Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday, January 8, 2020

No live meeting scheduled for January. January 2020 will be a packet only meeting.

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 Packet – January 8, 2020

DATE: December 19, 2019

NOTE: No live January meeting. January 2020 is a packet only meeting.

Enclosed are the following items related to the January packet.
Material is arranged in order of the agenda.

DUR Board Meeting Minutes – Appendix A

Update on Medication Coverage Authorization Unit/SoonerCare Opioid Initiative Update – Appendix B

Annual Review of Revcovi™ (Elapegademase-lvlr) – Appendix C

Annual Review of Gamifant® (Emapalumab-lzsg) – Appendix D

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

Annual Review of Firdapse® (Amifampridine) and 30-Day Notice to Prior Authorize Ruzurgi® (Amifampridine) – Appendix F

30-Day Notice to Prior Authorize Korlym® (Mifepristone) – Appendix G

Industry News and Updates – Appendix H

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

Future Business

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Packet – January 8, 2020
No live January meeting. January 2020 is a packet only meeting.

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. DUR Board Meeting Minutes – See Appendix A
A. December 11, 2019 DUR Minutes
B. December 11, 2019 DUR Recommendations Memorandum

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

2. Update on Medication Coverage Authorization Unit/SoonerCare Opioid Initiative Update – See Appendix B
A. Pharmacy Helpdesk Activity for December 2019
B. Medication Coverage Activity for December 2019
C. SoonerCare Opioid Initiative Update

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

3. Annual Review of Revcovi™ (Elapegademase-lvlr) – See Appendix C
A. Introduction
B. Current Prior Authorizations Criteria
C. Utilization of Revcovi™ (Elapegademase-lvlr)
D. Prior Authorization of Revcovi™ (Elapegademase-lvlr)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

4. Annual Review of Gamifant® (Emapalumab-lzsg) – See Appendix D
A. Current Prior Authorization Criteria
B. Utilization of Gamifant® (Emapalumab-lzsg)
C. Prior Authorization of Gamifant® (Emapalumab-lzsg)
D. Market News and Updates
E. College of Pharmacy Recommendations

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

5. Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution) – See Appendix E
A. Current Prior Authorization Criteria
B. Utilization of Glaucoma Medications
C. Prior Authorization of Glaucoma Medications
D. Market News and Updates
E. Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Glaucoma Medications

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

6. Annual Review of Firdapse® (Amifampridine) and 30-Day Notice to Prior Authorize Ruzurgi® (Amifampridine) – See Appendix F
A. Introduction
B. Current Prior Authorization Criteria

C. Utilization of Firdapse® (Amifampridine)
D. Prior Authorization of Firdapse® (Amifampridine)
E. Market News and Updates
F. Ruzurgi® (Amifampridine) Product Summary
G. College of Pharmacy Recommendations

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

7. 30-Day Notice to Prior Authorize Korlym® (Mifepristone) – See Appendix G

A. Introduction
B. Market News and Updates
C. Korlym® (Mifepristone) Product Summary
D. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

8. Industry News and Updates – See Appendix H

A. Introduction
B. News and Updates

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

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

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

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

A. Short-Acting Beta$_2$ Agonists
B. Hemophilia Medications
C. Leukemia Medications
D. Anticonvulsants
E. Anti-Migraine Medications

**Future business subject to change.*

Appendix A

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 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 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

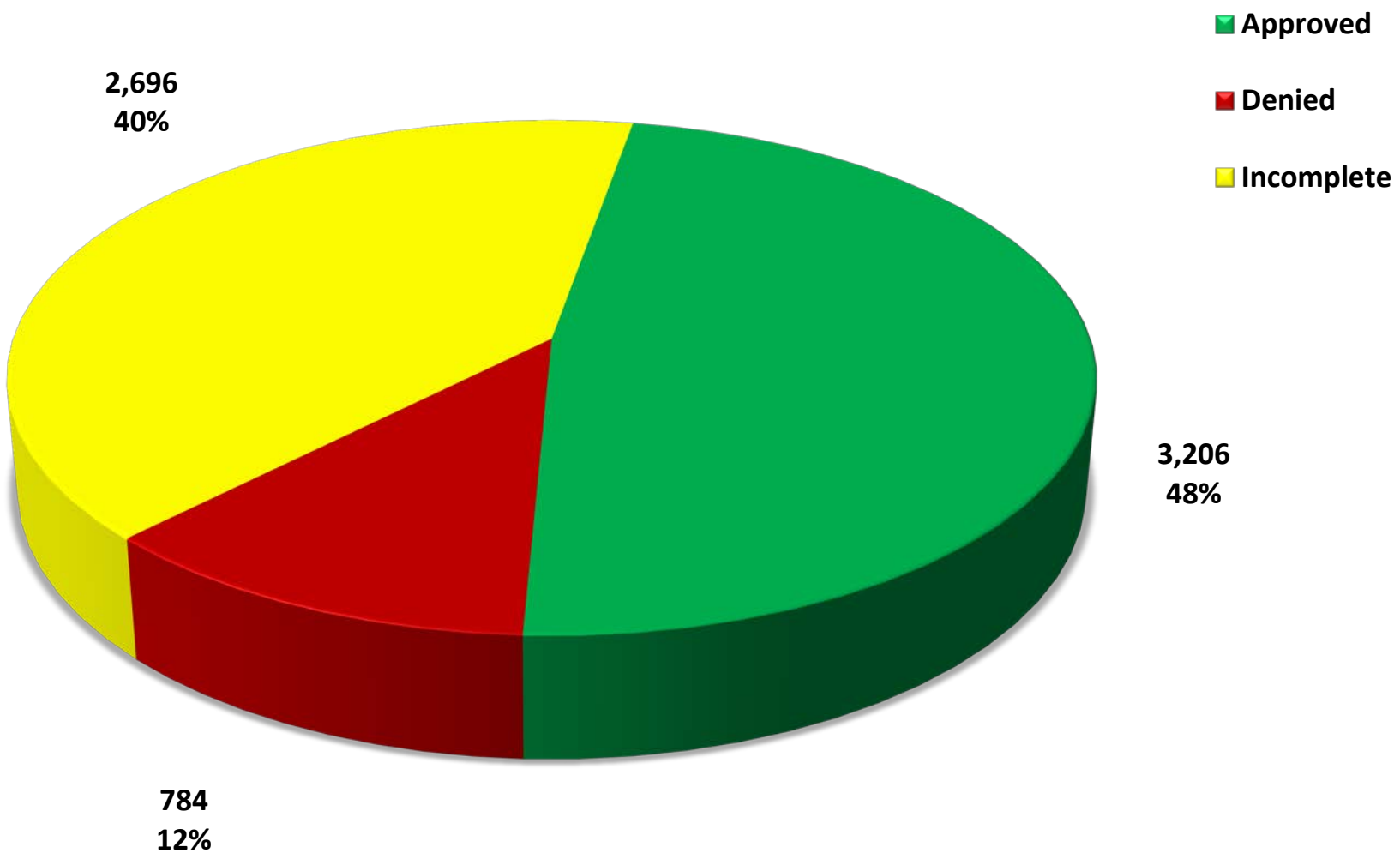
NO ACTION REQUIRED.

Recommendation 17: Future Business

NO ACTION REQUIRED.

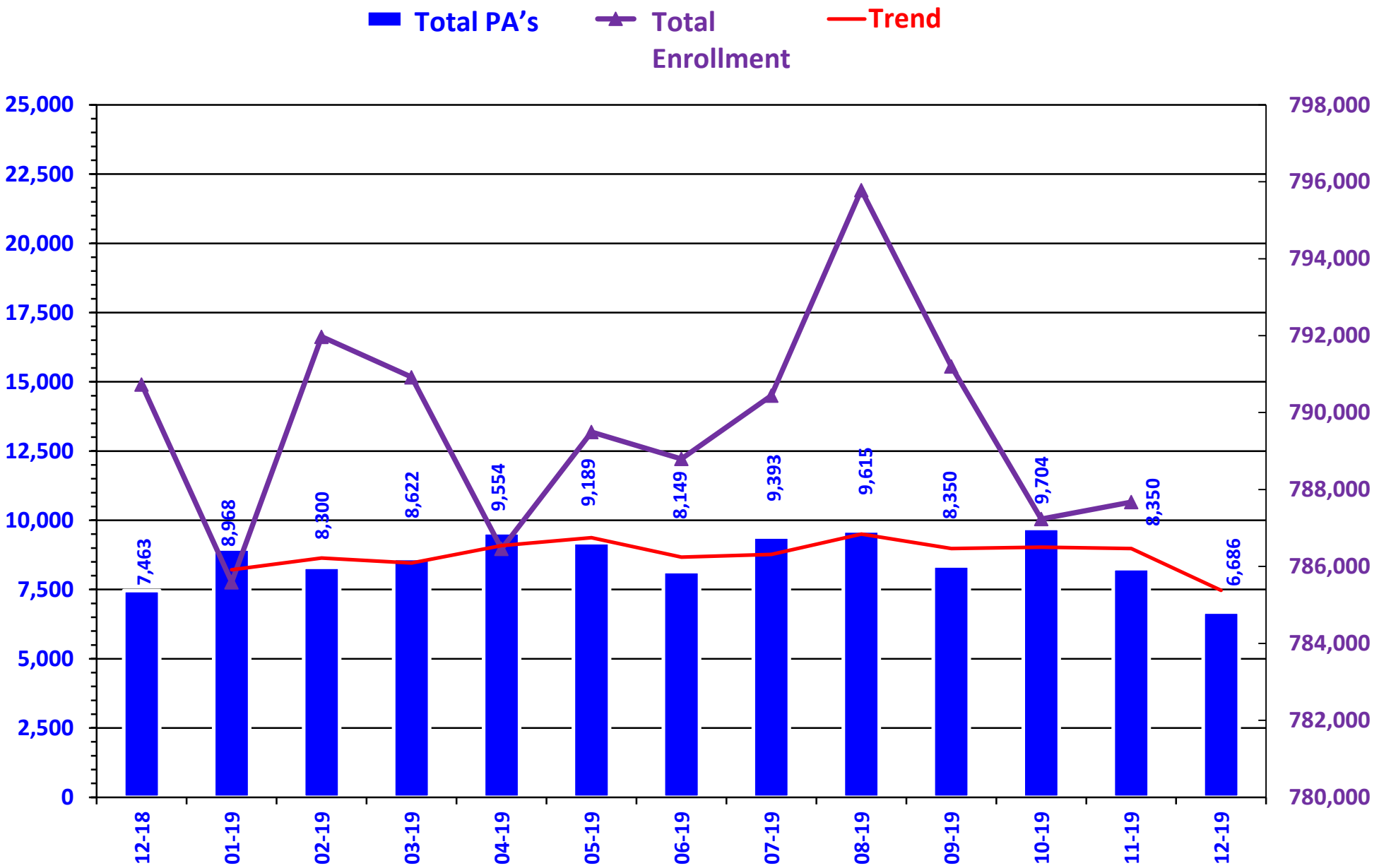
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: DECEMBER 2019*



PA totals include approved/denied/incomplete/overrides
**Current as of December 26th, 2019*

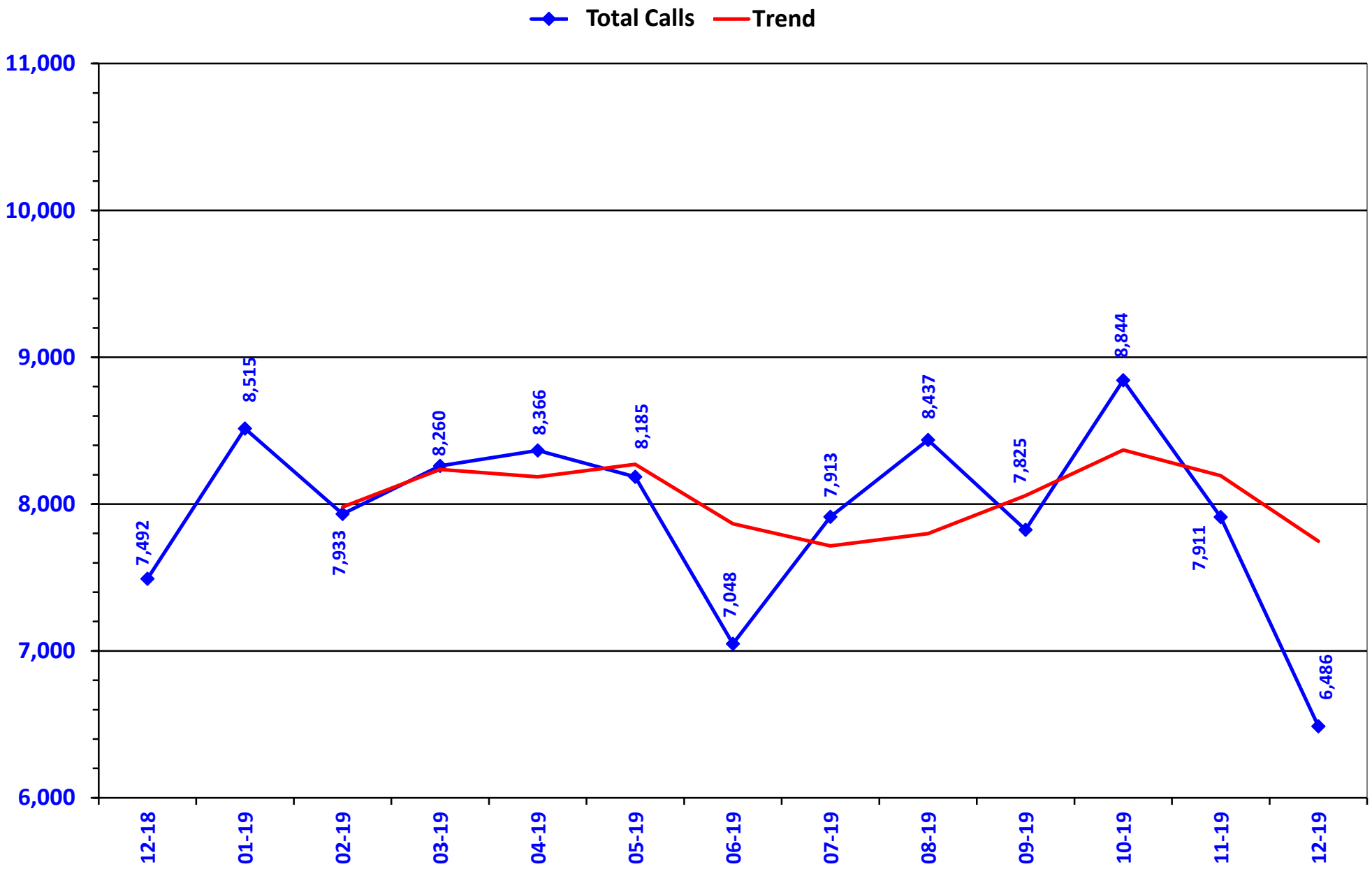
PRIOR AUTHORIZATION REPORT: DECEMBER 2018 – DECEMBER 2019*



PA totals include approved/denied/incomplete/overrides

**Current as of December 26th, 2019*

CALL VOLUME MONTHLY REPORT:
DECEMBER 2018 – DECEMBER 2019*



PA totals include approved/denied/incomplete/overrides
**Current as of December 26th, 2019*

Prior Authorization Activity

12/1/2019 Through 12/26/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	58	0	12	36	360
Analgesic - Narcotic	256	114	18	124	148
Antiasthma	94	23	24	47	318
Antibiotic	33	18	0	15	340
Anticonvulsant	150	63	23	64	285
Antidepressant	142	30	27	85	346
Antidiabetic	207	68	35	104	339
Antihemophilic Factor	10	5	0	5	299
Antihistamine	17	3	4	10	85
Antimigraine	113	27	41	45	147
Antineoplastic	84	60	6	18	174
Antiulcers	93	32	16	45	126
Anxiolytic	14	3	1	10	237
Atypical Antipsychotics	229	124	17	88	352
Biologics	111	56	15	40	261
Bladder Control	43	9	17	17	328
Blood Thinners	243	136	15	92	338
Botox	26	15	6	5	237
Buprenorphine Medications	70	12	5	53	69
Cardiovascular	54	20	8	26	314
Chronic Obstructive Pulmonary Disease	145	58	21	66	212
Constipation/Diarrhea Medications	95	25	17	53	194
Contraceptive	26	15	1	10	338
Dermatological	250	65	79	106	150
Diabetic Supplies	402	233	14	155	217
Endocrine & Metabolic Drugs	67	37	7	23	149
Erythropoietin Stimulating Agents	17	8	5	4	118
Fibromyalgia	119	6	5	108	360
Gastrointestinal Agents	122	33	21	68	185
Glaucoma	13	6	2	5	88
Growth Hormones	61	47	3	11	138
Hepatitis C	120	82	10	28	8
HFA Rescue Inhalers	27	1	0	26	202
Insomnia	26	4	3	19	153
Insulin	118	46	4	68	333
Multiple Sclerosis	19	11	6	2	193
Muscle Relaxant	38	5	15	18	25
Nasal Allergy	38	5	15	18	249
Neurological Agents	88	38	11	39	240
NSAIDs	17	1	3	13	360
Ocular Allergy	17	0	3	14	0
Ophthalmic Anti-infectives	12	1	1	10	13
Osteoporosis	16	7	1	8	364
Other*	268	67	43	158	288
Otic Antibiotic	10	2	2	6	8
Pediculicide	28	1	2	25	7
Respiratory Agents	52	23	8	21	144
Statins	11	1	7	3	78
Stimulant	500	241	46	213	350
Synagis	111	57	16	38	116

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Testosterone	38	10	7	21	302
Thyroid	10	2	4	4	361
Topical Antifungal	21	6	4	11	209
Topical Corticosteroids	50	1	30	19	84
Vitamin	45	20	15	10	137
Pharmacotherapy	49	38	1	10	267
Emergency PAs	1	1	0	0	
Total	**5,094**	**2,032**	**722**	**2,340**	
Overrides					
Brand	29	16	1	12	241
Compound	18	13	0	5	46
Cumulative Early Refill	2	0	0	2	0
Diabetic Supplies	8	7	1	0	131
Dosage Change	346	328	0	18	13
High Dose	5	3	0	2	240
Ingredient Duplication	6	6	0	0	11
Lost/Broken Rx	65	61	0	4	13
MAT Override	196	147	3	46	67
NDC vs Age	243	152	30	61	262
NDC vs Sex	4	4	0	0	82
Nursing Home Issue	42	40	0	2	20
Opioid MME Limit	119	60	6	53	90
Opioid Quantity	26	20	2	4	167
Other*	38	34	0	4	10
Quantity vs. Days Supply	391	240	19	132	268
STBS/STBSM	12	7	0	5	61
Stolen	13	12	0	1	24
Temporary Unlock	1	1	0	0	29
Third Brand Request	28	23	0	5	17
Overrides Total	**1,592**	**1,174**	**62**	**356**	
Total Regular PAs + Overrides	**6,686**	**3,206**	**784**	**2,696**	

Denial Reasons	
Unable to verify required trials.	2,115
Does not meet established criteria.	801
Lack required information to process request.	547
Other PA Activity	
Duplicate Requests	365
Letters	10,292
No Process	2
Changes to existing PAs	488
Helpdesk Initiated Prior Authorizations	544
PAs Missing Information	4

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

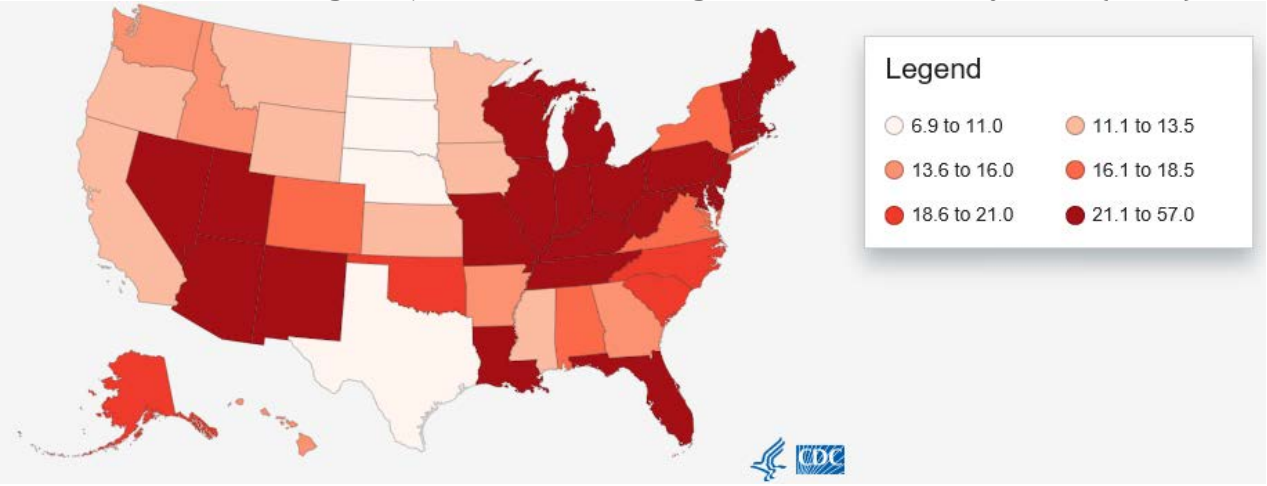
SoonerCare Opioid Initiative Update

Oklahoma Health Care Authority
January 2020

Introduction[1]

In the United States, opioids were involved in 47,600 deaths in 2017, 775 of which were in Oklahoma. Oklahoma saw a 6.5% decrease in the drug overdose death rate from 2016 to 2017, this is in contrast to the 13.2% increase seen in 2016. The following map from the Centers for Disease Control and Prevention (CDC) highlights the age-adjusted rates of drug overdose deaths by state for 2017.

CDC Number and Age-Adjusted Rates of Drug Overdose Deaths by State (2017)



Morphine Milligram Equivalent (MME) Summary[2,3,4,5,6,7,8,9]

Morphine is considered the "gold standard" for the treatment of pain and is used as the basis for comparison via morphine milligram equivalent (MME). The MME provides a conversion factor from one opioid to another and gives a standard for comparison. The following are MME recommendations or alerts from various government organizations, medical groups, quality measurement programs, and law enforcement:

- CDC: The CDC recommends clinicians prescribe the lowest effective opioid dosage when a patient begins opioid therapy for chronic pain, and encourages caution for doses exceeding 50 MME per day and avoidance of doses exceeding 90 MME per day.
- Centers for Medicare and Medicaid Services (CMS): In January 2019, CMS finalized new opioid policies for Medicare drug plans. CMS recommended that residents of long-term care facilities, those in hospice care, patients receiving palliative care or end-of-life care, and patients being treated for active cancer-related pain should be excluded from these interventions. It was also recommended that these policies not impact patients' access to medication assisted treatment (MAT), such as buprenorphine. In addition, it was stated that the MME thresholds and day supply limits are not prescribing limits and the

patient or their prescriber can request an expedited or standard coverage determination from the plan for approval of higher amounts or a longer days' supply. The following CMS safety edits became effective on January 1, 2019:

- 7-day supply limit for opioid naïve patients (hard edit)
- Opioid care coordination edit at 90 MME which alerts pharmacists to review when the patient's cumulative MME per day reaches or exceeds 90 across all opioid prescriptions; the 90 MME threshold identifies potentially high-risk patients who may benefit from closer monitoring and care coordination
- Some plans may implement a hard edit when a patient's cumulative opioid daily dosage reaches 200 MME or greater
- Concurrent opioid and benzodiazepine use or duplicative long-acting opioid therapy (soft edits)

- Oklahoma Senate Bill (SB) 1446: In May 2018, SB 1446 was signed into law and places a 7-day limit on initial opioid prescriptions for acute pain. The State Board of Osteopathic Examiners, Oklahoma State Medical Association, Oklahoma Hospital Association, and several medical associations endorsed a best practice document released in October 2018 to clarify some of the details in Oklahoma SB 1446 on opioid prescribing, including instructing prescribers to thoroughly document their rationale for prescribing >100 MME.
- Oklahoma Bureau of Narcotics and Dangerous Drugs (OBNDD) Prescription Monitoring Program (PMP): In February 2018, the OBNDD via the AWARE system initiated 3 clinical alerts featured on the PMP. The clinical alerts were designed to help providers identify at-risk patients. One of the alerts included patients who exceed a daily MME of 100. Current Oklahoma law requires prescribers to check the PMP upon an initial opioid prescription and then at least every 180 days.
- Pharmacy Quality Alliance (PQA) Opioid Measures: PQA, a nationally recognized organization that develops measures to promote appropriate medication use and reporting of performance information related to medications, developed 3 opioid measures including 1 specific to opioid analgesics at "high dosages" in persons without cancer. The measure defined "high dosages" as 120 MME or greater.

The following table contains MMEs based on strength and quantities for commonly prescribed opioid medications. Daily MMEs in red font exceed the CDC recommendation of 90 MME per day.

Drug/Strength	Quantity	Day Supply	Daily MME
Immediate-Release (IR) Products			
codeine 30mg	120	30	18
hydrocodone/APAP 5mg/325mg	120	30	20
hydrocodone/APAP 7.5mg/325mg	120	30	30
hydrocodone/APAP 10mg/325mg	120	30	40
hydromorphone IR 2mg	120	30	32
hydromorphone IR 4mg	120	30	64
hydromorphone IR 8mg	120	30	128

Drug/Strength	Quantity	Day Supply	Daily MME
oxycodone IR 15mg	120	30	90
oxycodone IR 20mg	120	30	120
oxycodone/APAP 7.5mg/325mg	120	30	45
Extended-Release (ER) Products			
fentanyl patch 25mcg	10	30	60
fentanyl patch 37.5mcg	10	30	90
fentanyl patch 50mcg	10	30	120
fentanyl patch 75mcg	10	30	180
Hysingla® ER (hydrocodone ER) 100mg	30	30	100
Hysingla® ER (hydrocodone ER) 120mg	30	30	120
Oxycontin® (oxycodone ER) 30mg	60	30	90

MME = morphine milligram equivalent; APAP = acetaminophen

SoonerCare MME Claims Analysis[1,3,5,6,7,10,11,12,13]

In July 2018, the Drug Utilization Review (DUR) Board voted to lower the SoonerCare opioid MME limit to 100 to coincide with the OBNDD clinical alert on the Oklahoma PMP database. In July 2019, the DUR Board voted to lower the MME limit to 90 to coincide with CDC and CMS recommendations. MME limits were phased in gradually beginning in January 2019 with final implementation effective October 2019. Members requiring >90 cumulative MME day require prior authorization with clinically significant reasoning for use of >90 cumulative MME day. Members with a cancer diagnosis as well as medications for opioid use disorder are excluded from the MME edit.

The following table details SoonerCare MME data for Schedule II medications from January 1, 2019 to November 30, 2019. The table excludes members with an oncology diagnosis in medical claims history over the specified time period evaluated. Combination products containing buprenorphine and naloxone used for MAT were excluded from the analysis. The average cumulative MME per day decreased by 21.6% since January 2019 at the start of the MME edit implementation. In addition, the number of members with more than 120 MME per claim decreased by 78.0%.

Month/Year	Avg. Cumulative MME Per Day	Avg. MME Claim Per Day	# of Members >120 MME Per Claim*
January 2019	51	41	395
February 2019	45	40	350
March 2019	44	40	339
April 2019	44	39	296
May 2019	43	39	274
June 2019	42	39	269
July 2019	42	39	222
August 2019	40	38	86
September 2019	40	38	88
October 2019	40	37	96
November 2019	40	38	87

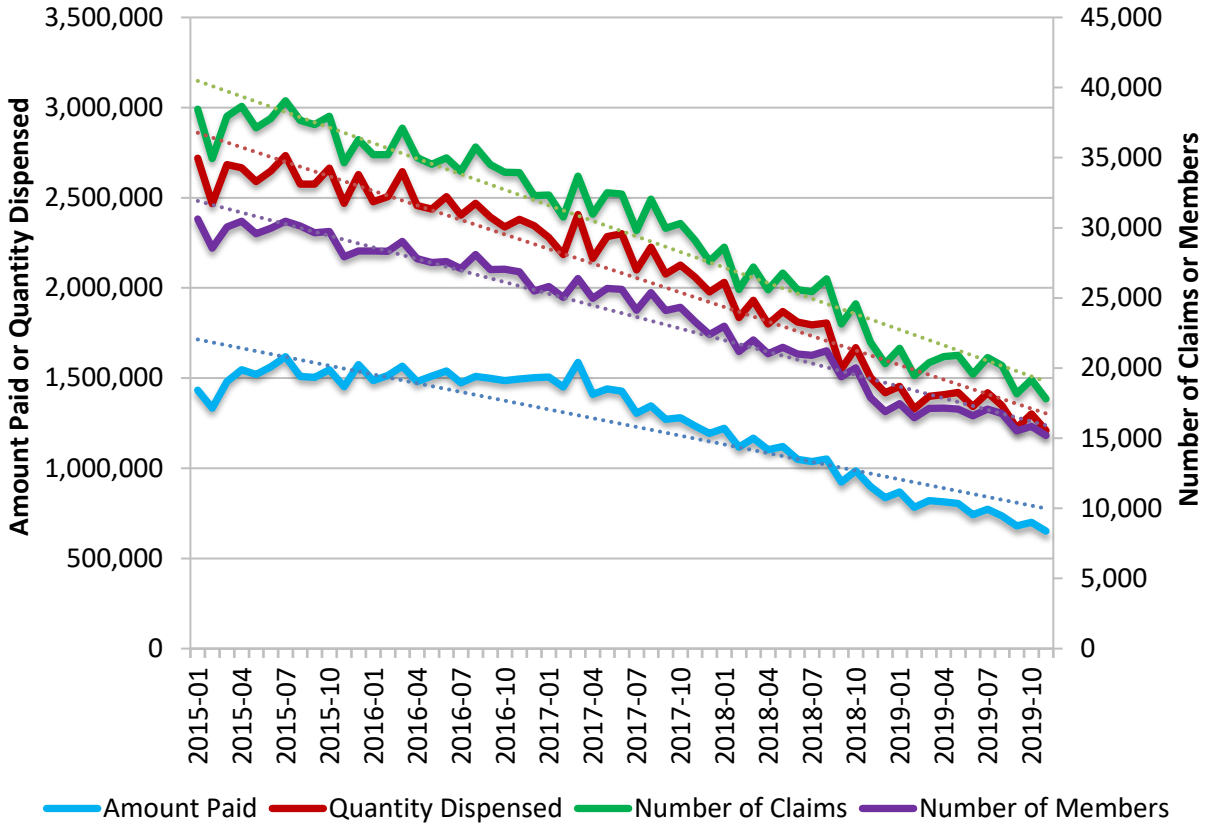
MME = morphine milligram equivalent; Avg. = average; # = number; > = greater than

*Excludes members with an oncology-related diagnosis.

In addition to the MME edits implemented in 2019, previous edits limiting the number of solid dosage form, immediate-release (IR) opioid units per claim to a maximum quantity of 120 units per 30-day supply were implemented in late 2014 and early 2015. Numerous opioid educational efforts have been undertaken by the OHCA and the College of Pharmacy including pain management practice facilitation, naloxone education and access, Lock-In program expansion, as well as newsletter articles and educational mailings. These efforts have coincided with laws passed by the Oklahoma legislature including mandatory PMP checks, which were implemented in November 2015, and a 7-day limit on initial opioid prescriptions for acute pain, which was implemented in November 2018.

The following chart shows the utilization trends of all opioid analgesics. All parameters have followed a linear decline since implementation of the quantity limit; linear trends are noted in the chart by dotted lines for each parameter.

Opioid Analgesic Trends: January 2015 to November 2019
Number of Claims, Amount Paid, Quantity Dispensed, Number of Members



[1] Centers for Disease Control and Prevention (CDC). Drug Overdose Deaths. Available online at: https://www.cdc.gov/drugoverdose/data/statedeaths.html. Last revised 06/27/2019. Last accessed 12/13/2019.
[2] CDC. Calculating Total Daily Dose of Opioids for Safer Dosage. Available online at: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. Last accessed 12/13/2019.
[3] CDC. CDC Guidelines for Prescribing Opioids for Chronic Pain. Available online at: https://www.cdc.gov/drugoverdose/prescribing/guideline.html. Last revised 03/18/2016. Last accessed 12/13/2019.
[4] Optum, Inc. Shining a Light on MEDs: Understanding morphine equivalent dose. Available online at: http://helioscomp.com/docs/default-source/White-Paper/cln14-15209_med-white-paper_final.pdf. Issued 2017. Last accessed 12/13/2019.
[5] Centers for Medicare and Medicaid Services (CMS). 2019 Medicare Part D Opioid Policies: Information for Pharmacies. Available online at: https://www.pharmacist.com/sites/default/files/audience/CMSPartDOpioid%20Pharmacy%20Tip%20Sheet_20181206_508.pdf. Last accessed 12/13/2019.
[6] Gerszewski A. Attorney General Hunter Applauds House and Senate Members for Passing Host of Opioid Commission Recommendations. Office of Oklahoma Attorney General. Available online at: http://www.oag.ok.gov/attorney-general-hunter-applauds-house-and-senate-members-for-passing-host-of-opioid-commission-recommendations. Issued 05/02/2018. Last accessed 12/13/2019.
[7] Oklahoma Medical Board. Compliance and Best Practice for an Act Regulating the Use of Opioid Drugs Oklahoma Senate Bills 1446 & 848. Available online at: http://www.okmedicalboard.org/download/884/Opioid_Best_Practices.pdf. Last revised 06/03/2019. Last accessed 12/13/2019.
[8] Oklahoma Prescription Monitoring Program (PMP). Clinical Alerts. Available online at: http://pmp.obn.ok.gov/blog-entry/clinical-alerts. Last accessed 12/13/2019.
[9] Pharmacy Quality Alliance (PQA). PQA Performance Measures. Available online at: https://www.pqaalliance.org/pqa-measures. Last accessed 12/13/2019.
[10] Oklahoma Health Care Authority (OHCA). Pharmacy Lock-In Program. Available online at: http://www.okhca.org/providers.aspx?id=8738&linkidentifier=id&itemid=8738. Last accessed 12/13/2019.
[11] OHCA. Provider Checkup: Fall 2016, Vol. 1. Available online at: https://content.govdelivery.com/accounts/OKHCA/bulletins/15f40c9#link_1472585927433. Issued 09/20/2016. Last accessed 12/13/2019.
[12] OHCA. Opioid Prescribing Guidelines. Available online at: https://www.okhca.org/providers.aspx?id=15481. Last accessed 12/13/2019.
[13] OHCA. Pain Management Program. Available online at: www.okhca.org/painmanagement. Last accessed 12/13/2019.

Appendix C

Fiscal Year 2019 Annual Review of Revcovi™ (Elapegademase-lvlr)

Oklahoma Health Care Authority
January 2020

Introduction[1,2,3]

Adenosine deaminase (ADA) deficiency is an autosomal recessive genetic disorder caused by mutations in the *ADA* gene. The ADA enzyme is found in all cells, including red and white blood cells, and works by catalyzing the deamination of adenosine and deoxyadenosine (dAXP) which are then excreted. In the absence of functional ADA enzyme, there is intracellular accumulation of dAXP and adenosine and subsequent cellular toxicity. Additionally, excessive levels of dAXP can block DNA synthesis. In approximately 90% of cases, ADA deficiency leads to severe combined immunodeficiency (ADA-SCID) with dysfunction of T, B, and natural killer (NK) cells that presents in the first few months of life.

ADA deficiency has an overall incidence of 1 in 200,000 live births. Most ADA-SCID patients present with life-threatening infections, chronic persistent diarrhea, and failure to thrive in the first months of life. Neurologic abnormalities, including cognitive deficits, can occur as a result of the metabolic abnormalities of ADA deficiency. ADA-SCID is typically fatal in the first 2 years of life without treatment. Diagnosis of ADA deficiency is established by demonstrating absent or very low (<1% of normal) ADA activity in red blood cells (RBCs), which is accompanied by increased levels of adenosine and 2'dAXP in plasma. Increased dAXP in RBCs is indicative for ADA deficiency. The addition of T-cell receptor excision circles (TRECS) testing, a surrogate marker for new T-cell production, to newborn screening tests has led to significant improvements in the diagnosis of ADA-SCID. Additionally, the guidelines from the American Academy of Allergy, Asthma, and Immunology (AAAAI) recommend testing for biallelic mutations in the *ADA* gene to further confirm ADA deficiency.

Exposure to contagious illnesses should be minimized as best as possible. The ADA-SCID treatment guidelines recommend that all patients initially receive enzyme replacement therapy (ERT) as an immediate stabilizing measure, while planning definitive treatment with either of 2 equal, first-line options: human leukocyte antigen (HLA)-matched sibling or family donor allogenic hematopoietic stem cell transplantation (HSCT) or autologous hematopoietic stem cell gene therapy (HSC-GT). HSC-GT is not currently available in the United States. If HLA-matched sibling donor/family donor HSCT or HSC-GT are not available or have failed, ERT can be continued or reinstituted and HSCT with alternative donors should be considered. There are currently 2 U.S. Food and Drug Administration (FDA) approved ERTs indicated for the treatment of ADA-SCID: Adagen® (pegademase bovine) and Revcovi™ (elapegademase-lvlr).

ERT has the potential to protect from neurologic injury caused by increased levels of adenosine and dAXP. ERT leads to a rapid increase in plasma ADA activity and over a period of 4 to 8 weeks, results in the return of RBC dAXP levels to nearly undetectable levels. An increase in B-cell numbers is evident within the first month of therapy in some patients, whereas T-cell

numbers typically begin to increase by 2 to 4 months. Production of antibodies also normalizes. Early treatment can reverse metabolic toxicity to the thymus and nonlymphoid organs, further stabilizing patients before HSCT or HSC-GT. In most patients, ERT should be used as a "bridge" for relatively short periods (a few months to approximately 2 years) before undergoing HSCT or HSC-GT. The deterioration in lymphocyte counts and function over time might lead to a decrease in antiviral immunity and tumor surveillance, contributing to an increased risk of malignancies. For these reasons, the guidelines do not recommend that continuous ERT treatment last beyond 5 to 8 years, and that long-term ERT treatment is only appropriate for patients when neither HSCT nor HSC-GT have been available or effective.

Current Prior Authorization Criteria

Revcovi™ (Elapegademase-lvlr) Approval Criteria:

1. An FDA approved diagnosis of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients; and
    a. Diagnosis of ADA deficiency should be confirmed by demonstrating biallelic mutations in the *ADA* gene; and
2. Revcovi™ must be prescribed by, or in consultation with, a physician who specializes in the treatment of immune deficiency disorders; and
3. The member must have failed to respond to a bone marrow transplant or not be a current suitable candidate for a bone marrow transplant; and
4. Prescriber must agree to monitor trough plasma ADA activity, trough deoxyadenosine (dAXP) levels, and/or total lymphocyte counts to ensure efficacy and compliance and to monitor for neutralizing antibodies when suspected; 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. Initial approvals will be for the duration of 6 months at which time the prescriber must confirm improvement or stabilization in ADA activity or dAXP levels or improvement in immune function. Subsequent approvals will require the prescriber to verify the member is still not a current suitable candidate for a bone marrow transplant.

Utilization of Revcovi™ (Elapegademase-lvlr): Fiscal Year 2019

Revcovi™ (Elapegademase-lvlr) Fiscal Year 2019 Utilization: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1	2	$394,261.74	$197,130.87	$7,040.39	60	56

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

- There were no paid pharmacy claims for Revcovi™ (elapegademase-lvlr) during fiscal year 2018 (fiscal year 2018 = 07/01/2017 to 06/30/2019) to allow for a fiscal year comparison.
- There were no paid medical claims for Revcovi™ (elapegademase-lvlr) during fiscal year 2018 or 2019.

Demographics of Members Utilizing Revcovi™ (Elapegademase-lvlr)

- Due to the limited number of members utilizing Revcovi™ (elapegademase-lvlr) during fiscal year 2019, detailed demographic information could not be provided.

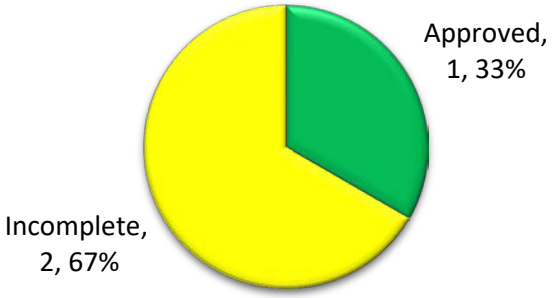
Top Prescriber Specialties of Revcovi™ (Elapegademase-lvlr) by Number of Claims

- The only prescriber specialty listed on paid pharmacy claims for Revcovi™ (elapegademase-lvlr) during fiscal year 2019 was pediatric pulmonologist.

Prior Authorization of Revcovi™ (Elapegademase-lvlr)

There were 3 prior authorization requests submitted for 1 unique member for Revcovi™ (elapegademase-lvlr) 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[4,5,6,7,8]

Discontinuation(s):

- **Adagen® (pegademase bovine):** Leadiant Biosciences announced the discontinuation of Adagen® citing a permanent shortage of the active ingredient. The discontinuation of the product is not due to quality, safety, or efficacy concerns. Leadiant estimated inventory of Adagen® to be depleted by late-March 2019. Adagen® is FDA approved for ERT for ADA deficiency in patients with ADA-SCID who are not suitable candidates for, or who have failed a bone marrow transplantation. A trial of Adagen® was previously a part of the Revcovi™ (elapegademase-lvlr) prior authorization criteria, but has been removed as a result of the Adagen® discontinuation.

News:

- **November 2019:** An investigative report by Kaiser Health News revealed that despite FDA manufacturing facility inspectors recommending against approval, Revcovi™ (elapegademase-lvlr) was FDA approved. Inspectors noted that Revcovi™ failed a sterility test after the vials tested positive for *Delftia acidovorans*; however, the drug filling machine stayed in use despite the contaminant. The manufacturer of Revcovi™, Leadiant Biosiences, said their written responses to the FDA observations were considered “adequate” by the FDA.

Pipeline:

- **ADA-SCID Gene Therapy:** Strimvelis®, an autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence, is a 1-time gene therapy that replaces the defective gene coding for ADA. Strimvelis® has been available in Europe since 2016 for ADA-SCID patients who cannot be treated by a bone marrow transplant, but is currently only administered at a single facility in Italy and has had limited uptake since launch. Orchard Therapeutics, the manufacturer of Strimvelis®, says it is planning to build a manufacturing plant for the therapy and expand the roll-out of the drug to other clinical centers in Europe. The benefits of Strimvelis® have been shown in 1 study involving 12 patients from 6 months to 6 years of age with ADA-SCID. Patients in the study had no appropriate bone marrow donor and alternative treatments had failed or were not available. All patients were treated with Strimvelis® and were still alive 3 years after treatment. The rate of severe infections declined after treatment and continued to decline with longer-term follow-up beyond 3 years. Orchard is also developing another gene therapy, OTL-101, for ADA-SCID, in development for both the European and United States markets. The FDA granted Orchard Rare Pediatric Disease designation for OTL-101. To be granted Rare Pediatric Disease designation, a drug must be designed for the treatment of a serious or life-threatening disease which affects <200,000 patients in the United States and which primarily includes patients between 0 and 18 years of age. Due to this designation the company may qualify for a Pediatric Priority Review voucher at the time the drug gets approved for this indication. That voucher could then be redeemed to receive priority review of a subsequent marketing application for a different product or be transferable to another company. More than 40 ADA-SCID patients have been treated with OTL-101. All patients have survived up to 5 years after treatment, and OTL-101 has restored patients' immune function with a favorable safety profile.

Recommendations

The College of Pharmacy does not recommend any changes to the current Revcovi™ (elapegademase-lvlr) prior authorization criteria at this time.

[1] Kohn DB, Hershfield MS, Puck JM, et al. Consensus approach for the management of severe combined immune deficiency caused by adenosine deaminase deficiency. *J Allergy Clin Immunol* 2018; 43(3)852-863. doi: 10.1016/j.jaci.2018.08.024.
[2] Rubinstein A. Adenosine deaminase deficiency: treatment. *UpToDate*. Available online at: https://www.uptodate.com/contents/adenosine-deaminase-deficiency-pathogenesis-clinical-manifestations-and-diagnosis?topicRef=3955&source=see_link. Last revised 03/26/2019. Last accessed 12/13/2019.
[3] Rubinstein A. Adenosine deaminase deficiency: Pathogenesis, clinical manifestations, and diagnosis. *UpToDate*. Available online at: https://www.uptodate.com/contents/adenosine-deaminase-deficiency-pathogenesis-clinical-manifestations-and-diagnosis?search=ada%20scid&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Last revised 03/26/2019. Last accessed 12/13/2019.
[4] OptumRx. Rx Highlights. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxhighlights/RxHighlights2019_January.pdf. Issued 01/2019. Last accessed 12/12/2019.
[5] Lupkin S. FDA Keeps Brand-Name Drugs On A Fast Path To Market — Despite Manufacturing Concerns. *Kaiser Health News*. Available online at: https://khn.org/news/fda-keeps-brand-name-drugs-on-a-fast-path-to-market-%E2%80%95-despite-manufacturing-concerns/. Issued 11/05/2019. Last accessed 12/12/2019.
[6] Strimvelis. The European Medicines Agency. Available online at: https://www.ema.europa.eu/en/medicines/human/EPAR/strimvelis. Last revised 05/09/2018. Last accessed 12/13/2019.
[7] Orchard Therapeutics. Orchard Therapeutics Announces That OTL-101 Has Received a Rare Pediatric Disease Designation. *B3C Newswire*. Available online at: https://www.b3cnewswire.com/201707241613/orchard-therapeutics-announces-that-otl-101-has-received-a-rare-paediatric-disease-designation.html. Issued 07/24/2017. Last accessed 12/13/2019.
[8] Orchard Therapeutics. Orchard Therapeutics Presents Two-Year Follow-Up Data Versus Historical Control from Registrational Trial of OTL-101 for the Treatment of ADA-SCID. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/02/22/1740293/0/en/Orchard-Therapeutics-Presents-Two-Year-Follow-Up-Data-Versus-Historical-Control-from-Registrational-Trial-of-OTL-101-for-the-Treatment-of-ADA-SCID.html. Issued 02/22/2019. Last accessed 12/13/2019.

Appendix D

Fiscal Year 2019 Annual Review of Gamifant® (Emapalumab-lzsg)

Oklahoma Health Care Authority
January 2020

Current Prior Authorization Criteria

Gamifant® (Emapalumab-lzsg) Approval Criteria:

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

8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
9. Approvals will be for the duration of 6 months with reauthorization granted if the prescriber documents the member is responding well to treatment, no unacceptable toxicity has occurred, and the member has not received hematopoietic stem cell transplantation (HSCT).

Utilization of Gamifant® (Emapalumab-lzsg): Fiscal Year 2019

There was no SoonerCare utilization, including pharmacy and medical claims, of Gamifant® (emapalumab-lzsg) during fiscal year 2019 (fiscal year 2019 = 07/01/2018 to 06/30/2019).

Prior Authorization of Gamifant® (Emapalumab-lzsg)

There were no prior authorization requests submitted for Gamifant® (emapalumab-lzsg) during fiscal year 2019.

Market News and Updates[1,2]

Guideline Update(s):

- **June 2019:** The Hemophagocytic Lymphohistiocytosis (HLH) Steering Committee of the Histiocyte Society developed recommendations based on expert opinions derived from an interdisciplinary working group for the diagnosis and treatment of HLH in adults, as a complement to previously published recommendations. In adult patients, HLH is often secondary to infection, malignancy, or underlying autoimmune diseases. However, diagnostic and treatment protocols pertain primarily to pediatric patients, who are likely to have primary HLH. This leads to several challenges in treating HLH in adults. For example, the HLH-2004 diagnostic criteria developed for children are commonly applied but are not validated for adults. Another challenge in HLH diagnosis is that patients may present with a phenotype indistinguishable from sepsis or multiple organ dysfunction syndrome. Treatment algorithms targeting hyperinflammation are frequently based on pediatric protocols, which may result in overtreatment and unnecessary toxicity in adults. The intent of these recommendations is to facilitate knowledge transfer between physicians caring for pediatric and adult patients with HLH, with the aim to improve the outcome for adult patients affected by HLH. Key points from these recommendations include the following:
    - Although hyperferritinemia often triggers the workup, this parameter is less specific in adults than in pediatric patients, and no single clinical or laboratory feature has sensitivity and specificity to unequivocally diagnose HLH in adults
    - Among malignancies, lymphoma can be difficult to diagnose; positron emission tomography (PET) scanning, biopsy, and collaboration with pathologists who have expertise in lymphoma are advised
    - Genetic testing is not generally advised in adults
    - There is no one-size-fits-all treatment approach, given that pathogenesis and treatment needs vary among patients with macrophage activation syndrome, malignancy-HLH (at diagnosis and following chemotherapy), immunotherapy-associated HLH, and infection-triggered HLH

- The HLH-94 treatment protocol, which includes etoposide, dexamethasone, and cyclosporine, is highly effective and advised; however, dosing and duration need to be tailored to the secondary HLH subtype, as well as to comorbidities, performance status, and response
- Secondary infections can be misconstrued as HLH relapse; opportunistic infection prophylaxis is suggested
- Refractory cases may require allogeneic transplantation

Recommendations

The College of Pharmacy does not recommend any changes to the current Gamifant® (emapalumab-lzsg) prior authorization criteria at this time.

[1] La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. *Blood* 2019; 133(23):2465-2477.

[2] Stein BL. Managing Hemophagocytic Lymphohistiocytosis. *NEJM Journal Watch*. Available online at: https://www.jwatch.org/na49330/2019/06/12/managing-hemophagocytic-lymphohistiocytosis. Issued 06/12/2019. Last accessed 12/03/2019.

Appendix E

Fiscal Year 2019 Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rocklatan® (Netarsudil/ Latanoprost 0.02%/0.005% Ophthalmic Solution)

Oklahoma Health Care Authority
January 2020

Current Prior Authorization Criteria

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		
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		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
latanoprost (Xalatan® 0.005%)	bimatoprost (Lumigan® 0.01%, 0.03%)	latanoprost (Xelpros® 0.005%)
travoprost (Travatan-Z® 0.004%)	tafluprost (Zioptan® 0.0015%)	latanoprostene bunod (Vyzulta® 0.024%)
Rho Kinase Inhibitors		
netarsudil (Rhopressa® 0.02%)		

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

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.

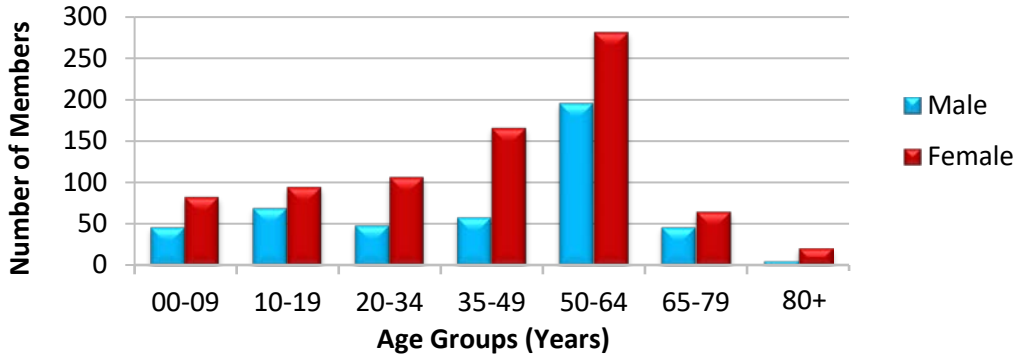
Utilization of Glaucoma Medications: Fiscal Year 2019

Comparison of Fiscal Years

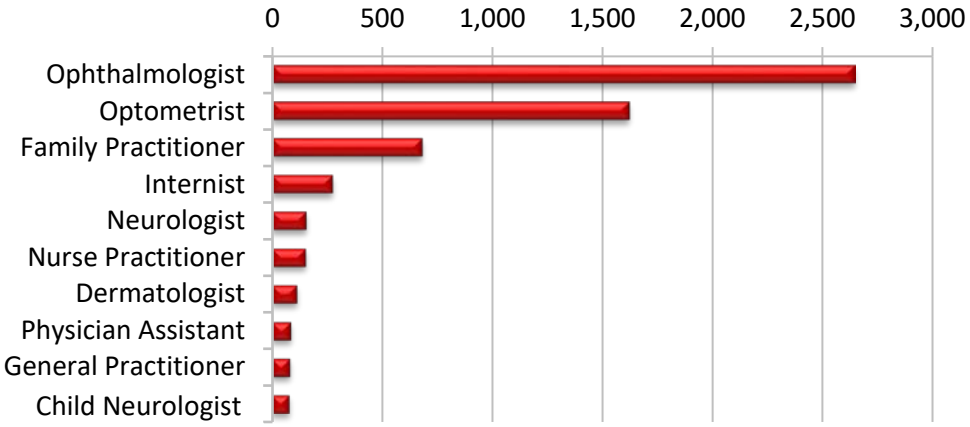
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	1,307	6,166	$566,314.53	$91.84	$2.66	87,865	212,622
2019	1,293	6,197	$586,039.51	$94.57	$2.68	81,843	218,970
% Change	**-1.10%**	**0.50%**	**3.50%**	**3.00%**	**0.80%**	**-6.90%**	**3.00%**
Change	**-14**	**31**	**$19,724.98**	**$2.73**	**$0.02**	**-6,022**	**6,348**

*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 Glaucoma Medications

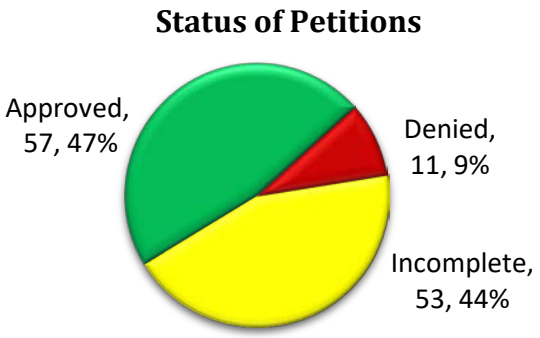


Top Prescriber Specialties of Glaucoma Medications by Number of Claims



Prior Authorization of Glaucoma Medications

There were 121 prior authorization requests submitted for glaucoma medications during fiscal year 2019. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2019.



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

Anticipated Patent Expiration(s):

- Combigan® (brimonidine/timolol 0.2%/0.5%): January 2023
- Alphagan-P® (brimonidine 0.1%): March 2024
- Vyzulta® (latanoprostene bunod 0.024%): October 2025
- Lumigan® (bimatoprost 0.01%): June 2027
- Zioptan® (tafluprost 0.0015%): May 2029
- Xelpros® (latanoprost 0.005%): September 2029
- Simbrinza® (brinzolamide/brimonidine 0.2%/1%): October 2030
- Rhopressa® (netarsudil 0.02%): March 2034
- Rocklatan® (netarsudil/latanoprost 0.02%/0.005%): March 2034

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

- **March 2019:** Aerie Pharmaceuticals, Inc. reported that the FDA approved Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution), a once-daily ophthalmic drop that is a fixed-dose combination of latanoprost, a prostaglandin analog (PGA), and netarsudil, a Rho kinase (ROCK) inhibitor specifically designed to target the trabecular meshwork (the eye's principal drainage pathway). Netarsudil is the active ingredient in Rhopressa® (netarsudil ophthalmic solution 0.02%) which was launched by Aerie in April 2018.

Pipeline:

- **Bimatoprost Sustained-Release (SR) Implant:** The FDA accepted a New Drug Application (NDA) in July 2019 for bimatoprost SR, a first-in class SR biodegradable implant for the reduction of intraocular pressure (IOP) in patients with primary open-angle glaucoma or ocular hypertension (HTN). In the 2 Phase 3 ARTEMIS studies, bimatoprost SR reduced IOP by 30% over the 12-week primary efficacy period, meeting the predefined criteria for non-inferiority to the study comparator, timolol. The ARTEMIS studies evaluated 1,122 patients on the efficacy and safety of bimatoprost SR versus timolol, a FDA standard comparator for registrational clinical trials, in patients with open-angle glaucoma or ocular HTN. After 3 treatments with bimatoprost SR, >80% of patients remained treatment free and did not need additional treatment to maintain IOP control for at least 12 months. Bimatoprost SR was well tolerated in the majority of patients. The FDA is expected to take action on the NDA by the end of the first half of 2020.

- **NB1111:** NB1111 is a prodrug of tetrahydrocannabinol (THC-valine-hemisuccinate; THCVHS), which has no physiological activity itself, but is designed to help transport the active part of the molecule, THC, into the eye. Once inside the eye, NB1111 is cleaved by enzymes in the eye, and THC is then released to bind to cannabinoid receptors. THC has been shown in both human and animal experiments since the 1970's to reduce IOP; however, the cannabinoid chemistry was not conducive to direct ocular delivery. NB1111 is unique because this is the first time a direct topical application of THC has been shown in animal experiments to have a sustained lowering of IOP, supporting development as a drug. In October 2019, Emerald Bioscience, Inc. announced data demonstrating the superiority of its formulation of NB1111 in lowering IOP in the eye in a validated animal model. NB1111 was compared to the current IOP-lowering standards-of-care for treating glaucoma: latanoprost and timolol. IOP was measured in normotensive (normal ocular pressure) rabbits following a single topical dose of NB1111 compared to latanoprost and timolol. NB1111 demonstrated a statistically superior intensity as well as duration of IOP decline. Additionally, Emerald Bioscience, Inc., announced data validating mechanisms of action of NB1111 by testing the active component of the prodrug, THC, in human donor tissue. The data demonstrated THC's ability to lower IOP in the eye by enhancing drainage of ocular fluid over the trabecular meshwork, 1 of the major tissues for regulating IOP in the eye. The meshwork is known to contain a high density of cannabinoid receptors, indicating NB1111's potential as a promising drug candidate to treat glaucoma and possibly other ocular disorders that threaten the optic nerve. THC also lowered biomarkers associated with inflammation and fibrosis, indicating a previously unrecognized interaction between the endocannabinoid system and the inflammatory cascade in the eye.
- **OTX-TIC:** OTX-TIC is designed to be a bioresorbable intracameral implant containing micronized travoprost that is injected into the anterior chamber of the eye and is intended for patients with glaucoma with a target duration of drug delivery of 4 to 6 months. Preclinical studies in beagles have demonstrated an acceptable safety profile, maintenance of drug levels in the aqueous humor, and a sustained lowering of IOP. OTX-TIC is designed to directly address compliance issues by delivering travoprost over the course of several months with a single implant. In May 2018, the first patient was treated with OTX-TIC in a Phase 1, multi-center, open-label, prospective, proof-of-concept clinical trial. This trial will evaluate the safety, efficacy, durability, and tolerability of OTX-TIC in patients with primary open-angle glaucoma or ocular HTN.
- **OTX-TP:** OTX-TP is a drug product candidate that is intended for insertion into the canaliculus to deliver travoprost to the ocular surface for up to 90 days without preservatives. The goal of OTX-TP is to deliver a continuous steady release of travoprost throughout the treatment period. Ocular Therapeutix is currently enrolling patients in a Phase 3 trial with OTX-TP to evaluate the reduction of IOP connected to glaucoma and ocular HTN.

Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution) Product Summary[9,10]

Indication(s): Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution) is a fixed dose combination of a ROCK inhibitor and a prostaglandin F2α analog indicated for the reduction of elevated IOP in patients with open-angle glaucoma or ocular HTN.

Dosing:

- 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. If a dose is missed, treatment should continue with the next dose 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. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes apart.

Mechanism of Action: Rocklatan® is comprised of 2 components: netarsudil and latanoprost. Each of these 2 components decrease elevated IOP. Elevated IOP represents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and glaucomatous visual field loss. Rocklatan® is believed to reduce IOP by increasing the outflow of aqueous humor.

Warnings and Precautions:

- Pigmentation: Rocklatan® contains latanoprost which has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue, and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered. After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients.
- Eyelash Changes: Rocklatan® contains latanoprost which may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.
- Intraocular Inflammation: Rocklatan® contains latanoprost which should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because it may exacerbate inflammation.
- Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost. Rocklatan® should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.
- Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. Rocklatan® should be used with caution in patients with a

history of herpetic keratitis. Rocklatan® should be avoided in cases of active herpes simplex keratitis because it may exacerbate inflammation.

- Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.
- Use with Contact Lenses: Contact lenses should be removed prior to the administration of Rocklatan® and may be reinserted 15 minutes after administration.

Contraindication(s): None.

Adverse Reactions: The most common adverse reaction experienced during clinical studies was conjunctival hyperemia (59%). Other common adverse reactions were instillation site pain (20%), corneal verticillata (15%), and conjunctival hemorrhage (11%).

Use in Specific Populations:

- Pregnancy: There are no adequate and well-controlled studies of Rocklatan® ophthalmic solution or its pharmacologically active ingredients (netarsudil and latanoprost) in pregnant women to inform any drug associated risk. However, systemic exposure to netarsudil from ocular administration is low. Reproduction studies of latanoprost showed embryofetal lethality in rabbits. No embryofetal lethality was observed at a dose approximately 15 times higher than the recommended human ophthalmic dose (RHOD). Intravenous (IV) administration of netarsudil to pregnant rats and rabbits during organogenesis did not produce adverse embryofetal effects at clinically relevant systemic exposures. Rocklatan® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Lactation: There are no data on the presence of netarsudil or latanoprost in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to netarsudil following topical ocular administration is low, and it is not known whether measurable levels of netarsudil would be present in maternal milk following topical ocular administration.
- Pediatric Use: The safety and effectiveness of Rocklatan® in pediatric patients have not been established.
- Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly patients and younger patients using Rocklatan®.

Efficacy: 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 Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution) into the Tier-1 category of the Glaucoma Medications Product Based Prior Authorization (PBPA) due to 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-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		
acetazolamide (Diamox® 500mg caps; 125mg, 250mg tabs)+		dorzolamide/timolol (Cosopt® PF 2%/0.5%)
brinzolamide (Azopt® 1%)		methazolamide (Neptazane® 25mg, 50mg tabs)+

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
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

Utilization Details of Glaucoma Medications: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
LATANOPROST SOL 0.005%	1,958	488	$28,427.53	$0.49	$14.52
TRAVATAN Z DRO 0.004%	765	210	$195,791.60	$6.97	$255.94
TIMOLOL MAL SOL 0.5%	623	244	$7,443.88	$0.29	$11.95
COMBIGAN SOL 0.2%/0.5%	441	108	$102,258.26	$6.28	$231.88
ACETAZOLAMID TAB 250MG	374	110	$33,121.76	$2.85	$88.56
DORZOL/TIMOL SOL 22.3/6.8MG/ML	356	123	$7,460.01	$0.42	$20.96
BRIMONIDINE SOL 0.2%	283	109	$4,175.98	$0.39	$14.76
ACETAZOLAMID CAP 500MG ER	230	87	$14,644.27	$2.02	$63.67
SIMBRINZA SUS 1%/0.2%	202	59	$33,766.85	$4.54	$167.16
DORZOLAMIDE SOL 2%	192	54	$4,273.15	$0.55	$22.26
ALPHAGAN P SOL 0.1%	145	48	$36,351.55	$6.04	$250.70
AZOPT SUS 1%	98	31	$26,128.32	$5.77	$266.62
TIMOLOL GEL SOL 0.5%	93	40	$11,843.67	$3.52	$127.35
ACETAZOLAMID TAB 125MG	73	23	$5,128.86	$2.46	$70.26
TIMOLOL MAL SOL 0.25%	57	33	$664.67	$0.32	$11.66

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
RHOPRESSA SOL 0.02%	27	10	$6,328.21	$7.40	$234.38
LEVOBUNOLOL SOL 0.5% OP	11	2	$184.68	$0.62	$16.79
TIMOLOL MAL SOL 0.5%	9	3	$172.07	$0.66	$19.12
TIER-1 SUBTOTAL	**5,937**	**1,782**	**$518,165.32**	**$2.47**	**$87.28**
TIER-2 PRODUCTS					
LUMIGAN SOL 0.01%	136	22	$38,753.58	$8.43	$284.95
BIMATOPROST SOL 0.03%	11	2	$1,367.48	$3.60	$124.32
PILOCARPINE SOL 4%	6	1	$489.82	$1.30	$81.64
PILOCARPINE SOL 1%	3	3	$239.64	$1.02	$79.88
PILOCARPINE SOL 2%	2	1	$158.43	$1.41	$79.22
TIER-2 SUBTOTAL	**158**	**29**	**$41,008.95**	**$7.19**	**$259.55**
SPECIAL PA PRODUCTS					
BRIMONIDINE SOL 0.15%	29	6	$6,320.77	$6.70	$217.96
METHAZOLAMID TAB 50MG	24	4	$9,912.10	$13.73	$413.00
DORZOL/TIMOL SOL 2%/0.5% PF	15	4	$2,059.67	$4.58	$137.31
ALPHAGAN P SOL 0.15%	12	1	$3,853.40	$10.70	$321.12
VYZULTA SOL 0.024%	10	2	$3,433.85	$11.72	$343.39
COSOPT PF SOL 2%/0.5%	6	2	$1,009.52	$5.61	$168.25
METHAZOLAMID TAB 25MG	5	1	$160.71	$1.07	$32.14
TIMOLOL GEL SOL 0.25%	1	1	$115.22	$3.03	$115.22
SPECIAL PA SUBTOTAL	**102**	**21**	**$26,865.24**	**$8.67**	**$263.38**
TOTAL	**6,197**	**1,293***	**$586,039.51**	**$2.68**	**$94.57**

*Total number of unduplicated members.
PF = preservative free; PA = prior authorization
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 12/2019. Last accessed 12/17/2019.
[2] Aerie Pharmaceuticals. Aerie Pharmaceuticals Announces U.S. FDA Approval of Rocklatan™ (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% for the Reduction of Intraocular Pressure in Patients with Open-Angle Glaucoma or Ocular Hypertension. *Business Wire*. Available online at: https://investors.aeriepharma.com/news-releases/news-release-details/aerie-pharmaceuticals-announces-us-fda-approval-rocklatantm. Issued 03/12/2019. Last accessed 12/17/2019.
[3]Allergan Plc. U.S. FDA Accepts Allergan's New Drug Application for Bimatoprost Sustained-Release in Patients with Open-Angle Glaucoma or Ocular Hypertension. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/us-fda-accepts-allergans-new-drug-application-for-bimatoprost-sustained-release-in-patients-with-open-angle-glaucoma-or-ocular-hypertension-300886238.html. Issued 07/17/2019. Last accessed 12/17/2019.
[4] Emerald Bioscience, Inc. Glauconix Presents Data Validating Impact of Emerald Bioscience's Prodrug on the Ocular Endocannabinoid System in Glaucoma. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/15/1929750/0/en/Glauconix-Presents-Data-Validating-Impact-of-Emerald-Bioscience-s-Prodrug-on-the-Ocular-Endocannabinoid-System-in-Glaucoma.html. Issued 10/15/2019. Last accessed 12/17/2019.
[5] Emerald Bioscience, Inc. Emerald Bioscience's NB1111 Demonstrates Superiority in Lowering Intraocular Pressure Compared to Global Standard of Care Glaucoma Treatment in Preclinical Model. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/15/1929766/0/en/Emerald-Bioscience-s-NB1111-Demonstrates-Superiority-in-Lowering-Intraocular-Pressure-Compared-to-Global-Standard-of-Care-Glaucoma-Treatment-in-Preclinical-Model.html. Issued 10/15/2019. Last accessed 12/17/2019.
[6] Ocular Therapeutix. OTX-TIC (travoprost implant). Available online at: https://www.ocutx.com/research/otx-tic/. Last accessed 12/17/2019.
[7] Ocular Therapeutix. OTX-TP (travoprost insert). Available online at: https://www.ocutx.com/research/otx-tp/. Last accessed 12/17/2019.
[8] Ocular Therapeutix. Ocular Therapeutix Announces Topline Results of Phase 3 Clinical Trial of OTX-TP for the Treatment of Glaucoma. *Business Wire*. Available online at: https://www.drugs.com/clinical_trials/ocular-therapeutix-announces-topline-results-phase-3-clinical-trial-otx-tp-glaucoma-18153.html. Issued 05/20/2019. Last accessed 12/17/2019.
[9] 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 12/17/2019.
[10] 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 12/17/2019.

Appendix F

Fiscal Year 2019 Annual Review of Firdapse® (Amifampridine) and 30-Day Notice to Prior Authorize Ruzurgi® (Amifampridine)

Oklahoma Health Care Authority
January 2020

Introduction[1,2,3]

Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disorder which principally affects the proximal parts of the extremities. LEMS is caused by autoantibodies to presynaptic P/Q-type voltage-gated calcium channels (VGCCs) that effectively decrease acetylcholine (ACh) release, inhibit neuromuscular transmission, and disrupt the ability of nerve cells to send signals to muscle cells. This results in the clinical manifestation of the disease such as muscle fatigue, diminished physical functionality, and impairments in activities of daily living (ADL). LEMS can be associated with certain neoplastic conditions, the most common being small cell lung cancer (SCLC), where its onset precedes or coincides with the diagnosis of cancer. LEMS can occur at any age. The prevalence of LEMS specifically in pediatric patients is not known, but LEMS is estimated to affect 1 in 100,000 people in the United States.

Current Prior Authorization Criteria

Firdapse® (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. A quantity limit of 240 tablets per 30 days will apply; and
6. Initial approvals will be for 6 months. Continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with the requested medication.

Utilization of Firdapse® (Amifampridine): Fiscal Year 2019

There was no SoonerCare utilization of Firdapse® (amifampridine) or Ruzurgi® (amifampridine) during fiscal year 2019.

Prior Authorization of Firdapse® (Amifampridine)

There were no prior authorization requests submitted for Firdapse® (amifampridine) or Ruzurgi® (amifampridine) during fiscal year 2019.

Market News and Updates[4,5,6]

Anticipated Patent Expiration(s):

- Firdapse® (amifampridine): November 2025
- Ruzurgi® (amifampridine): May 2026

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

- **May 2019:** The FDA approved Ruzurgi® (amifampridine) tablets for the treatment of LEMS in patients 6 years to younger than 17 years of age. The decision for approval is based on evidence derived from adequate and well-controlled studies, pharmacokinetic data in adult patients with LEMS, pharmacokinetic modeling and simulation to identify the dosing regimen in pediatric patients, and safety data from pediatric patients 6 years to younger than 17 years of age. In particular, the effectiveness of Ruzurgi® was established in a randomized, double-blind, placebo-controlled withdrawal study of 32 adult patients comparing patients continuing on Ruzurgi® to patients who were switched to placebo. The results indicated greater perceived weakening in the patients switched to placebo, while patients that continued on Ruzurgi® experienced less impairment. Firdapse®, the previous treatment approval for LEMS is only for adults, which makes Ruzurgi® the first FDA approved treatment for pediatric patients with LEMS.

News:

- **June 2019:** Catalyst Pharmaceuticals, Inc. announced it filed a suit against the FDA and several related parties challenging the approval of Ruzurgi® for the treatment of LEMS in pediatric patients. The complaint alleges that the defendants' approval of Ruzurgi® violated multiple provisions of FDA regulations regarding labeling, resulting in misbranding in violation of the Federal Food, Drug, and Cosmetic Act (FDCA). Additional allegations include that the FDA violated Catalyst's statutory rights to Orphan Drug exclusivity and to New Chemical Entity exclusivity under the FDCA. The suit seeks an order vacating the FDA's approval of Ruzurgi®.

Ruzurgi® (Amifampridine) Product Summary[7]

Indication(s): Ruzurgi® (amifampridine) is a potassium channel blocker indicated for the treatment of LEMS in patients 6 years to younger than 17 years of age.

Dosing:

- Ruzurgi® is supplied as 10mg oral tablets.
- The recommended dosing in patients 6 years to younger than 17 years of age weighing ≥45kg is as follows:
    - The initial recommended dosage is 15mg to 30mg daily, in divided doses.

    - Doses can be increased daily in 5mg to 10mg increments, divided in up to 5 doses daily.
    - The maximum recommended single dose is 30mg, and the maximum recommended daily dose is 100mg.
- The recommended dosing in patients 6 years to younger than 17 years of age weighing <45kg is as follows:
    - The initial recommended dose is 7.5mg to 15mg daily, in divided doses.
    - Doses can be increased daily in 2.5mg to 5mg increments, divided in up to 5 doses daily.
    - The maximum recommended single dose is 15mg, and the maximum recommended daily dose is 50mg.
- When patients require a dosage in <5mg increments, have difficulty swallowing, or require feeding tubes, a 1mg/mL suspension can be prepared. *Refer to the Ruzurgi® prescribing information for further details regarding preparation of an oral suspension.*
- 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.

Mechanism of Action: The mechanism by which amifampridine exerts its therapeutic effect in LEMS patients has not been fully elucidated. Amifampridine is a broad spectrum potassium channel blocker.

Contraindication(s): Ruzurgi® is contraindicated in patients with a history of seizures or hypersensitivity to amifampridine or other aminopyridines.

Adverse Reactions: The most common adverse reactions (2 to 10%) experienced during clinical studies with Ruzurgi® were paresthesia/dysesthesia, abdominal pain, dyspepsia, dizziness, and nausea.

Use in Specific Populations:
- Pregnancy: There are no data on the developmental risks associated with the use of Ruzurgi® in pregnant women. Animal studies to assess the potential adverse effects of amifampridine on embryo fetal development have not been conducted.
- Lactation: There are no data on the presence of amifampridine or the 3-N-acetyl-amifampridine metabolite in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of Ruzurgi® have been established in patients 6 years to younger than 17 years of age. The safety and effectiveness of Ruzurgi® in pediatric patients younger than 6 years of age have not been established.
- Renal Impairment: Ruzurgi® should be initiated at the lowest recommended starting dose in patients with renal impairment and patients should be closely monitored for adverse reactions. No dosage recommendations for Ruzurgi® can be made for patients with end-stage renal disease [ESRD; creatinine clearance (CrCl) <15mL/min] or in patients requiring dialysis.
- Hepatic Impairment: Ruzurgi® is extensively metabolized by NAT2, and hepatic impairment may cause an increase in exposure. In patients with any degree of hepatic

impairment, Ruzurgi® should be initiated at the lowest recommended starting dose and patients should be closely monitored for adverse reactions.

- NAT2 Poor Metabolizers: Patients who are known NAT2 poor metabolizers should be initiated at the lowest recommended starting dose of Ruzurgi® and monitored closely for adverse reactions. Dose modifications of Ruzurgi® should be considered as needed based on clinical effect and tolerability.

Efficacy: The effectiveness of Ruzurgi® for the treatment of LEMS was established in a randomized, double-blind, placebo-controlled withdrawal study of 32 adult patients in which patients were taking Ruzurgi® for at least 3 months prior to entering the study. The study compared patients continuing on Ruzurgi® to patients who were switched to placebo. The primary measure of efficacy was the categorization of the degree of change in the Triple Timed Up and Go test (3TUG) upon withdrawal of active medication, when compared with the time-matched average of the 3TUG assessments at baseline. The 3TUG is a measure of the time it takes a patient to rise from a chair, walk 3 meters, and return to the chair for 3 consecutive laps without pause. The secondary efficacy endpoint was the self-assessment scale for LEMS-related weakness (W-SAS). The patients that continued on Ruzurgi® experienced less impairment and perceived weakening than those receiving placebo ($P<0.0001$).

Product Comparison:

Medication	Ruzurgi®	Firdapse®
Generic Name	amifampridine	amifampridine **phosphate**
Date of FDA Approval	May 6, 2019	November 28, 2018
Manufacturer	Jacobus Pharmaceutical Company, Inc.	Catalyst Pharmaceuticals, Inc.
Indication	LEMS in **pediatric patients** 6 years to younger than 17 years of age	LEMS in **adults**
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 in a refrigerator 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 Tablet	$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 Firdapse® (amifampridine) prior authorization criteria with the following 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. 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] Lennon VA, Kryzer TJ, Griesmann GE, et al. Calcium-channel antibodies in the Lambert-Eaton syndrome and other paraneoplastic syndromes. *N Engl J Med* 1995; 332(22):1467-1474.

[2] Sanders DB. Lambert-Eaton myasthenic syndrome: diagnosis and treatment. *Ann NY Acad Sci* 2003; 998:500-508.

[3] Titulaer MJ, Lang B, Verschuuren JJ. Lambert-Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies. *Lancet Neurol* 2011; 10(12):1098-1107.

[4] 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 11/2019. Last accessed 12/16/2019.

[5] FDA. FDA approves first treatment for children with Lambert-Eaton myasthenic syndrome, a rare autoimmune disorder. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-children-lambert-eaton-myasthenic-syndrome-rare-autoimmune-disorder. Last revised 05/06/2019. Last accessed 12/16/2019.

[6] Catalyst Pharmaceuticals, Inc. Catalyst Pharmaceuticals Files Federal Lawsuit Against U.S. Food and Drug Administration. *Globe Newswire*. Available online at: https://ir.catalystpharma.com/news-releases/news-release-details/catalyst-pharmaceuticals-files-federal-lawsuit-against-us-food. Issued 06/12/2019. Last accessed 12/16/2019.

[7] 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.

Appendix G

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

Oklahoma Health Care Authority
January 2020

Introduction[1,2,3]

Cushing's syndrome, also called hypercortisolism, is an endocrine disorder that results from long-term exposure to excess levels of cortisol. The most common cause of Cushing's syndrome is the long-term, high-dose use of corticosteroids. Other patients develop endogenous Cushing's syndrome because their bodies produce too much cortisol. Pituitary adenomas can secrete increased amounts of adrenocorticotropic hormone (ACTH), which can cause an overproduction of cortisol. Ectopic ACTH syndrome and tumors of the adrenal gland can cause similar problems with cortisol imbalance. Endogenous Cushing's syndrome is rare and is estimated to occur in approximately 40 to 70 people out of every 1 million. Common symptoms of Cushing's disease include upper body obesity, severe fatigue and muscle weakness, high blood pressure, elevated blood sugar, easy bruising, and bluish-red stretch marks on the skin. The prognosis for patients with Cushing's syndrome depends on the cause of the disease. Most cases of Cushing's syndrome can be cured and many patients with Cushing's syndrome show significant improvement with treatment. Treatment of Cushing's syndrome is also dependent on the cause of excess cortisol. If the cause is long-term use of a medication being used to treat another disorder, the physician may reduce the dose of the medication until symptoms are under control. If the cause is a pituitary adenoma, surgery or radiotherapy may be used. Surgery, radiotherapy, chemotherapy, immunotherapy, or a combination of these may be used to treat ectopic ACTH syndrome. According to the Endocrine Society Clinical Practice Guideline for the Treatment of Cushing's syndrome, surgical resection of the causal lesion(s) is generally the first-line approach. The choice of second-line treatments, including medication, bilateral adrenalectomy, and radiation therapy (for corticotrope tumors), must be individualized for each patient.

Market News and Updates[4]

Anticipated Patent Expiration(s):

- Korlym® (mifepristone): August 2038

Korlym® (Mifepristone) Product Summary[5]

Indication(s): 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.

- Limitations of Use: Korlym® (mifepristone) should not be used for the treatment of T2DM unrelated to endogenous Cushing's syndrome.

Dosing:

- Korlym® is supplied as 300mg oral tablets.
- 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 per day.
- In patients with renal impairment, the dose should not exceed 600mg once daily.
- In patients with mild-to-moderate hepatic impairment, the dose should not exceed 600mg once daily. Mifepristone should not be used in patients with severe hepatic impairment.
- The recommended dose should not exceed 900mg once daily with concomitant administration with strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, nefazodone).

Mechanism of Action: 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.

Contraindication(s):

- Pregnancy
- Patients 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, due to an increased risk of adverse events
- Patients receiving systemic corticosteroids for lifesaving purposes (e.g., immunosuppression after organ transplantation) because mifepristone antagonizes the effects of glucocorticoids
- Women with a history of unexplained vaginal bleeding or with endometrial hyperplasia with atypia or endometrial carcinoma
- Patients with known hypersensitivity to mifepristone or to any of the product components

Warnings and Precautions:

- <u>Adrenal Insufficiency:</u> Patients receiving mifepristone may experience adrenal insufficiency. Serum cortisol levels do not provide an accurate assessment of hypoadrenalism in patients receiving mifepristone because serum cortisol levels remain elevated and may even increase during treatment with mifepristone. It is recommended to closely monitor patients for signs and symptoms of adrenal insufficiency, including weakness, nausea, increased fatigue, hypotension, and hypoglycemia. If adrenal insufficiency is suspected, treatment with mifepristone should be discontinued immediately and corticosteroids administered without delay. High doses of supplemental corticosteroids may be needed to overcome the glucocorticoid receptor blockage produced by mifepristone. Factors considered in deciding the duration of corticosteroid treatment should include the long half-life of mifepristone. Treatment

with mifepristone at a lower dose can be resumed after resolution of adrenal insufficiency. Patients should also be evaluated for precipitating causes of hypoadrenalism (e.g., infection, trauma).

- Hypokalemia: In a study of patients with Cushing's syndrome, hypokalemia was observed in 44% of subjects during treatment with mifepristone. Hypokalemia should be corrected prior to initiating mifepristone. During administration of mifepristone, serum potassium should be measured 1 to 2 weeks after starting or increasing the dose of mifepristone and periodically thereafter. Hypokalemia can occur at any time during mifepristone treatment. Mifepristone-induced hypokalemia should be treated with intravenous (IV) or oral potassium supplementation based on event severity. If hypokalemia persists in spite of potassium supplementation, it is recommended to consider adding mineralcorticoid antagonists.
- Vaginal Bleeding and Endometrial Changes: Being an antagonist of the progesterone receptor, mifepristone promotes unopposed endometrial proliferation that may result in endometrium thickening, cystic dilatation of endometrial glands, and vaginal bleeding. Mifepristone should be used with caution in women who have hemorrhagic disorders or who are receiving concurrent anticoagulant therapy. Women who experience vaginal bleeding during mifepristone treatment should be referred to a gynecologist for further evaluation.
- QT Interval Prolongation: Mifepristone prolongs the QTc interval in a dose-related manner. There is little or no experience with high exposure, concomitant dosing with other QT-prolonging drugs, or potassium channel variants resulting in a long QT interval. To minimize risk, it is recommended to use the lowest effective dose.
- Exacerbation/Deterioration of Conditions Treated with Corticosteroids: Use of mifepristone in patients who receive corticosteroids for other conditions (e.g., autoimmune disorders) may lead to exacerbation or deterioration of such conditions, as mifepristone antagonizes the desired effects of glucocorticoids in these clinical settings. For medical conditions in which chronic corticosteroid therapy is lifesaving (e.g., immunosuppression in organ transplantation), mifepristone is contraindicated.
- Use of Strong CYP3A Inhibitors: Mifepristone should be used with caution in patients taking ketoconazole and other strong inhibitors of CYP3A, such as itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, atazanavir, amprenavir, fosamprenavir, clarithromycin, conivaptan, lopinavir/ritonavir, posaconazole, saquinavir, telithromycin, or voriconazole, as these could increase the concentration of mifepristone in the blood. The benefit of concomitant use of these agents should be carefully weighed against the potential risks. Mifepristone should be used in combination with strong CYP3A inhibitors only when necessary, and in such cases the dose should be limited to 900mg per day.
- *Pneumocystis jiroveci* Infection: Patients with endogenous Cushing's syndrome are at risk of opportunistic infections such as *Pneumocystis jiroveci* pneumonia during mifepristone treatment. Patients may present with respiratory distress shortly after initiation of mifepristone. Appropriate diagnostic tests should be undertaken and treatment should be considered for *Pneumocystis jiroveci* infection.
- Potential Effects of Hypercortisolemia: Mifepristone does not reduce serum cortisol levels. Elevated cortisol levels may activate mineralocorticoid receptors which are also

expressed in cardiac tissues. In patients with underlying heart conditions, including heart failure and coronary vascular disease, caution should be used.

Adverse Reactions: The most common (≥20%) adverse reactions experienced with mifepristone in clinical studies in Cushing's syndrome included nausea, fatigue, headache, decreased blood potassium, arthralgia, vomiting, peripheral edema, hypertension, dizziness, decreased appetite, and endometrial hypertrophy.

Use in Specific Populations:

- Pregnancy: Mifepristone is contraindicated in pregnancy because the use of mifepristone results in pregnancy loss. There are no data that assess the risk of birth defects in women exposed to mifepristone during pregnancy. Available data limited to exposure following a single dose of mifepristone during pregnancy showed a higher rate of major birth defects compared to the general population comparator. The patient should be apprised of the potential hazard to a fetus.
- Lactation: Mifepristone is present in human milk; however, there are no data on the amount of mifepristone in human milk, the effects on the breastfed infant, or the effects on milk production during long-term use of mifepristone. To minimize exposure to a breastfed infant, women who discontinue or interrupt mifepristone treatment may consider pumping and discarding milk during treatment and for 18 to 21 days after the last dose, before breastfeeding.
- Females and Males of Reproductive Potential: Due to its anti-progestational activity, mifepristone causes pregnancy loss. Pregnancy testing should be performed before the initiation of treatment with mifepristone or if treatment is interrupted for more than 14 days in females of reproductive potential. It is recommended to use non-hormonal contraception for the duration of treatment and for 1 month after stopping treatment. Mifepristone interferes with the effectiveness of hormonal contraceptives.
- Pediatric Use: The safety and effectiveness of mifepristone in pediatric patients have not been established.
- Geriatric Use: Clinical studies of mifepristone did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.
- Renal Impairment: The maximum dose should not exceed 600mg per day in renally-impaired patients.
- Hepatic Impairment: In patients with mild-to-moderate hepatic impairment, the maximum dose should not exceed 600mg per day. The pharmacokinetics of mifepristone in patients with severe hepatic impairment has not been studied, and mifepristone should not be used in these patients.

Efficacy: An uncontrolled, open-label, 24-week, multicenter clinical study was conducted to evaluate the safety and efficacy of mifepristone in the treatment of endogenous Cushing's syndrome. The study enrolled 50 patients with clinical and biochemical evidence of hypercortisolemia despite prior surgical treatment and radiotherapy. The reasons for medical treatment were failed surgery, recurrence of disease, and poor medical candidate(s) for surgery. Of the 50 patients, 43 patients (86%) had Cushing's disease, 4 patients (8%) had

ectopic corticotropin (ACTH) secretion, and 3 patients (6%) had adrenal carcinoma. Baseline characteristics included: mean age of 45 years (range 26 to 71), mean body mass index (BMI) of 36kg/m^2 (range 24 to 66), mean weight 100kg (range 61 to 199), and mean waist circumference was 119cm (range 89 to 178). Baseline urinary free cortisol level was 365µg per 24 hour. Patients belonged to 1 of 2 cohorts: a "diabetes" cohort (29 patients, 26 with T2DM and 3 with glucose intolerance), and a "hypertension" cohort (21 patients). Efficacy was evaluated separately in the 2 cohorts. Mifepristone treatment was started in all patients at a dose of 300mg once daily. The study protocol allowed an increase in dose to 600mg after 2 weeks, and then by additional 300mg increments every 4 weeks to a maximum of 900mg per day for patients <60kg, or 1,200mg per day for patients >60kg, based on clinical tolerance and clinical response.

- Results in the Diabetes Cohort: Patients in the diabetes cohort underwent standard oral glucose tolerance tests at baseline and periodically during the clinical study. Anti-diabetic medications were allowed; however, they had to be kept stable during the trial and patients had to be on stable anti-diabetes regimens prior to enrollment. The primary efficacy analysis was an analysis of responders. A responder was defined as a patient who had a ≥25% reduction from baseline in glucose area under the curve (AUC). The primary efficacy analysis was conducted in the modified intent-to-treat population (N=25) defined as all patients who received a minimum of 30 days of mifepristone. A total of 15 of 25 patients (60%) were treatment responders [95% confidence interval (CI): 39%, 78%]. Mean hemoglobin A1c (HbA1c) was 7.4% in the 24 patients with HbA1c values at baseline and week 24. For these 24 patients, the mean reduction in HbA1c was 1.1% (95% CI; -1.6, -0.7) from baseline to the end of the trial. A total of 14 of 24 patients had above normal HbA1c levels at baseline, ranging between 6.7% and 10.4%; all of these patients had reductions in HbA1c by the end of the study (range -0.4 to -4.4%) and 8 of 14 patients (57%) had normalized HbA1c levels at trial end. Anti-diabetes medications were reduced in 7 of the 15 T2DM patients taking anti-diabetes medications and remained constant in the others.
- Results in the Hypertension Cohort: There were no changes in the mean systolic and diastolic blood pressures at the end of the trial relative to baseline in the modified intent-to-treat population (N=21).
- Signs and Symptoms of Cushing's Syndrome in Both Cohorts: Individual patients showed varying degrees of improvement in Cushing's syndrome manifestations such as cushingoid appearance, acne, hirsutism, striae, psychiatric symptoms, and excess total body weight. Due to the variability in clinical presentation and variability of response in this open label trial, it is uncertain whether these changes could be ascribed to the effects of mifepristone.

Cost: The Wholesale Acquisition Cost (WAC) of Korlym® (mifepristone) is $499 per 300mg tablet resulting in a cost of $59,880 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 diagnosis of 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 had a 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] National Institute of Health: National Institute of Neurological Disorders and Stroke. Cushing's Syndrome Information Page. Available online at: https://www.ninds.nih.gov/Disorders/All-Disorders/Cushings-Syndrome-Information-Page. Last revised 03/27/2019. Last accessed 12/16/2019.

[2] Nieman LK. Medical Therapy of Hypercortisolism (Cushing's Syndrome). *UpToDate*. Available online at: https://www.uptodate.com/contents/medical-therapy-of-hypercortisolism-cushings-syndrome?search=korlym&source=search_result&selectedTitle=3~48&usage_type=default&display_rank=2#H6330490. Last revised 10/30/2018. Last accessed 12/16/2019.

[3] Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2015; 100(8):2807–2831. doi:10.1210/jc.2015-1818

[4] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 12/2019. Last accessed 12/16/2019.

[5] Korlym® (mifepristone) Prescribing Information. Corcept Therapeutics Incorporated. 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 12/04/2019.

Appendix H

Industry News and Updates

Oklahoma Health Care Authority
January 2020

Introduction

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

News and Updates[1,2]

News:

- **Biosimilars:** The U.S. Food and Drug Administration (FDA) announced efforts to make the development of biosimilars and interchangeable insulin products more efficient. The draft guidance allows biosimilar drug manufacturers to skip certain clinical trials if they meet certain conditions, including that the proposed product is close enough to a product that has already been approved. The guidance also clarifies the information and data that would be needed to gain FDA approval. Acting FDA Commissioner Dr. Brett Giroir stated that increasing competition among insulin products could potentially lower costs for payers and patients, while increasing access and product choice.
- **N-nitrosodimethylamine (NDMA):** The FDA is investigating whether metformin is contaminated with NDMA. The move is part of the FDA's push to investigate a range of drugs for the presence of NDMA. The FDA stated that the investigation follows other countries' findings of low levels of NDMA in metformin medications, and that it would recommend recalls as appropriate. Zantac® (ranitidine) was recalled in 2019 for the presence of NDMA and the FDA later added that levels of contamination of ranitidine "are similar to the levels you would expect to be exposed to if you ate common food like grilled or smoked meats." The European Union (EU) watchdog the European Medicines Agency (EMA) is also asking companies to test metformin medications in the EU for NDMA after reports in Singapore of finding the NDMA impurity in some metformin products. The EMA described the risk so far as very low, urging patients to continue taking their medication because the danger of not adequately controlling diabetes was far higher.

---

[1] Garcia L. FDA seeks to clear hurdles for biosimilar insulin in attempt to cut costs for diabetes patients. *San Antonia Express News*. Available online at: https://www.expressnews.com/business/health-care/article/FDA-seeks-to-clear-hurdles-for-biosimilar-insulin-14869167.php. Issued 11/29/2019. Last accessed 12/02/2019.

[2] O'Donnell C, Burger L. FDA Probes Diabetes Drug Metformin for Carcinogen NDMA. *Pharmacy Learning Network*. Available online at: https://www.managedhealthcareconnect.com/content/fda-probes-diabetes-drug-metformin-carcinogen-ndma?hmpid=YmV0aGFueS1ob2xkZXJyZWFkQG91aHNjLmVkdQ. Issued 12/06/2019. Last accessed 12/10/2019.

Appendix I

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 Statement

For Immediate Release: December 5th, 2019

Statement from Janet Woodcock, M.D., director of FDA's Center for Drug Evaluation and Research, on impurities found in diabetes drugs outside the U.S.

The FDA has been investigating the presence of genotoxic impurities, called nitrosamines, in some types of drugs. Over the past year and a half, several drug products including angiotensin II receptor blockers (ARBs) and ranitidine, commonly known as Zantac, have been found to contain small amounts of nitrosamines such as N-Nitrosodimethylamine (NDMA). During this time, there has been an ongoing investigation into the presence of nitrosamines in other drug products. This effort is focused on ensuring the drugs used by Americans continue to meet strict quality standards.

The FDA is aware that some metformin in other countries were reported to have low levels of NDMA. Based on the information available, the levels of NDMA seen outside the U.S. are within the range that is naturally occurring in some foods and in water. While the FDA is aware that some regulatory agencies outside the U.S. may be recalling some metformin drugs, there are no metformin recalls affecting the U.S. market at this time. The FDA is investigating whether metformin in the U.S. market contains NDMA, and whether it is above the acceptable daily intake limit of 96 nanograms. The agency will also work with companies to test samples of metformin sold in the U.S. and will recommend recalls as appropriate if high levels of NDMA are found. If as part of the investigation, metformin drugs are recalled, the FDA will provide timely updates to patients and health care professionals.

The FDA recommends prescribers continue to use metformin when clinically appropriate, as the FDA investigation is still ongoing, and there are no alternative medications that treat this condition in the same way. NDMA is a common contaminant found in water and foods including cured and grilled meats, dairy products and vegetables. Everyone is exposed to some level of NDMA. The FDA and the international scientific community do not expect it to cause harm when ingested at low levels. Genotoxic substances such as NDMA may increase the risk of cancer if people are exposed to them above acceptable levels and over long periods of time, but a person taking a drug that contains NDMA at-or-below the acceptable daily intake limit every day for 70 years is not expected to have an increased risk of cancer.

FDA NEWS RELEASE

For Immediate Release: December 12th, 2019

FDA authorizes first test to aid in newborn screening for Duchenne Muscular Dystrophy

The FDA authorized marketing of the first test to aid in newborn screening for Duchenne Muscular Dystrophy (DMD), a rare genetic disorder that causes progressive muscle deterioration and weakness.

The GSP Neonatal Creatine Kinase-MM kit authorized is intended to aid in screening newborns for DMD. Newborn screening is a series of tests to help health care professionals identify serious diseases and conditions shortly after birth. As part of this screening, a newborn screening card is used to collect a small amount of blood from a prick of an infant's heel, sometimes called a heel stick. The collected, dried blood samples are used to test for a variety of diseases and conditions.

While the number and type of diseases and conditions tested on each state's newborn screening panel can vary, there has been a national effort to harmonize screening practices across state newborn screening programs in the U.S. As a result of the collaboration between the federal Advisory Committee on Heritable Disorders in Newborns and Children and the American College of Medical Genetics, as well as governmental, non-governmental, advocacy, and private partners, the Recommended Uniform Screening Panel (RUSP) was developed and adopted. The RUSP is a list of core and secondary conditions for screening newborns that the U.S. Department of Health and Human Services recommends for states to screen as part of their state universal newborn screening programs.

The authorization of the GSP Neonatal Creatine Kinase-MM kit enables laboratories to add this test to their newborn screening panel if they choose to do so, but this authorization does not signal a recommendation for DMD to be added to the RUSP as a condition for which newborn screening is recommended. The GSP

Neonatal Creatine Kinase-MM kit is not intended for DMD diagnosis or for screening of other forms of muscular dystrophies.
The GSP Neonatal Creatine Kinase-MM kit works by measuring the concentration of a type of protein called CK-MM, which is part of a group of proteins called creatine kinase. Creatine kinase is found in muscle tissue and CK-MM enters the blood stream in increased amounts when there is muscle damage. This test measures the levels of CK-MM from the dried blood samples collected from the prick of a newborn's heel 24 to 48 hours after birth. Elevated levels of CK-MM detected by the kit may indicate presence of DMD. Results showing elevated CK-MM must be confirmed using other testing methods, such as muscle biopsies, genetic, and other laboratory tests.
DMD, while rare, is the most common type of muscular dystrophy. It is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. The first symptoms are usually seen between 3 and 5 years of age and worsen over time. The disease often occurs in people without a known family history of the condition and primarily affects boys, but in rare cases it can affect girls. DMD occurs in about 1 in 3,600 male live-born infants worldwide. People with DMD progressively lose the ability to perform activities independently and often require use of a wheelchair by their early teens. As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary. The U.S. Centers for Disease Control and Prevention (CDC) advises that early diagnosis could lead to more personalized care for each person living with muscular dystrophy and may give each of them a better chance to reach his or her full potential. The CDC has also found that there was an average of 2.5 years between when a parent or caregiver noticed the first signs and symptoms of DMD, and when a diagnosis of DMD was made.
The FDA reviewed the GSP Neonatal Creatine Kinase-MM kit through the de novo premarket review pathway, a regulatory pathway for low-to-moderate risk devices of a new type. During this process, the FDA evaluated data from a clinical study of 3,041 newborns whose dried blood samples were tested for protein levels that are associated with DMD. In the study, the kit was able to accurately identify the 4 screened newborns that had DMD-causing genetic mutations. The device manufacturer also tested 30 samples from newborns with clinically confirmed cases of DMD, all of which were correctly identified by the test.
Along with this authorization, the FDA is establishing criteria, called special controls, that must be met for tests of this type, including certain design verification, design validation, and labeling requirements. When met, these special controls, along with general controls, provide a reasonable assurance of safety and effectiveness for tests of this type. This action also creates a new regulatory classification, which means that subsequent devices of the same type, with the same intended use, may go through the FDA's 510(k) pathway, whereby devices can obtain clearance by demonstrating substantial equivalence to a predicate device.
Risks associated with use of the kit include false negative test results. As part of the clinical study, the device manufacturer performed genetic testing, an accepted method of diagnosing DMD, on 173 patient samples including a subset of patients identified as negative by the GSP Neonatal Creatine Kinase-MM kit. Genetic testing on the negative samples did not identify any DMD-causing genetic variants, confirming the negative screening results by the GSP Neonatal Creatine Kinase-MM kit.
The FDA granted marketing authorization of the GSP Neonatal Creatine Kinase-MM kit to PerkinElmer.

FDA NEWS RELEASE

For Immediate Release: December 12th, 2019

FDA grants accelerated approval to first targeted treatment for rare DMD mutation

The FDA granted accelerated approval to Vyondys 53 (golodirsen) injection to treat DMD patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. It is estimated that about 8% of patients with DMD have this mutation.
Vyondys 53 was approved under the accelerated approval pathway, which provides for the approval of drugs that treat serious or life-threatening diseases and generally offer a meaningful advantage over existing treatments. Approval under this pathway can be based on adequate and well-controlled studies showing the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit to patients (i.e., how patients feel or function or whether they survive). This pathway provides earlier patient access to promising new drugs while the company conducts clinical trials to verify the predicted clinical benefit.
The accelerated approval of Vyondys 53 is based on the surrogate endpoint of an increase in dystrophin production in the skeletal muscle observed in some patients treated with the drug. The FDA has concluded that the data submitted by the applicant demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in patients with DMD who have a confirmed mutation of the dystrophin gene

amenable to exon 53 skipping. A clinical benefit of the drug, including improved motor function, has not been established. In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease, and the lack of available therapy.
Vyondys 53 was evaluated in a 2-part clinical study. The first part included 12 DMD patients, with 8 patients receiving Vyondys 53 and 4 receiving placebo. The second part of the study was open-label, and included the 12 patients enrolled in part 1 of the study, and 13 additional patients who had not previously received the treatment. In the study, dystrophin levels increased, on average, from 0.10% of normal at baseline to 1.02% of normal after 48 weeks of treatment with the drug or longer.
As part of the accelerated approval process, the FDA is requiring the company to conduct a clinical trial to confirm the drug's clinical benefit. The ongoing study is designed to assess whether Vyondys 53 improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. If the trial fails to verify clinical benefit, the FDA may initiate proceedings to withdraw approval of the drug.
The most common side effects reported by participants receiving Vyondys 53 in clinical studies were headache, fever, cough, vomiting, abdominal pain, nasopharyngitis, and nausea. Hypersensitivity reactions, including rash, fever, itching, hives, skin irritation, and skin peeling, have occurred in patients who were treated with Vyondys 53.
Additionally, renal toxicity was observed in animals who received golodirsen. Although renal toxicity was not observed in the clinical studies with Vyondys 53, renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Renal function should be monitored in patients taking Vyondys 53.
The FDA granted this application Fast Track and Priority Review designations. Vyondys 53 also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. In addition, the manufacturer received a rare pediatric disease priority review voucher. The FDA's rare pediatric disease priority review voucher program is intended to encourage development of new drugs and biologics to prevent and treat rare diseases in children.
Approval of Vyondys 53 was granted to Sarepta Therapeutics of Cambridge, Massachusetts.

FDA NEWS RELEASE

For Immediate Release: December 13th, 2019

FDA approves use of drug to reduce risk of cardiovascular (CV) events in certain adult patient groups

The FDA approved the use of Vascepa (icosapent ethyl) as an adjunctive therapy to reduce the risk of CV events among adults with elevated triglyceride levels of ≥150mg/dL. Patients must also have either established CV disease or diabetes and 2 or more additional risk factors for CV disease. Patients are advised to continue physical activity and maintain a healthy diet.
Vascepa is the first FDA approved drug to reduce CV risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy. Statins are drugs used to treat elevated cholesterol levels and reduce the risk of CV events.
High levels of triglycerides can play a role in the hardening of arteries or thickening of the artery wall, which can increase the risk of a heart attack or stroke; however, the mechanisms of action that contribute to reduced CV events among patients taking Vascepa are not completely understood.
Vascepa's efficacy and safety were established in a study with 8,179 patients who were either 45 years and older with a documented history of coronary artery, cerebrovascular, carotid artery, and peripheral artery disease, or 50 years and older with diabetes and additional risk factors for CV disease. Patients who received Vascepa were significantly less likely to experience a CV event, such as a stroke or heart attack. Vascepa's active ingredient is the omega-3 fatty acid, eicosapentaenoic acid, derived from fish oil. Vascepa is taken orally.
In clinical trials, Vascepa was associated with an increased risk of atrial fibrillation or atrial flutter requiring hospitalization. The incidence of atrial fibrillation was greater among patients with a history of atrial fibrillation or atrial flutter. Vascepa was also associated with an increased risk of bleeding events. The incidence of bleeding was higher among patients who were also taking other medications that increase the risk of bleeding, such as aspirin, clopidogrel, or warfarin at the same time.
Patients with allergies to fish or shellfish should be advised about the potential for allergic reactions. They should discontinue treatment and seek medical attention if any allergic reactions occur.

The most common side effects reported in the clinical trials for Vascepa were musculoskeletal pain, peripheral edema, atrial fibrillation, and arthralgia.
Vascepa was initially approved in 2012 for adults with severe triglyceride levels. This supplemental application received priority review. The FDA grants priority review to applications for drugs that, if approved, would improve the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions.
The approval of Vascepa was granted to Amarin Pharma, Inc.

Current Drug Shortages Index (as of December 17th, 2019):

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***
Buspirone HCl Tablets	***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***
Isocarboxazid Tablets	***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***
Leuprolide Acetate (Lupron Depot; Lupron Depot Ped) 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***
Methotrexate Sodium 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***
Nelarabine (Arranon) 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***
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***
Thioridazine Hydrochloride Tablets	***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***