphoma subtype; or
d. As a single-agent in members who have received ≥1 line of therapy.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1. Chronic, accelerated, or blast phase CML; and
2. Newly diagnosed or resistant/intolerant to other Tyrosine Kinase Inhibitors (TKIs).

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

1. As a single-agent 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.

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

1. Relapsed/refractory FL; and
2. Progression of disease following 2 or more lines of systemic therapy; and

3. As a single-agent.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1. Member must have 1 of the following:
    a. T315I mutation; or
    b. Intolerant or resistant to all other Tyrosine Kinase Inhibitors (TKIs); or
    c. Post-hematopoietic stem cell transplantation in patients with prior accelerated or blast phase prior to transplant or who have relapsed.

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

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

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

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

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

1. Failure of 1 or more lines of therapy.

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

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

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

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

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

1. Non-germinal center DLBCL; and

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

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

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

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

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

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

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

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

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

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

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

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

1. Large B-cell lymphoma [including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Relapsed/refractory disease; and
3. Member must be 18 years of age or older; and

4. Member must not have primary central nervous system lymphoma; and
5. Member must have had 2 or more lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells, must be trained in the management of cytokine release syndrome (CRS) and neurologic toxicities, and must comply with the REMS requirements.

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

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

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

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

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

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

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

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

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

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

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

1. Member must have 1 of the following:
    a. Primary treatment of advanced phase CML with disease progression to accelerated phase; or
    b. Post-hematopoietic stem cell transplant in patients who have relapsed; or
    c. T315I mutation; or
    d. Members who are intolerant or resistant to 2 or more Tyrosine Kinase Inhibitors (TKIs); and

2. As a single-agent only.

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

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

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

1. Member must have 1 of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

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

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

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

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

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

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

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

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

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

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

a. First-line therapy; or
b. Second-line therapy or subsequent therapy.

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

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

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

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

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

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

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

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

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

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

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

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

Utilization of Leukemia Medications: Fiscal Year 2019

Please note, several medications in this report have indications for diagnoses other than leukemia. All paid claims for fiscal year 2019 for these medications have been included in this report to accurately reflect medication utilization.

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	43	253	$2,800,372.13	$11,068.66	$366.49	16,630	7,641
2019	42	263	$3,044,272.21	$11,575.18	$392.81	14,066	7,750
% Change	**-2.30%**	**4.00%**	**8.70%**	**4.60%**	**7.20%**	**-15.40%**	**1.40%**
Change	**-1**	**10**	**$243,900.08**	**$506.52**	**$26.32**	**-2,564**	**109**

*Total number of unduplicated members.
Cost do not reflect rebated prices or net costs.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Fiscal Year 2019 Utilization: Medical Claims

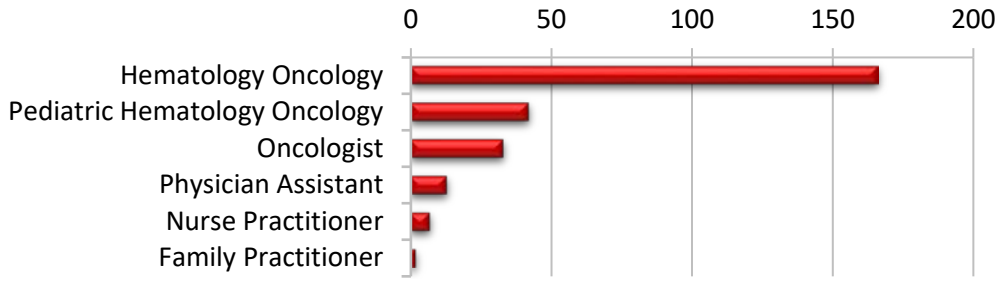
Fiscal Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim	Total Units
2019	6	17	$250,557.04	$14,738.65	2,134

*Total number of unduplicated members. +Total number of unduplicated claims.
Cost do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Demographics of Members Utilizing Leukemia Medications: Pharmacy Claims

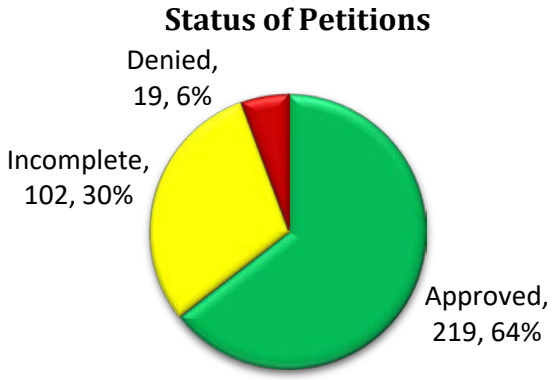
- Due to the limited number of members utilizing leukemia medications during fiscal year 2019, detailed demographic information could not be provided.

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



Prior Authorization of Leukemia Medications

There were 340 prior authorization requests submitted for leukemia medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



Market News and Updates[6,7]

Anticipated Patent Expiration(s):

- Folotyn® (pralatrexate): May 2025
- Sprycel® (dasatinib): September 2026
- Synribo® (omacetaxine): October 2026
- Bosulif® (bosutinib): November 2026
- Beleodaq® (belinostat): October 2027
- Xospata® (gilteritinib): January 2031
- Copiktra® (duvelisib): May 2032
- Zelboraf® (vemurafenib): June 2032
- Tasigna® (nilotinib): October 2032
- Venclexta® (venetoclax): September 2033
- Zydelig® (idelalisib): September 2033
- Iclusig® (ponatinib): December 2033
- Idhifa® (enasidenib): September 2034
- Imbruvica® (ibrutinib): October 2034
- Tibsovo® (ivosidenib): March 2035
- Daurismo™ (glasdegib): April 2036
- Calquence® (acalabrutinib): July 2036

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

- **August 2017:** The FDA approved Idhifa® (enasidenib) for the treatment of adult patients with relapsed or refractory AML with an isocitrate dehydrogenase-2 (IDH2) mutation.
- **September 2018:** The FDA approved Lumoxiti™ (moxetumomab pasudotox-tdfk), a CD22-directed cytotoxin, for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who have received at least 2 prior systemic therapies, including treatment with a purine nucleoside analog (PNA).
- **November 2018:** The FDA approved Daurismo™ (glasdegib) in combination with low-dose cytarabine (LDAC), for the treatment of newly-diagnosed AML in patients who are 75 years of age or older or who have comorbidities that preclude intensive induction chemotherapy.
- **November 2018:** The FDA approved Xospata® (gilteritinib) for treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation.

- **December 2018:** The FDA approved Asparlas™ (calaspargase pegol-mknl) an asparagine-specific enzyme, as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients age 1 month to 21 years. Asparlas™ provides for a longer interval between doses compared to other available pegaspargase products.
- **May 2019:** The FDA approved Tibsovo® (ivosidenib) for the treatment of newly-diagnosed AML with a susceptible IDH1 mutation in patients who are at least 75 years of age or who have comorbidities that preclude the use of intensive induction chemotherapy.

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

- **March 2018:** The FDA approved Tasigna® (nilotinib) for the treatment of pediatric patients 1 year of age or older with newly-diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP), Ph+ CML-CP resistant, or those intolerant to prior tyrosine kinase inhibitor (TKI) therapy.
- **May 2019:** The FDA approved Venclexta® (venetoclax) for the treatment of adult patients with CLL or SLL in combination with obinutuzumab (Gazyva®).
- **May 2019:** The FDA approved the addition of overall survival (OS) data in the labeling for Xospata® (gilteritinib). Approval was based on the ADMIRAL trial in which 371 adult patients with relapsed or refractory AML with specified mutations were randomized (2:1) to receive gilteritinib 120mg once daily (N=247) over continuous 28-day cycles or prespecified salvage chemotherapy (N=124). The median OS was 9.3 months for patients receiving gilteritinib and 5.6 months for those in the chemotherapy arm (P=0.0004).
- **November 2019:** The FDA approved Calquence® (acalabrutinib) for the treatment of adults with CLL or SLL.

Product Summaries[8,9,10,11,12,13]

Asparlas™ (Calaspargase pegol-mknl):

- **Therapeutic Class:** Asparagine-specific enzyme
- **Indication(s):** A component of a multi-agent chemotherapeutic regimen for the treatment of ALL in pediatric and young adult patients 1 month to 21 years of age
- **How Supplied:** 3,750 units/5mL sterile solution in a single-dose vial (SDV)
- **Dose:** 2,500 units/m^2 intravenously (IV) no more frequently than every 21 days
- **Cost:** Wholesale Acquisition Cost (WAC) of $4,800.00 per SDV; cost will vary due to body surface area-based dosing and duration variability

Daurismo™ (Glasdegib):

- **Therapeutic Class:** Hedgehog pathway inhibitor
- **Indication(s):** For use in combination with LDAC, for the treatment of newly-diagnosed AML in adult patients who are 75 years of age or older or who have comorbidities that preclude the use of intensive induction chemotherapy
- **How Supplied:** 25mg and 100mg oral tablets

- **Dose:** 100mg orally once daily on days 1 to 28 in combination with cytarabine 20mg subcutaneously (sub-Q) twice daily on days 1 to 10 of each 28-day cycle
- **Cost:** WAC of $296.19 per 25mg tablet and $592.38 per 100mg tablet; $16,586.64 per 28 days based on recommended dose of 100mg once daily

Idhifa® (Enasidenib):

- **Therapeutic Class:** IDH2 inhibitor
- **Indication(s):** Treatment of adults with relapsed or refractory AML with an IDH2 mutation
- **How Supplied:** 50mg and 100mg oral tablets
- **Dose:** 100mg orally once daily
- **Cost:** WAC of $900.99 for either 50mg tablet or 100mg tablet; $27,029.70 per 30 days based on recommended dose of 100mg once daily

Lumoxiti™ (Moxetumomab Pasudotox-tdfk):

- **Therapeutic Class:** CD22-directed cytotoxin
- **Indication(s):** Treatment of adult patients with relapsed/refractory HCL who have received 2 prior systemic therapies, including treatment with a PNA
- **How Supplied:** 1mg lyophilized powder in a SDV
- **Dose:** 0.04mg/kg IV on days 1, 3, and 5 of a 28-day cycle
- **Cost:** WAC of $2,114.58 per SDV; cost will vary due to weight-based dosing and duration variability

Tibsovo® (Ivosidenib):

- **Therapeutic Class:** IDH1 inhibitor
- **Indication(s):** Treatment of AML with a susceptible IDH1 mutation in newly-diagnosed patients who are 75 years of age or older or who have comorbidities that preclude use of intensive induction chemotherapy, and in adult patients with relapsed or refractory AML
- **How Supplied:** 250mg oral tablets
- **Dose:** 500mg orally once daily
- **Cost:** WAC of $457.01 per 250mg tablet; $27,420.60 per 30 days based on recommended dose of 500mg daily

Xospata® (Gilteritinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation
- **How Supplied:** 40mg oral tablets
- **Dose:** 120mg orally once daily
- **Cost:** WAC of $262.50 per 40mg tablet; $23,625.00 per 30 days based on recommended dose of 120mg daily

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); and
- The prior authorization of Asparlas® (calaspargase pegol-mknl), Daurismo® (glasdegib), Idhifa® (enasidenib), Lumoxiti® (moxetumomab pasudotox-tdfk), Tibsovo® (ivosidenib), and Xospata® (gilteritinib) with the following criteria listed in red

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

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

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]:

2. As a single-agent ~~in relapsed/refractory disease~~.

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

1. Newly-diagnosed AML; and
2. In combination with low-dose cytarabine (LDAC); and
3. Members 75 years of age older or who have significant comorbid conditions [severe cardiac disease, ECOG performance status ≥2, or serum creatinine (SCr) >1.3].

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

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

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

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

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

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

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

1. Newly diagnosed AML in members 75 years of age older or who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. IDH1 mutation; or
2. Relapsed/refractory AML; and
    a. As a single-agent; and
    b. IDH1 mutation.

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

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

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

1. Relapsed/refractory AML; and
2. FLT3 mutation; and
3. As a single-agent.

Utilization Details of Leukemia Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT	TOTAL	TOTAL	TOTAL	CLAIMS/	COST/
DASATINIB PRODUCTS					
SPRYCEL TAB 100MG	101	17	$1,300,253.92	5.94	$12,873.80
SPRYCEL TAB 70MG	17	4	$126,235.26	4.25	$7,425.60
SPRYCEL TAB 50MG	15	2	$106,047.35	7.5	$7,069.82
SPRYCEL TAB 20MG	7	2	$70,068.71	3.5	$10,009.82
SPRYCEL TAB 140MG	2	1	$27,387.32	2	$13,693.66
SUBTOTAL	**142**	**26**	**$1,629,992.56**	**5.46**	**$11,478.82**
IBRUTINIB PRODUCTS					
IMBRUVICA TAB 420MG	26	6	$307,820.95	4.33	$11,839.27
IMBRUVICA CAP 140MG	12	2	$54,631.07	6	$4,552.59
IMBRUVICA TAB 560MG	11	2	$130,804.74	5.5	$11,891.34
IMBRUVICA TAB 280MG	2	2	$24,167.18	1	$12,083.59
IMBRUVICA TAB 140MG	2	1	$22,756.92	2	$11,378.46
SUBTOTAL	**53**	**13**	**$540,180.86**	**4.08**	**$10,192.09**

PRODUCT	TOTAL	TOTAL	TOTAL	CLAIMS/	COST/
NILOTINIB PRODUCTS					
TASIGNA CAP 200MG	14	2	$163,386.91	7	$11,670.49
TASIGNA CAP 150MG	11	3	$145,248.24	3.67	$13,204.39
SUBTOTAL	**25**	**5**	**$308,635.15**	**5**	**$12,345.41**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	19	2	$189,847.06	9.5	$9,991.95
SUBTOTAL	**19**	**2**	**$189,847.06**	**9.5**	**$9,991.95**
PONATINIB PRODUCTS					
ICLUSIG TAB 45MG	11	2	$182,289.93	5.5	$16,571.81
ICLUSIG TAB 15MG	5	2	$99,407.39	2.5	$19,881.48
SUBTOTAL	**16**	**4**	**$281,697.32**	**4**	**$17,606.08**
BOSUTINIB PRODUCTS					
BOSULIF TAB 100MG	3	1	$33,605.49	3	$11,201.83
SUBTOTAL	**3**	**1**	**$33,605.49**	**3**	**$11,201.83**
IDELALISIB PRODUCTS					
ZYDELIG TAB 150MG	3	1	$32,172.03	3	$10,724.01
SUBTOTAL	**3**	**1**	**$32,172.03**	**3**	**$10,724.01**
ACALABRUTINIB PRODUCTS					
CALQUENCE CAP 100MG	2	1	$28,141.74	2	$14,070.87
SUBTOTAL	**2**	**1**	**$28,141.74**	**2**	**$14,070.87**
TOTAL	**263**	**42***	**$3,044,272.21**	**6.26**	**$11,575.18**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBERS	COST/ CLAIM
BRENTUXIMAB VEDOTIN J9042	12	4	$203,608.00	3	$16,967.33
OBINUTUZUMAB J9301	4	1	$37,683.00	4	$9,420.75
BLINATUMOMAB J9039	1	1	$9,266.04	1	$9,266.04
TOTAL	**17^**	**6***	**$250,557.04**	**2.83**	**$14,738.65**

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

[1] Chiorazzi N, Rai KR, and Ferrarini M. Chronic lymphocytic leukemia. *N Eng J Med* 2005; 352:804-815.
[2] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. *CA Cancer J Clin* 2018; 68:7-30.
[3] National Comprehensive Cancer Network (NCCN) Guidelines. CLL/SLL V 2.2019. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Last accessed 02/04/2020.
[4] Hallek M. Chronic lymphocytic leukemia: 2015 update on diagnosis, risk stratification, and treatment. *American Journal of Hematology* 2015; 90:446-460.
[5] National Comprehensive Cancer Network (NCCN) Guidelines. AML v 3.2020. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Last accessed 01/24/2020.
[6] 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 01/2020. Last accessed 01/28/2020.
[7] FDA: Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 01/09/2020. Last accessed 01/14/2020.
[8] Asparlas™ Prescribing Information. Servier Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761102s000lbl.pdf. Last revised 12/2018. Last accessed 01/14/2020.
[9] Daurismo™ Prescribing Information. Pfizer. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210656s000lbl.pdf. Last revised 11/2018. Last accessed 01/14/2020.
[10] Idhifa® Prescribing Information. Celgene Corporation. Available online at: https://media2.celgene.com/content/uploads/idhifa-pi.pdf. Last revised 09/2019. Last accessed 01/28/2020.
[11] Lumoxiti™ Prescribing Information. AstraZeneca. Available online at: https://www.azpicentral.com/lumoxiti/lumoxiti.pdf#page=1. Last revised 01/2019. Last accessed 01/14/2020.
[12] Tibsovo® Prescribing Information. Agios Pharmaceuticals. Available online at: https://www.tibsovopro.com/pdf/prescribinginformation.pdf. Last revised 05/2019. Last accessed 01/14/2020.
[13] Xospata® Prescribing Information. Astellas Pharma. Available online at: https://astellas.us/docs/xospata.pdf. Last revised 05/2019. Last accessed 01/14/2020.

Appendix L

30-Day Notice to Prior Authorize Azedra® (Iobenguane I-131)

Oklahoma Health Care Authority
February 2020

Introduction[1]

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

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

Market News and Updates[2,3]

Anticipated Patent Expiration(s):

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

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

- **July 2018:** The FDA approved Azedra® (iobenguane I-131) for the treatment of adult and pediatric patients (12 years of age and older) with iobenguane scan-positive, unresectable, locally advanced or metastatic pheochromocytoma or PPGL who require systemic anticancer therapy.

Azedra® (Iobenguane I-131) Product Summary[4]

Azedra® (Iobenguane I-131):

- **Therapeutic Class:** Radioactive therapeutic agent
- **Indication(s):** Treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic PPGL
- **How Supplied:** 555MBq/mL (15mCi/mL) of I-131 (as iobenguane I-131) and 0.006mg/mL of iobenguane in a 30mL single-dose vial (SDV); supplied in dosimetric (2mL) and therapeutic (22.5mL) presentations

- **Dose:** Administered intravenously (IV) as a dosimetric dose followed by 2 therapeutic doses administered 90 days apart:
  - Dosimetric dose: 185 to 222MBq (5 to 6mCi) if >50kg or 3.7MBq/kg (0.1mCi/kg) if ≤50kg
  - Therapeutic dose: 18,500MBq (500mCi) if >62.5kg or 296MBq/kg (8mCi/kg) if ≤62.5kg
- **Cost:** Wholesale Acquisition Cost (WAC) of $9,060.00 per dosimetric dose vial and $101,925.00 per therapeutic dose vial; treatment cost will vary depending on patient weight

Recommendations

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

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

[1] Kantorovich V, Pacak K. Pheochromocytoma and paraganglioma. *Prog Brian Res* 2010; 182:343-73.
[2] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm?resetfields=1. Last revised 12/2019. Last accessed 12/30/2019.
[3] FDA. Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 12/05/2019. Last accessed 12/30/2019.
[4] Azedra® (iobenguane I-131) Prescribing Information. Progenics Pharmaceuticals, Inc. Available online at: https://azedra.com/full-prescribing-information.pdf. Last revised 08/2018. Last accessed 02/03/2020.

Appendix M

Fiscal Year 2019 Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei]

Oklahoma Health Care Authority
February 2020

Current Prior Authorization Criteria

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

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

Hemlibra® (Emicizumab-kxwh) Approval Criteria:

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

a. Member's current prophylaxis therapy is not adequate to prevent spontaneous bleeding episodes; or
b. Member is unable to maintain venous access for prophylactic infusions; and
c. Treatment plan must be made to address breakthrough bleeds and procedures; and
d. Routine lab screening must occur for factor VIII inhibitor while using Hemlibra® since this would change the treatment plan for bleeds and procedures; and

6. First dose must be given in a health care facility; and
7. In order to calculate appropriate dosing, the member's recent weight must be provided and have been taken within the last 3 months.
8. Initial approvals will be for 3 months of therapy. Subsequent approvals will be the duration of 1 year if there has been a decrease in the member's spontaneous bleeding episodes since beginning Hemlibra® treatment.

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

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

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

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

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

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

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

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

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

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

Standards of Care for Pharmacies Providing Factor Replacement Products can be found on the OHCA website in the Hemophilia Therapeutic Category at www.okhca.org/pa.

Utilization of Factor Replacement Products: Fiscal Year 2019

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units	Cost Per Utilizer Per Year
2018	85	697	$18,748,696.44	$26,899.13	12,131,607	$220,572.90
2019	87	670	$22,244,623.15	$33.2009.93	12,785,505	$255,685.32
% Change	**2.40%**	**-3.90%**	**18.60%**	**23.40%**	**5.40%**	**15.91%**
Change	**2**	**-27**	**$3,495,926.71**	**$6,301.80**	**654,898**	**$35,112.42**

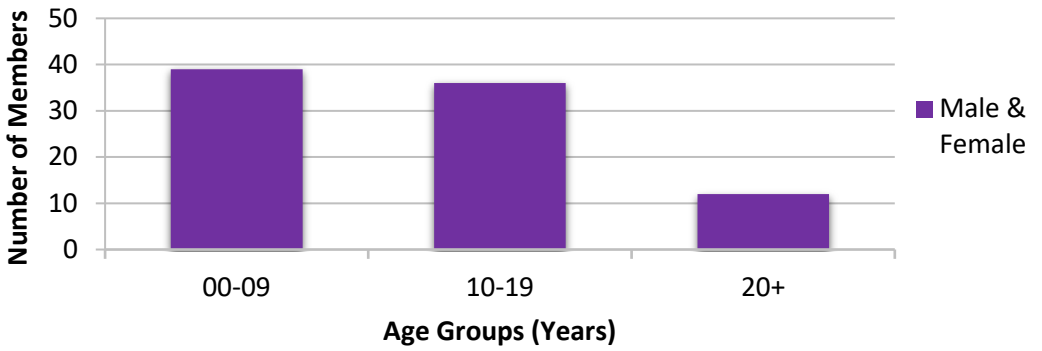
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2018 = 07/01/2017 to 06/30/2018; Fiscal year 2019 = 07/01/2018 to 06/30/2019

Fiscal Year Comparison: Medical Claims

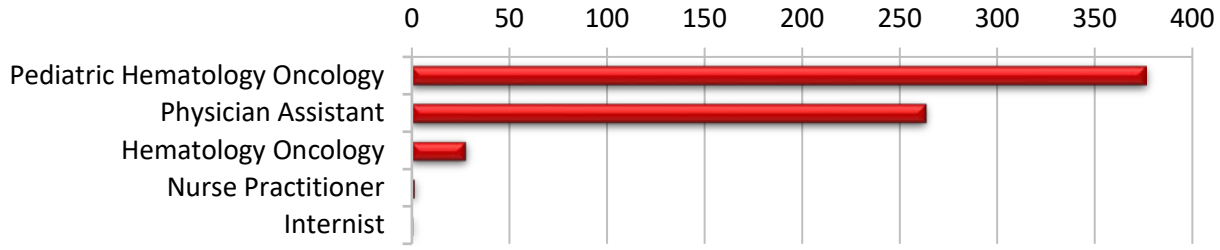
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units	Cost Per Utilizer Per Year
2018	11	25	$1,213,298.95	$48,537.95	614,176	$110,299.90
2019	7	23	$877,963.91	$38,172.34	439,018	$125,423.41
% Change	**-36.4%**	**-0.8%**	**-27.65%**	**-21.4%**	**39.9%**	**13.71%**
Change	**-4**	**2**	**-$335,335.04**	**-$10,365.61**	**-178,158**	**$15,123.51**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2018 = 07/01/2017 to 06/30/2018; Fiscal year 2019 = 07/01/2018 to 06/30/2019

Demographics of Members Utilizing Factor Replacement Products: Pharmacy Claims



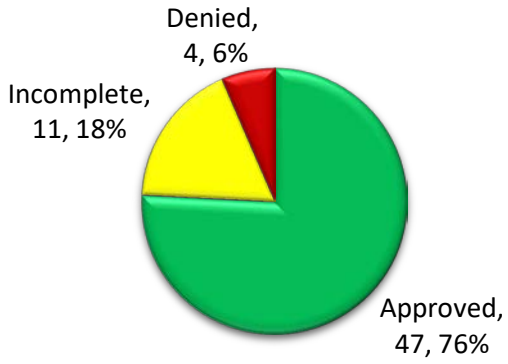
Top Prescriber Specialties of Factor Replacement Products By Number of Claims: Pharmacy Claims



Prior Authorization of Factor Replacement Products

There were 62 prior authorization requests for 25 unique members submitted for factor replacement products during state fiscal year (SFY) 2019. The following chart shows the status of the submitted petitions for SFY 2019.

Status of Petitions



- There were 22 pharmacies with attestations for the Standards of Care (SOC) signed for SFY 2019. There are currently 20 pharmacies with attestations for the SOC signed for SFY 2020. This decrease can be attributed to 3 pharmacies within the same company that decided to have 1 location be the dispensing pharmacy.

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

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

- **February 2019:** Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei]

New Indication Approval(s):

- **October 2019:** Wilate® [von Willebrand factor/coagulation factor VIII (FVIII) complex (human)] was approved by the FDA to be used for routine prophylaxis to reduce the frequency of bleeding episodes or for on-demand treatment of bleeding episodes in adolescents and adults with Hemophila A.

Pipeline Update(s):

- **Eptacog Beta:** Eptacog Beta is a recombinant human factor VIIa (FVIIa) which has been studied in patients with hemophila A and hemophilia B with inhibitors. It is currently under review by the FDA.
- **Fitusiran:** Fitusiran is a ribonucleic acid interfering (RNAi) therapeutic agent targeting antithrombin. Alnylam and Sanofi began enrolling patients in Phase 3 studies in 2018. There are 6 active clinical trials for fitusiran as a subcutaneous (sub-Q) treatment under investigation in patients with hemophilia A and B with and without inhibitors. Studies have included adults and as young as infants.
- **Marzeptacog alfa (MarzAA):** Marzeptacog alfa is a sub-Q FVIIa treatment for patients with hemophilia A or B with inhibitors. At the annual American Society of Hematology (ASH) meeting in December 2019, Catalyst Biosciences presented posters showing promising results from their Phase 2 clinical trial of marzeptacog alfa. Marzeptacog alfa significantly lowered the number of bleeding episodes. A Phase 3 study is planned for 2020.
- **BIVV001 (rFVIIIFc-VWF-XTEN):** BIVV001 is a recombinant FVIII which uses Fc fusion technology and adds a region of von Willebrand factor and XTEN polypeptides to potentially extend its time in circulation. In a Phase 1/2 trial the FVIII half-life was extended to 38 hours or 43 hours, depending on the dose, which is a significant improvement over the average FVIII half-life of 12 hours. A Phase 3 clinical trial is now under way.
- **Concizumab:** Concizumab is a monoclonal antibody engineered to create factor X (FX), through a series of chemical and molecular reactions, for the treatment of hemophilia A and B with or without inhibitors. After positive results were reported from a pair of Phase 2 trials, Novo Nordisk plans to proceed with a Phase 3 clinical trial.
- **Marstacimab:** Marstacimab is a monoclonal antibody designed to treat hemophilia A and B patients, with or without inhibitors, by blocking tissue factor pathway inhibitor (TFPI). A recently completed Phase 1/2 trial evaluated the safety and efficacy of marstacimab. Pfizer has announced plans to begin a Phase 3 study.
- **Gene Therapy:**

Factor Deficiency	Gene Therapy*	Phase
Factor VIII (Hemophilia A)	valoctogene roxaparvovec (BMN 270)	3; FDA submission
	SB 525	3
	SPK 8011	3
	SPK 8016 (Hemophilia A and B with inhibitor)	1/2
	BAX 888	1/2
	DXT 201	1/2
	TAK-754	1

Factor Deficiency	Gene Therapy*	Phase
Factor IX (Hemophilia B)	finanacogene elaparvovec (SPK 9001)	3
	etranacogene dezaparvovec (AMT-061)	3
	FLT 180a	2/3
	AMT-060	1/2
	SBFIX	1/2
	AskBio 009	1/2
	SB-FIX	1

*The information in this chart has been compiled by the Oklahoma Health Care Authority. This information may not be an all-inclusive list of gene therapies targeted at treating hemophilia A and B. This information was collected from various sources and is subject to change. This is to be used for informational purposes only.

Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] Product Summary[18]

FDA Approval(s): Feburary 2019

Indication(s): For use in adults and children with hemophilia A for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

Dosing: One unit of Esperoct® per kg of body weight will raise the FVIII level by 2 international units per deciliter [IU/dL]

- Bleeding Episodes/On-Demand Treatment:
  - Minor bleeding episodes should be treated with 40 IU/kg (≥12 years) or 65 IU/kg (≤12 years). One dose should be sufficient.
  - Moderate bleeding episodes should be treated with the same dose as minor bleeding episodes, but an additional dose may be administered after 24 hours.
  - Major bleeding episodes should be treated with 50 IU/kg (≥12 years) or 65 IU/kg (≤12 years). Additional dose(s) may be administered approximately every 24 hours.
- Perioperative Bleeding Management:
  - Minor procedures (e.g., tooth extraction) should be treated with 50 IU/kg (≥12 years) or 65 IU/kg (≤12 years). Additional dose(s) may be administered approximately every 24 hours if necessary.
  - Major procedures (e.g., intracranial, intra-abdominal, intrathoracic, joint replacement) should be treated with 50 IU/kg (≥12 years) or 65 IU/kg (≤12 years). Additional dose(s) may be administered approximately every 24 hours for the first week and then approximately every 48 hours until wound healing has occured.
- Routine Prophylaxis:
  - Adults and adolescents (≥12 years): Recommended starting dose of 50 IU/kg every 4 days which may be adjusted to more or less frequently based on bleeding episodes. May be dosed to achieve a specific target FVIII activity level depending on severity of hemophilia.
  - Children (≤12 years): Recommended starting dose of 65 IU/kg twice weekly which may be adjusted to more or less frequently based on bleeding episodes. May be

dosed to achieve a specific target FVIII activity level depending on severity of hemophilia.

Prolonged Half-Life: Esperoct® is a glycopegylated recombinant anti-hemophilic FVIII. The FVIII in Esperoct® is conjugated to a 40-kDa polyethylene glycol molecule which increases the half-life and decreases the clearance compared to the non-pegylated molecule. Esperoct® has a half-life ranging from 14.7 to 21.7 hours depending on the age of the patient. Factor VIII has an average half-life of 12 hours.

Cost Comparison:

Factor Replacement Product	Cost Per Unit	Cost for 4 Weeks of Prophylaxis Therapy
Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei]¥	**$2.23***	**$34,788***
Advate® [antihemophilic factor (recombinant)]+	$1.29**	$10,836 - $21,672**

Costs do not reflect rebated prices or net costs.
*Wholesale Acquistion Cost (WAC)
**Specialty Pharmaceutical Allowable Cost (SPAC)
¥Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei] dosing 65 IU/kg twice weekly for a 30kg patient.
+Advate® dosing 20 to 40 IU/kg every other day for a 30kg patient.

Recommendations

The Oklahoma Health Care Authority recommends the prior authorization of Esperoct®[antihemophilic factor (recombinant), glycopegylated-exei] with the following criteria:

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

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

At this time the Oklahoma Health Care Authority does not recommend any changes to the current Standards of Care for pharmacies providing factor replacement products.

Utilization Details of Factor Replacement Products: Fiscal Year 2019

Pharmacy Claims: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ADVATE PRODUCTS					
ADVATE INJ 1500 UNIT	33	8	$809,601.70	$1,480.08	$24,533.38
ADVATE INJ 2000 UNIT	29	5	$942,379.14	$1,438.75	$32,495.83
ADVATE INJ 1000 UNIT	28	10	$524,055.74	$951.10	$18,716.28
ADVATE INJ 500 UNIT	19	7	$207,783.90	$821.28	$10,935.99
ADVATE INJ 4000 UNIT	4	1	$298,148.76	$3,138.41	$74,537.19
ADVATE INJ 250 UNIT	2	2	$9,188.98	$296.42	$4,594.49
ADVATE INJ 3000 UNIT	1	1	$38,770.17	$5,538.60	$38,770.17
SUBTOTAL	**116**	**17**	**$2,829,928.39**	**$1,323.01**	**$24,395.93**
KOGENATE PRODUCTS					
KOGENATE FS INJ 2000 UNIT	61	11	$1,868,499.33	$1,314.92	$30,631.14
KOGENATE FS INJ 1000 UNIT	58	11	$881,458.42	$881.46	$15,197.56
KOGENATE FS INJ 500 UNIT	48	9	$342,384.85	$346.19	$7,133.02
KOGENATE FS INJ 3000 UNIT	7	1	$282,794.26	$1,442.83	$40,399.18
KOGENATE FS INJ 250 UNIT	3	2	$4,209.38	$73.85	$1,403.13
SUBTOTAL	**177**	**20**	**$3,379,346.24**	**$922.56**	**$19,092.35**
FEIBA PRODUCTS					
FEIBA INJ 2500 UNIT	21	3	$7,788,614.56	$14,264.86	$370,886.41
FEIBA INJ 1000 UNIT	2	1	$16,614.86	$1,510.44	$8,307.43
SUBTOTAL	**23**	**3**	**$7,805,229.42**	**$14,012.98**	**$339,357.80**
ELOCTATE PRODUCTS					
ELOCTATE INJ 1500 UNIT	30	4	$835,765.68	$1,230.88	$27,858.86
ELOCTATE INJ 500 UNIT	13	1	$60,096.62	$1,036.15	$4,622.82
ELOCTATE INJ 2000 UNIT	5	1	$84,392.97	$602.81	$16,878.59
ELOCTATE INJ 750 UNIT	3	1	$72,072.69	$858.01	$24,024.23
ELOCTATE INJ 1000 UNIT	2	2	$19,716.80	$579.91	$9,858.40
ELOCTATE INJ 250 UNIT	1	1	$841.60	$420.80	$841.60
SUBTOTAL	**54**	**6**	**$1,072,886.36**	**$1,076.11**	**$19,868.27**
WILATE PRODUCTS					
WILATE 1000-1000 UNIT	24	5	$318,726.31	$692.88	$13,280.26
WILATE 500-500 UNIT	18	4	$128,903.44	$345.59	$7,161.30
SUBTOTAL	**42**	**6**	**$447,629.75**	**$537.37**	**$10,657.85**
ALPROLIX PRODUCTS					
ALPROLIX INJ 1000 UNIT	10	1	$73,346.79	$289.91	$7,334.68
ALPROLIX INJ 4000 UNIT	9	1	$560,218.61	$2,188.35	$62,246.51
ALPROLIX INJ 2000 UNIT	6	1	$175,011.65	$1,041.74	$29,168.61
ALPROLIX INJ 500 UNIT	5	2	$36,579.15	$254.02	$7,315.83
ALPROLIX INJ 3000 UNIT	5	1	$1,892.69	$15.90	$378.54
ALPROLIX INJ 250 UNIT	1	1	$2,978.82	$106.39	$2,978.82
SUBTOTAL	**36**	**3**	**$850,027.71**	**$878.13**	**$23,611.88**
HELIXATE PRODUCTS					
HELIXATE FS INJ 2000 UNIT	1	1	$2,540.40	$2,540.40	$2,540.40
SUBTOTAL	**1**	**1**	**$2,540.40**	**$2,540.40**	**$2,540.40**
ALPHANATE PRODUCTS					
ALPHANATE INJ 1000 UNIT	10	2	$106,728.95	$567.71	$10,672.90
ALPHANATE INJ 250 UNIT	6	1	$22,107.40	$122.82	$3,684.57
ALPHANATE INJ 1500 UNIT	4	1	$80,316.24	$669.30	$20,079.06
ALPHANATE INJ 500 UNIT	2	1	$3,056.00	$509.33	$1,528.00

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ALPHANATE INJ 2000 UNIT	1	1	$2,197.35	$732.45	$2,197.35
SUBTOTAL	**23**	**2**	**$214,405.94**	**$431.40**	**$9,322.00**
XYNTHA PRODUCTS					
XYNTHA SOLOF INJ 2000 UNIT	2	1	$72,829.30	$1,213.82	$36,414.65
XYNTHA INJ 1000 UNIT	1	1	$1,275.00	$1,275.00	$1,275.00
SUBTOTAL	**3**	**2**	**$74,104.30**	**$1,214.82**	**$24,701.43**
ADYNOVATE PRODUCTS					
ADYNOVATE INJ 1000 UNIT	13	3	$274,482.65	$1,737.23	$21,114.05
ADYNOVATE INJ 2000 UNIT	11	3	$340,849.28	$1,578.01	$30,986.30
ADYNOVATE INJ 3000 UNIT	9	1	$566,956.62	$2,249.83	$62,995.18
ADYNOVATE INJ 1500 UNIT	3	2	$61,687.43	$1,233.75	$20,562.48
ADYNOVATE INJ 500 UNIT	3	2	$22,476.89	$321.10	$7,492.30
SUBTOTAL	**39**	**4**	**$1,266,452.87**	**$1,697.66**	**$32,473.15**
NUWIQ PRODUCTS					
NUWIQ KIT 500 UNIT	19	4	$307,100.28	$1,323.71	$16,163.17
NUWIQ KIT 1000 UNIT	14	4	$407,015.54	$1,833.40	$29,072.54
NUWIQ KIT 3000 UNIT	10	1	$938,539.39	$5,100.76	$93,853.94
NUWIQ KIT 250 UNIT	4	2	$18,972.38	$412.44	$4,743.10
NUWIQ KIT 2500 UNIT	2	1	$148,981.65	$6,477.46	$74,490.83
NUWIQ KIT 2000 UNIT	1	1	$19,755.06	$4,938.77	$19,755.06
SUBTOTAL	**50**	**6**	**$1,840,364.30**	**$2,588.42**	**$36,807.29**
MONOCLATE PRODUCTS					
MONOCLATE-P INJ 1500 UNIT	1	1	$16,692.55	$1,669.25	$16,692.55
SUBTOTAL	**1**	**1**	**$16,692.55**	**$1,669.26**	**$16,692.55**
HUMATE PRODUCTS					
HUMATE-P SOL 2400 UNIT	6	4	$105,931.00	$6,620.69	$17,655.17
HUMATE-P SOL 500-1200 UNIT	4	4	$18,697.74	$1,869.77	$4,674.44
HUMATE-P SOL 250-600 UNIT	3	3	$2,218.77	$554.69	$739.59
SUBTOTAL	**13**	**8**	**$126,847.51**	**$4,228.25**	**$9,757.50**
RIXUBIS PRODUCTS					
RIXUBIS INJ 1000 UNIT	3	3	$6,909.60	$987.09	$2,303.20
RIXUBIS INJ 2000 UNIT	2	1	$10,416.63	$2,604.16	$5,208.32
RIXUBIS INJ 500 UNIT	1	1	$4,231.91	$1,057.98	$4,231.91
RIXUBIS INJ 3000 UNIT	1	1	$3,923.27	$3,923.27	$3,923.27
RIXUBIS INJ 250 UNIT	1	1	$1,504.26	$376.06	$1,504.26
SUBTOTAL	**8**	**4**	**$26,985.67**	**$1,349.28**	**$3,373.21**
NOVOSEVEN PRODUCTS					
NOVOSEVEN RT INJ 5MG	1	1	$103,456.55	$103,456.55	$103,456.55
NOVOSEVEN RT INJ 8MG	1	1	$33,146.87	$33,146.87	$33,146.87
SUBTOTAL	**2**	**2**	**$136,603.42**	**$68,301.71**	**$68,301.71**
BENEFIX PRODUCTS					
BENEFIX INJ 2000 UNIT	4	3	$26,550.84	$2,950.09	$6,637.71
SUBTOTAL	**4**	**3**	**$26,550.84**	**$2,950.09**	**$6,637.71**
KOVALTRY PRODUCTS					
KOVALTRY INJ 1000 UNIT	11	1	$212,908.60	$1,314.25	$19,355.33
SUBTOTAL	**11**	**1**	**$212,908.60**	**$1,314.25**	**$19,355.33**
IDELVION PRODUCTS					
IDELVION SOL 500 UNIT	4	1	$22,455.09	$2,245.51	$5,613.77
IDELVION SOL 1000 UNIT	1	1	$4,205.27	$4,205.27	$4,205.27
SUBTOTAL	**5**	**1**	**$26,660.36**	**$2,423.67**	**$5,332.07**
HEMLIBRA PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
HEMLIBRA INJ 60MG/0.4ML	25	4	$605,147.11	$900.52	$24,205.88
HEMLIBRA INJ 30MG/ML	14	2	$163,759.91	$553.24	$11,697.14
HEMLIBRA INJ 150/ML	13	2	$818,777.95	$2,249.39	$62,982.92
HEMLIBRA INJ 105/0.7ML	7	3	$284,747.05	$1,452.79	$40,678.15
SUBTOTAL	**59**	**7**	**$1,872,432.02**	**$1,225.41**	**$31,736.14**
COAGADEX PRODUCTS					
COAGADEX INJ 250 UNIT	2	**1**	$4,120.94	$2,060.47	$2,060.47
SUBTOTAL	**2**	**1**	**$4,120.94**	**$2,060.47**	**$2,060.47**
CORIFACT PRODUCTS					
CORIFACT INJ 1000-1600 UNIT	1	1	$11,905.56	$11,905.56	$11,905.56
SUBTOTAL	**1**	**1**	**$11,905.56**	**$11,905.56**	**$11,905.56**
TOTAL	**670**	**87***	**$22,244,623.15**	**$1,718.00**	**$33,200.93**

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

Medical Claims: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J7189 FACTOR VIIA RECOMBINANT (NOVOSEVEN)	12	1	$825,506.84	$68,792.23
J7192 FACTOR VIII RECOMBINANT (ADVATE, KOGENATE FS, RECOMBINATE)	11	6	$52,457.07	$4,768.82
TOTAL	**23+**	**7***	**$877,963.91**	**$38,172.34**

+Total number of unduplicated claims.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2019 = 07/01/2018 to 06/30/2019

---

[1] Barrett J. New Treatment for Hemophilia A Receives FDA Approval. *Pharmacy Times*. Available online at: https://www.pharmacytimes.com/news/new-treatment-for-hemophilia-a-receives-fda-approval. Issued 02/19/2019. Last accessed 01/16/2020.

[2] Octapharma USA. FDA Approves Octapharma's WILATE® for Hemophilia A in Adult and Adolescent Patients. Available online at: https://www.octapharmausa.com/en/news-contact/news-single-view.html?tx_ttnews%5Btt_news%5D=1127&cHash=a01d65a6cc16f0d4d21c4151a4335e05. Issued 10/09/2019. Last accessed 01/16/2020.

[3] Investigational Treatments. Available online at: https://hemabio.com/pipeline/. Last accessed 01/28/2020.

[4] Inacio P. Fitusiran Clinical Development Among 2018 Corporate Goals, Alnylam Pharmaceuticals Says. *Hemophilia News Today*. Available online at: https://hemophilianewstoday.com/2018/01/12/hemophilia-clinical-program-fitusiran-among-2018-goals-alnylam-pharmaceuticals-announces/. Issued 01/12/2018. Last accessed 01/21/2020.

[5] U.S. National Library of Medicine. Clinicaltrials.gov. Available online at: https://clinicaltrials.gov/ct2/results?cond=hemophilia&term=fitusiran&cntry=&state=&city=&dist=&Search=Search. Last accessed 01/21/2020.

[6] Pena A. New Early Data Support Catalyst's MarzAA in Treating Acute Bleeds in Hemophilia. *Hemophilia News Today*. Available online at: https://hemophilianewstoday.com/2019/12/10/early-data-support-phase-3-trial-catalysts-marzaa-treating-acute-bleeds-hem-a-b/. Issued 12/10/2019. Last accessed 01/18/2020.

[7] National Hemophilia Foundation. Investigators Report Progress on New Subcutaneous Therapy. Available online at: https://www.hemophilia.org/Newsroom/Industry-News/Investigators-Report-Progress-on-New-Subcutaneous-Therapy. Issued 07/25/2019. Last accessed 01/18/2020.

[8] National Hemophilia Foundation. Sanofi Presents Final Trial Data for rFVIII Candidate. Available online at: https://www.hemophilia.org/Newsroom/Industry-News/Sanofi-Presents-Final-Trial-Data-for-rFVIII-Candidate. Issued 07/22/2019. Last accessed 01/18/2020.

[9] National Hemophilia Foundation. Investigational Marstacimab Shows Promise in Laboratory Assays. Available online at: https://www.hemophilia.org/Newsroom/Industry-News/Investigational-Marstacimab-Shows-Promise-in-Laboratory-Assays. Issued 09/03/2019. Last accessed 01/18/2020.

[10] National Hemophilia Foundation. Sangamo and Pfizer Announce Progress in Gene Therapy Trial at ASH. Available onlint at: https://www.hemophilia.org/Newsroom/Industry-News/Sangamo-and-Pfizer-Announce-Progress-in-Gene-Therapy-Trial-at-ASH. Issued 12/09/2019. Last accessed 01/18/2020.
[11] National Hemophilia Foundation. UniQure Reaches Enrollment Goal in Phase 3 Gene Therapy Trial. Available online at: https://www.hemophilia.org/Newsroom/Industry-News/UniQure-Reaches-Enrollment-Goal-in-Phase-3-Gene-Therapy-Trial. Issued 12/06/2019. Last accessed 01/18/2020.
[12] National Hemophilia Foundation. BioMarin Provides Trial Updates for Hemophilia A Gene Therapy. Available online at: https://www.hemophilia.org/Newsroom/Industry-News/BioMarin-Provides-Trial-Updates-for-Hemophilia-A-Gene-Therapy. Issued 06/03/2019. Last accessed 01/18/2020.
[13] Malcolm E. Gene Therapy. *Hemophilia News Today*. Available online at: https://hemophilianewstoday.com/gene-therapy/. Last accessed 01/18/2020.
[14] Park B. BLA Submitted for Gene Therapy to Treat Hemophilia A. *MPR*. Available online at: https://www.empr.com/home/news/drugs-in-the-pipeline/bla-submitted-for-gene-therapy-to-treat-hemophilia-a/. Issued 12/30/2019. Last accessed 01/18/2020.
[15] Pena A. Takeda Presents Early Data About Improving Efficiency of Hemophilia A and B Gene Therapy. *Hemophilia News Today*. Available online at: https://hemophilianewstoday.com/2019/12/18/takeda-presents-early-data-about-improving-efficiency-of-hemophilia-a-and-b-gene-therapy/. Issued 12/18/2019. Last accessed 01/18/2020.
[16] SB-525 for Hemophilia A. *Hemophilia News Today*. Available online at: https://hemophilianewstoday.com/sb-525/. Last revised 01/08/2020. Last accessed 01/21/2020.
[17] U.S. National Library of Medicine. Clinicaltrials.gov. Available online at: https://clinicaltrials.gov/. Last accessed 12/31/2019.
[18] Esperoct® Prescribing Information. Novo Nordisk, Inc. Available online at: https://www.fda.gov/vaccines-blood-biologics/esperoct. Last revised 07/19/2019. Last accessed 01/16/2020.

Appendix N

Fiscal Year 2019 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant)

Oklahoma Health Care Authority
February 2020

Current Prior Authorization Criteria

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®)			ergotamine sublingual tablet (Ergomar®)
			sumatriptan injection (Imitrex®)
			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 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 dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
5. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent 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.
6. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).

Emgality® (Galcanezumab-gnlm) Approval Criteria [Migraine Diagnosis]:*

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

   b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
   a. Hormone replacement therapy or hormone-based contraceptives; and
   b. Chronic insomnia; and
   c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 2[¥] agents with different mechanisms of action. ([¥]The manufacturer of Emgality® has currently provided a supplemental rebate to require a trial with 2 other migraine preventative therapies; however, Emgality® will follow the original criteria and require trials with 3 other migraine preventative therapies if the manufacturer chooses not to participate in supplemental rebates.) This includes, but is not limited to:
   a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
   b. Select anticonvulsant therapy; or
   c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
   a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
   b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
   c. Opioids (≥10 days/month for >3 months); and
   d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
   e. Ergotamine-containing medications (≥10 days/month for >3 months); and
   f. Triptans (≥10 days/month for >3 months); and
8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Medication must be prescribed by or in consultation with a neurologist; and
10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for

continued approval. Continuation approvals will be granted for the duration of 1 year; and

14. A quantity limit of 1 syringe or pen per 30 days will apply. Requests for an initial loading dose (240mg administered as 2 consecutive 120mg injections) will be approved for a quantity limit override upon meeting Emgality® approval criteria.

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

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

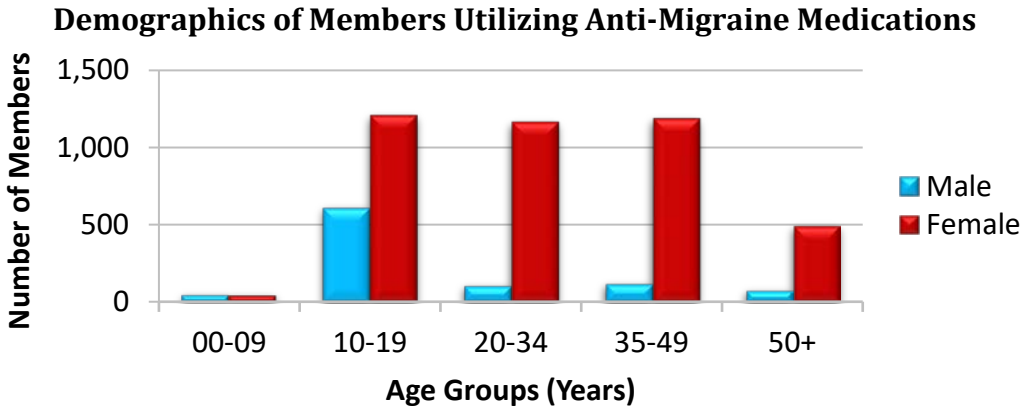
8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Aimovig®, Ajovy®) recommended as treatment (not necessarily prescribed 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. Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. A patient-specific, clinically significant reason why member cannot use Emgality® (galcanezumab-gnlm) must be provided; and
14. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
15. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig®, a quantity limit of 1 syringe or autoinjector per 30 days will apply.; and
    b. For Ajovy®, a quantity limit of 1 syringe or autoinjector per 30 days will apply. Requests for quarterly dosing (675mg every 3 months) will be approved for a quantity limit override upon meeting Ajovy® approval criteria.

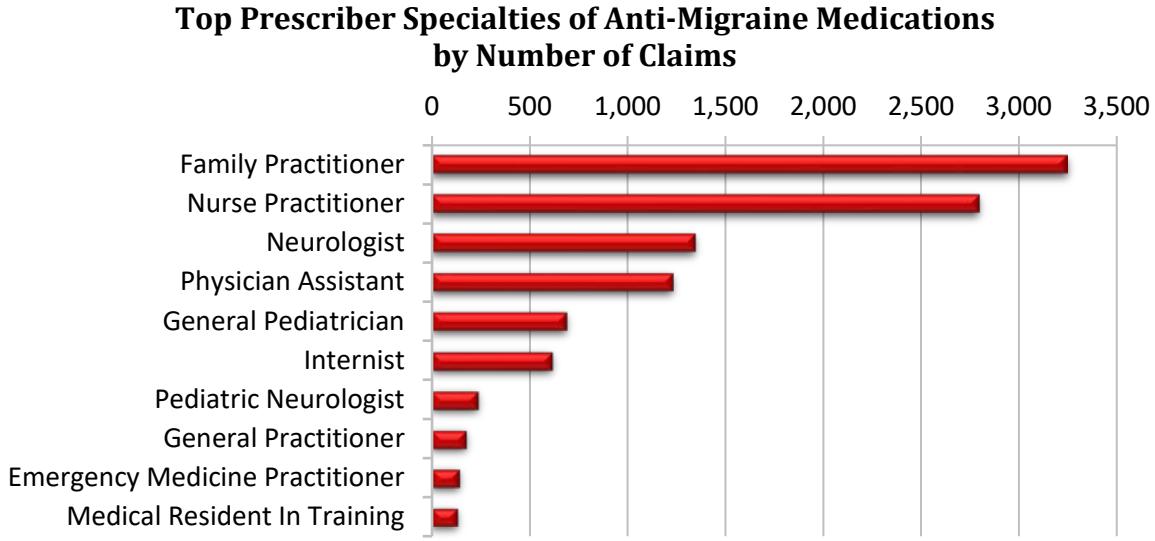
Utilization of Anti-Migraine Medications: Fiscal Year 2019

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	5,292	11,655	$289,878.37	$24.87	$1.53	125,939	189,004
2019	5,038	11,251	$375,000.48	$33.33	$1.99	121,390	188,873
% Change	**-4.80%**	**-3.50%**	**29.40%**	**34.00%**	**30.10%**	**-3.60%**	**-0.10%**
Change	**-254**	**-404**	**$85,122.11**	**$8.46**	**$0.46**	**-4,549**	**-131**

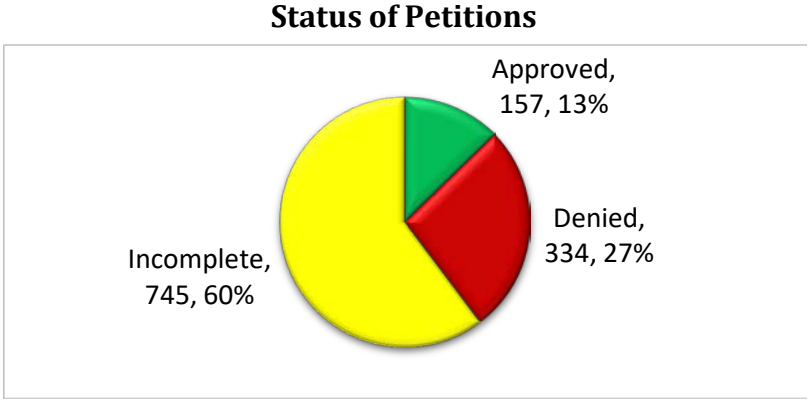
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2018 = 07/01/2017 to 06/30/2018; Fiscal year 2019 = 07/01/2018 to 06/30/2019





Prior Authorization of Anti-Migraine Medications

There were 1,236 prior authorization requests submitted for anti-migraine medications during fiscal year 2019. Computer edits are in place to detect lower tiered medications in a member's claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2019.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13]

Anticipated Patent Expiration(s):

- Zomig® (zolmitriptan nasal spray): May 2021
- Treximet® (sumatriptan/naproxen tablets): April 2026
- Tosymra™ (sumatriptan nasal spray): July 2031
- Onzetra® Xsail® (sumatriptan nasal powder): October 2034

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

- **January 2019:** Dr. Reddy's Laboratories and Promius Pharma announced the FDA approval of Tosymra™ (sumatriptan nasal spray) for the acute treatment of migraine with or without aura.
- **June 2019:** The FDA approved Emgality® (galcanezumab-gnlm) for the treatment of episodic cluster headache in adults. The effectiveness of Emgality® for the treatment of episodic cluster headache was demonstrated in a placebo-controlled, clinical trial of 106 patients. The trial measured the average number of cluster headaches per week for 3 weeks and compared the average change from baseline in the Emgality® and placebo groups. During the 3-week period, patients taking Emgality® experienced 8.7 fewer weekly cluster headache attacks than they did at baseline, compared to 5.2 fewer attacks for patients on placebo. Emgality® was first approved by the FDA in September 2018 for the preventive treatment of migraine in adults.
- **October 2019:** The FDA approved Reyvow™ (lasmiditan) for the acute treatment of migraine with or without aura in adults.
- **December 2019:** The FDA approved Ubrelvy™ (ubrogepant) for the acute treatment of migraine with or without aura in adults. Ubrelvy™ is the first oral calcitonin gene-related peptide (CGRP) receptor antagonist approved for the acute treatment of migraine.
- **January 2020:** The FDA approved an autoinjector formulation of Ajovy® (fremanezumab-vfm). Ajovy® was previously available as a syringe formulation. The Ajovy® prior authorization criteria has been adjusted to reflect the new formulation *(see Current Prior Authorization Criteria section of this report.)*

News:

- **March 2019:** According to a systematic review and pooled meta-analysis published in *Pain*, flunarizine, a calcium channel blocker, may be a safe, effective, and well-tolerated prophylactic treatment for episodic migraine. According to the authors, flunarizine has not gained the same level of popularity as similar cardiovascular (CV) medications used for migraine prevention, despite its effectiveness, excellent safety profile, and recommendation in guidelines as a first-line prophylactic therapy. Through an examination of available published trials, investigators sought to characterize the safety and efficacy of flunarizine. A systematic review of the literature published up to November 2017 was conducted. Randomized controlled trials (RCTs) that evaluated flunarizine for episodic migraine prophylaxis were examined. The primary outcome was the mean reduction in 28-day migraine attack frequency, expressed as the mean difference between groups. Secondary outcomes included treatment-related adverse events and migraine intensity and duration, and the percentage of responders (i.e.,

those reporting ≥50% decrease in headache frequency). Of the 879 studies identified, 25 were selected for inclusion and data synthesis. Based on 5 trials (N=249), flunarizine was found to reduce the frequency of attacks by 0.4 per 28 days [mean difference, −0.44; 95% confidence interval (CI), −0.61 to −0.26]. In 3 studies (N=113), the percentage of responders was greater in patients taking flunarizine versus placebo [odds ratio (OR), 8.86; 95% CI, 3.57 to 22.0]. In 7 trials (N=1,151), the prophylactic efficacy of flunarizine was comparable with that of propranolol (mean difference, −0.08; 95% CI, −0.34 to 0.18), in other studies, flunarizine and propranolol were found to have comparable efficacy on migraine intensity (2 studies; 135 participants; mean difference, 0.22; 95% CI, 0.12 to 0.57) and on migraine duration (5 studies; 1,063 participants; mean difference, 0.60; 95% CI, −1.48 to 2.69). Weight gain and daytime somnolence were the 2 most commonly reported adverse events. According to the authors, who called for new RCTs that adhere to current methodologic standards, "Ultimately, flunarizine seems to be a well-tolerated alternative for patients with contraindications for beta blockers."

- **August 2019:** The American Academy of Neurology (AAN) and American Headache Society (AHS) have published updated guidelines on the prevention and treatment of migraine in children and adolescents. In the guidelines, the authors highlight that a key component in preventing and treating migraine is maintaining a strong patient-provider relationship. The guidelines come after the authors reviewed literature published from January 2003 to August 2017 and are an update of the recommendations published by the AAN in 2004. The studies lacked sufficient evidence that preventive medications, including divalproex, onabotulinumtoxinA, amitriptyline, nimodipine, or flunarizine, had more or less of an impact on the frequency of migraine compared to placebo. However, there are medications that could more positively impact headache frequency than placebo. According to the authors, children with migraine who take propranolol may be more likely to have at least a 50% reduction in headache frequency compared to their counterparts taking placebo. In addition, topiramate and cinnarizine may be able to better limit headache frequency than placebo. The authors also determined, through their systematic review, that children with migraine who are taking amitriptyline are more likely to experience a reduction in headache frequency if a clinician provides cognitive behavioral therapy rather than headache education in addition to the medication. Furthermore, counseling patients on lifestyle and behavioral factors that influence headache frequency is key in prevention of pediatric migraines.
- **January 2020:** The Institute for Clinical and Ecominoic Review (ICER) reviewed 3 treatments for acute migraine: Reyvow™ (lasmiditan), Ubrelvy™ (ubrogepant) and rimegepant. While the first 2 have been approved, the latter remains under regulatory review. David Rind, ICER's chief medical officer, said: "These new therapies appear to be less effective overall than triptans and are expected to be much more expensive. However, for those patients who are unable to take triptans or who don't get adequate benefit from them, the evidence does demonstrate that all 3 new therapies improve or relieve migraine symptoms in 10% to 20% more patients than respond to placebo. To reach commonly-cited thresholds of cost-effectiveness, these therapies would require prices significantly below what some analysts are currently projecting." ICER's value-

based price benchmark range for lasmiditan, rimegepant, and ubrogepant is $2,200 to $3,200 per year.

Pipeline:

- **Atogepant:** According to findings from a Phase 2b/3 study presented at the 2019 AHS Annual Meeting, orally administered atogepant, a CGRP receptor antagonist, demonstrated a statistically significant and clinically relevant reduction in mean migraine days compared with placebo while eliciting no treatment-related serious adverse events. At the lowest dose of atogepant administered (10mg once daily, N=92), there was a 4.0-day reduction in mean monthly migraine days compared with a reduction of 2.85 days in the placebo arm (adjusted P=0.0236). This benefit remained consistent across 5 doses of atogepant explored in the study. At the largest dose (60mg twice daily, N=87), there was a 4.14-day mean reduction in monthly migraine days (adjusted P=0.0031). Additional Phase 3 studies are currently evaluating atogepant for episodic and chronic migraines. For episodic migraine, the treatment is being tested at 10mg, 30mg, and 60mg once daily. For chronic migraine, a 30mg twice daily dose is being explored along with 60mg once daily.
- **Rimegepant:** Results of a Phase 3 clinical trial for rimegepant were published in *The New England Journal of Medicine* in July 2019. In the trial, patients were either given a single dose of rimegepant or placebo. The co-primary endpoints were pain freedom and freedom from the symptom that bothers the patient the most (MBS) at 2 hours after receiving the drug. The trial hit its co-primary endpoints. All of the patients in the trial were adults and had at least a 1-year history of migraine and 2 to 8 migraine attacks of moderate or severe intensity per month. Of the 1,186 patients, 594 received the drug and 592 received placebo. Of those, 537 in the rimegepant group and 535 in the placebo group were evaluable for efficacy. In the rimegepant cohort, 19.6% were pain-free 2 hours after receiving the drug, while 12% were pain-free in the placebo group. In addition, 37.6% of patients in the rimegepant group were free from their MBS 2 hours after dosing compared to 25.2% in the placebo group.
- **Eptinezumab:** In July 2019, Alder BioPharmaceuticals provided new data from post-hoc analyses from 2 Phase 3 clinical trials for eptinezumab at the AHS Annual Meeting. Highlights from the new data presented show 18.1% of episodic migraine patients treated with 100mg of eptinezumab experienced no migraine days for at least half of the study period (≥3 months), compared with 4.9% of placebo-treated patients. The FDA accepted the Biologics License Application (BLA) filing for eptinezumab in April 2019, and set a Prescription Drug User Fee Act (PDUFA) target action date of February 21, 2020. If approved, eptinezumab will be the first-to-market intravenous therapy for migraine prevention.
- **Vazegepant:** Biohaven Pharmaceutical announced positive topline results from a randomized, dose-ranging, placebo-controlled, Phase 2/3 clinical trial evaluating the efficacy and tolerability of intranasal vazegepant 5mg, 10mg, and 20mg versus placebo in 1,673 patients for the acute treatment of migraine. Vazegepant 10mg and 20mg was statistically superior to placebo on the co-primary endpoints of pain freedom and freedom from MBS at 2 hours using a single dose. The benefits of vazegepant were

durable and sustained without rescue medication through 48 hours (nominal P<0.05). Additional study results are anticipated to be presented at upcoming scientific meetings in 2020.

Tosymra™ (Sumatriptan Nasal Spray) Product Summary[14]

Indication(s): Tosymra™ (sumatriptan nasal spray) is a serotonin $(5\text{-HT})_{1B/1D}$ receptor agonist (triptan) indicated for the acute treatment of migraine with or without aura in adults.
Limitation(s) of Use:

- Tosymra™ should be used only if a clear diagnosis of migraine has been established
- Tosymra™ is not indicated for the preventive treatment of migraine
- Tosymra™ is not indicated for the treatment of cluster headache

Dosing:

- Tosymra™ delivers 10mg of sumatriptan and is supplied as a ready-to-use, single-dose, disposable unit. Each carton contains 6 units.
- The recommended dose of Tosymra™ is 10mg given as a single spray in 1 nostril. The maximum cumulative dose that may be given in a 24-hour period is 30mg, with doses of Tosymra™ separated by at least 1 hour. Tosymra™ may also be given at least 1 hour following a dose of another sumatriptan product.

Efficacy: The efficacy of Tosymra™ is based on the relative bioavailability of Tosymra™ nasal spray compared to sumatriptan subcutaneous (sub-Q) injection (4mg) in healthy adults.

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Tosymra™ (sumatriptan 10mg nasal spray)	**$97.50**	**$292.50**
sumatriptan 20mg nasal spray	$41.53	$83.06
sumatriptan 6mg/0.5mL sub-Q injection	$32.29	$64.58

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.
sub-Q = subcutaneous
*Cost per maximum cumulative dose based on FDA recommended dosing.

Reyvow™ (Lasmiditan Tablets) Product Summary[15]

Indication(s): Reyvow™ (lasmiditan) is a serotonin $(5\text{-HT})_{1F}$ receptor agonist indicated for the acute treatment of migraine with or without aura in adults.
Limitation(s) of Use:

- Reyvow™ is not indicated for the preventive treatment of migraine

Dosing:

- Reyvow™ is supplied as 50mg and 100mg tablets.
- The recommended dose is 50mg, 100mg, or 200mg taken orally, as needed. No more than 1 dose should be taken in 24 hours.

Contraindication(s): None

Warnings and Precautions:

- Driving Impairment: Lasmiditan may cause significant driving impairment. In a driving study, administration of single 50mg, 100mg, or 200mg doses of lasmiditan significantly impaired subjects' ability to drive. Additionally, more sleepiness was reported at 8 hours following a single dose of lasmiditan compared to placebo. Patients should be advised not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle or operating machinery, for at least 8 hours after each dose of lasmiditan. Patients who cannot follow this advice should not take lasmiditan. Patients and prescribers should be aware that patients may not be able to assess their own driving competence and the degree of impairment caused by lasmiditan.
- Central Nervous System (CNS) Depression: CNS depression, including dizziness and sedation, may be caused by lasmiditan. Because of the potential for lasmiditan to cause sedation, other cognitive and/or neuropsychiatric adverse reactions, and driving impairment, lasmiditan should be used with caution if used in combination with alcohol or other CNS depressants.
- Serotonin Syndrome: In clinical trials, reactions consistent with serotonin syndrome were reported in patients treated with lasmiditan who were not taking any other drugs associated with serotonin syndrome. Serotonin syndrome may also occur with lasmiditan during coadministration with serotonergic drugs. Lasmiditan should be discontinued if serotonin syndrome is suspected.
- Medication Overuse Headache: Overuse of acute migraine medications (e.g., ergotamines, triptans, opioids, or a combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (i.e., medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in the frequency of migraine attacks. Detoxification of patients including withdrawal of the overused drugs and treatment of withdrawal symptoms may be necessary.

Adverse Reactions: The most common adverse reaction(s) (≥5% and greater than placebo) in lasmiditan clinical studies were dizziness, fatigue, paresthesia, and sedation.

Use in Specific Populations:

- Pregnancy: There are no adequate data on the developmental risk associated with the use of lasmiditan in pregnant women. In animal studies, adverse effects on development (increased incidences of fetal abnormalities, increased embryofetal and offspring mortality, decreased fetal body weight) occurred at maternal exposures less than (rabbit) or greater than (rat) those observed clinically.
- Lactation: There are no data on the presence of lasmiditan in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of lasmiditan have not been established in pediatric patients.
- Geriatric Use: In controlled clinical trials, dizziness occurred more frequently in patients who were at least 65 years of age compared to patients who were younger than 65

years of age. A larger increase in systolic blood pressure also occurred in patients 65 years of age and older compared to patients who were younger than 65 years of age. Clinical trials did not include sufficient number of subjects 65 years of age and older to determine whether there is a difference in efficacy in these patients compared to younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease(s) or other drug therapy(ies).

- Hepatic Impairment: No dosage adjustment is needed for patients with mild or moderate hepatic impairment (Child-Pugh A or B). Lasmiditan has not been studied in patients with severe hepatic impairment (Child-Pugh C) and its use in not recommended for use in these patients.

Efficacy: The efficacy of lasmiditan in the acute treatment of migraine was demonstrated in 2 randomized, double-blind, placebo-controlled trials. These studies enrolled patients with a history of migraine with and without aura according to the International Classification of Headache Disorders diagnostic criteria. Patients were predominantly female (84%) and white (78%), with a mean age of 42 years (range 18 to 81 years). At baseline, 22% of patients were taking preventive medication for migraine. Study 1 randomized patients to lasmiditan 100mg (N=744), 200mg (N=745), or placebo (N=742) and Study 2 randomized patients to lasmiditan 50mg (N=750), 100mg (N=754), 200mg (N=750), or placebo (N=751). Patients were allowed to take a rescue medication 2 hours after taking lasmiditan; however, opioids, barbiturates, triptans, and ergots were not allowed within 24 hours of lasmiditan administration. The primary efficacy analyses were conducted in patients that treated a migraine with moderate-to-severe pain within 4 hours of the onset of the attack. The efficacy of lasmiditan was established by an effect on pain freedom at 2 hours and MBS freedom at 2 hours compared to placebo for Studies 1 and 2. Pain freedom was defined as a reduction of moderate or severe headache pain to no pain, and MBS freedom was defined as the absence of the self-identified MBS (photophobia, phonophobia, or nausea). Among patients who selected a MBS, the most commonly selected MBS was photophobia (54%), followed by nausea (24%), and phonophobia (22%). In both studies, the percentage of patients achieving pain freedom and MBS freedom 2 hours after treatment was significantly greater among patients receiving lasmiditan at all doses compared to those receiving placebo.

Efficacy Endpoints	Study 1			Study 2			
	Lasmiditan 100mg	Lasmiditan 200mg	Placebo	Lasmiditan 50mg	Lasmiditan 100mg	Lasmiditan 200mg	Placebo
Pain Free at 2 hours							
N	498	503	515	544	523	521	534
% Responders	28.3	31.8	15.3	28.3	31.4	38.8	21.0
Difference from placebo (%)	13	16.5		7.3	10.4	17.8	
P-value	<0.001	<0.001		0.006	<0.001	<0.001	

Efficacy Endpoints	Study 1			Study 2			
	Lasmiditan 100mg	Lasmiditan 200mg	Placebo	Lasmiditan 50mg	Lasmiditan 100mg	Lasmiditan 200mg	Placebo
MBS Free at 2 hours							
N	464	467	480	502	491	478	509
% Responders	41.2	40.7	29.6	40.8	44.0	48.7	33.2
Difference from placebo (%)	11.6	11.1		7.6	10.8	15.5	
P-value	<0.001	<0.001		0.014	<0.001	<0.001	

N = number; % = percentage; MBS = most bothersome symptom

Cost: Cost information for Reyvow™ (lasmiditan) is not currently available.

Ubrelvy™ (Ubrogepant Tablets) Product Summary[16]

Indication(s): Ubrelvy™ (ubrogepant) is a CGRP receptor antagonist indicated for the acute treatment of migraine with or without aura in adults.
Limitation(s) of Use:

- Ubrelvy™ is not indicated for the preventive treatment of migraine

Dosing:

- Ubrelvy™ is supplied as 50mg and 100mg tablets. It is supplied in unit-dose packets and each packet contains 1 tablet. Ubrelvy™ is available in boxes containing 6, 8, 10, 12, or 30 packets.
- The recommended dose is 50mg or 100mg taken orally, as needed. If needed, a second dose may be administered at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200mg.
- In patients with severe hepatic or severe renal impairment, the recommended dose is 50mg. If needed, a second 50mg dose may be taken at least 2 hours after the initial dose.
- The safety of treating more than 8 migraines in a 30-day period has not been established.

Contraindication(s): Concomitant use with strong CYP3A4 inhibitors

Adverse Reactions: The most common adverse reaction(s) (incidence ≥2% and greater than placebo) in ubrogepant clinical studies were nausea and somnolence.

Use in Specific Populations:

- Pregnancy: There are no adequate data on the developmental risk associated with the use of ubrogepant in pregnant women. In animal studies, adverse effects on embryofetal development were observed following administration of ubrogepant during pregnancy (increased embryofetal mortality in rabbits) or during pregnancy and lactation (decreased body weight in offspring in rats) at doses greater than those used clinically and which were associated with maternal toxicity.

- Lactation: There are no data on the presence of ubrogepant in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of ubrogepant have not been established in pediatric patients.
- Geriatric Use: In pharmacokinetic studies, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects. Clinical studies of ubrogepant did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.
- Hepatic Impairment: In patients with pre-existing mild (Child-Pugh Class A), moderate (Child-Pugh Class B), or severe hepatic impairment (Child-Pugh Class C), ubrogepant exposure was increased by 7%, 50%, and 115%, respectively. No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Dose adjustment for ubrogepant is recommended with severe hepatic impairment.
- Renal Impairment: The renal route of elimination plays a minor role in the clearance of ubrogepant. No dose adjustment is recommended for patients with mild or moderate renal impairment. Dose adjustment is recommended for patients with severe renal impairment and use of ubrogepant should be avoided in patients with end-stage renal disease.

Efficacy: The efficacy of ubrogepant for the acute treatment of migraine was demonstrated in 2 randomized, double-blind, placebo-controlled trials. Study 1 randomized patients to placebo (N=559) or ubrogepant 50mg (N=556) or 100mg (N=557) and Study 2 randomized patients to placebo (N=563) or ubrogepant 50mg (N=562). In all studies, patients were instructed to treat a migraine with moderate-to-severe headache pain intensity. A second dose of study medication (ubrogepant or placebo), or the patient's usual acute treatment for migraine, was allowed between 2 to 48 hours after the initial treatment for a non-responding or recurrent migraine headache. Up to 23% of patients were taking preventive medications for migraine at baseline. None of these patients were on concomitant preventive medication that act on the CGRP pathway. The primary efficacy analyses were conducted in patients who treated a migraine with moderate-to-severe pain. The efficacy of ubrogepant was established by pain freedom at 2 hours post-dose and MBS freedom at 2 hours post-dose, compared to placebo, for Studies 1 and 2. Pain freedom was defined as a reduction of moderate or severe headache pain to no pain, and MBS freedom was defined as the absence of the self-identified MBS (i.e., photophobia, phonophobia, or nausea). Among patients who selected a MBS, the most commonly selected was photophobia (56%), followed by phonophobia (24%), and nausea (19%). In both studies, the percentage of patients achieving headache pain freedom and MBS freedom 2 hours post-dose was significantly greater among patients receiving ubrogepant compared to those receiving placebo.

Efficacy Endpoints	Study 1			Study 2	
	Ubrogepant 50mg	Ubrogepant 100mg	Placebo	Ubrogepant 50mg	Placebo
Pain Free at 2 hours					
N	422	448	456	464	456
% Responders	19.2	21.2	11.8	21.8	14.3
Difference from placebo (%)	7.4	9.4		7.5	
P-value	0.002	<0.001		0.007	
MBS Free at 2 hours					
N	420	448	454	463	456
% Responders	38.6	37.7	27.8	38.9	27.4
Difference from placebo (%)	10.8	9.9		11.5	
P-value	<0.001	<0.001		<0.001	
Pain Relief at 2 hours					
N	422	448	456	464	456
% Responders	60.7	61.4	49.1	62.7	48.2
P-value	<0.001	<0.001		<0.001	
Sustained Pain Freedom 2 to 24 hours					
N	418	441	452	457	451
% Responders	12.7	15.4	8.6	14.4	8.2
P-value	NS	0.002		0.005	

N = number; % = percentage; MBS = most bothersome symptom; NS = not statistically significant (NS)

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Ubrelvy™ (ubrogepant) 100mg tablets	**$85.00**	**$170.00**
rizatriptan 10mg tablets	$0.76	$2.28
sumatriptan 100mg tablets	$0.60	$1.20

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

Recommendations

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

1. The placement of Tosymra™ (sumatriptan nasal spray), Reyvow™ (lasmiditan), and Ubrelvy™ (ubrogepant) into the Special Prior Authorization (PA) Tier with the following criteria as shown in red.
2. Updating the Emgality® (galcanezumab-gnlm) PA criteria as shown in in red based on new FDA approved indication(s).

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®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan (Reyvow™)
			sumatriptan injection (Imitrex®)
			sumatriptan injection (Zembrace® SymTouch®)
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan nasal spray (Tosymra™)
			ubrogepant (Ubrelvy™)

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

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response or a patient-specific, clinically significant reason why a Tier-1 product is not appropriate for the member; 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 Zembrace® SymTouch® or Tosymra™ will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
5. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent 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.
6. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
7. Use of Reyvow™ (lasmiditan) or Ubrelvy™ (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications.

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

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

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

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

Utilization Details of Anti-Migraine Medications: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
SUMATRIPTAN TAB 50MG	3,013	1,587	$46,383.29	$1.08	$15.39	12.37%
SUMATRIPTAN TAB 100MG	2,950	1,174	$45,013.89	$1.06	$15.26	12.00%
SUMATRIPTAN TAB 25MG	1,985	1,165	$34,378.21	$1.22	$17.32	9.17%
RIZATRIPTAN TAB 10MG	1,107	521	$17,819.11	$0.69	$16.10	4.75%
RIZATRIPTAN TAB 10MG ODT	852	382	$17,673.38	$0.92	$20.74	4.71%
RIZATRIPTAN TAB 5MG ODT	437	248	$9,144.52	$0.94	$20.93	2.44%
RIZATRIPTAN TAB 5MG	418	227	$6,853.94	$0.71	$16.40	1.83%
RELPAX TAB 40MG	121	51	$62,343.13	$40.91	$515.23	16.62%
RELPAX TAB 20MG	55	30	$25,397.28	$38.60	$461.77	6.77%
SUMAT-NAPROX TAB 85-500MG	8	4	$1,590.80	$6.63	$198.85	0.42%
TIER-1 SUBTOTAL	**10,946**	**5,389**	**$266,597.55**	**$1.48**	**$24.36**	**71.08%**
TIER-2 PRODUCTS						
ZOMIG SPR 5MG	38	10	$17,038.88	$14.95	$448.39	4.54%
ZOLMITRIPTAN TAB 5MG	21	8	$471.23	$0.77	$22.44	0.13%
NARATRIPTAN TAB 2.5MG	18	6	$465.28	$1.03	$25.85	0.12%
ZOLMITRIPTAN TAB 2.5MG	13	3	$424.89	$1.09	$32.68	0.11%
ZOMIG SPR 2.5MG	12	4	$5,301.10	$14.73	$441.76	1.41%
ZOLMITRIPTAN TAB 5MG ODT	12	5	$373.13	$1.15	$31.09	0.10%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ZOLMITRIPTAN TAB 2.5 MG	8	4	$297.61	$1.36	$37.20	0.08%
NARATRIPTAN TAB 1MG	3	3	$92.79	$2.44	$30.93	0.02%
TIER-2 SUBTOTAL	**125**	**43**	**$24,464.91**	**$6.92**	**$195.72**	**6.51%**
SPECIAL PRIOR AUTHORIZATION PRODUCTS						
SUMATRIPTAN INJ 6MG/0.5ML	26	5	$7,449.93	$16.63	$286.54	1.99%
SUMATRIPTAN SPR 20MG/ACT	14	3	$4,132.86	$25.83	$295.20	1.10%
ELETRIPTAN TAB 40MG	13	2	$1,229.16	$5.64	$94.55	0.33%
SUMATRIPTAN INJ 6MG/0.5ML	8	1	$3,919.39	$18.49	$489.92	1.05%
SUMATRIPTAN INJ 6MG/0.5ML	3	1	$93.93	$3.13	$31.31	0.03%
ELETRIPTAN TAB 20MG	3	2	$329.34	$4.70	$109.78	0.09%
SPECIAL PA SUBTOTAL	**67**	**14**	**$17,154.61**	**$15.07**	**$256.04**	**4.59%**
CGRP PRODUCTS						
EMGALITY INJ 120MG/ML	77	38	$45,825.03	$19.34	$595.13	12.22%
AIMOVIG INJ 70MG/ML	21	7	$11,844.63	$18.80	$564.03	3.16%
AIMOVIG INJ 140DOSE	8	3	$4,526.75	$10.99	$565.84	1.21%
EMGALITY INJ 120MG/ML	4	3	$2,862.01	$24.67	$715.50	0.76%
AIMOVIG INJ 140MG/ML	3	1	$1,724.99	$20.54	$575.00	0.46%
CGRP SUBTOTAL	**113**	**52**	**$66,783.41**	**$18.49**	**$591.00**	**17.81%**
TOTAL	**11,251**	**5,038***	**$375,000.48**	**$1.99**	**$33.33**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
CGRP = calcitonin gene-related peptide
Fiscal year 2019 = 07/01/2018 to 06/30/2019

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm?resetfields=1. Last revised 01/2020. Last accessed 01/13/2020.

[2] Dr. Reddy's. Dr. Reddy's Laboratories and Its U.S. Subsidiary, Promius Pharma, Announce FDA Approval for Tosymra™ (Sumatriptan Nasal Spray) 10mg, in the U.S. Market. *Biospace*. Available online at: https://www.biospace.com/article/releases/dr-reddy-s-laboratories-and-its-u-s-subsidiary-promius-pharma-announce-fda-approval-for-tosymra-sumatriptan-nasal-spray-10-mg-in-the-u-s-market/. Issued 01/29/2019. Last accessed 01/09/2020.

[3] FDA News Release. FDA approves first treatment for episodic cluster headache that reduces the frequency of attacks. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-episodic-cluster-headache-reduces-frequency-attacks. Issued 06/04/2019. Last accessed 01/09/2020.

[4] FDA News Release. FDA approves new treatment for patients with migraine. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-patients-migraine. Issued 10/11/2019. Last accessed 01/09/2020.

[5] FDA News Release. FDA approves new treatment for adults with migraine. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-adults-migraine. Issued 12/23/2019. Last accessed 01/14/2020.

[6] Levy S. FDA approves Teva's Ajovy auto-injector device. *Drug Store News*. Available online at: https://drugstorenews.com/fda-approves-tevas-ajovy-auto-injector-device?oly_enc_id=6022E7647590A6Z&utm_source=omeda&utm_medium=email&utm_campaign=NL_DSN+AM&utm_keyword=. Issued 01/29/2020. Last accessed 01/30/2020.

[7] Rothbard G. Flunarizine May Be Safe and Effective for Episodic Migraine Prophylaxis. *Neurology Advisor*. Available online at: https://www.neurologyadvisor.com/topics/migraine-and-headache/flunarizine-may-be-safe-and-effective-for-episodic-migraine-prophylaxis/. Issued 03/21/2019. Last accessed 01/14/2020.

[8] Murphy C. AAN, AHS Issue Updated Guidelines for Pediatric Migraines. *Neurology Consult*. Available online at: https://www.consultant360.com/exclusive/neurology/migraine/aan-ahs-issue-updated-guidelines-pediatric-migraine. Issued 08/2019. Last accessed 01/14/2020.

[9] ICER expects new migraine drug prices to exceed their worth. *The Pharma Letter*. Available online at: https://www.thepharmaletter.com/article/icer-expects-new-migraine-drug-prices-to-exceed-their-worth. Issued 01/13/2020. Last accessed 01/24/2020.

[10] Inman S. Atogepant Effectively Prevents Migraine in Phase 2b/3 Trial. *Neurology Live*. Available online at: https://www.neurologylive.com/conferences/ahs-2019/atogepant-effectively-prevents-migraine-in-phase-2b3-trial. Issued 07/13/2019. Last accessed 01/09/2020.

[11] Terry M. Biohaven's Rimegepant for Migraines Heads to the FDA for Approval Following Successful Trial. *BioSpace*. Available online at: https://www.biospace.com/article/biohaven-s-migraine-drug-shows-superiority-for-freedom-from-pain-in-phase-iii/. Issued 07/11/2019. Last accessed 01/09/2020.

[12] Alder BioPharmaceuticals. Alder BioPharmaceuticals Reports Second Quarter 2019 Financial and Operating Results. *Globe Newswire*. Available online at: https://investor.alderbio.com/news-releases/news-release-details/alder-biopharmaceuticalsr-reports-second-quarter-2019-financial. Issued 08/06/2019. Last accessed 01/14/2020.

[13] Biohaven Pharmaceuticals. Biohaven Achieves Positive Topline Results in Pivotal Phase 2/3 Study of Vazegepant, the First and Only Intranasal CGRP Receptor Antagonist in Clinical Development for the Acute Treatment of Migraine. *PR Newswire*. Available online at: https://www.biohavenpharma.com/investors/news-events/press-releases/12-17-2019. Issued 12/17/2019. Last accessed 01/14/2020.

[14] Tosymra™ (sumatriptan nasal spray) Prescribing Information. Upsher-Smith Laboratories, LLC. Available online at: https://www.upsher-smith.com/wp-content/uploads/TOS-MI.pdf. Last revised 07/2019. Last accessed 01/09/2020.

[15] Reyvow™ (lasmiditan) Prescribing Information. Lilly USA, LLC. Available online at: http://pi.lilly.com/us/reyvow-uspi.pdf. Issued 10/2019. Last accessed 01/13/2020.

[16] Ubrelvy™ (Ubrogepant) Prescribing Information. Allergan. Available online at: https://media.allergan.com/products/Ubrelvy_pi.pdf. Last revised 12/2019. Last accessed 01/09/2020.

Appendix O

Fiscal Year 2019 Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Xcopri® (Cenobamate)

Oklahoma Health Care Authority
February 2020

Current Prior Authorization Criteria

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

Briviact® (Brivaracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants; and
4. 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
5. 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.

Carnexiv™ (Carbamazepine Injection) Approval Criteria:

1. An FDA approved indication; and
2. Initial prescription must be written by a neurologist; and
3. Member must currently be stable on oral carbamazepine; and

4. Member must have a current condition in which oral administration is temporarily not feasible and needing Carnexiv™ for replacement therapy; and
5. Approval length will be for a maximum of 7 days of therapy. Further approval may be granted if prescriber documents an ongoing need for Carnexiv™ intravenous (IV) therapy over carbamazepine oral formulations.

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. 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. 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 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.

Aptiom® (Eslicarbazepine) Approval Criteria:

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

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

1. An FDA approved diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants; and
4. Afinitor® must be used as adjunctive treatment; and
5. The member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. The member must not be taking St. John's wort concurrently with Afinitor®; and
7. The prescriber must verify that Afinitor® trough levels and adverse reactions (e.g., non-infectious pneumonitis, stomatitis, hyperglycemia, dyslipidemia, thrombocytopenia, neutropenia, febrile neutropenia) will be monitored, and dosing changes or discontinuations will correspond with recommendations in the drug labeling; and
8. Verification from the prescriber that female members will use contraception while receiving Afinitor® therapy and for 8 weeks after the last dose of Afinitor® and that male members with female partners of reproductive potential will use contraception while receiving Afinitor® therapy and for 4 weeks after the last dose of Afinitor®; and
9. The member's recent body surface area (BSA) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
10. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Felbatol® (Felbamate) Approval Criteria:

1. Initial prescription must be written by a neurologist; and
2. Member must have failed therapy with at least 3 other anticonvulsants.

Spritam® (Levetiracetam) Approval Criteria:

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

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

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

Banzel® (Rufinamide) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome (LGS); and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants.

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. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
6. 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
7. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Qudexy® XR (Topiramate Extended-Release) 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 quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (150mg and 200mg).

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. 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).

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Refractory complex seizures in adults and pediatric patients 10 years of age or older; or
   b. Infantile spasms in children 1 month to 2 years of age; and
2. Authorization of generic vigabatrin (in place of brand Sabril®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
3. Members with refractory complex seizures must have previous trials of at least 3 other anticonvulsants; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the SABRIL REMS program and maintain enrollment throughout therapy.

Utilization of Anticonvulsants: Fiscal Year 2019

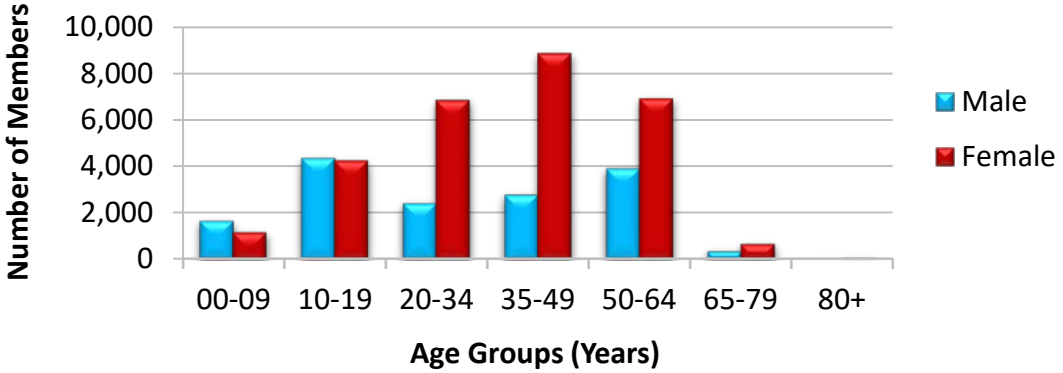
The following utilization data includes anticonvulsants used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate. Please note, the following utilization data does not include Afinitor® (everolimus) for the diagnosis of tuberous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

Comparison of Fiscal Years

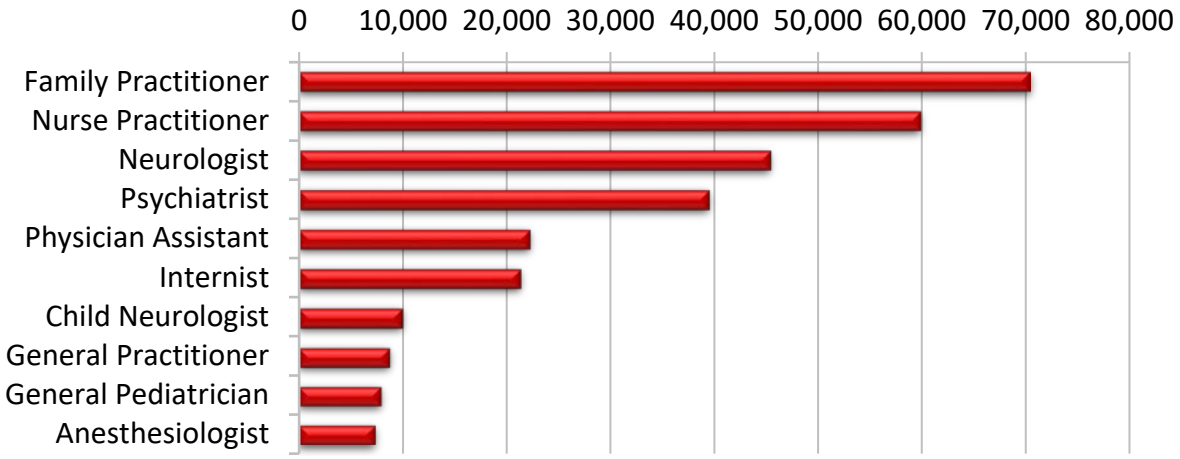
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	45,800	329,438	$26,394,474.62	$80.12	$2.63	31,734,176	10,023,351
2019	44,223	318,777	$26,907,879.08	$84.41	$2.77	31,091,690	9,719,497
% Change	**-3.40%**	**-3.20%**	**1.90%**	**5.40%**	**5.30%**	**-2.00%**	**-3.00%**
Change	**-1,577**	**-10,661**	**$513,404.46**	**$4.29**	**$0.14**	**-642,486**	**-303,854**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Demographics of Members Utilizing Anticonvulsants



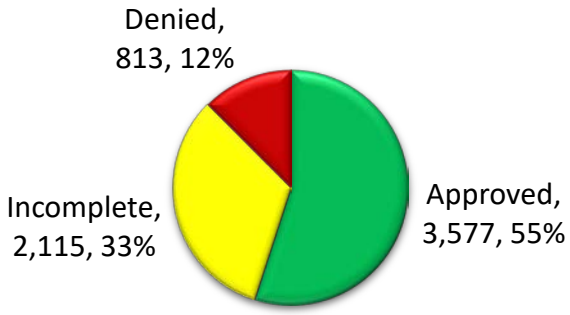
Top Prescriber Specialties of Anticonvulsants by Number of Claims



Prior Authorization of Anticonvulsants

There were 6,505 prior authorization requests submitted for anticonvulsants during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Briviact® [brivaracetam tablets, oral solution, intravenous (IV) solution]: February 2021
- Vimpat® (lacosamide tablets, oral solution, IV solution): March 2022
- Banzel® (rufinamide tablets, oral suspension): May 2023
- Sympazan™ (clobazam oral films): April 2024
- Diacomit® (stiripentol capsules, oral suspension): August 2025* (*Diacomit® does not have any unexpired patents; however, it does currently have exclusivity through August 2025.)
- Fycompa® (perampanel tablets, oral suspension): July 2026
- Oxtellar XR® [oxcarbazepine extended-release (ER) tablets]: April 2027
- Nayzilam® (midazolam nasal spray): January 2028
- Trokendi XR® (topiramate ER capsules): April 2028
- Aptiom® (eslicarbazepine tablets): August 2032
- Carnexiv™ (carbamazepine IV solution): February 2033

- Qudexy® XR (topiramate ER capsules): March 2033
- Spritam® (levetiracetam tablets for oral suspension): March 2034
- Epidiolex® (cannabidiol oral solution): June 2035

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

- **May 2019:** The FDA approved Nayzilam® (midazolam nasal spray) for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients 12 years of age and older with epilepsy. Nayzilam® is the first FDA-approved nasal delivery option for treating seizure clusters and is supplied as a single-dose nasal spray unit that can be carried with the patient. Each Nayzilam® nasal spray unit contains 5mg midazolam per 0.1mL solution. Nayzilam® allows for administration by a non-health care professional in patients actively seizing.
- **November 2019:** The FDA approved Xcopri® (cenobamate) for the treatment of adult patients with partial-onset seizures. Cenobamate is currently pending controlled substance scheduling by the U.S. Drug Enforcement Administration (DEA).
- **January 2020:** The FDA approved Valtoco® (diazepam nasal spray) for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients 6 years of age and older with epilepsy. Valtoco® is the first nasal spray approved by the FDA as a rescue treatment for patients aged 6 years and older. Valtoco® is supplied as a single-dose nasal spray device containing 5mg, 7.5mg, or 10mg diazepam per 0.1mL solution. Similar to Nayzilam®, Valtoco® allows for administration by a non-health care professional in patients actively seizing.
- **January 2020:** The FDA expanded the approved indications for Sabril® (vigabatrin) to include the adjunctive treatment of refractory complex partial seizures in patients 2 years of age and older who have responded inadequately to several alternative treatments; vigabatrin is not indicated as a first-line agent. Vigabatrin was previously approved for this indication in patients 10 years of age and older. Sabril® was first FDA approved in 2009 and is also indicated for the treatment of infantile spasms in infants 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.

Xcopri® (Cenobamate) Product Summary[9]

Indication(s): Xcopri® (cenobamate) is indicated for the treatment of partial-onset seizures in adult patients.

Dosing:

- Xcopri® is supplied as 12.5mg, 25mg, 50mg, 100mg, 150mg, and 200mg oral tablets.
- The recommended initial dosage of cenobamate is 12.5mg once daily, titrated to the recommended maintenance dose of 200mg once daily.
- The recommended dosage and titration schedule is included in the following table (Table 1). The recommended dosage and titration schedule should not be exceeded due

to the potential for serious adverse reactions (*refer to Xcopri® prescribing information for specific warnings and precautions*).

- The maximum recommended dosage of cenobamate is 400mg once daily.
- Cenobamate may be taken any time of the day, with or without food. Cenobamate tablets should be swallowed whole with liquid, and the tablets should not be crushed or chewed.
- For patients with mild-to-moderate hepatic impairment, the maximum recommended dosage of cenobamate is 200mg once daily. Cenobamate is not recommended for use in patients with severe hepatic impairment.
- If cenobamate is discontinued, the dosage should be gradually reduced over a period of at least 2 weeks, unless safety concerns require abrupt withdrawal.
- The safety and effectiveness of cenobamate have not been established in pediatric patients.

Table 1. Recommended Dosage of Cenobamate for Partial-Onset Seizures in Adult Patients

Initial Dosage	
Week 1 and 2	12.5mg once daily
Titration Regimen	
Week 3 and 4	25mg once daily
Week 5 and 6	50mg once daily
Week 7 and 8	100mg once daily
Week 9 and 10	150mg once daily
Maintenance Dosage	
Week 11 and thereafter	200mg once daily
Maximum Dosage	
If needed based on clinical response and tolerability, dose may be increased above 200mg by increments of 50mg once daily every 2 weeks to 400mg	400mg once daily

Mechanism of Action: The precise mechanism by which cenobamate exerts its therapeutic effects in patients with partial-onset seizures is unknown. Cenobamate has been demonstrated to reduce repetitive neuronal firing by inhibiting voltage-gated sodium currents and is also a positive allosteric modulator of the gamma-aminobutyric acid ($GABA_A$) ion channel.

Contraindication(s):

- Familial short QT syndrome
- Hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri®

Adverse Reactions: In clinical trials, the most common adverse reactions (incidence of ≥10% and greater than placebo) that occurred in cenobamate-treated patients were somnolence, dizziness, fatigue, diplopia, and headache. The discontinuation rates because of adverse events were 11%, 9%, and 21% for patients randomized to receive cenobamate at doses of

100mg/day, 200mg/day, and 400mg/day, respectively, compared to 4% of patients randomized to receive placebo.

Efficacy: The efficacy of cenobamate for the treatment of partial-onset seizures was established in 2 multicenter, randomized, double-blind, placebo-controlled studies in adult patients (Study 1 and Study 2). The patients enrolled in the 2 studies had partial-onset seizures with or without secondary generalization and were not adequately controlled with 1 to 3 concomitant antiepileptic drugs (AEDs). During an 8-week baseline period, patients were required to have at least 3 or 4 partial-onset seizures per 28 days on average with no seizure-free period exceeding 3 to 4 weeks. Both studies had an 8-week baseline period to establish a baseline seizure frequency, then patients were randomized to a treatment arm. Patients entered a treatment period consisting of an initial treatment phase (6 weeks) and a subsequent maintenance phase (6 weeks for Study 1 and 12 weeks for Study 2). Study 1 compared doses of cenobamate 200mg/day with placebo, and Study 2 compared doses of cenobamate 100mg/day, 200mg/day, and 400mg/day with placebo. In the 2 studies, patients had a mean duration of epilepsy of approximately 24 years and median baseline seizure frequency of 8.5 seizures per 28 days. More than 80% of patients were taking 2 or more concomitant AEDs. The primary efficacy outcome in both studies was the percent change from baseline in seizure frequency per 28 days in the treatment period. The following table (Table 2) summarizes the change in seizure frequency in Study 1 and Study 2.

Table 2. Percent Change from Baseline in Seizure Frequency per 28 Days in the Treatment Period (Study 1 and Study 2)

Treatment Group	N	Median % Change*	P-Value¥
Study 1			
Placebo	108	-21.5	n/a
Cenobamate 200mg/day	113	-55.6	<0.0001**
Study 2			
Placebo	106	-24.3	n/a
Cenobamate 100mg/day	108	-36.3	0.006**
Cenobamate 200mg/day	109	-55.2	<0.001**
Cenobamate 400mg/day	111	-55.3	<0.001**

N = number; % = percentage; n/a = not applicable

*Median percent change from baseline in seizure frequency per 28 days (%); a negative percent change from baseline in seizure frequency indicates a reduction in seizure frequency from baseline

¥ P-value (compared to placebo)

**Statistically significant compared to placebo

Cost: Cost information for Xcopri® (cenobamate) is not yet available.

Recommendations

The College of Pharmacy recommends the prior authorization of Xcopri® (cenobamate) with the following criteria:

Xcopri® (Cenobamate) Approval Criteria:

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

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

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Refractory complex seizures in adults and pediatric patients ~~10~~ 2 years of age or older; or
   b. Infantile spasms in children 1 month to 2 years of age; and
2. Authorization of generic vigabatrin (in place of brand Sabril®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
3. Members with refractory complex seizures must have previous trials of at least 3 other anticonvulsants; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the SABRIL REMS program and maintain enrollment throughout therapy.

Utilization Details of Anticonvulsants: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
GABAPENTIN PRODUCTS					
GABAPENTIN CAP 300MG	35,217	10,356	$451,039.14	$12.81	3.4
GABAPENTIN TAB 600MG	24,413	5,017	$444,853.77	$18.22	4.9
GABAPENTIN TAB 800MG	18,366	3,039	$383,945.47	$20.91	6.0
GABAPENTIN CAP 100MG	9,942	3,702	$119,315.35	$12.00	2.7
GABAPENTIN CAP 400MG	6,121	1,611	$91,923.89	$15.02	3.8
GABAPENTIN SOL 250MG/5ML	786	152	$42,756.71	$54.40	5.2
NEURONTIN CAP 300MG	6	1	$5,626.16	$937.69	6.0
SUBTOTAL	**94,851**	**23,878**	**$1,539,460.49**	**$16.23**	**4.0**
LEVETIRACETAM PRODUCTS					
LEVETIRACETA SOL 100MG/ML	10,663	1,613	$228,035.68	$21.39	6.6
LEVETIRACETA TAB 500MG	9,207	2,038	$141,371.96	$15.35	4.5
LEVETIRACETA TAB 1000MG	5,621	936	$139,829.06	$24.88	6.0
LEVETIRACETA TAB 750MG	4,078	743	$85,934.30	$21.07	5.5
LEVETIRACETA TAB 250MG	1,487	335	$21,550.16	$14.49	4.4
LEVETIRACETA TAB 500MG ER	541	111	$13,955.21	$25.80	4.9
LEVETIRACETA TAB 750MG ER	478	89	$20,842.92	$43.60	5.4
KEPPRA XR TAB 500MG	99	10	$81,263.91	$820.85	9.9
KEPPRA XR TAB 750MG	66	9	$61,809.95	$936.51	7.3

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
ROWEEPRA TAB 500MG	63	45	$940.47	$14.93	1.4
KEPPRA TAB 1000MG	51	6	$62,976.29	$1,234.83	8.5
KEPPRA TAB 750MG	49	6	$52,521.14	$1,071.86	8.2
KEPPRA SOL 100MG/ML	47	6	$18,117.08	$385.47	7.8
KEPPRA TAB 500MG	38	4	$13,194.56	$347.23	9.5
LEVETIRACETM INJ 500/5ML	35	1	$3,144.63	$89.85	35.0
ROWEEPRA TAB 750MG	15	12	$317.56	$21.17	1.3
KEPPRA TAB 250MG	9	1	$8,507.28	$945.25	9.0
SPRITAM TAB 1000MG	2	1	$981.04	$490.52	2.0
ROWEEPRA XR TAB 500MG	1	1	$42.84	$42.84	1.0
SUBTOTAL	**32,550**	**5,967**	**$955,336.04**	**$29.35**	**5.5**
DIVALPROEX, VALPROATE, AND VALPROIC ACID PRODUCTS					
DIVALPROEX TAB 500MG DR	8,131	1,510	$134,525.13	$16.54	5.4
DIVALPROEX TAB 500MG ER	6,688	1,238	$196,552.94	$29.39	5.4
DIVALPROEX TAB 250MG DR	5,041	1,180	$70,728.43	$14.03	4.3
DIVALPROEX TAB 250MG ER	3,505	770	$95,475.67	$27.24	4.6
VALPROIC ACD SOL 250MG/5ML	2,283	307	$44,744.48	$19.60	7.4
DIVALPROEX CAP 125MG	1,808	307	$138,761.45	$76.75	5.9
DIVALPROEX TAB 125MG DR	1,730	389	$22,881.92	$13.23	4.4
VALPROIC ACD CAP 250MG	929	180	$27,517.99	$29.62	5.2
DEPAKOTE SPR CAP 125MG	115	15	$44,079.86	$383.30	7.7
DEPAKOTE ER TAB 500MG	77	8	$41,058.06	$533.22	9.6
DEPAKOTE ER TAB 250MG	49	5	$15,344.15	$313.15	9.8
DEPAKOTE TAB 500MG DR	47	5	$32,068.93	$682.32	9.4
DEPAKOTE TAB 250MG DR	32	3	$6,612.32	$206.64	10.7
DEPAKOTE TAB 125MG DR	9	1	$1,869.20	$207.69	9.0
SUBTOTAL	**30,444**	**5,918**	**$872,220.53**	**$28.65**	**5.1**
TOPIRAMATE PRODUCTS					
TOPIRAMATE TAB 50MG	9,315	2,714	$110,515.44	$11.86	3.4
TOPIRAMATE TAB 25MG	8,295	3,078	$92,690.23	$11.17	2.7
TOPIRAMATE TAB 100MG	7,847	1,650	$99,684.22	$12.70	4.8
TOPIRAMATE TAB 200MG	3,216	500	$47,407.03	$14.74	6.4
TOPIRAMATE CAP 15MG	534	131	$23,721.65	$44.42	4.1
TOPIRAMATE CAP 25MG	484	105	$30,387.83	$62.78	4.6
TROKENDI XR CAP 200MG	173	32	$198,265.19	$1,146.04	5.4
TROKENDI XR CAP 100MG	142	30	$98,259.79	$691.97	4.7
TROKENDI XR CAP 50MG	88	32	$29,095.07	$330.63	2.8
TOPAMAX TAB 100MG	41	6	$38,391.40	$936.38	6.8
TOPAMAX TAB 200MG	25	2	$27,032.28	$1,081.29	12.5
TOPIRAMATE CAP ER 200MG	20	2	$12,013.58	$600.68	10.0
TROKENDI XR CAP 25MG	14	8	$3,769.11	$269.22	1.8
TOPIRAMATE CAP ER 100MG	14	2	$6,565.96	$469.00	7.0

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TOPAMAX TAB 50MG	13	1	$1,073.11	$82.55	13.0
TOPIRAMATE CAP ER 150MG	11	1	$6,267.36	$569.76	11.0
TOPAMAX SPR CAP 25MG	10	2	$27,996.97	$2,799.70	5.0
TOPIRAMATE CAP ER 50MG	7	3	$3,597.66	$513.95	2.3
SUBTOTAL	**30,249**	**8,299**	**$856,733.88**	**$28.32**	**3.6**
LAMOTRIGINE PRODUCTS					
LAMOTRIGINE TAB 100MG	10,247	2,154	$117,294.53	$11.45	4.8
LAMOTRIGINE TAB 25MG	7,019	2,508	$82,289.63	$11.72	2.8
LAMOTRIGINE TAB 200MG	6,711	1,154	$85,151.47	$12.69	5.8
LAMOTRIGINE TAB 150MG	3,800	773	$45,803.93	$12.05	4.9
LAMOTRIGINE CHW 25MG	249	56	$7,742.03	$31.09	4.4
LAMOTRIGINE TAB 200MG ER	126	19	$20,590.25	$163.41	6.6
LAMOTRIGINE ODT 25MG	114	19	$69,133.89	$606.44	6.0
LAMOTRIGINE TAB 300MG ER	104	19	$20,643.19	$198.49	5.5
LAMOTRIGINE CHW 5MG	104	34	$3,044.63	$29.28	3.1
LAMICTAL TAB 150MG	95	8	$99,006.78	$1,042.18	11.9
LAMOTRIGINE ODT 50MG	82	18	$27,061.92	$330.02	4.6
LAMICTAL TAB 200MG	76	10	$77,956.68	$1,025.75	7.6
LAMOTRIGINE TAB 50MG ER	73	13	$9,072.08	$124.28	5.6
LAMOTRIGINE TAB 100MG ER	61	13	$4,910.65	$80.50	4.7
LAMICTAL XR TAB 200MG	56	6	$81,684.43	$1,458.65	9.3
LAMICTAL TAB 100MG	54	5	$54,988.70	$1,018.31	10.8
LAMOTRIGINE TAB 250MG ER	49	8	$29,756.06	$607.27	6.1
LAMOTRIGINE ODT 100MG	32	6	$11,009.58	$344.05	5.3
LAMOTRIGINE TAB 100MG	30	12	$11,216.18	$373.87	2.5
LAMICTAL ODT 100MG	23	2	$8,248.19	$358.62	11.5
LAMICTAL XR TAB 300MG	18	2	$34,202.54	$1,900.14	9.0
LAMOTRIGINE TAB 200MG	12	2	$2,318.89	$193.24	6.0
LAMICTAL ODT 200MG	12	1	$10,133.94	$844.50	12.0
LAMICTAL ODT 50MG	12	1	$7,948.62	$662.39	12.0
LAMOTRIGINE TAB 25MG ER	11	2	$928.03	$84.37	5.5
LAMICTAL CHW 25MG	11	1	$77,981.35	$7,089.21	11.0
LAMICTAL ODT 25MG	11	1	$4,701.43	$427.40	11.0
LAMICTAL XR TAB 50MG	9	1	$5,774.90	$641.66	9.0
LAMICTAL XR TAB 250MG	9	1	$15,558.28	$1,728.70	9.0
LAMICTAL XR TAB 100MG	6	1	$4,092.24	$682.04	6.0
SUBVENITE TAB 150MG	3	1	$40.28	$13.43	3.0
LAMICTAL KIT START 49	2	2	$1,062.92	$531.46	1.0
LAMOTRIGINE KIT ODT	1	1	$374.95	$374.95	1.0
SUBTOTAL	**29,222**	**6,854**	**$1,031,723.17**	**$35.31**	**4.3**
CLONAZEPAM PRODUCTS					
CLONAZEPAM TAB 1MG	12,431	2,564	$129,197.95	$10.39	4.8

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
CLONAZEPAM TAB 0.5MG	10,620	2,829	$108,304.58	$10.20	3.8
CLONAZEPAM TAB 2MG	3,461	641	$36,919.59	$10.67	5.4
CLONAZEPAM ODT 0.25MG	1,093	311	$39,079.65	$35.75	3.5
CLONAZEPAM ODT 0.125MG	570	203	$22,312.48	$39.14	2.8
CLONAZEPAM ODT 0.5MG	551	180	$23,532.86	$42.71	3.1
CLONAZEPAM ODT 1MG	305	105	$13,347.99	$43.76	2.9
CLONAZEPAM ODT 2MG	42	15	$2,230.76	$53.11	2.8
KLONOPIN TAB 2MG	12	1	$2,308.07	$192.34	12.0
SUBTOTAL	**29,085**	**6,849**	**$377,233.93**	**$12.97**	**4.2**
OXCARBAZEPINE PRODUCTS					
OXCARBAZEPIN TAB 300MG	10,084	2,142	$192,900.10	$19.13	4.7
OXCARBAZEPIN TAB 600MG	8,289	1,385	$246,877.78	$29.78	6.0
OXCARBAZEPIN TAB 150MG	6,241	1,592	$106,522.70	$17.07	3.9
OXCARBAZEPIN SUS 300MG/5ML	3,159	498	$375,989.42	$119.02	6.3
TRILEPTAL SUS 300MG/5ML	150	21	$100,750.69	$671.67	7.1
OXTELLAR XR TAB 600MG	133	23	$155,521.50	$1,169.33	5.8
OXTELLAR XR TAB 300MG	56	13	$17,238.56	$307.83	4.3
TRILEPTAL TAB 600MG	43	5	$79,884.97	$1,857.79	8.6
OXTELLAR XR TAB 150MG	32	7	$6,718.39	$209.95	4.6
TRILEPTAL TAB 300MG	8	1	$3,903.20	$487.90	8.0
SUBTOTAL	**28,195**	**5,687**	**$1,286,307.31**	**$45.62**	**5.0**
PREGABALIN PRODUCTS					
LYRICA CAP 150MG	2,942	582	$1,555,468.38	$528.71	5.1
LYRICA CAP 75MG	1,591	528	$766,516.82	$481.78	3.0
LYRICA CAP 100MG	1,584	408	$874,053.10	$551.80	3.9
LYRICA CAP 300MG	1,014	149	$444,120.66	$437.99	6.8
LYRICA CAP 50MG	737	290	$391,802.89	$531.62	2.5
LYRICA CAP 200MG	645	133	$310,509.59	$481.41	4.8
LYRICA CAP 225MG	248	40	$121,947.75	$491.72	6.2
LYRICA CAP 25MG	116	64	$55,278.08	$476.54	1.8
LYRICA SOL 20MG/ML	14	2	$10,329.58	$737.83	7.0
SUBTOTAL	**8,891**	**2,196**	**$4,530,026.85**	**$509.51**	**4.0**
CARBAMAZEPINE PRODUCTS					
CARBAMAZEPIN TAB 200MG	3,369	673	$123,599.48	$36.69	5.0
CARBAMAZEPIN CHW 100MG	624	114	$27,924.73	$44.75	5.5
CARBAMAZEPIN TAB 400MG ER	487	73	$80,062.19	$164.40	6.7
CARBAMAZEPIN CAP 300MG ER	370	55	$23,871.18	$64.52	6.7
CARBAMAZEPIN TAB 200MG ER	307	69	$25,214.05	$82.13	4.4
CARBAMAZEPIN SUS 100MG/5ML	263	32	$27,011.79	$102.71	8.2
CARBAMAZEPIN CAP 200MG ER	256	49	$16,525.41	$64.55	5.2
CARBAMAZEPIN TAB 100MG ER	229	62	$11,574.62	$50.54	3.7
EPITOL TAB 200MG	176	51	$6,594.37	$37.47	3.5

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
CARBAMAZEPIN CAP 100MG ER	112	34	$5,354.30	$47.81	3.3
TEGRETOL TAB 200MG	73	8	$28,354.33	$388.42	9.1
TEGRETOL-XR TAB 400MG	65	9	$25,074.79	$385.77	7.2
TEGRETOL SUS 100MG/5ML	58	7	$18,712.58	$322.63	8.3
CARBATROL CAP 200MG	56	5	$9,724.63	$173.65	11.2
TEGRETOL-XR TAB 200MG	42	4	$15,361.79	$365.76	10.5
CARBATROL CAP 300MG	27	4	$4,112.15	$152.30	6.8
SUBTOTAL	**6,514**	**1,249**	**$449,072.39**	**$68.94**	**5.2**
LACOSAMIDE PRODUCTS					
VIMPAT TAB 200MG	2,212	259	$1,811,434.15	$818.91	8.5
VIMPAT TAB 100MG	1,408	240	$1,050,511.15	$746.10	5.9
VIMPAT SOL 10MG/ML	1,041	131	$784,371.98	$753.48	7.9
VIMPAT TAB 150MG	918	128	$701,951.68	$764.65	7.2
VIMPAT TAB 50MG	669	120	$312,515.30	$467.14	5.6
VIMPAT INJ 200MG/20ML	2	1	$173.00	$86.50	2.0
SUBTOTAL	**6,250**	**879**	**$4,660,957.26**	**$745.75**	**7.1**
PHENYTOIN AND FOSPHENYTOIN PRODUCTS					
PHENYTOIN EX CAP 100MG	3,776	593	$118,345.95	$31.34	6.4
DILANTIN CAP 100MG	293	42	$49,035.61	$167.36	7.0
PHENYTOIN SUS 125MG/5ML	258	32	$8,891.81	$34.46	8.1
PHENYTOIN CHW 50MG	226	39	$10,121.89	$44.79	5.8
PHENYTOIN EX CAP 200MG	146	32	$11,379.34	$77.94	4.6
DILANTIN CAP 30MG	79	13	$8,784.61	$111.20	6.1
PHENYTOIN EX CAP 300MG	45	14	$3,699.92	$82.22	3.2
DILANTIN CHW 50MG	32	5	$3,494.54	$109.20	6.4
PHENYTEK CAP 200MG	7	3	$754.93	$107.85	2.3
DILANTIN-125 SUS 125MG/5ML	6	1	$374.91	$62.49	6.0
FOSPHENYTOIN INJ 100MG/2ML	5	2	$320.99	$64.20	2.5
CEREBYX INJ 100MG/2ML	1	1	$44.04	$44.04	1.0
SUBTOTAL	**4,874**	**777**	**$215,248.54**	**$44.16**	**6.3**
ZONISAMIDE PRODUCTS					
ZONISAMIDE CAP 100MG	3,110	446	$64,090.33	$20.61	7.0
ZONISAMIDE CAP 50MG	745	143	$13,626.56	$18.29	5.2
ZONISAMIDE CAP 25MG	455	107	$7,787.17	$17.11	4.3
ZONEGRAN CAP 100MG	25	3	$52,308.33	$2,092.33	8.3
SUBTOTAL	**4,335**	**699**	**$137,812.39**	**$31.79**	**6.2**
CLOBAZAM PRODUCTS					
CLOBAZAM SUS 2.5MG/ML	668	136	$235,491.43	$352.53	4.9
CLOBAZAM TAB 10MG	651	137	$26,298.70	$40.40	4.8
CLOBAZAM TAB 20MG	622	106	$48,545.09	$78.05	5.9
ONFI TAB 10MG	407	103	$400,731.31	$984.60	4.0
ONFI TAB 20MG	353	100	$744,337.04	$2,108.60	3.5

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
ONFI SUS 2.5MG/ML	333	84	$662,610.52	$1,989.82	4.0
SUBTOTAL	**3,034**	**666**	**$2,118,014.09**	**$698.09**	**4.6**
PHENOBARBITAL PRODUCTS					
PHENOBARB TAB 64.8MG	629	78	$25,584.39	$40.67	8.1
PHENOBARB ELX 20MG/5ML	482	113	$29,172.76	$60.52	4.3
PHENOBARB TAB 32.4MG	430	57	$18,948.99	$44.07	7.5
PHENOBARB SOL 20MG/5ML	283	76	$17,734.45	$62.67	3.7
PHENOBARB TAB 97.2MG	188	22	$9,800.69	$52.13	8.5
PHENOBARB TAB 30MG	122	21	$2,840.24	$23.28	5.8
PHENOBARB TAB 60MG	115	23	$2,367.73	$20.59	5.0
PHENOBARB TAB 16.2MG	85	15	$2,967.32	$34.91	5.7
PHENOBARB TAB 100MG	35	6	$573.94	$16.40	5.8
PHENOBARB TAB 15MG	10	4	$204.86	$20.49	2.5
SUBTOTAL	**2,379**	**415**	**$110,195.37**	**$46.32**	**5.7**
DIAZEPAM PRODUCTS					
DIAZEPAM GEL 10MG	1,258	794	$498,676.54	$396.40	1.6
DIAZEPAM GEL 20MG	393	191	$178,019.38	$452.98	2.1
DIASTAT ACDL GEL 5-10MG	141	96	$96,498.80	$684.39	1.5
DIASTAT ACDL GEL 12.5-20MG	88	40	$48,574.43	$551.98	2.2
DIAZEPAM GEL 2.5MG	74	62	$28,700.65	$387.85	1.2
DIASTAT PED GEL 2.5MG	36	30	$15,865.99	$440.72	1.2
SUBTOTAL	**1,990**	**1,213**	**$866,335.79**	**$435.34**	**1.6**
ETHOSUXIMIDE PRODUCTS					
ETHOSUXIMIDE CAP 250MG	654	110	$53,397.50	$81.65	5.9
ETHOSUXIMIDE SOL 250MG/5ML	520	84	$46,242.46	$88.93	6.2
ZARONTIN CAP 250MG	29	3	$8,688.04	$299.59	9.7
SUBTOTAL	**1,203**	**197**	**$108,328.00**	**$90.05**	**6.1**
PRIMIDONE PRODUCTS					
PRIMIDONE TAB 50MG	555	110	$8,318.58	$14.99	5.0
PRIMIDONE TAB 250MG	244	33	$4,535.57	$18.59	7.4
MYSOLINE TAB 250MG	17	2	$72,724.10	$4,277.89	8.5
SUBTOTAL	**816**	**145**	**$85,578.25**	**$104.88**	**5.6**
RUFINAMIDE PRODUCTS					
BANZEL TAB 400MG	360	41	$1,093,877.39	$3,038.55	8.8
BANZEL SUS 40MG/ML	254	34	$459,539.75	$1,809.21	7.5
BANZEL TAB 200MG	93	13	$78,545.22	$844.57	7.2
SUBTOTAL	**707**	**88**	**$1,631,962.36**	**$2,308.29**	**8.0**
ACETAZOLAMIDE PRODUCTS					
ACETAZOLAMID TAB 250MG	374	110	$33,121.76	$88.56	3.4
ACETAZOLAMID CAP 500MG ER	230	87	$14,644.27	$63.67	2.6
ACETAZOLAMID TAB 125MG	73	23	$5,128.86	$70.26	3.2
SUBTOTAL	**677**	**220**	**$52,894.89**	**$78.13**	**3.1**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
PERAMPANEL PRODUCTS					
FYCOMPA TAB 8MG	151	23	$119,559.75	$791.79	6.6
FYCOMPA TAB 6MG	127	27	$105,450.89	$830.32	4.7
FYCOMPA TAB 4MG	100	23	$87,599.85	$876.00	4.3
FYCOMPA SUS 0.5MG/ML	92	12	$104,666.30	$1,137.68	7.7
FYCOMPA TAB 10MG	69	8	$64,808.09	$939.25	8.6
FYCOMPA TAB 2MG	42	14	$15,729.37	$374.51	3.0
FYCOMPA TAB 12MG	36	7	$30,606.82	$850.19	5.1
SUBTOTAL	**617**	**114**	**$528,421.07**	**$856.44**	**5.4**
BRIVARACETAM PRODUCTS					
BRIVIACT TAB 100MG	271	40	$300,131.66	$1,107.50	6.8
BRIVIACT TAB 50MG	239	41	$231,347.72	$967.98	5.8
BRIVIACT SOL 10MG/ML	58	6	$55,656.56	$959.60	9.7
BRIVIACT TAB 75MG	27	4	$43,277.81	$1,602.88	6.8
BRIVIACT TAB 25MG	8	3	$9,172.06	$1,146.51	2.7
SUBTOTAL	**603**	**94**	**$639,585.81**	**$1,060.67**	**6.4**
FELBAMATE PRODUCTS					
FELBAMATE TAB 600MG	234	25	$64,011.62	$273.55	9.4
FELBAMATE SUS 600MG/5ML	117	11	$74,306.66	$635.10	10.6
FELBAMATE TAB 400MG	67	8	$3,856.43	$57.56	8.4
FELBATOL TAB 600MG	34	3	$59,886.29	$1,761.36	11.3
FELBATOL TAB 400MG	9	2	$13,311.28	$1,479.03	4.5
SUBTOTAL	**461**	**49**	**$215,372.28**	**$467.18**	**9.4**
CANNABIDIOL PRODUCTS					
EPIDIOLEX SOL 100MG/ML	343	97	$598,426.74	$1,744.68	3.5
SUBTOTAL	**343**	**97**	**$598,426.74**	**$1,744.68**	**3.5**
ESLICARBAZAPINE PRODUCTS					
APTIOM TAB 800MG	86	12	$110,067.95	$1,279.86	7.2
APTIOM TAB 600MG	72	9	$89,860.91	$1,248.07	8.0
APTIOM TAB 400MG	23	7	$19,457.01	$845.96	3.3
APTIOM TAB 200MG	9	4	$5,604.34	$622.70	2.3
SUBTOTAL	**190**	**32**	**$224,990.21**	**$1,184.16**	**5.9**
VIGABATRIN PRODUCTS					
SABRIL POW 500MG	134	22	$2,317,498.14	$17,294.76	6.1
VIGABATRIN PAK 500MG	28	9	$167,771.59	$5,991.84	3.1
SABRIL TAB 500MG	16	3	$268,159.23	$16,759.95	5.3
VIGABATRIN TAB 500MG	1	1	$20,684.01	$20,684.01	1.0
SUBTOTAL	**179**	**35**	**$2,774,112.97**	**$15,497.84**	**5.1**
TIAGABINE PRODUCTS					
TIAGABINE TAB 4MG	27	5	$9,684.13	$358.67	5.4
TIAGABINE TAB 12MG	23	2	$8,090.91	$351.78	11.5
TIAGABINE TAB 2MG	17	3	$5,812.27	$341.90	5.7

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
GABITRIL TAB 16MG	6	1	$2,767.90	$461.32	6.0
TIAGABINE TAB 16MG	1	1	$349.71	$349.71	1.0
SUBTOTAL	**74**	**12**	**$26,704.92**	**$360.88**	**6.2**
METHSUXIMIDE PRODUCTS					
CELONTIN CAP 300MG	44	5	$14,823.55	$336.90	8.8
SUBTOTAL	**44**	**5**	**$14,823.55**	**$336.90**	**8.8**
TOTAL	**318,777**	**44,223***	**$26,907,879.08**	**$84.41**	**7.2**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019
The utilization details above include anticonvulsants used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate. Please note, the above utilization data does not include Afinitor® (everolimus) for the diagnosis of tuberous sclerosis complex (TSC)-associated partial-onset seizures; utilization data for everolimus is included in the annual review of oncology medications.

---

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 01/2020. Last accessed 01/21/2020.

[2] UCB. UCB Announces Nayzilam® (Midazolam) Nasal Spray Now Approved by FDA to Treat Intermittent, Stereotypic Episodes of Frequent Seizure Activity in People Living with Epilepsy in the U.S. Available online at: https://www.ucb.com/stories-media/Press-Releases/article/UCB-announces-NAYZILAM-midazolam-nasal-spray-now-approved-by-FDA-to-treat-intermittent-stereotypic-episodes-of-frequent-seizure-activity-in-people-living-with-epilepsy-in-the-U-S. Issued 05/20/2019. Last accessed 01/21/2020.

[3] Nayzilam® (Midazolam) Prescribing Information. UCB. Available online at: https://www.ucb.com/_up/ucb_com_products/documents/Nayzilam%20COL%20Rev.%205-2019.pdf. Last revised 05/2019. Last accessed 01/21/2020.

[4] SK Life Science. FDA Approves Xcopri® (Cenobamate Tablets), an Anti-Epileptic Drug (AED) from SK Biopharmaceuticals, Co., Ltd., and U.S. Subsidiary SK Life Science, Inc. Available online at: https://www.sklifescienceinc.com/pdf/FDA_Approves_XCOPRI_(cenobamate_tablets)_an_Anti-Epileptic_Drug_(AED)_from_SK_Biopharmaceuticals_Co._Ltd._and_U.S._Subsidiary_SK_Life_Science_Inc.pdf. Issued 11/21/2019. Last accessed 01/21/2020.

[5] Neurelis. Neurelis Announces FDA Approval for Seizure Rescue Treatment Valtoco® (Diazepam Nasal Spray) That Incorporates the Science of Intravail® for Consistent and Reliable Absorption. Available online at: https://www.neurelis.com/neurelis-announces-fda-approval-seizure-rescue-treatment-valtocor-diazepam-nasal-spray-incorporates. Issued 01/13/2020. Last accessed 01/21/2020.

[6] Valtoco® (Diazepam) Prescribing Information. Neurelis. Available online at: https://www.valtoco.com/sites/default/files/VALTOCO_Prescribing_Information.pdf. Last revised 01/2020. Last accessed 01/21/2020.

[7] Levy S. FDA Approves New Indication for Lundbeck's Sabril®. *Drug Store News*. Available online at: https://drugstorenews.com/fda-approves-new-indication-lundbecks-sabril?utm_source=omeda&utm_medium=email&utm_campaign=NL_DSN+AM&utm_keyword=&oly_enc_id=6022E7647590A6Z. Issued 01/28/2020. Last accessed 01/29/2020.

[8] Sabril® (Vigabatrin) Prescribing Information. Lundbeck. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020427s021,022006s023lbl.pdf. Last revised 01/2020. Last accessed 01/29/2020.

[9] Xcopri® (Cenobamate) Prescribing Information. SK Life Science, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212839s000lbl.pdf. Last revised 11/2019. Last accessed 01/22/2020.

Appendix P

Fiscal Year 2019 Annual Review of Osteoporosis Medications 30-Day Notice to Prior Authorize Evenity® (Romosozumab-aqqg)

Oklahoma Health Care Authority
February 2020

Current Prior Authorization Criteria

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

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization
*Must be used in combination with a bisphosphonate to count as a trial.
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 why 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: Fiscal Year 2019

Comparison of Fiscal Years: Pharmacy Claims

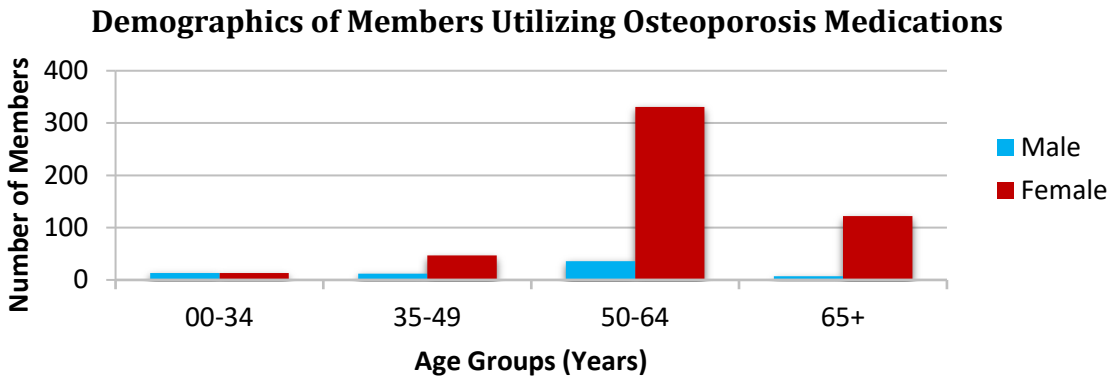
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	587	3,039	$187,867.70	$61.82	$2.00	18,887	93,817
2019	581	2,377	$277,674.87	$116.82	$2.68	18,558	103,642
% Change	**-1.0%**	**-21.8%**	**47.8%**	**89.0%**	**34.0%**	**-1.7%**	**10.5%**
Change	**-6**	**-662**	**$89,807.17**	**$55.00**	**$0.68**	**-329**	**9,825**

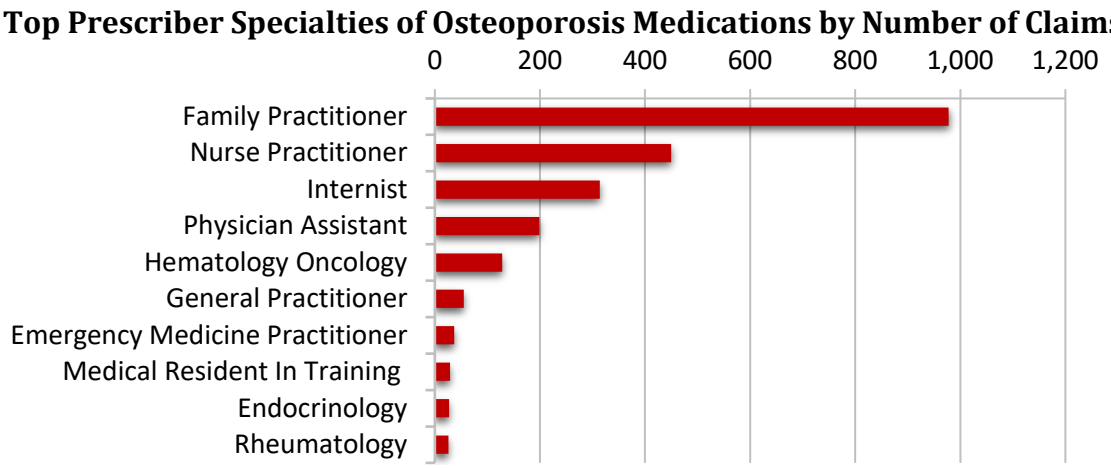
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2018 = 07/01/2017 to 06/30/2018; Fiscal year 2019 = 07/01/2018 to 06/30/2019

Fiscal Year 2019 Utilization: Medical Claims

*Total Members	†Total Claims	Total Cost	Cost/Claim	Claims/Member
173	537	$688,191.33	$1,281.55	3.10

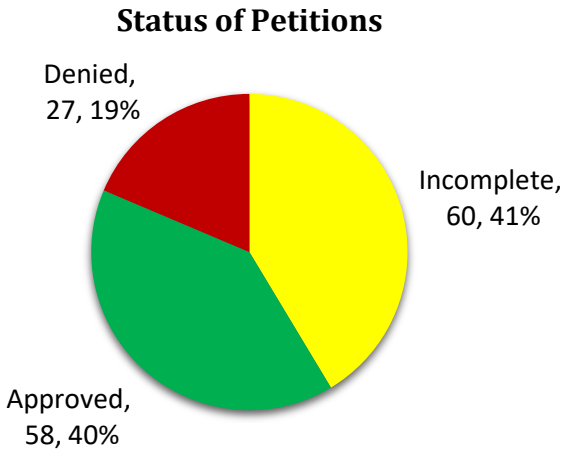
*Total number of unduplicated members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal year 2019 = 07/01/2018 to 06/30/2019





Prior Authorization of Osteoporosis Medications

There were 145 prior authorization requests submitted for osteoporosis medications during fiscal year 2019. 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 fiscal year 2019.



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

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

- **April 2019:** The FDA approved Evenity® (romosozumab-aqqg) to treat osteoporosis in postmenopausal women at high-risk of fracture. The safety and efficacy of Evenity® were demonstrated in 2 clinical trials involving a total of more than 11,000 women with postmenopausal osteoporosis. In the first trial, Evenity® lowered the risk of a new vertebral fracture by 73% compared to placebo. In the second trial, 1 year of treatment with Evenity® followed by alendronate reduced nonvertebral fractures and the risk of a new vertebral fracture by 50% compared to 2 years of alendronate alone. Evenity® contains a *Boxed Warning* stating that it may increase the risk of heart attack, stroke, and cardiovascular (CV) death and should not be used in patients who have had a heart attack or stroke within the previous year.
- **October 2019:** The FDA approved a New Drug Application (NDA) for PF708 submitted under the 505(b)(2) regulatory pathway, with Forteo® (teriparatide injection) as the reference drug, for the treatment of osteoporosis in patients at high-risk for fractures. Pfenex is conducting a comparative human factors study between PF708 and Forteo® as requested by the FDA to support the designation of PF708 as therapeutically equivalent ("A" rated) to Forteo®. Alvogen will launch PF708 once the FDA has made its decision on a therapeutic equivalence rating according to Chief Executive Officer of Pfenex.

News:

- **April 2019:** Public Citizen, a consumer advocacy group, requested that the FDA upgrade the vertebral fracture risk associated with the discontinuation of Prolia® (denosumab) to a *Boxed Warning*. The petition also urged FDA officials to require Amgen to notify doctors and to update the risk evaluation and mitigation strategy (REMS) in order to increase physician and patient awareness about the risks associated with treatment cessation. It would discourage abrupt cessation of treatment or the introduction of drug holidays without adequate consideration of alternative anti-resorptive treatment options to protect patients from vertebral fractures. The request was based on evidence showing that cessation of denosumab is associated with an increased risk of multiple vertebral fractures.

Guideline Update(s):

- **May 2019:** The Endocrine Society published updated clinical practice guidelines for the pharmacological management of osteoporosis in postmenopausal women. The guidelines recommend treating postmenopausal women at high-risk of fractures (especially those who have experienced a recent fracture) with pharmacological therapies, as the benefits outweigh the risks. Bisphosphonates (alendronate, risedronate, zoledronic acid, and ibandronate) and denosumab should be used to

reduce fracture risk in postmenopausal women at high-risk of fractures. Fracture risk should be reassessed after 3 to 5 years of bisphosphonate therapy and after 5 to 10 years of denosumab therapy. Women who remain at high-risk of fractures should continue therapy, whereas those who are at low-to-moderate-risk of fractures should be considered for a "bisphosphonate holiday." In postmenopausal women with osteoporosis at very high-risk of fracture, guidelines recommend teriparatide or abaloparatide treatment for up to 2 years for the reduction of vertebral and nonvertebral fractures. In patients at high-risk of fracture with a low-risk of deep vein thrombosis (DVT) and for whom bisphosphonates or denosumab are not appropriate, or with a high-risk of breast cancer, raloxifene or bazedoxifene can be used to reduce the risk of vertebral fractures. Calcium and vitamin D can be used as an adjunct to osteoporosis therapies. Bone mineral density (BMD) should be monitored every 1 to 3 years by dual-energy X-ray absorptiometry at the spine and hip to assess the response to treatment.

- **September 2019:** The American Society for Bone and Mineral Research (ASBMR) engaged the Center for Medical Technology Policy (CMTP) to help develop a consensus of a broad multistakeholder coalition regarding recommendations for secondary prevention in people aged 65 years or older with a hip or vertebral fracture. The consensus includes a recommendation to communicate 3 messages to patients and their caregivers consistently throughout the process: patients are at high-risk for more fractures, especially over the next 1 to 2 years; bone fractures lead to increase morality and a decline in mobility or independence; however, there are actions they can take to reduce their risk. Consensus recommendations include to regularly assess the risk of falling in people aged 65 years or older who have ever had a hip or vertebral fracture, and to employ strategies to reduce fall risks such as minimizing the use of medications associated with increased fall risk. A daily supplement of at least 800 IU vitamin D per day and daily calcium supplementation for those who are unable to achieve an intake of 1200mg/day of calcium from food sources can help reduce fracture risks. First-line pharmacologic therapy options for hip or vertebral fracture include: oral bisphosphonates such as alendronate, risedronate, or intravenous (IV) zoledronic acid; and subcutaneous (sub-Q) denosumab, if oral bisphosphonates pose difficulties. The optimal duration of pharmacologic therapy for people aged 65 years and older with a hip or vertebral fracture is not known. Most published guidelines recommend that the need for therapy with bisphosphonates be reassessed after 3 to 5 years, and patients who are stopping anabolic agents or denosumab should be placed on an anti-resorptive therapy.

Evenity® (Romosozumab-aqqg) Product Summary[7]

Indication(s): Evenity® (romosozumab-aqqg) is a sclerostin inhibitor indicated for the treatment of osteoporosis in postmenopausal women at high-risk for fracture or patients who have failed or are intolerant to other available osteoporosis therapies.

- Limitation(s) of Use: Duration of use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

Boxed Warning: Potential risk of myocardial infarction (MI), stroke, and CV death

Dosing:

- Evenity® is available as a 105mg/1.17mL solution supplied in single-use prefilled syringes. A full dose of romosozumab requires 2 single-use prefilled syringes.
- The recommended dose is 210mg administered as 2 sub-Q injections, 1 after the other, for a total dose of 210mg. The dose should be administered once every month for 12 doses in the abdomen, thigh, or upper arm.
- Romosozumab should be administered by a health care provider.
- Patients should receive adequate supplementation with calcium and vitamin D during treatment.

Mechanism of Action: Romosozumab inhibits the action of sclerostin, a regulatory factor in bone metabolism. Romosozumab increases bone formation and, to a lesser extent, decreases bone resorption.

Contraindication(s):

- Hypocalcemia
- Known hypersensitivity to Evenity® or any of its ingredients

Warnings and Precautions:

- Major Adverse Cardiac Events (MACE): Patients should be monitored for symptoms of MI and stroke and should be instructed to seek prompt medical attention if symptoms occur.
- Hypersensitivity: Hypersensitivity reactions including angioedema, erythema multiforme, dermatitis, rash, and urticarial have occurred in romosozumab-treated patients. Romosozumab should be discontinued if a clinically significant allergic reaction occurs.
- Hypocalcemia: Patients should be adequately supplemented with calcium and vitamin D during treatment with romosozumab.
- Osteonecrosis of the Jaw: Patients should be monitored for symptoms of osteonecrosis of the jaw. Consideration should be given to discontinuation of therapy based on a benefit-risk assessment.
- Atypical Femoral Fracture: Patients should be evaluated for new or unusual thigh, hip, or groin pain to rule out an incomplete femur fracture.

Adverse Reactions(s): The most common adverse reactions (≥5%) reported with romosozumab in clinical trials were arthralgia and headache.

Use in Specific Populations:

- Pregnancy: Evenity® is not indicated for use in women of reproductive potential. Weekly administration of romosozumab to pregnant rats during the period of organogenesis

produced skeletal abnormalities in the offspring. Administration of romosozumab to rats prior to mating and through to the end of lactation produced minimal to slight decreases in femoral bone mineral density and/or cortical circumferences in the offspring.

- Lactation: Evenity® is not indicated for use in women of reproductive potential. In animal studies where pregnant rats were given weekly doses of romosozumab through mating and lactation, romosozumab was dose-dependently present in the serum of offspring on postnatal day 21 at 0.01 to 2.4 times maternal exposure due to gestational and/or lactational exposure.
- Pediatric Use: The safety and effectiveness of romosozumab have not been established in pediatric patients.
- Geriatric Use: No overall differences in safety or efficacy were observed between patients older than 65 years and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: No dose adjustment is required in patients with renal impairment. Patients with severe renal impairment or receiving dialysis are at greater risk of developing hypocalcemia.

Efficacy:

- The safety and efficacy of romosozumab were evaluated in a randomized, double-blind, placebo-controlled study of postmenopausal women, 55 to 90 years of age, with BMD T-scores ≤−2.5. Patients received sub-Q injections of romosozumab (N=3,589) or placebo (N=3,591) for 12 months. Romosozumab significantly reduced the incidence of new vertebral fractures and clinical fracture (a composite endpoint of symptomatic vertebral fracture and nonvertebral fracture) through month 12 compared to placebo. However, 88% of these clinical fractures were nonvertebral fractures, and the incidence of nonvertebral fractures was not statistically significantly different when comparing romosozumab to placebo at month 12 or month 24. Romosozumab significantly increased BMD at the lumbar spine, total hip, and femoral neck compared with placebo at month 12. The treatment differences in BMD were 12.7% at the lumbar spine, 5.8% at the total hip, and 5.2% at the femoral neck. After romosozumab discontinuation, BMD returns to approximately baseline levels within 12 months in the absence of follow-on anti-resorptive therapy. A total of 154 transiliac crest bone biopsy specimens were obtained from 139 postmenopausal women with osteoporosis at month 2, month 12, and/or month 24. At month 2 in women treated with romosozumab, histomorphometric indices of bone formation at trabecular and endocortical surfaces were increased. These effects on bone formation were accompanied by a decrease in indices of bone resorption. At month 12, both bone formation and resorption indices were decreased with romosozumab, while bone volume, and trabecular and cortical thickness were increased.
- In a second study, romosozumab was evaluated in a randomized, double-blind, alendronate-controlled, event-driven study of postmenopausal women 55 to 90 years of age, with BMD T-score ≤−2.5, and either 1 moderate or severe vertebral fracture or 2

mild vertebral fractures or BMD T-score ≤−2.0, and either 2 moderate or severe vertebral fractures or a history of a proximal femur fracture. Romosozumab significantly reduced the incidence of new vertebral fracture at 24 months and the risk of clinical fracture through the end of the primary analysis period. The median duration of subject follow-up for the primary analysis period was 33 months. Romosozumab significantly increased BMD at the lumbar spine, total hip, and femoral neck compared with alendronate at month 12, and 12 months of treatment with romosozumab followed by 12 months of treatment with alendronate significantly increased BMD compared with alendronate alone.

Cost: The Wholesale Acquisition Cost (WAC) of Evenity® is $912.49 per pre-filled syringe, resulting in an approximate cost per 12-month treatment of $21,899.87. This cost is based on 2 syringes per dose for a maximum of 12 doses. The cost does not include the supplement costs of calcium and vitamin D during treatment with Evenity®. Patients who require osteoporosis therapy after 12 months, may need to continue therapy with an anti-resorptive agent.

Recommendations

The College of Pharmacy recommends the prior authorization of Evenity® (romosozumab-aqqg) with the following criteria:

Evenity® (Romosozumab-aqqg) Approval Criteria:

1. An FDA approved diagnosis of osteoporosis in postmenopausal women at high-risk for fracture; and
2. Member meets 1 of the following:
   a. History of osteoporotic fracture; or
   b. Multiple risk factors for fracture (e.g., T-score ≤-2.5 at the total hip or femoral neck, smoking, corticosteroid use, rheumatoid arthritis); or
   c. Failed or are intolerant to other available osteoporosis therapies; and
3. Prescriber must verify member has not had a myocardial infarction or stroke within the preceding year; and
4. Prescriber must verify calcium levels will be monitored and pre-existing hypocalcemia will be corrected prior to starting therapy; and
5. Member must take adequate calcium and vitamin D supplements during treatment with Evenity® to reduce the risk of hypocalcemia; and
6. Evenity® must be administered by a health care provider; and
7. Approvals will be for a maximum total duration of 1 year of therapy.

Utilization Details of Osteoporosis Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
ALENDRONATE PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ALENDRONATE TAB 70MG	1,811	447	$18,739.73	$0.25	$10.35
ALENDRONATE TAB 35MG	177	41	$2,014.38	$0.28	$11.38
ALENDRONATE TAB 10MG	89	25	$1,218.32	$0.33	$13.69
ALENDRONATE TAB 5MG	25	5	$370.60	$0.33	$14.82
SUBTOTAL	**2,102**	**508**	**$22,343.03**	**$0.26**	**$10.63**
ZOLEDRONIC ACID PRODUCTS					
ZOLEDRONIC INJ 5MG/100ML	2	2	$139.77	$0.19	$69.89
SUBTOTAL	**2**	**2**	**$139.77**	**$0.19**	**$69.89**
IBANDRONATE PRODUCTS					
IBANDRONATE TAB 150MG	106	38	$2,382.44	$0.38	$22.48
SUBTOTAL	**106**	**38**	**$2,382.44**	**$0.38**	$22.48
TIER-1 SUBTOTAL	**2,210**	**541**	**$24,865.24**	**$0.27**	**$11.25**
TIER-2 PRODUCTS					
RISEDRONATE PRODUCTS					
RISEDRONATE TAB 35MG	36	4	$1,296.52	$1.28	$36.01
RISEDRONATE TAB 150MG	12	1	$606.52	$1.68	$50.54
RISEDRONATE TAB 5MG	10	1	$1,055.74	$3.62	$105.57
SUBTOTAL	**58**	**6**	**$2,958.78**	**$1.78**	**$51.01**
TIER-2 SUBTOTAL	**58**	**6**	**$2,958.78**	**$1.78**	**$51.01**
SPECIAL PA PRODUCTS					
ABALOPARATIDE PRODUCTS					
TYMLOS INJ 3120MG/1.56ML	1	1	$1,757.85	$58.59	$1,757.85
SUBTOTAL	**1**	**1**	**$1,757.85**	**$58.59**	**$1,757.85**
TERIPARATIDE PRODUCTS					
FORTEO SOL 600MCG/2.4ML	64	9	$206,439.34	$113.18	$3,225.61
SUBTOTAL	**64**	**9**	**$206,439.34**	**$113.18**	**$3,225.61**
DENOSUMAB PRODUCTS					
PROLIA SOL 60MG/ML	36	26	$40,277.66	$6.23	$1,118.82
SUBTOTAL	**36**	**26**	**$40,277.66**	**$6.23**	**$1,118.82**
ALENDRONATE PRODUCTS					
ALENDRONATE SOL 70MG/75ML	4	1	$809.76	$6.75	$202.44
ALENDRONATE TAB 40MG	3	1	$411.30	$4.57	$137.10
BINOSTO TAB 70MG	1	1	$154.94	$1.84	$154.94
SUBTOTAL	**8**	**3**	**$1,376.00**	**$4.68**	**$172.00**
SPECIAL PA SUBTOTAL	**109**	**39**	**$249,850.85**	**$29.01**	**$2,292.21**
TOTAL	**2,377**	**581***	**$277,674.87**	**$2.68**	**$116.82**

PA = prior authorization
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2019 = 07/01/2018 to 06/30/2019

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
PROLIA J0897	43	34	$35,799.33	$832.54
XGEVA J0897	296	55	$641,384.52	$2,166.84
IBANDRONATE SODIUM J1740	3	1	$569.37	$189.79
ZOLEDRONIC ACID J3489	205	85	$10,438.11	$50.92
TOTAL	**537[+]**	**173***	**$688,191.33**	**$1,281.55**

*Total number of unduplicated members.
[+]Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal year 2019 = 07/01/2018 to 06/30/2019

[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 12/2019. Last accessed 12/30/2019.
[2] FDA. FDA approves new treatment for osteoporosis in postmenopausal women at high risk of fracture. Available online at: http://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-osteoporosis-postmenopausal-women-high-risk-fracture. Last revised 04/09/2019. Last accessed 01/02/2020.
[3] Pfenex Inc. Pfenex Receives U.S. FDA Approval for PF708 to Treat Osteoporosis. *PR Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/07/1925635/0/en/Pfenex-Receives-U-S-FDA-Approval-for-PF708-to-Treat-Osteoporosis.html. Issued 10/07/2019. Last accessed 01/03/2020.
[4] Consumer watchdog petitions FDA for black box warning on Amgen's Prolia. *FiercePharma*. Available online at: https://www.fiercepharma.com/pharma/consumer-watchdog-petitions-fda-for-black-box-warning-amgen-s-prolia. Last revised 04/18/2019. Last accessed 01/02/2020.
[5] Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2019; 104(5):1595-1622. doi: 10.1210/jc.2019-00221.
[6] Robert BC, Gemma A, Robert AA, et al. Secondary Fracture Prevention: Consensus Clinical Recommendations from a Multistakeholder Coalition. *Journal of Bone and Mineral Research* 2019; [Epub ahead of print]. DOI: 10.1002/jbmr.3877
[7] Evenity® (romosozumab-aqqg) Prescribing Information. Amgen. Available online at: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/evenity/evenity_pi.ashx. Last revised 12/2019. Last accessed 01/02/2020.

Appendix Q

Fiscal Year 2019 Annual Review of Inhaled Short-Acting Beta$_2$ Agonists and 30-Day Notice to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder)

Oklahoma Health Care Authority
February 2020

Current Prior Authorization Criteria

Tier-1 products are covered with no prior authorization necessary.

Short-Acting Beta$_2$ Agonists Tier-2 Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member cannot use all available Tier-1 medications.
3. Approval of generic levalbuterol HFA requires a patient-specific, clinically significant reason the member cannot use the brand formulation.

Short-Acting Beta$_2$ Agonists	
Tier-1	**Tier-2**
albuterol HFA (ProAir® HFA)*	albuterol HFA (generic)
albuterol inhalation powder (ProAir® RespiClick®)	levalbuterol HFA (generic)¥
albuterol HFA (Proventil® HFA)*	
albuterol HFA (Ventolin® HFA)*	
levalbuterol HFA (Xopenex® HFA)*	

*Brand preferred.
¥Additional criteria applies.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC is unavailable.

Xopenex® (Levalbuterol) Nebulizer Solution Approval Criteria:

1. A free-floating 90 days of therapy per 365 days will be in place.
2. Use of this product in excess of 90 days of therapy in 365 day period will require a patient-specific, clinically significant reason why the member is unable to use long-acting bronchodilators and/or inhaled corticosteroids (ICS) therapy for long-term control as recommended in the National Asthma Education and Prevention Program (NAEPP) guidelines; and
3. A patient-specific, clinically significant reason why the member cannot use a metered-dose inhaler (MDI) must be provided; and
4. Clinical exceptions will be made for clients with chronic obstructive pulmonary disease (COPD); and
5. A quantity limit of 288mL per 30 days will apply.

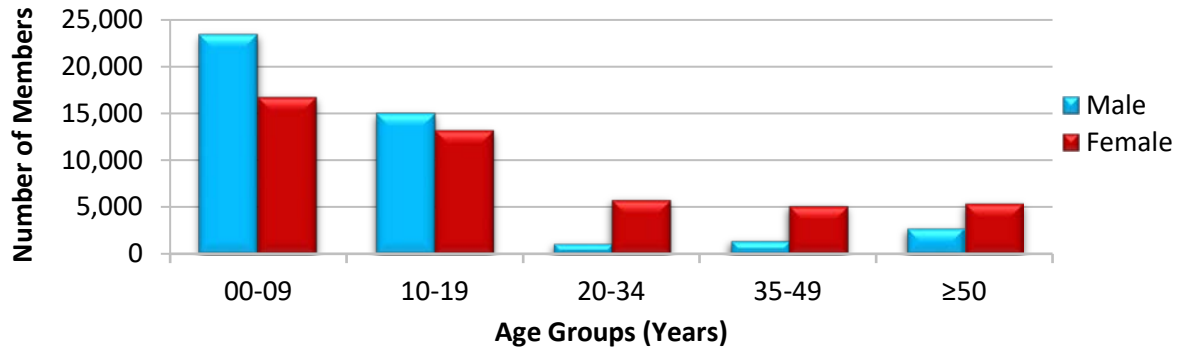
Utilization of Inhaled Short-Acting Beta$_2$ Agonists: Fiscal Year 2019

Comparison of Fiscal Years

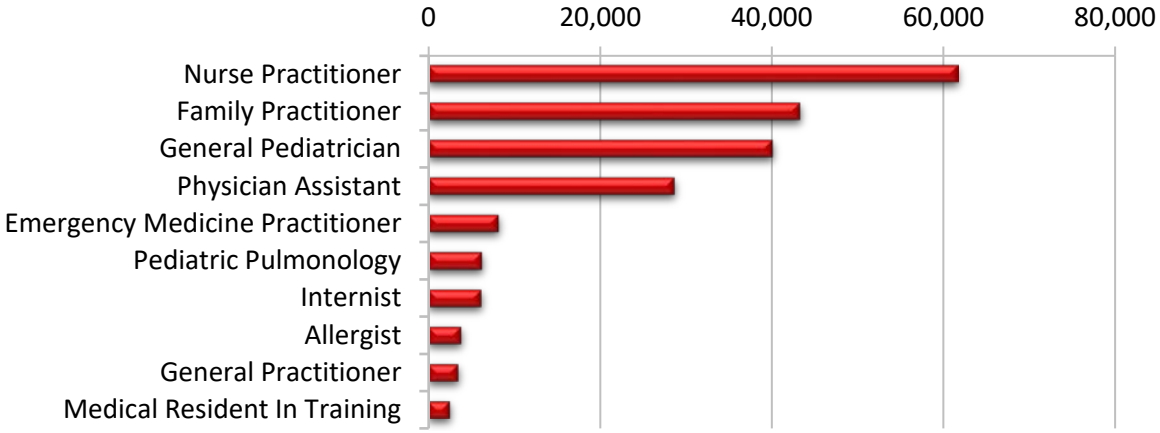
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	95,816	228,287	$15,077,181.83	$66.04	$3.11	10,907,656	4,848,808
2019	89,974	212,784	$14,528,304.92	$68.28	$3.20	9,940,043	4,545,884
% Change	**-6.10%**	**-6.80%**	**-3.60%**	**3.40%**	**2.90%**	**-8.90%**	**-6.20%**
Change	**-5,842**	**-15,503**	**-$548,876.91**	**$2.24**	**$0.09**	**-967,613**	**-302,924**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal year 2018 = 07/01/2017 to 06/30/2018; Fiscal year 2019 = 07/01/2018 to 06/30/2019

Demographics of Members Utilizing Inhaled Short-Acting Beta$_2$ Agonists



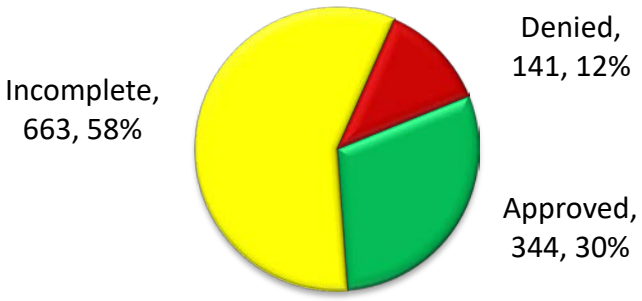
Top Prescriber Specialties of Inhaled Short-Acting Beta$_2$ Agonists by Number of Claims



Prior Authorization of Inhaled Short-Acting Beta$_2$ Agonists

There were 1,148 prior authorization requests submitted for inhaled short-acting beta$_2$ agonists during fiscal year 2019. The following chart shows the status of the submitted petitions during fiscal year 2019.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Ventolin® (albuterol HFA): August 2026, however, an authorized generic is currently available
- ProAir® (albuterol HFA): May 2031, however, an authorized generic is currently available
- ProAir RespiClick® (albuterol sulfate inhalation powder): January 2032
- ProAir® Digihaler™ (albuterol sulfate inhalation powder): August 2035

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

- **December 2018:** Teva Pharmaceutical Industries Ltd. reported that the FDA approved ProAir® Digihaler™ (albuterol sulfate inhalation powder), the first and only digital inhaler with built-in sensors which connects to a companion mobile application and provides inhaler use information to people with asthma. ProAir® Digihaler™ is indicated for the treatment or prevention of bronchospasm in patients aged 4 years and older with reversible obstructive airway disease, and for prevention of exercise-induced bronchospasm in patients aged 4 years and older. ProAir® Digihaler™ contains a built-in electronic module that automatically detects, records, and stores data on inhaler events, including peak inspiratory flow rate (L/min). ProAir® Digihaler™ may be used with, and transmits information to, a mobile application (app) ProAir® Digihaler™ does not need to be connected to the mobile app in order for patients to take their medicine.

Guideline Update(s):

- **April 2019:** The Global Initiative for Asthma (GINA) released the 2019 updates to the Pocket Guide for Asthma Management and Prevention, as well as an updated version of the Pocket Guide on "Diagnosis and Management of Difficult-to-Treat and Severe Asthma in Adolescent and Adult Patients". The 2019 GINA strategy report represents the most significant change in asthma management in over 30 years. GINA no longer recommends starting treatment of asthma with short-acting beta$_2$-agonist (SABA) reliever inhalers on their own. Instead, GINA recommends that all adults and adolescents with asthma should receive either symptom-driven (for mild asthma) or daily inhaled anti-inflammatory controller treatment to reduce their risk of serious exacerbations and to control symptoms. Due to the known dangers of the overuse of SABAs, and current research including evidence that even mild asthma involves inflammation, the GINA guidelines now recommend that adult and adolescent patients

with asthma be prescribed a low dose inhaled corticosteroid (ICS)/long-acting beta$_2$ agonist (LABA) to be used for symptom relief, and for asthma that is more than mild, use of this type of medication regularly plus either a SABA or ICS/LABA for quick relief. The only low dose ICS/LABA in the United States with a rapid enough acting LABA component to be included in this new paradigm is Symbicort® 80mcg (budesonide 80mcg/formoterol 4.5mcg), which contains formoterol, a quick-acting and long-lasting bronchodilator. Dulera® (mometasone/formoterol) also contains formoterol, but the corticosteroid doses available are only medium and high dose, without a low-dose option.

ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) Product Summary[8]

Indication(s): ProAir® Digihaler™ (albuterol sulfate inhalation powder) is a drug product containing a beta$_2$-adrenergic agonist indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

Dosing:

- ProAir® Digihaler™ is supplied as a dry powder inhaler containing 200 inhalation doses that meters 117mcg of albuterol sulfate (equivalent to 97mcg of albuterol base) from the device reservoir and delivers 108mcg of albuterol sulfate (equivalent to 90mcg of albuterol base) from the mouthpiece per actuation.
- ProAir® Digihaler™ contains a QR code and a built-in electronic module which automatically detects, records, and stores data on inhaler events, including peak inspiratory flow rate (L/min).
- ProAir® Digihaler™ may pair with and transmit data to the mobile app via Bluetooth® wireless technology where inhaler events are categorized. Use of the App is not required for administration of medication to the patient.
- For the treatment or prevention of bronchospasm in adults and children 4 years of age and older, the recommended dosing regimen is 2 inhalations every 4 to 6 hours. In some patients, 1 inhalation every 4 hours may be sufficient.
- For the treatment of the prevention of exercise-induced bronchospasm in adults and children 4 years of age and older, the recommended regimen is 2 inhalations 15 to 30 minutes before exercise.
- ProAir® Digihaler™ does not require priming and should not be used with a spacer or volume holding chamber.
- ProAir® Digihaler™ should be kept clean and dry at all times. Routine maintenance is not required. If the mouthpiece needs cleaning, the mouthpiece should be gently wiped with a dry cloth or tissue as needed. The inhaler should not be washed or any part of the inhaler put in water.
- ProAir® Digihaler™ inhaler has a dose counter. The inhaler should be discarded 13 months after opening the foil pouch, when the counter displays 0, or after the expiration date on the product, whichever comes first.

Efficacy: The approval of ProAir® Digihaler™ was based on adequate and well-controlled efficacy studies of albuterol sulfate inhalation powder (ProAir RespiClick®) in adult and pediatric patients.

Cost Comparison:

Medication	Cost Per 1 Inhaler (200 doses)
ProAir® Digihaler™ (albuterol sulfate inhalation powder)	**$146.67**
ProAir RespiClick® (albuterol sulfate inhalation powder)	$60.09
ProAir® HFA (albuterol sulfate HFA)	$32.55

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.

Recommendations

The College of Pharmacy recommends the placement of ProAir® Digihaler™ (albuterol sulfate inhalation powder) into Tier-2 of the Short-Acting Beta$_2$ Agonist Rescue Inhalers Product Based Prior Authorization Tier chart with the following criteria:

Tier-1 products are covered with no prior authorization necessary.

Rescue Inhalers Tier-2 Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member cannot use all available Tier-1 medications.
3. Approval of generic levalbuterol HFA requires a patient-specific, clinically significant reason the member cannot use the brand formulation.

Short-Acting Beta$_2$ Agonists	
Tier-1	**Tier-2**
albuterol HFA (ProAir® HFA)*	albuterol HFA (generic)
albuterol inhalation powder (ProAir® RespiClick®)	**albuterol inhalation powder (ProAir® Digihaler™)¥**
albuterol HFA (Proventil® HFA)*	levalbuterol HFA (generic)¥
albuterol HFA (Ventolin® HFA)*	
levalbuterol HFA (Xopenex® HFA)*	

*Brand preferred.
¥Additional criteria applies.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC is unavailable.

ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason the member requires the ProAir® Digihaler™ formulation over all available Tier-1 medications must be provided; and
3. The prescriber agrees to closely monitor member adherence; and

4. Members should be capable and willing to use the Companion Mobile App and follow the *Instructions for Use* and ensure the ProAir® Digihaler™ Companion Mobile App is compatible with their specific smartphone; and
5. Members' phone camera must be functional and able to scan the inhaler QR code and register the ProAir® Digihaler™ inhaler; and
6. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and patient compliance greater than 80% with prescribed therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

Utilization Details of Inhaled Short-Acting Beta$_2$ Agonists: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
PROAIR HFA	140,631	64,182	$11,624,422.18	$3.43	$82.66	80.01%
PROVENTIL HFA	12,106	6,461	$1,254,640.93	$4.19	$103.64	8.64%
VENTOLIN HFA	886	664	$58,159.82	$2.68	$65.64	0.40%
XOPENEX HFA	488	230	$41,839.48	$3.14	$85.74	0.29%
PROAIR RESPICLICK	14	4	$1,188.07	$3.05	$84.86	0.01%
SUBTOTAL	**154,125**	**71,541**	**$12,980,250.48**	**$3.49**	**$84.22**	**89.35%**
TIER-2 PRODUCTS						
ALBUTEROL HFA	2,964	2,578	$146,322.80	$2.07	$49.37	1.01%
LEVALBUTEROL AER 45/ACT	27	14	$1,818.40	$2.54	$67.35	0.01%
SUBTOTAL	**2,991**	**2,592**	**$148,141.20**	**$2.31**	**$49.53**	**1.02%**
NEBULIZER SOLUTION PRODUCTS						
ALBUTEROL NEB 0.083%	35,406	22,059	$567,185.14	$1.12	$16.02	3.90%
ALBUTEROL NEB 1.25MG/3ML	10,636	7,889	$400,407.77	$3.37	$37.65	2.76%
ALBUTEROL NEB 0.63MG/3ML	6,692	4,990	$266,926.41	$3.28	$39.89	1.84%
LEVALBUTEROL NEB 0.63MG	1,439	877	$81,921.22	$3.33	$56.93	0.56%
LEVALBUTEROL NEB 1.25MG	708	384	$37,251.34	$2.90	$52.61	0.26%
LEVALBUTEROL NEB 0.31MG	406	306	$22,043.30	$3.88	$54.29	0.15%
ALBUTEROL NEB 0.5%	363	244	$13,994.93	$2.43	$38.55	0.10%
XOPENEX NEB 1.25/3ML	11	1	$8,345.63	$30.35	$758.69	0.06%
LEVALBUTEROL NEB 1.25/0.5ML	7	7	$1,837.50	$18.01	$262.50	0.01%
SUBTOTAL	**55,668**	**36,757**	**$1,399,913.24**	**$6.33**	**$25.15**	**9.64%**
TOTAL	**212,784**	**89,974***	**$14,528,304.92**	**$3.20**	**$68.28**	**100%**

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

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 01/2020. Last accessed 01/03/2020.

[2] Teva Pharmaceutical Industries, Ltd. Teva Announces FDA Approval of First and Only Digital Inhaler with Built-In Sensors-ProAir® Digihaler™ (albuterol sulfate 117mcg) Inhalation Powder. *Business Wire*. Available online at: https://apnews.com/c4eda18019434172848f5f5ab6857cf0. Issued 12/21/2018. Last accessed 01/07/2020.

[3] GalxoSmithKline. GSK Announces Availability of Authorized Generic Albuterol Sulfate Inhaler for Treatment or Prevention of Bronchospasm. *Asthma and Allergy Foundation of America*. Available online at: https://community.aafa.org/blog/gsk-to-offer-generic-version-of-ventolin-hfa-albuterol-inhaler. Issued 01/17/2019. Last accessed 01/07/2020.

[4] ProAir® HFA (albuterol) – First-Time Generic. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/new-generics/newgenerics_proairhfa_2019-0122.pdf. Issued 2019. Last accessed 01/07/2020.

[5] Dever S. 2019 Asthma Guideline Recommends Major Change in Management. *Asthma and Allergy Care*. Available online at: https://www.allergyandasthmacare.com/2019/06/2019-asthma-guideline-recommends-major-change-in-management.html. Issued 06/09/2019. Last accessed 01/03/2020.

[6] Reddel HK, FitzGerald JM, Bateman ED, et al. GINA 2019: a fundamental change in asthma management. *Eur Respir J* 2019; 53:1901046. doi: 10.1183/13993003.01046-2019

[7] Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available online at: www.ginasthma.org. Last accessed 01/07/2020.

[8] ProAir® Digihaler™ Prescribing Information. Teva Respiratory, LLC. Available online at: https://www.proairdigihaler.com/globalassets/proair_digihaler/Proair_Digihaler_PI.pdf. Last revised 12/2018. Last accessed 01/07/2020.

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 RELEASES

For Immediate Release: January 9th, 2020

FDA approves the first targeted therapy to treat a rare mutation in patients with gastrointestinal stromal tumors (GIST)

The FDA approved Ayvakit (avapritinib) for the treatment of adults with unresectable or metastatic GIST – a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine – harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation. This approval includes GIST that harbors a PDGFRA D842V mutation, which is the most common exon 18 mutation. Ayvakit is a kinase inhibitor, meaning it blocks a type of enzyme called a kinase and helps keeps the cancer cells from growing.

GISTs arise from specialized nerve cells found in the walls of the gastrointestinal tract. One or more mutations in the DNA of 1 of these cells may lead to the development of GIST. These cells aid in the movement of food through the intestines and control various digestive processes. More than half of GISTs start in the stomach. Most of the others start in the small intestine, but GISTs can start anywhere along the gastrointestinal tract. The activating mutations in PDGFRA have been linked to the development of GISTs, and up to approximately 10% of GIST cases involve mutations of this gene.

The FDA approved Ayvakit based on the results of a clinical trial involving 43 patients with GIST harboring a PDGFRA exon 18 mutation, including 38 patients with PDGFRA D842V mutation. Patients received Ayvakit 300mg or 400mg orally once daily until disease progression or they experienced unacceptable toxicity. The recommended dose was determined to be 300mg once daily. The trial measured how many patients experienced complete or partial shrinkage of their tumors during treatment. For patients harboring a PDGFRA exon 18 mutation, the overall response rate was 84%, with 7% having a complete response and 77% having a partial response. For the subgroup of patients with PDGFRA D842V mutations, the overall response rate was 89%, with 8% having a complete response and 82% having a partial response. While the median duration of response was not reached, 61% of the responding patients with exon 18 mutations had a response lasting 6 months or longer (31% of patients with an ongoing response were followed for less than 6 months).

Common side effects for patients taking Ayvakit were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash, and dizziness. Ayvakit can cause intracranial hemorrhage in which case the dose should be reduced, or the drug should be discontinued. Ayvakit can also cause central nervous system effects including cognitive impairment, dizziness, sleep disorders, mood disorders, speech disorders, and hallucinations. If this happens, depending on the severity, Ayvakit should be withheld and then resumed at the same or reduced dose upon improvement or permanently discontinued.

Health care professionals should advise pregnant women that Ayvakit may cause harm to a developing fetus or newborn baby. Additionally, the FDA advises health care professionals to tell females of reproductive potential, and males with female partners of reproductive potential, to use effective contraception during treatment with Ayvakit and for 6 weeks after the final dose.

The FDA granted this application Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious condition, when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Ayvakit was also granted Fast Track designation, which expedites the review of drugs to treat serious conditions and fill an unmet medical need. Ayvakit received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Ayvakit to Blueprint Medicines Corporation.

FDA NEWS RELEASE

For Immediate Release: January 21st, 2020

FDA approves first treatment for thyroid eye disease

The FDA approved Tepezza (teprotumumab-trbw) for the treatment of adults with thyroid eye disease, a rare condition where the muscles and fatty tissues behind the eye become inflamed, causing the eyes to be pushed

forward and bulge outwards. The approval represents the first drug approved for the treatment of thyroid eye disease.
Thyroid eye disease is associated with the outward bulging of the eye that can cause a variety of symptoms such as eye pain, double vision, light sensitivity, or difficulty closing the eye. This disease impacts a relatively small number of Americans, with more women than men affected. Although this condition impacts relatively few individuals, thyroid eye disease can be incapacitating. For example, the troubling ocular symptoms can lead to the progressive inability of people with thyroid eye disease to perform important daily activities, such as driving or working.
Tepezza was approved based on the results of 2 studies (Study 1 and 2) consisting of a total of 170 patients with active thyroid eye disease who were randomized to either receive Tepezza or a placebo. Of the patients who were administered Tepezza, 71% in Study 1 and 83% in Study 2 demonstrated a greater than 2 millimeter reduction in proptosis as compared to 20% and 10% of subjects who received placebo, respectively.
The most common adverse reactions observed in patients treated with Tepezza were muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing loss, dry skin, dysgeusia, and headache. Tepezza should not be used if pregnant, and women of child-bearing potential should have their pregnancy status verified prior to beginning treatment and should be counseled on pregnancy prevention during treatment and for 6 months following the last dose of Tepezza.
The FDA granted this application Priority Review, in addition to Fast Track and Breakthrough Therapy Designation. Additionally, Tepezza received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases or conditions. Development of this product was also in part supported by the FDA Orphan Products Grants Program, which provides grants for clinical studies on safety and efficacy of products for use in rare diseases or conditions.
The FDA granted the approval of Tepezza to Horizon Therapeutics Ireland DAC.

FDA NEWS RELEASE

For Immediate Release: January 23rd, 2020

FDA approves first treatment option specifically for patients with epithelioid sarcoma, a rare soft tissue cancer

The FDA granted accelerated approval to Tazverik (tazemetostat) for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection. Epithelioid sarcoma is a rare sub-type of soft tissue sarcoma that often occurs in young adults.
Tazverik blocks activity of the EZH2 methyltransferase, which may help keep the cancer cells from growing. Most cases of epithelioid sarcoma begin in the soft tissue under the skin of an extremity, though it can start in other areas of the body. Surgical removal is considered the main treatment when the cancer is localized to 1 area of the body. Chemotherapy or radiation may also be given. However, there is a high likelihood for local and regional spread of the disease even with treatment and approximately 50% of patients have metastatic disease at the time of diagnosis. Metastatic disease is considered life-threatening to the patient.
Tazverik's approval was based on the results of a clinical trial enrolling 62 patients with metastatic or locally advanced epithelioid sarcoma. During the clinical trial, patients received 800mg of Tazverik twice a day until the disease progressed or the patient reached an unacceptable level of toxicity. Tumor response assessments were performed every 8 weeks during the clinical trial. The trial measured how many patients experienced complete or partial shrinkage of their tumors during treatment. The overall response rate was 15%, with 1.6% of patients having a complete response and 13% having a partial response. Of the 9 patients that had a response, 6 (67%) patients had a response lasting 6 months or longer.
The most common side effects for patients taking Tazverik were pain, fatigue, nausea, decreased appetite, vomiting, and constipation. Patients treated with Tazverik are at increased risk of developing secondary malignancies including: T-cell lymphoblastic lymphoma, myelodysplastic syndrome, and acute myeloid leukemia. The FDA advises health care professionals to tell females of reproductive potential to use effective contraception during treatment with Tazverik and for 6 months after the final dose. Males with a female partner of reproductive potential should use effective contraception during treatment with Tazverik and for 3 months after the final dose. Females who are pregnant or breastfeeding should not take Tazverik because it may cause harm to a developing fetus or newborn baby. Tazverik must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.
Tazverik was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients.

Further clinical trials may be required to verify and describe Tazverik's clinical benefit. Tazverik 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 Tazverik to Epizyme, Inc.

Current Drug Shortages Index (as of January 23rd, 2020):

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

Alogliptin Tablets	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Bacitracin Ophthalmic Ointment	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Carisoprodol Tablets, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Diltiazem Hydrochloride ER (Twice-a-Day) Capsules	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Disulfiram Tablets	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***

Eprosartan Mesylate Tablets	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Latanoprost Ophthalmic Solution 0.005%	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoprolol Tartrate 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***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***

Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Ranitidine Tablets/Capsules	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Triamcinolone Acetonide (Triesence) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***
Vinblastine Sulfate Injection	***Currently in Shortage***
Vincristine Sulfate Injection, USP (Preservative-Free)	***Currently in Shortage***