OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
January 13, 2021

No live meeting scheduled for January.
January 2021 will be a packet only meeting.

Oklahoma Health Care Authority (OHCA)
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: Michyla Adams, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – January 13, 2021

NOTE: No live January meeting. January 2021 is a packet only meeting.

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

Approval of DUR Board Meeting Minutes – Appendix A

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

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

Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe) – Appendix D

Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Durysta™ (Bimatoprost Implant) – Appendix E

Annual Review of Antiviral Medications – Appendix F

Annual Review of Korlym® (Mifepristone) – Appendix G

Annual Review of Turalio® (Pexidartinib) – Appendix H

Annual Review of Inrebic® (Fedratinib) and Elzonris® (Tagraxofusp-erzs) – Appendix I

30-Day Notice to Prior Authorize Imcivree™ (Setmelanotide) – Appendix J

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

Future Business

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Packet – January 13, 2021
No live January meeting. January 2021 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. Approval of DUR Board Meeting Minutes – See Appendix A

A. December 9, 2020 DUR Minutes
B. December 9, 2020 DUR Recommendations Memorandum
C. Correspondence

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

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

A. Pharmacy Helpdesk Activity for December 2020
B. Medication Coverage Activity for December 2020
C. SoonerCare Opioid Initiative Update

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

3. Annual Review of Gonadotropin Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) – See Appendix C

A. Current Prior Authorization Criteria
B. Utilization of GnRH Medications
C. Prior Authorization of GnRH Medications
D. Market News and Updates
E. Fensolvi® (Leuprolide Acetate) Product Summary
F. Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of GnRH Medications

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

4. Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe) – See Appendix D

A. Current Prior Authorization Criteria
B. Utilization of Antihyperlipidemics
C. Prior Authorization of Antihyperlipidemics
D. Market News and Updates
E. Nexletol® (Bempedoic Acid) Product Summary
F. Nexlizet™ (Bempedoic Acid/Ezetimibe) Product Summary
G. Cost Comparison: LDL-C Lowering Therapies as an Adjunct to Statins
H. College of Pharmacy Recommendations
I. Utilization Details of Antihyperlipidemics

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

5. Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Durysta™ (Bimatoprost Implant) – 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. Durysta™ (Bimatoprost Implant) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Glaucoma Medications

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

6. Annual Review of Antiviral Medications – See Appendix F

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

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

7. Annual Review of Korlym® (Mifepristone) – See Appendix G

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

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

8. Annual Review of Turalio® (Pexidartinib) – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Turalio® (Pexidartinib)
D. Prior Authorization of Turalio® (Pexidartinib)
E. College of Pharmacy Recommendations

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

9. Annual Review of Inrebic® (Fedratinib) and Elzonris® (Tagraxofusp-erzs) – See Appendix I

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)
D. Prior Authorization of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)
E. College of Pharmacy Recommendations

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

10. 30-Day Notice to Prior Authorize Imcivree™ (Setmelanotide) – See Appendix J

A. Introduction
B. Imcivree™ (Setmelanotide) Product Summary
C. College of Pharmacy Recommendations

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

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

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

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

A. Anticonvulsants
B. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
C. Anti-Migraine Medications
D. Osteoporosis Medications
E. Leukemia Medications

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

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

Appendix A

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

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

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

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

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

PRESENT FOR PUBLIC COMMENT:	
N/A	

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

ACTION: NONE REQUIRED

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

3A: NOVEMBER 4, 2020 DUR MINUTES

3B: NOVEMBER 4, 2020 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Muchmore

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

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

4A: INTRODUCTION

4B: SOONERCARE MAINTENANCE DRUG LIST

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

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

5A: PHARMACY HELPDESK ACTIVITY FOR NOVEMBER 2020

5B: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2020

5C: PEDIATRIC ANTIPSYCHOTIC MONITORING PROGRAM UPDATE

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

ACTION: NONE REQUIRED

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

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

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

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

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

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

7B: PRODUCT SUMMARIES

7C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

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

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

8A: LENVIMA® (LENVATINIB) PRODUCT SUMMARY

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Borders

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

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF SKIN CANCER MEDICATIONS**

9A: INTRODUCTION

9B: CURRENT PRIOR AUTHORIZATION CRITERIA

9C: UTILIZATION OF SKIN CANCER MEDICATIONS

9D: PRIOR AUTHORIZATION OF SKIN CANCER MEDICATIONS

9E: MARKET NEWS AND UPDATES

9F: COLLEGE OF PHARMACY RECOMMENDATIONS

9G: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED; WILL BE AN ACTION ITEM IN FEBRUARY 2021

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

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

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

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

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

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

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

AGENDA ITEM NO. 16: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Ha
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
NO LIVE MEETING SCHEDULED FOR JANUARY 2021. JANUARY 2021 WILL BE A PACKET ONLY MEETING.
17A: ANTIVIRAL MEDICATIONS
17B: GLAUCOMA MEDICATIONS
17C: GONADOTROPIN-RELEASING HORMONE (GNRH) MEDICATIONS
17D: HYPERLIPIDEMIA MEDICATIONS
*Future product and class reviews subject to change.
Materials included in agenda packet; Non-presentation/Questions only
ACTION: NONE REQUIRED

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

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

Memorandum

Date: December 11, 2020

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

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

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

Recommendation 1: Maintenance Drug List

NO ACTION REQUIRED.

Recommendation 2: Pediatric Antipsychotic Monitoring Program Update

NO ACTION REQUIRED.

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

VOTE ITEM AT FEBRUARY MEETING

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

VOTE ITEM AT FEBRUARY MEETING

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Recommendation 5: Prior Authorization of Lenvima® (Lenvatinib)

VOTE ITEM AT FEBRUARY MEETING

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

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

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

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

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

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

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

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

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

Recommendation 6: Annual Review of Skin Cancer Medications

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Antidepressants

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Thrombocytopenia Medications

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 14: Future Business

No live DUR meeting is scheduled for January 2021. January 2021 will be a packet only meeting.

NO ACTION REQUIRED.

I respectfully address the DUR board regarding the review of the NMOSD category. Unfortunately, I am unable to attend in person and kindly request my testimony be read.
I am the Director of the OMRF Multiple Sclerosis Center of Excellence in Oklahoma City where we manage longitudinally over 3000 patients with demyelinating diseases to include MS, Neuromyelitis Optica (NMOSD), and MOGAD.
My work in demyelinating diseases for over 20 years, both in the clinical and research areas, has grated me lengthy exposure to NMOSD. This is a very rare disease characterized by acute events of neurological dysfunction, primarily affecting the optic nerves and spinal cord, often leading to blindness and paralysis. Different from other related disease, such as Multiple Sclerosis, NMOSD tends to have minimal recovery, leaving individuals with this condition with profound disability. Up to three fourths of the patients with NMOSD attacks have residual permanent neurological deficits.
Given the clinical features of the disease as previously described, the only effective approach is one of reduction of the risk of relapses, as there is no available cure.
The neuro-immunology community has been extremely excited about the results of recent clinical trials on novel approaches to manage NMOSD, resulting in the approval of the FDA of three different treatment options, namely eculizumab (Soliris), satralizumab (Enspryng), and Uplizna (inebilizumab). Despite this rag-to-riches story in the ability to treat NMOSD, as clinicians we continue to encounter particular characteristics of the patient's health, co-morbidities, physical abilities (visual and dexterity) and NMO evolution, that make the selection of one agent over the other being highly advisable. Consequently, I humbly but strongly request the DUR board not impose a step therapy restriction to the use of any of these treatments, allowing experienced clinicians, along with the participation of their patients, select the treatment that is best suited for them.

OMRF
DISCOVERIES THAT MAKE A DIFFERENCE

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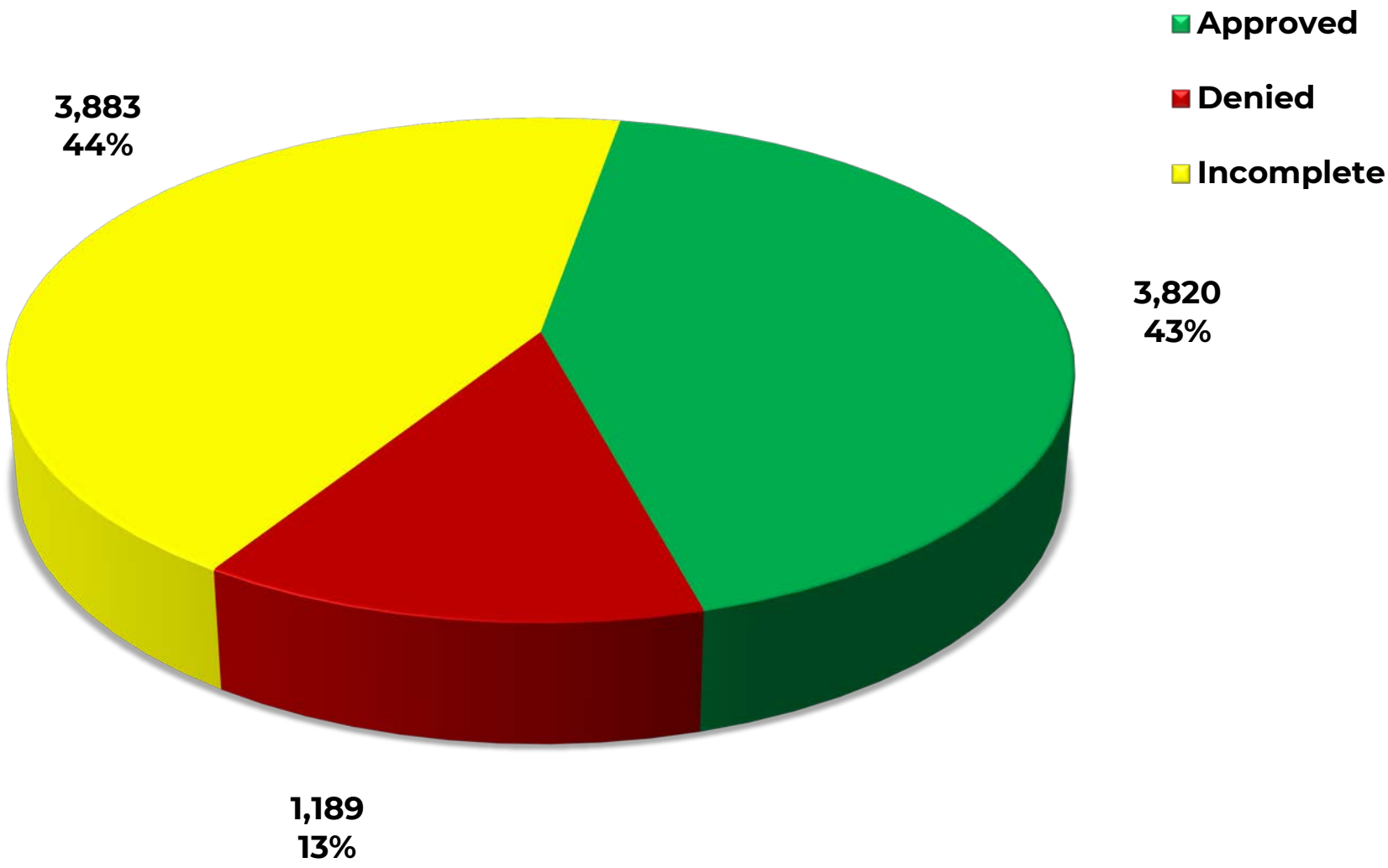
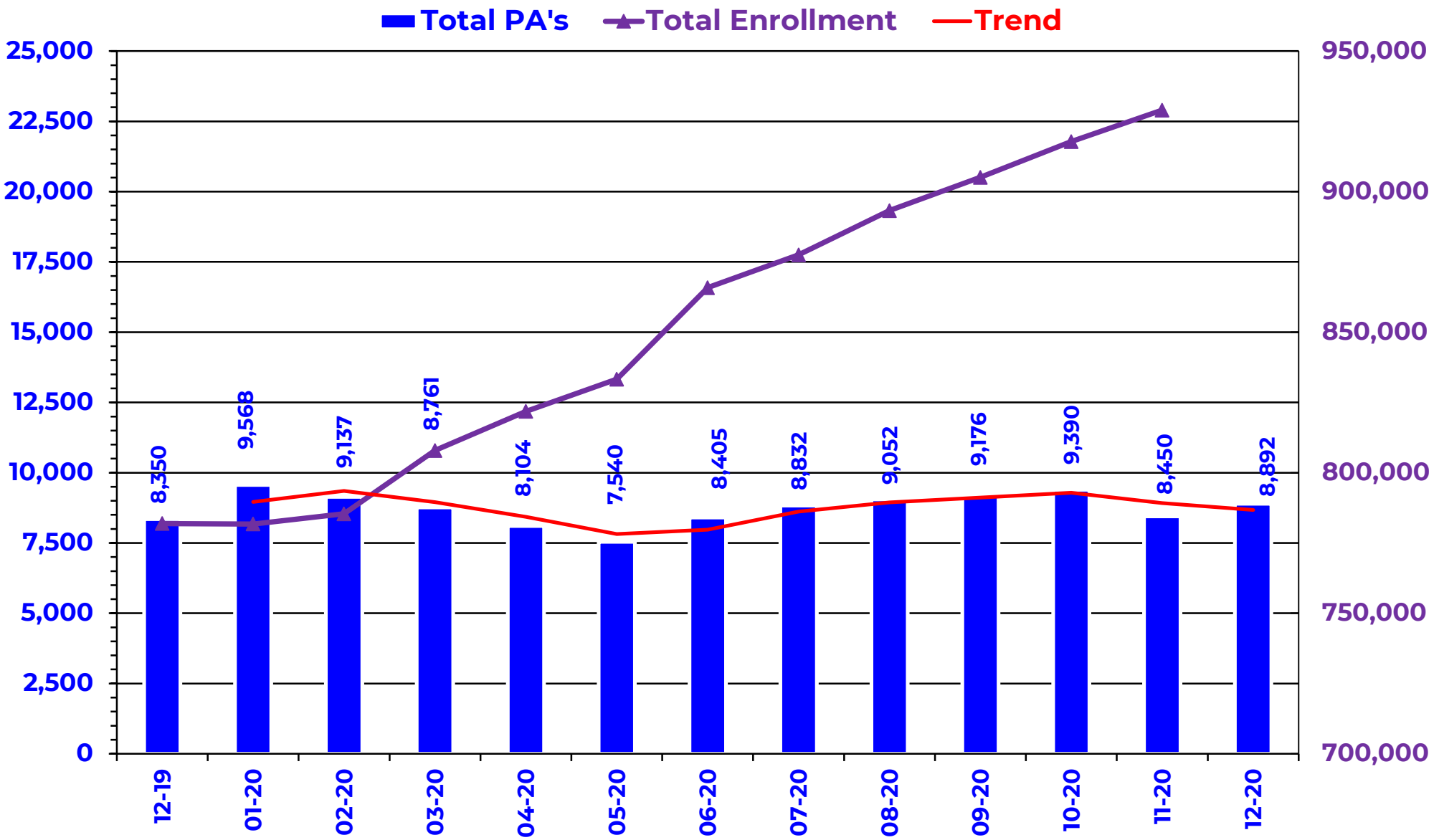
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: DECEMBER 2020



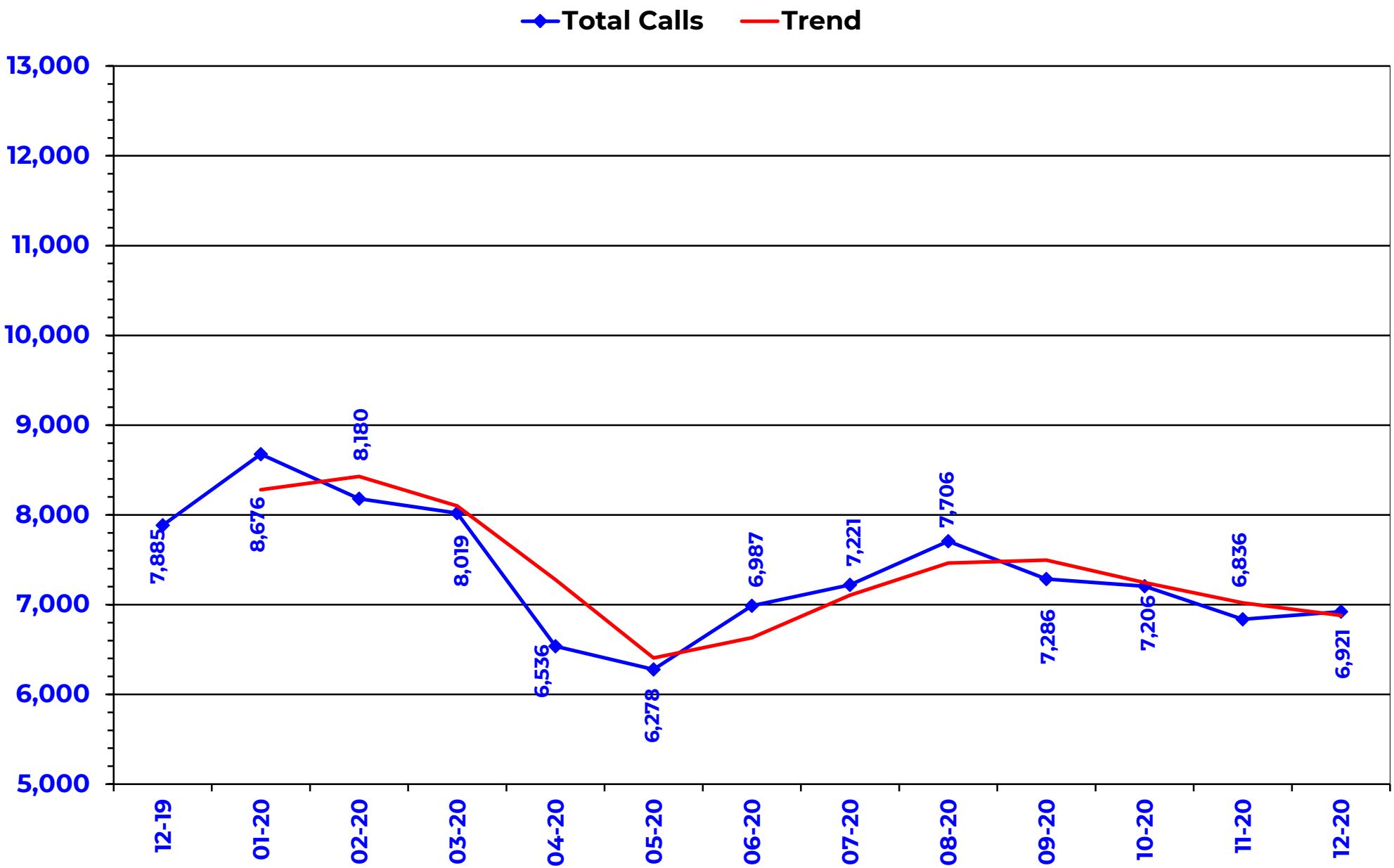
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: DECEMBER 2019 – DECEMBER 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: DECEMBER 2019 – DECEMBER 2020



Prior Authorization Activity

12/1/2020 Through 12/31/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	79	16	9	54	341
Analgesic - NonNarcotic	28	1	9	18	358
Analgesic, Narcotic	311	101	34	176	150
Angiotensin Receptor Antagonist	11	3	2	6	358
Antiasthma	41	12	13	16	264
Antibiotic	40	18	3	19	92
Anticonvulsant	183	70	9	104	310
Antidepressant	204	36	23	145	330
Antidiabetic	409	112	70	227	348
Antihemophilic Factor	13	10	0	3	281
Antihistamine	23	9	3	11	358
Antimigraine	265	33	98	134	197
Antineoplastic	99	58	8	33	163
Antiparasitic	11	4	2	5	15
Antiulcers	65	10	10	45	133
Anxiolytic	25	1	3	21	359
Atypical Antipsychotics	335	150	42	143	343
Biologics	175	94	20	61	266
Bladder Control	54	4	22	28	360
Blood Thinners	358	187	19	152	323
Botox	61	39	15	7	297
Buprenorphine Medications	62	9	2	51	60
Calcium Channel Blockers	14	3	0	11	220
Cardiovascular	55	23	4	28	317
Chronic Obstructive Pulmonary Disease	198	36	62	100	343
Constipation/Diarrhea Medications	159	38	43	78	218
Contraceptive	49	24	5	20	323
Dermatological	379	96	103	180	172
Diabetic Supplies	668	349	62	257	213
Endocrine & Metabolic Drugs	74	40	6	28	135
Fish Oils	17	1	4	12	359
Gastrointestinal Agents	135	28	35	72	201
Glaucoma	20	2	3	15	104
Growth Hormones	104	58	13	33	132
Hematopoietic Agents	12	5	2	5	320
Hepatitis C	111	70	15	26	9
Insomnia	44	3	12	29	175
Insulin	144	45	9	90	331
Miscellaneous Antibiotics	10	0	1	9	0
Muscle Relaxant	53	2	15	36	80
Nasal Allergy	58	9	15	34	145
Neurological Agents	78	23	20	35	225
Neuromuscular Agents	10	1	4	5	358
NSAIDs	37	1	5	31	360
Ocular Allergy	26	2	6	18	84
Ophthalmic Anti-infectives	17	9	0	8	26
Osteoporosis	23	9	5	9	341
Other*	299	64	50	185	246
Otic Antibiotic	15	1	4	10	26
Pediculicide	28	1	5	22	55
Respiratory Agents	18	10	0	8	146

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Statins	28	2	14	12	218
Stimulant	832	378	80	374	352
Synagis	93	38	11	44	104
Testosterone	81	17	15	49	312
Thyroid	11	1	3	7	355
Topical Antifungal	27	3	2	22	115
Topical Corticosteroids	74	1	41	32	55
Vitamin	58	11	30	17	159
Pharmacotherapy	129	123	0	6	303
Emergency PAs	0	0	0	0	
Total	7,103	2,531	1,128	3,444	

Overrides					
Brand	30	16	1	13	272
Compound	14	12	0	2	19
Cumulative Early Refill	3	2	0	1	5
Diabetic Supplies	7	6	0	1	48
Dosage Change	372	347	4	21	14
High Dose	2	2	0	0	358
Ingredient Duplication	4	2	0	2	7
Lost/Broken Rx	111	101	0	10	15
MAT Override	236	156	5	75	67
NDC vs Age	286	172	17	97	258
NDC vs Sex	5	5	0	0	81
Nursing Home Issue	28	26	0	2	16
Opioid MME Limit	80	39	4	37	130
Opioid Quantity	30	28	1	1	148
Other*	64	58	0	6	8
Quantity vs. Days Supply	461	277	27	157	220
STBS/STBSM	19	11	2	6	95
Third Brand Request	26	20	0	6	13
Overrides Total	**1,789**	**1,289**	**61**	**439**	
Total Regular PAs + Overrides	**8,892**	**3,820**	**1,189**	**3,883**	

Denial Reasons	
Unable to verify required trials.	3,219
Does not meet established criteria.	1,222
Lack required information to process request.	625
Other PA Activity	
Duplicate Requests	769
Letters	15,153
No Process	7
Changes to existing PAs	627
Helpdesk Initiated Prior Authorizations	643
PAs Missing Information	14

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

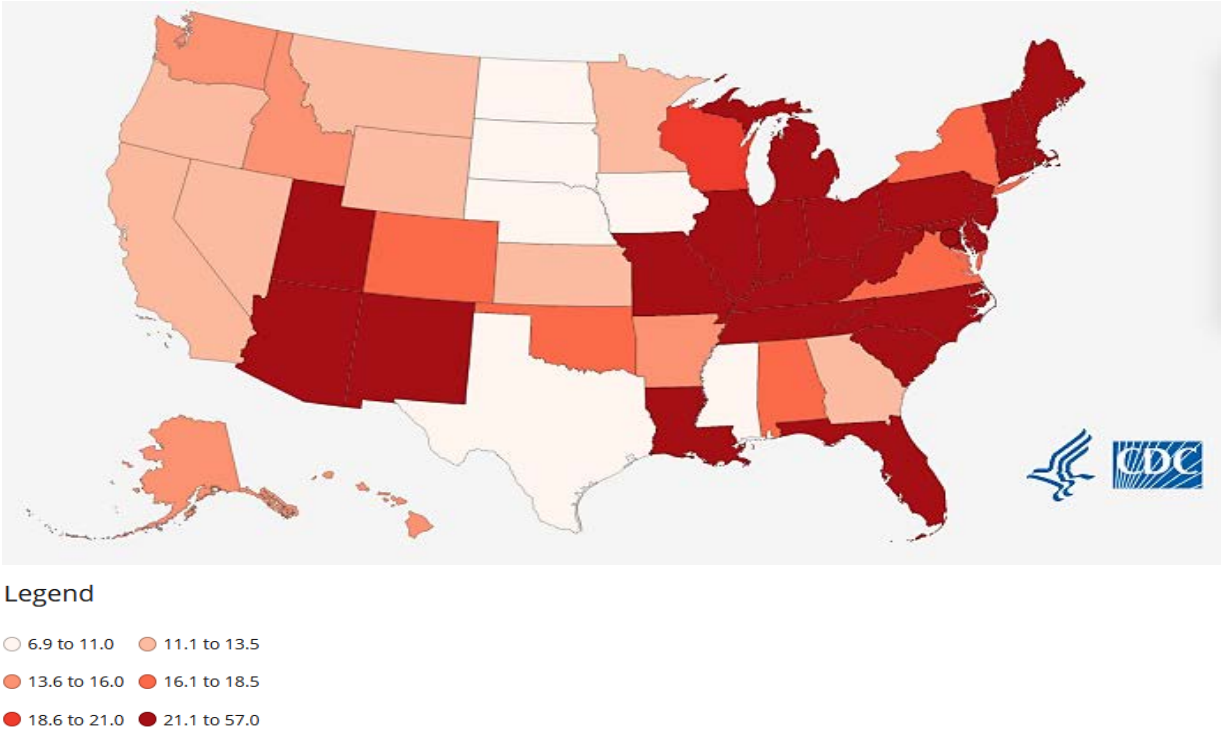
SoonerCare Opioid Initiative Update

Oklahoma Health Care Authority
January 2021

Introduction[1]

In the United States there were 67,367 drug overdose deaths in 2018, 716 of which were in Oklahoma. Oklahoma saw an 8.46% decrease in the drug overdose death rate from 2017 to 2018. This decrease exceeds the 6.5% decrease from 2016 to 2017 and is in contrast to the 13.2% increase seen in 2016. Additionally, Oklahoma saw a statistically significant change in drug overdose death rates involving prescription opioids from 2017 to 2018. The number of deaths from prescription opioids decreased 35.8% from 2017 to 2018 in Oklahoma. The following map from the Centers for Disease Control and Prevention (CDC) highlights the age-adjusted rates of drug overdose deaths by state for 2018.

CDC Number and Age-Adjusted Rates (per 100,000) of Drug Overdose Deaths by State (2018)



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 opioid to opioid 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. Starting in 2020, patients with sickle cell disease were also excluded from the safety 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 limitations 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 MME across all opioid prescriptions; the 90 MME threshold identifies potentially high-risk patients who may benefit from closer monitoring and care coordination
    - Due to the increased burden on the health care system as a result of the COVID-19 pandemic, it was recommended that plans waive requirements for pharmacist consultation with the prescriber to confirm intent of opioid use in order to lessen the administrative burden on prescribers and pharmacists (all other existing opioid point-of-sale safety edits should be continued during the pandemic)
  - 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 placed a 7-day supply 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 is a nationally recognized organization that develops measures to promote appropriate medication use and reporting of performance information related to medications. They have developed the PQA Opioid Measure Set which includes 7 measures to provide important tools to address the opioid epidemic. Included are measures to evaluate the use of opioids at high dosages (≥90 MME/day, previously ≥120 MME/day), from multiple prescribers and pharmacies, and concurrent opioid use with benzodiazepines. Additionally, initial opioid prescribing measures are included to evaluate new prescriptions at high dosages (≥50 MME/day), for long duration (>7 cumulative day supply), or for long-acting or extended-release opioids. Patients with a cancer diagnosis, sickle cell disease, or those receiving hospice care are excluded.

The following table contains MMEs based on strength and quantities for commonly prescribed opioid medications. Daily MMEs in red font exceed the CDC and CMS 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
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/hour	10	30	60
fentanyl patch 37.5mcg/hour	10	30	90
fentanyl patch 50mcg/hour	10	30	120

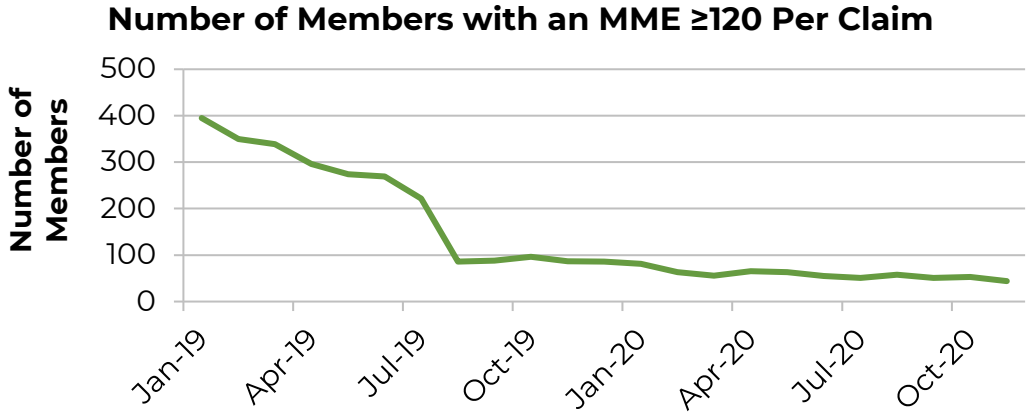
Drug/Strength	Quantity	Day Supply	Daily MME
fentanyl patch 75mcg/hour	10	30	180
Hysingla® ER (hydrocodone ER) 100mg	30	30	100
Hysingla® ER (hydrocodone ER) 120mg	30	30	120
Oxycontin® (oxycodone ER) 30mg	60	30	90

MME = morphine milligram equivalent; APAP = acetaminophen; IR = immediate-release; ER = extended-release

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 MME to coincide with the OBNDD clinical alert on the Oklahoma PMP database. Then in July 2019, the DUR Board voted to lower the MME limit to 90 MME 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 per day require prior authorization with patient-specific, clinically significant reasoning for use of >90 cumulative MME per day. Members with an oncology, hemophilia, or sickle cell diagnosis are excluded from the MME edit. Additionally, medications for MAT of opioid use disorder (OUD) are excluded from the MME edit.

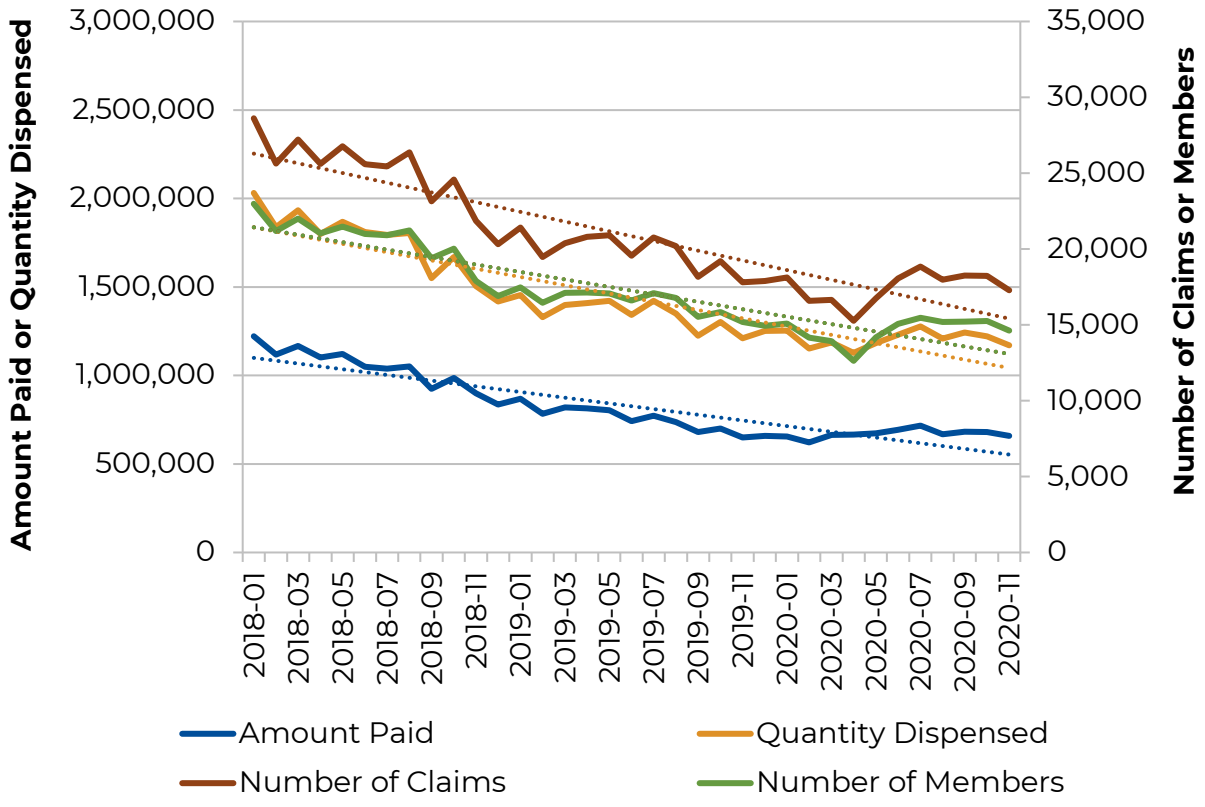
The following chart shows SoonerCare data for the number of unduplicated utilizing members with an MME ≥120 per claim for Schedule II medications from January 1, 2019 to November 30, 2020. The data excludes members with an oncology, hemophilia, or sickle cell diagnosis in medical claims history over the specified time period. Combination products containing buprenorphine and naloxone used for MAT of OUD were excluded from the analysis as well. Since the start of the MME edit implementation in January 2019, the number of members with an MME ≥120 per claim has decreased by 88.9%. Further, since the final implementation of the MME limit in October 2019, the number of members with ≥120 MME per claim has decreased by 54.2%.



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 Oklahoma Health Care Authority (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 supply 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 2018 to November 2020



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Appendix C

Fiscal Year 2020 Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Fensolvi® (Leuprolide Acetate) and Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix)

Oklahoma Health Care Authority
January 2021

Current Prior Authorization Criteria

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

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

Supprelin® LA (Histrelin) and Synarel® (Nafarelin) Approval Criteria:

1. An FDA approved indication of central precocious puberty confirmed by submitting the following:
    a. Documentation of onset of symptoms prior to 8 years of age in females and 9 years of age in males; and
    b. Documentation that bone age is advanced 1 year beyond the chronological age; and
    c. Lab assessment:
        i. Documentation of abnormal basal gonadotropin levels; or
        ii. Documentation of pubertal response to a gonadotropin-releasing hormone analog stimulation test; and
2. Approvals may be granted with documentation of failed trials of lower tiered products or an FDA approved indication not covered by a lower tiered product.

Lupaneta Pack™ [Leuprolide Acetate for Depot Suspension (3.75mg for Intramuscular Injection) and Norethindrone Acetate Tablet (5mg for Oral Administration)] Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the individual components must be provided.

Orilissa® (Elagolix) Approval Criteria:

1. An FDA approved indication of moderate-to-severe pain associated with endometriosis; and
2. Member must be 18 years of age or older; and
3. Member must not have known osteoporosis; and
4. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
5. Female members of reproductive potential must be willing to use effective non-hormonal contraception during treatment with Orilissa® and for at least 1 week after discontinuing treatment; and
6. Member must not have severe hepatic impairment (Child-Pugh C); and
7. Member must not be taking a strong organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and
8. Orilissa® must be prescribed by, or in consultation with, an obstetrician/gynecologist or a specialist with expertise in the treatment of endometriosis; and
9. A failed trial at least 1 month in duration with nonsteroidal anti-inflammatory drugs (NSAIDs) or a patient-specific, clinically significant reason why the member cannot use NSAIDs must be provided; and
10. A failed trial at least 3 months in duration of hormonal contraceptives or a patient-specific, clinically significant reason why the member cannot use hormonal contraceptives must be provided; and
11. Dosing and lifetime approval duration will be limited based on the following:
    a. Coexisting condition of moderate hepatic impairment (Child-Pugh B):
        i. 150mg once daily for a maximum of 6 months; or
    b. Normal liver function or mild hepatic impairment (Child-Pugh A):
        i. 150mg once daily for a maximum of 24 months; or
        ii. 200mg twice daily for a maximum of 6 months.

Utilization of GnRH Medications: Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	121	318	$1,580,898.26	$4,971.38	$73.22	1,676	21,590
2020	151	364	$1,884,575.73	$5,177.41	$80.65	3,847	23,368
% Change	**24.80%**	**14.50%**	**19.20%**	**4.10%**	**10.10%**	**129.50%**	**8.20%**
Change	**30**	**46**	**$303,677.47**	**$206.03**	**$7.43**	**2,171**	**1,778**

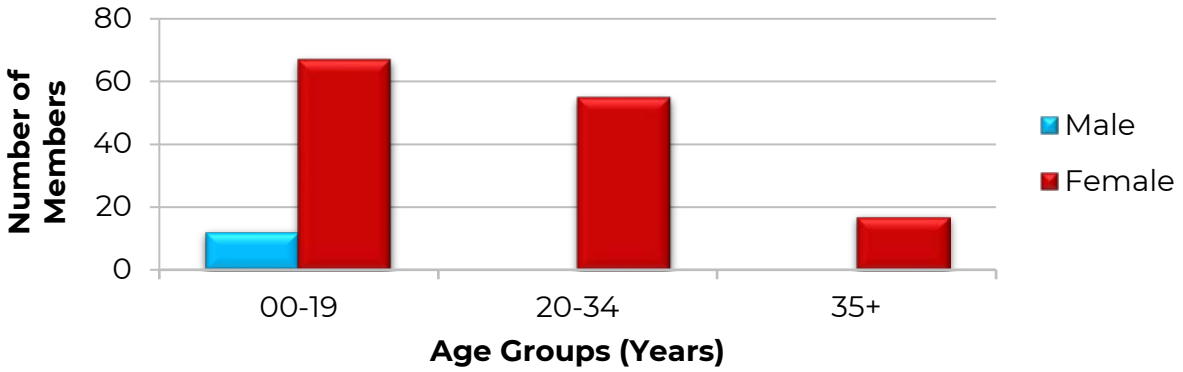
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Comparison of Fiscal Years: Medical Claims

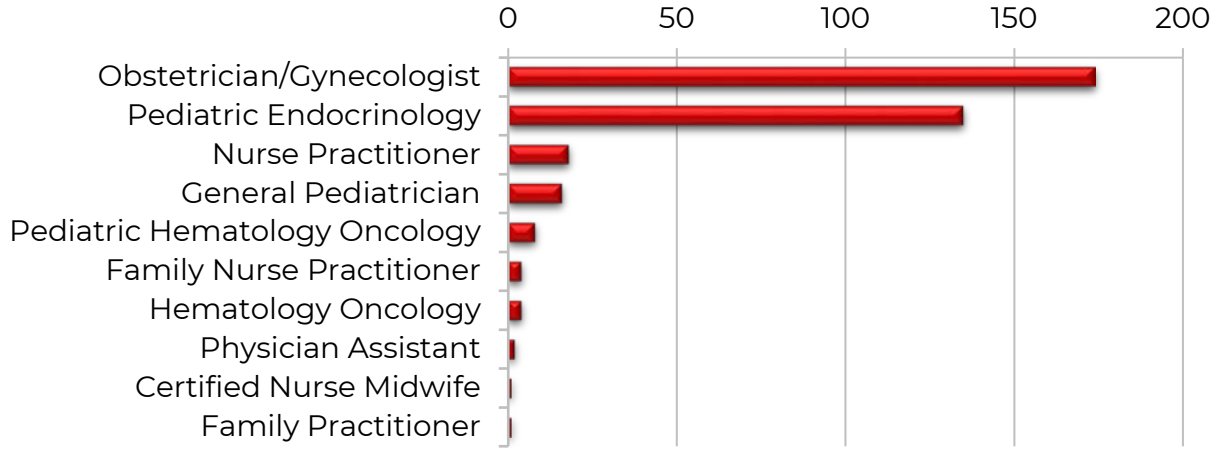
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	53	119	$135,656.91	$1,139.97	301
2020	91	182	$186,176.97	$1,022.95	433
% Change	**71.70%**	**52.94%**	**37.24%**	**-10.27%**	**43.85%**
Change	**38**	**63**	**$50,520.06**	**-$117.02**	**132**

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

Demographics of Members Utilizing GnRH Medications: Pharmacy Claims

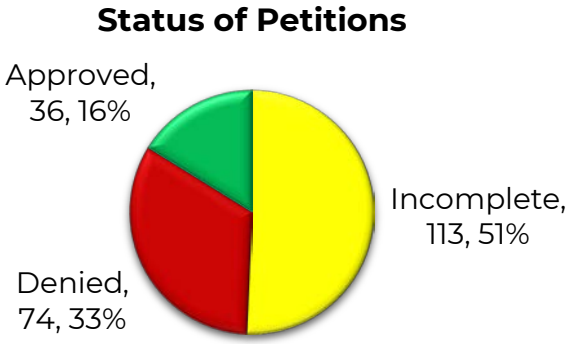


Top Prescriber Specialties of GnRH Medications by Number of Claims: Pharmacy Claims



Prior Authorization of GnRH Medications

There were 223 prior authorization requests submitted for GnRH medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



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

Anticipated Patent Expiration(s):

- Fensolvi® (leuprolide acetate): October 2023
- Oriahnn™ (elagolix/estradiol/norethindrone and elagolix): September 2024
- Supprelin® LA (histrelin): June 2026
- Triptodur® (triptorelin): June 2029
- Lupron Depot® (leuprolide): February 2031
- Orilissa® (elagolix): September 2036

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

- **May 2020:** The FDA approved Fensolvi® (leuprolide acetate) for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). Fensolvi® is an injectable polymeric matrix formulation of leuprolide which forms a solid drug delivery depot when administered subcutaneously (sub-Q) and is designed to release the medication at a controlled rate over a 6-month period. CPP is defined as the onset of puberty prior to 8 years of age in females or 9 years of age in males and occurs in approximately 1 in 5,000 to 10,000 children. CPP is much more common in females than in males. The primary goal of medical treatment for CPP is the preservation of height potential, as untreated CPP can result in the premature cessation of growth and short stature as an adult. However, many patients with slowly-progressive or non-progressive forms of CPP achieve an adult height within their target range without the use of medical therapy. When the decision to initiate treatment is made, the standard of care for treatment of CPP consists of GnRH analogs such as leuprolide, histrelin, nafarelin, and triptorelin.
- **May 2020:** The FDA approved Oriahnn™ (elagolix/estradiol/ norethindrone and elagolix) for the management of heavy menstrual bleeding associated with uterine leiomyomas, also known as fibroids, in premenopausal women. Oriahnn™ is a combination of elagolix (a GnRH receptor antagonist), estradiol (an estrogen), and norethindrone

(a progestin) and is available in an oral capsule formulation. Oriahnn™ is the first non-surgical, oral medication approved by the FDA for this indication. Uterine fibroids are benign neoplasms originating from uterine smooth muscle tissue and are the most common solid pelvic tumors in women. Many women with fibroids are asymptomatic and can be monitored without active treatment. However, approximately 20 to 50% of women with fibroids are symptomatic, with the most common symptoms being excessive menstrual bleeding and pelvic discomfort or pressure. Although hysterectomy is the most common surgical treatment for fibroids, accounting for 39% of hysterectomies performed in the United States, medical therapy is available as an alternative option for women who anticipate future childbearing or wish to retain their uteri. Options for medical therapy include oral contraceptives, nonsteroidal anti-inflammatory drugs (NSAIDs), and GnRH analogs.

Pipeline:

- **Linzagolix:** ObsEva is conducting Phase 3 studies of linzagolix for patients with endometriosis or uterine fibroids. Linzagolix is an oral, once daily GnRH receptor antagonist. Linzagolix may lower estradiol in a dose-dependent manner, potentially allowing the estradiol level to be maintained within an optimal range to reduce bone mineral density loss. Linzagolix is being evaluated both as monotherapy and in combination with hormonal add-back therapy (estradiol 1mg/ norethindrone acetate 0.5mg). The Phase 3 EDELWEISS 2 and EDELWEISS 3 studies for endometriosis-associated pelvic pain are currently ongoing. Additionally, in July 2020 ObsEva announced positive results from the Phase 3 PRIMROSE 1 study of linzagolix for the management of heavy menstrual bleeding due to uterine fibroids. ObsEva plans to submit a New Drug Application (NDA) to the FDA in the first half of 2021 for linzagolix for the management of heavy menstrual bleeding associated with uterine fibroids.
- **Relugolix:** Myovant is conducting Phase 3 studies of relugolix for the treatment of endometriosis-associated pain and for heavy menstrual bleeding associated with uterine fibroids. Relugolix is an oral GnRH receptor antagonist being studied in combination with estradiol 1mg and norethindrone acetate 0.5mg. The Phase 3 LIBERTY 1 and LIBERTY 2 studies in patients with heavy menstrual bleeding associated with uterine fibroids have been completed. The primary endpoint in both studies was the proportion of women achieving menstrual blood loss volume <80mL and a ≥50% reduction from baseline in menstrual blood volume during the last 35 days of the 24-week treatment period. In LIBERTY 1 and LIBERTY 2, the primary endpoint was met in 73.4% and 71.2% of patients receiving relugolix combination therapy vs. 18.9% and

14.7% treated with placebo, respectively. In August 2020, the FDA accepted Myovant's NDA for relugolix/estradiol/norethindrone combination therapy for the treatment of women with heavy menstrual bleeding associated with uterine fibroids. The Prescription Drug User Fee Act (PDUFA) action date is June 01, 2021.

Fensolvi® (Leuprolide Acetate) Product Summary[12]

Indication(s): Fensolvi® (leuprolide acetate) is a GnRH agonist indicated for the treatment of pediatric patients 2 years of age and older with CPP.

How Supplied: 45mg leuprolide acetate in a kit containing 2 trays:

- Syringe A Tray: This tray contains a syringe prefilled with diluent for reconstitution (ATRIGEL Delivery System) and a white plunger rod (to be used with Syringe B).
  - The ATRIGEL Delivery System is a polymeric delivery system consisting of a biodegradable polymer formulation dissolved in a biocompatible solvent. Immediately prior to administration, the syringe containing the ATRIGEL Delivery System is mixed with the syringe containing lyophilized leuprolide acetate until a uniform suspension is achieved.
- Syringe B Tray: This tray contains a syringe prefilled with 45mg lyophilized leuprolide acetate powder and a safety needle.

Dosing: 45mg administered by sub-Q injection once every 6 months

- Must be administered by a health care professional
- Response should be monitored at 1 to 2 months following initiation of therapy (and as needed) with a GnRH agonist stimulation test, basal serum luteinizing hormone (LH) levels, or serum concentration of sex steroid levels to confirm adequate suppression of pituitary gonadotropins, sex steroids, and secondary sexual characteristics
- Height should be measured every 3 to 6 months; bone age should be monitored periodically
- Treatment should be discontinued at the appropriate age of onset of puberty

Mechanism of Action: Leuprolide acetate is a GnRH agonist which causes potent inhibition of gonadotropin secretion [LH and follicle stimulating hormone (FSH)] when given continuously in therapeutic doses. After a period of initial stimulation, leuprolide acetate causes downregulation of GnRH receptors when administered chronically. This results in a reduction in the release of LH and FSH and subsequent suppression of ovarian and testicular production of estradiol and testosterone, respectively. The inhibitory effects of leuprolide acetate are reversible upon discontinuation of drug therapy.

Contraindication(s):

- Hypersensitivity to GnRH, GnRH agonists, or any of the components of Fensolvi®
- Pregnancy

Warnings and Precautions:

- Initial Rise of Gonadotropins and Sex Steroid Levels: During the early phase of therapy, gonadotropins and sex steroid levels may rise above baseline due to the initial stimulatory effect of leuprolide acetate. Increased signs and symptoms of puberty including vaginal bleeding may be observed during the first weeks of treatment or after subsequent doses. The prescriber should be notified if these symptoms persist beyond the second month after administration.
- Psychiatric Events: In postmarketing reports, patients taking GnRH agonists have reported psychiatric events such as emotional lability, crying, irritability, impatience, anger, and aggression. Patients should be monitored for the development or worsening of psychiatric symptoms during treatment with Fensolvi®.
- Convulsions: In postmarketing reports, convulsions have been observed in patients receiving GnRH agonists. Convulsions have been observed in patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and in patients taking medications such as bupropion and selective serotonin reuptake inhibitors (SSRIs). Convulsions have also been observed in patients without any of these conditions.

Use in Specific Populations:

- Pregnancy: Use of Fensolvi® is contraindicated in pregnancy and may cause fetal harm based on findings from animal studies and the drug's mechanism of action. Pregnancy should be excluded prior to initiating treatment in women of reproductive potential. Non-hormonal methods of contraception should be used during treatment.
- Lactation: No data are available on the presence of leuprolide acetate in animal or human milk, the effects on breastfed infants, or the effects on milk production.
- Females and Males of Reproductive Potential: Fertility is expected to be decreased while on treatment with Fensolvi®, but this is believed to be reversible upon discontinuation. There is no evidence that pregnancy rates are affected following discontinuation.
- Pediatric Use: The safety and effectiveness of Fensolvi® for the treatment of CPP were established in pediatric patients 2 years of age and older.

Adverse Reactions: In an open-label, single-arm study of 64 pediatric patients, the most common adverse reactions (reported in ≥5% of patients

treated with Fensolvi®) included injection site pain, nasopharyngitis, pyrexia, headache, cough, abdominal pain, injection site erythema, nausea, constipation, vomiting, upper respiratory tract infection, bronchospasm, productive cough, and hot flush. Additionally, psychiatric adverse reactions of emotional disorders and irritability occurred in 2% of patients treated with Fensolvi®.

Efficacy: The safety and efficacy of Fensolvi® were established in an uncontrolled, open-label, single-arm study which included 64 children 4 to 9 years of age (62 females and 2 males) with CPP. All patients were naïve to GnRH agonist treatment, received at least 1 dose of Fensolvi® 45mg at a dosing interval of 24 weeks, and were observed for 12 months. The primary endpoint was suppression of peak stimulated LH concentrations to <4IU/L by month 6 and was achieved in 87% of pediatric patients with CPP. Additionally, at month 6, estradiol and testosterone levels were suppressed in 97% and 100% of patients, respectively. These laboratory endpoints were measured after GnRH agonist stimulation. Treatment with Fensolvi® also stopped or reversed progression of clinical signs of puberty and resulted in reductions in growth velocity and bone age.

Cost Comparison:

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

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

Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) Product Summary[13,14]

Indication(s): Oriahnn™ (elagolix/estradiol/norethindrone and elagolix) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

- Limitation of Use: Use should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

Boxed Warning: Thromboembolic Disorders and Vascular Events

- Estrogen and progestin combinations, including Oriahnn™, increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events
- Oriahnn™ is contraindicated in women with current or history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women older than 35 years of age who smoke and women with uncontrolled hypertension (HTN)

How Supplied: 2 capsules (a morning capsule and an evening capsule):

- Morning capsule: Contains elagolix 300mg, estradiol 1mg, and norethindrone acetate 0.5mg
- Evening capsule: Contains elagolix 300mg
- Packaged in a carton with 4 weekly blister packs, each containing 7 morning capsules and 7 evening capsules

Dosing:

- 1 capsule (elagolix/estradiol/norethindrone) by mouth in the morning and 1 capsule (elagolix) in the evening
- Each dose should be taken at approximately the same time each day, with or without food
- Missed doses may be taken within 4 hours of the time the dose was due
- Missed doses that are >4 hours late should be skipped; the missed dose should not be taken with the next scheduled dose

Mechanism of Action: Oriahnn™ contains a combination of 3 medications: elagolix (a GnRH receptor antagonist), estradiol (an estrogen), and norethindrone acetate (a progestin).

- Elagolix binds competitively to GnRH receptors in the pituitary gland, causing suppression of LH and FSH and a subsequent decrease in the blood concentrations of ovarian sex hormones estradiol and progesterone. This ultimately reduces bleeding associated with uterine fibroids.
- Estradiol binds to nuclear receptors in estrogen-responsive tissues. The addition of estradiol may help to decrease bone loss that could occur due to a decrease in circulating estrogen from using elagolix alone.
- Norethindrone binds to nuclear receptors in progesterone-responsive tissues. The addition of norethindrone may help protect the uterus from potential adverse endometrial effects of unopposed estrogen.

Contraindication(s):

- High risk of arterial, venous thrombotic, or thromboembolic disorder

- Pregnancy
- Known osteoporosis
- Current or history of breast cancer, or other hormonally-sensitive malignancies
- Known liver impairment or disease
- Undiagnosed abnormal uterine bleeding
- Known hypersensitivity to ingredients in Oriahnn™
- Organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations

Warnings and Precautions:

- Thromboembolic Disorders and Vascular Events: Use is contraindicated in women with current or history of thrombotic or thromboembolic disorders and women at increased risk for these events. In general, risk is greatest for women older than 35 years of age who smoke or for women with uncontrolled HTN, dyslipidemia, vascular disease, or obesity.
- Bone Loss: Use of Oriahnn™ is contraindicated in women with known osteoporosis. Bone mineral density loss increases with increased duration of use and may not be completely reversibly after stopping treatment.
- Hormonally-Sensitive Malignancies: Use of Oriahnn™ is contraindicated in women with current or history of breast cancer and in women at an increased risk of hormonally-sensitive malignancies (e.g., patients with mutations in BRCA genes).
- Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders: In clinical studies of Oriahnn™, depression, depressed mood, and tearfulness occurred at a higher percentage than placebo (3% vs. 1%, respectively). Additionally, suicidal ideation and behavior occurred in a separate study of elagolix at lower doses for a different indication, with 1 completed suicide reported.
- Hepatic Impairment and Transaminase Elevations: Use Oriahnn™ is contraindicated in women with known hepatic impairment or disease. Elevations >3 times the upper limit of normal (ULN) in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were seen in 1.1% and 1.3% of patients treated with Oriahnn™ in clinical studies, respectively. Peak elevations of 8 times the ULN for ALT and 6 times the ULN for AST were observed.
- Elevated Blood Pressure (BP): Use Oriahnn™ is contraindicated in women with uncontrolled HTN. Elevations in systolic (5.1mmHg) and diastolic (2.1mmHg) BP were observed in patients treated with Oriahnn™ relative to placebo. Women with well-controlled HTN should continue to monitor BP and discontinue treatment if BP increases

significantly. Women without a history of HTN should also monitor BP during treatment.

- Gallbladder Disease or History of Cholestatic Jaundice: A small increase in the relative risk of developing gallbladder disease exist for patients using estrogens. The risks and benefits of treatment with Oriahnn™ should be evaluated in women with a history of cholestatic jaundice associated with estrogen use or pregnancy, and Oriahnn™ should be discontinued if jaundice occurs.
- Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy: The ability to recognize pregnancy may be impaired while taking Oriahnn™ due to its effects on the intensity, duration, and amount of menstrual bleeding. The effects of hormonal contraception on Oriahnn™ efficacy are unknown. Non-hormonal contraception should be used during treatment with Oriahnn™ and for 1 week after discontinuation.
- Effects on Carbohydrate and Lipid Metabolism: Oriahnn™ may decrease glucose tolerance resulting in increased glucose levels. Additionally, in patients with established hypertriglyceridemia, the use of estrogen therapy may increase plasma triglyceride levels leading to pancreatitis. The use of elagolix is associated with increased total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides.
- Alopecia: In Phase 3 studies, hair loss and hair thinning occurred more frequently in patients taking Oriahnn™ (3.5%) compared to placebo (1%). Additionally, almost one-third of affected patients discontinued treatment due to alopecia. In most of the affected women, hair loss continued when treatment was stopped, and it is unknown whether the hair loss is reversible.
- Effect on Other Laboratory Results: Serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin) may be increased in patients using estrogen and progestin combinations. This may reduce the free concentration of thyroid or corticosteroid levels, potentially necessitating higher replacement doses for patients with hypothyroidism or hypoadrenalism.
- Risk of Allergic Reactions Due to the Inactive Ingredient FD&C Yellow No. 5 (Tartrazine): Susceptible patients may experience allergic-type reactions to the inactive ingredient FD&C Yellow No. 5 (tartrazine) contained in Oriahnn™. Incidence of tartrazine sensitivity is low in the general population, but the risk is higher in patients who also have aspirin hypersensitivity.

Use in Specific Populations:

- Pregnancy: Use of Oriahnn™ is contraindicated in pregnant women. Based on animal data, exposure to elagolix in early pregnancy may

increase the risk of early pregnancy loss. There are insufficient human data to determine whether there is increased risk of major birth defects or miscarriage. In Phase 3 studies, there was 1 pregnancy reported out of 453 women who received Oriahnn™. The pregnancy resulted in a spontaneous abortion with estimated fetal exposure to Oriahnn™ occurring in the first 18 days of pregnancy.

- Lactation: There are no data available on the presence of elagolix in human milk, the effects on the breastfed child, or the effects on milk production. Estrogen and progestin medications can be detected in human milk and can reduce milk production.
- Females and Males of Reproductive Potential: Pregnancy should be excluded prior to initiating treatment with Oriahnn™ as this medication may delay the ability to recognize the occurrence of pregnancy. Non-hormonal contraception should be used during treatment and for 1 week after discontinuation.
- Pediatric Use: Safety and effectiveness of Oriahnn™ have not been established in pediatric patients.
- Renal Impairment: No dose adjustment is required in women with any degree of renal impairment or end-stage renal disease, including women on dialysis.
- Hepatic Impairment: Use of Oriahnn™ is contraindicated in women with any hepatic impairment or disease. Estradiol-associated adverse effects are expected to be increased in patients with hepatic impairment due to increased blood levels of estradiol. Additionally, elagolix-associated adverse effects are expected to be increased in patients with moderate and severe hepatic impairment due to increased elagolix exposures (3-fold and 7-fold for moderate and severe impairment, respectively).

Adverse Reactions: The most common adverse reactions with Oriahnn™ (occurring in ≥5% of patients and at a greater frequency than placebo) were hot flush, headache, fatigue, and metrorrhagia. Additionally, the most common adverse reactions leading to study discontinuation were nausea, headache, alopecia, metrorrhagia, menorrhagia, and hot flush.

Efficacy: The safety and efficacy of Oriahnn™ were established in 2 identical randomized, double-blind, placebo-controlled studies (UF-1 and UF-2). In the 2 studies, a total of 790 premenopausal women (412 in UF-1 and 378 in UF-2) with heavy menstrual bleeding were randomized to receive Oriahnn™ or placebo for 6 months. The median age of patients in both studies was 43 years and ranged from 25 to 53 years of age. Additionally, 68% of women were black or African American.

- Inclusion Criteria: Patients were eligible for inclusion if they were premenopausal women between 18 years and 51 years of age at the

time of screening and had an ultrasound-confirmed diagnosis of uterine fibroids. Additionally, included patients had heavy menstrual bleeding, defined at baseline as having at least 2 menstrual cycles with >80mL of menstrual blood loss (assessed by alkaline hematin, an objective and validated method of quantifying blood volume on sanitary products).

- Exclusion Criteria: Patients were excluded if they were pregnant or had a persistent or complex ovarian cyst, cancer, pelvic inflammatory disease, a history of osteoporosis, or a bone mineral density T-score of ≤-1.5 at the lumbar spine, total hip, or femoral neck.
- Primary Endpoint: The primary endpoint was menstrual blood loss <80mL during the final month and ≥50% reduction in menstrual blood loss from baseline to the final month.
- Results: In UF-1 and UF-2, the primary endpoint was met in 68.5% and 76.5% of patients receiving Oriahnn™ vs. 8.7% and 10% of patients receiving placebo, respectively (P<0.001 in both studies).

Cost Comparison:

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

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), Specialty Pharmaceutical Allowable Cost (SPAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.
*Cost per unit based on each capsule for Oriahnn™, each tablet for norgestimate/ethinyl estradiol, and each package for Lupron Depot®.
⁺Cost per year based on 1 capsule twice daily for Oriahnn™, 1 tablet daily for norgestimate/ethinyl estradiol, 1 injection monthly for Lupron® Depot 1-month kit, and 1 injection every 3 months for Lupron® Depot 3-month kit.

Recommendations

The College of Pharmacy recommends moving Supprelin® LA (histrelin) and Synarel® (nafarelin) to Tier-1 based on net costs and recommends the placement of Fensolvi® (leuprolide) into Tier-3 of the GnRH Medications Product Based Prior Authorization (PBPA) category with the following criteria (additions and changes shown in red):

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

1. An FDA approved diagnosis of central precocious puberty confirmed by submitting the following:

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

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

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

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

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

Oriahnn™ (Elagolix/Estradiol/Norethindrone and Elagolix) Approval Criteria:

1. An FDA approved diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women; and
2. Member must be 18 years of age or older; and
3. Member must not have any contraindications to Oriahnn™ therapy including:
    a. Osteoporosis; and
    b. Pregnancy; and
        i. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
        ii. Female members of reproductive potential must be willing to use effective non-hormonal contraception during treatment with Oriahnn™ and for at least 1 week after discontinuing treatment; and

c. Hepatic impairment or disease; and
d. Undiagnosed abnormal uterine bleeding; and
e. High risk of arterial, venous thrombotic, or thromboembolic disease; and
f. Current or history of breast cancer or other hormonally-sensitive malignancies; and
g. Known hypersensitivity to ingredients in Oriahnn™; and
h. Concomitant use with an organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and

4. Oriahnn™ must be prescribed by, or in consultation with, an obstetrician/gynecologist or a specialist with expertise in the treatment of uterine leiomyomas (fibroids); and
5. A failed trial at least 1 month in duration with nonsteroidal anti-inflammatory drugs (NSAIDs) or a patient-specific, clinically significant reason why the member cannot use NSAIDs must be provided; and
6. A failed trial at least 3 months in duration of hormonal contraceptives or a patient-specific, clinically significant reason why the member cannot use hormonal contraceptives must be provided; and
7. A quantity limit of 56 capsules per 28 days will apply; and
8. Lifetime approval duration will be limited to a maximum of 24 months.

Utilization Details of GnRH Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
GONADOTROPIN-RELEASING HORMONE (GnRH) AGONIST PRODUCTS						
LUPRON DEP-PED INJ 30MG	102	39	$982,043.18	$9,627.87	2.62	52.11%
LUPRON DEPOT INJ 11.25MG	57	39	$221,062.32	$3,878.29	1.46	11.73%
LUPRON DEPOT INJ 3.75MG	40	19	$51,573.76	$1,289.34	2.11	2.74%
LUPRON DEP-PED INJ 11.25MG	29	14	$216,292.04	$7,458.35	2.07	11.48%
TRIPTODUR SUS 22.5MG	17	11	$283,911.27	$16,700.66	1.55	15.06%
LUPRON DEP-PED INJ 7.5MG	12	3	$19,253.70	$1,604.48	4	1.02%
LUPRON DEPOT INJ 22.5MG	4	1	$18,749.78	$4,687.45	4	0.99%
LUPRON DEP-PED INJ 11.25MG	1	1	$3,061.63	$3,061.63	1	0.16%
LUPRON DEPOT INJ 7.5MG	1	1	$1,622.18	$1,622.18	1	0.09%
SUBTOTAL	**263**	**120***	**$1,797,569.86**	**$6,834.87**	**2.19**	**95.38%**
ELAGOLIX PRODUCTS						
ORILISSA TAB 150MG	74	28	$64,055.33	$865.61	2.64	3.40%
ORILISSA TAB 200MG	27	6	$22,950.54	$850.02	4.5	1.22%
SUBTOTAL	**101**	**34***	**$87,005.87**	**$861.44**	**2.97**	**4.62%**
TOTAL	**364**	**151***	**$1,884,575.73**	**$5,177.41**	**2.41**	**100.00%**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J9217 LEUPROLIDE DEPOT 7.5MG	108	57	$65,480.43	$606.30
J1950 LEUPROLIDE DEPOT 3.75MG	57	17	$120,400.43	$2,112.29
J9218 LEUPROLIDE INJ 1MG	17	17	$296.11	$17.42
TOTAL	**182**	**91**	**$186,176.97**	**$1,022.95**

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

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Appendix D

Fiscal Year 2020 Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/ Ezetimibe)

Oklahoma Health Care Authority
January 2021

Current Prior Authorization Criteria

Fibric Acid Derivative Medications*	
Tier-1	**Tier-2**
choline fenofibrate DR cap 45mg (Trilipix®)	choline fenofibrate DR cap 135mg (Trilipix®)
fenofibrate tab (Tricor®)	fenofibrate tab 135mg (Fenoglide®)
fenofibrate tab (Triglide®)	fenofibrate cap (Lipofen®)
fenofibrate micronized cap 67mg, 134mg (Lofibra®)	fenofibrate micronized cap (Antara®)
fenofibric acid tab 35mg (Fibricor®)	fenofibrate micronized cap 200mg (Lofibra®)
gemfibrozil tab (Lopid®)	fenofibric acid tab 105mg (Fibricor®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
DR = delayed release; cap = capsule; tab = tablet

Fibric Acid Derivative Medications Tier-2 Approval Criteria:

1. Laboratory documented failure with a Tier-1 medication after a 6 month trial; or
2. Documented adverse effect, drug interaction, or contraindication to all Tier-1 medication(s); or
3. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Juxtapid® (Lomitapide) and Kynamro® (Mipomersen) Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following criteria:
    a. A documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least 1 of the following:
        i. Documentation that both parents have untreated total cholesterol >250mg/dL; or

ii. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; and
2. Documented trial of high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
3. Documented trial of Repatha® (evolocumab) at least 12 weeks in duration; and
4. Member requires additional lowering of LDL cholesterol (LDL-C) (baseline, current, and goal LDL-C levels must be provided); and
5. Prescriber must be certified with Juxtapid® or Kynamro® Risk Evaluation and Mitigation Strategy (REMS) program.

Omega-3 Fatty Acids Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL) and controlled diabetes [fasting glucose <150mg/dL at the time of triglycerides measurement and hemoglobin A1c (HgA1c) <7.5%]; and
2. Previous failure with fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a previous failure of or a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®), which is available without prior authorization; and
4. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors Approval Criteria:

1. For Repatha® (evolocumab):
    a. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following:
        i. Documented functional mutation(s) in both low-density lipoprotein (LDL) receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
        ii. An untreated total cholesterol >500mg/dL and at least 1 of the following:
            1. Documented evidence of definite heterozygous familial hypercholesterolemia (HeFH) in both parents; or
            2. Presence of tendinous/cutaneous xanthoma prior to 10 years of age; or
    b. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or

    c. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and
        i. Documentation of established CVD; and
            1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or
2. For Praluent® (alirocumab):
    a. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or
    b. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established CVD; and
        i. Documentation of established CVD; and
            1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; and
3. Member must be 13 years of age or older for the diagnosis of HoFH or must be 18 years of age or older for all other FDA-approved diagnoses or indications; and
4. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
    a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
    b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
    c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
    d. Tier structure rules still apply; and
5. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
6. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
7. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent®. A quantity limit of 2 syringes or auto-injectors per 28 days will apply for Repatha® 140mg and a quantity limit of 1 auto-injector per 28 days will apply for Repatha® 420mg. Requests for the Repatha® 420mg dose will not be approved for multiple 140mg syringes or auto-injectors, but instead members should use (1) 420mg auto-injector; and
8. Initial approvals will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of the medication, and

compliance will be checked at that time and every 6 months thereafter for continued approval.

Statin Medications and Ezetimibe*	
Tier-1	**Special PA**
atorvastatin (Lipitor®)	fluvastatin (Lescol® & Lescol® XL)
ezetimibe (Zetia®)	lovastatin ER (Altoprev®)
lovastatin (Mevacor®)	pitavastatin calcium (Livalo®)
pravastatin (Pravachol®)	pitavastatin magnesium (Zypitamag™)
rosuvastatin tablet (Crestor®)	rosuvastatin capsule (Ezallor Sprinkle™)
simvastatin (Zocor®)	simvastatin suspension (FloLipid®)
	simvastatin/ezetimibe (Vytorin®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended-release; PA = prior authorization

Statin Medications and Ezetimibe Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher low-density lipoprotein (LDL) reduction cannot be used; and
2. Use of FloLipid® (simvastatin oral suspension) will require a patient specific, clinically significant reason why the member cannot use simvastatin oral tablets, even when the tablets are crushed; and
3. Use of Ezallor Sprinkle™ (rosuvastatin capsule) will require a patient-specific, clinically significant reason why the member cannot use rosuvastatin oral tablets, even when the tablets are crushed.

Welchol® (Colesevelam) Chewable Bar Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use other formulations of colesevelam, including oral tablets and packets for oral suspension, which are available without prior authorization, must be provided; and
3. A quantity limit of 30 chewable bars per 30 days will apply.

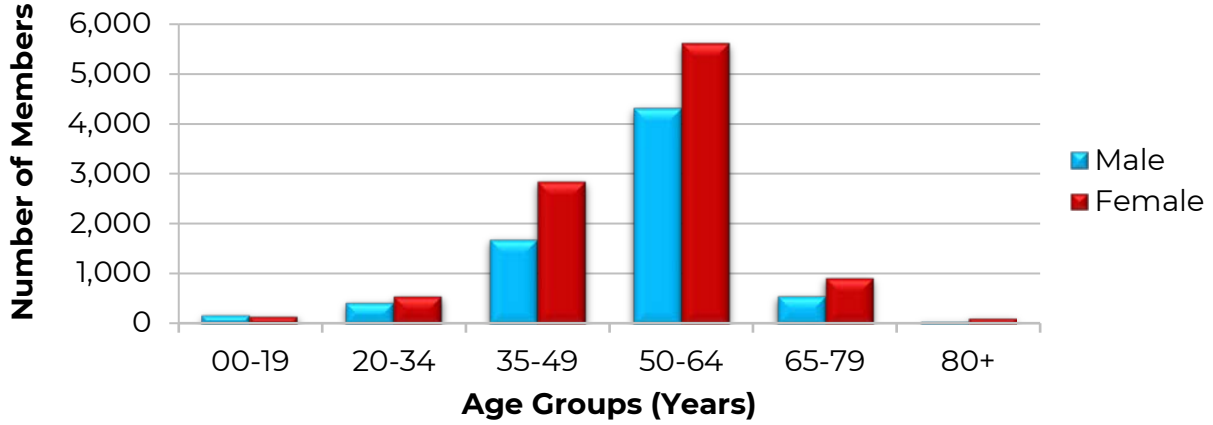
Utilization of Antihyperlipidemics: Fiscal Year 2020

Comparison of Fiscal Years

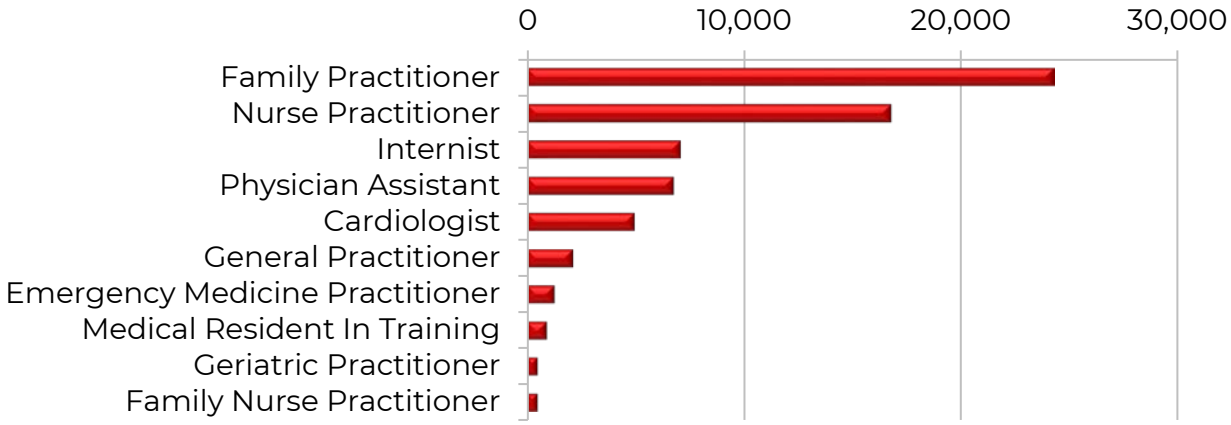
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	17,567	68,308	$1,122,593.99	$16.43	$0.32	3,700,247	3,562,428
2020	17,464	68,007	$1,122,603.99	$16.51	$0.30	3,919,905	3,751,928
% Change	**-0.6%**	**-0.4%**	**0.001%**	**0.5%**	**-6.3%**	**5.9%**	**5.3%**
Change	**-103**	**-301**	**$10.00**	**$0.08**	**-$0.02**	**219,658**	**189,500**

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

Demographics of Members Utilizing Antihyperlipidemics



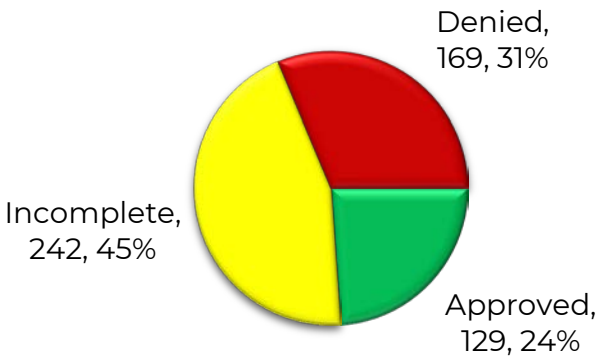
Top Prescriber Specialties of Antihyperlipidemics by Number of Claims



Prior Authorization of Antihyperlipidemics

There were 540 prior authorization requests submitted for antihyperlipidemics during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Welchol® (colesevelam chewable bar): April 2022
- Livalo® (pitavastatin calcium tablet): August 2024
- Nexletol® (bempedoic acid tablet): December 2025
- Nexlizet™ (bempedoic acid/ezetimibe tablet): December 2025
- Juxtapid® (lomitapide capsule): August 2027
- FloLipid® (simvastatin oral suspension): February 2030
- Zypitamag™ (pitavastatin magnesium tablet): January 2031
- Epanova® (omega-3-carboxylic acids capsule): January 2033
- Antara® (fenofibrate micronized capsule): May 2033
- Vascepa® (icosapent ethyl capsule): June 2033
- Ezallor Sprinkle™ (rosuvastatin capsule): February 2036

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

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

prevention, there was a 35% relative risk reduction in major CV events when compared to 16% for the high-risk primary prevention patients. Several committee members voiced concerns about approval for the high-risk primary prevention population because they only comprised 30% of the trial population.

- **February 2020:** The FDA approved Nexletol® (bempedoic acid), an oral, once-daily, non-statin, low-density lipoprotein cholesterol (LDL-C) lowering medication indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with established atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of LDL-C. Nexletol® is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL-C by inhibiting the production of cholesterol in the liver. The approval of Nexletol® was supported by multiple Phase 3 trials including over 3,000 patients. Nexletol® provided an average of 18% placebo-corrected LDL-C lowering when used with moderate or high intensity statins.
- **February 2020:** The FDA approved Nexlizet™ (bempedoic acid/ ezetimibe), an oral, once-daily, non-statin LDL-C lowering medication as adjunct therapy to diet and maximally tolerated statin therapy for adult patients with ASCVD or HeFH who require additional LDL-C lowering. Nexlizet™ has the same mechanism of action as Nexletol®, but also has an additional ingredient, ezetimibe, that inhibits cholesterol absorption in the intestines. The approval of Nexlizet™ is supported by a Phase 3 fixed combination drug product (FCDP) LDL-C lowering trial in which enrolled patients on maximally tolerated statins had a mean difference in LDL-C reduction of 38% when compared to placebo.

News:

- **October 2019:** *The New England Journal of Medicine* published a 20-year follow-up trial in children with familial hypercholesterolemia (FH). A total of 214 patients with FH, who were previously patients in a placebo-controlled trial evaluating the 2-year efficacy and safety of pravastatin, were invited for follow-up, together with their 95 unaffected siblings. These patients completed a questionnaire, provided blood samples, and underwent measurements of carotid intima-media thickness. Of the 214 patients in the original cohort, 184 patients (86%) were seen in follow-up, including 77 of the 95 siblings (81%). The mean LDL-C in the patients decreased from 237.3mg/dL to 160.7mg/dL, a decrease of 32% from baseline. Mean progression of carotid intima-media thickness over the entire follow-up period was 0.0056mm per year in patients with FH and 0.0057mm per year in the siblings. In this trial, the initiation of statin therapy during childhood

slowed the progression of carotid intima-media thickness and reduced the risk of CV disease in adulthood.

- **May 2020:** Results from a patient-reported outcome from the FOURIER trial showed that evolocumab, a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, did not impair cognition when added to statin therapy for LDL-C lowering. Patients in the trial answered questions at the beginning and end of the trial about their everyday function in a 23-item survey on memory and executive domains using the Everyday Cognition (ECog) scale. The survey revealed no differences in total scores and subdomain scores among the 82.2% of the FOURIER trial population that completed the survey. Patients in the trial who achieved a very low LDL-C (<20mg/dL) at week 4 showed similar declines in total cognitive scores as those whose LDL-C remained at or above 100mg/dL, thus showing no link between very low LDL-C and worse cognitive outcomes.
- **June 2020:** In a retrospective trial of Finnish women with ovarian cancer, statin use was associated with a large reduction in cancer-specific mortality. A 40% reduction in ovarian cancer mortality compared with non-statin users was observed in over 10,000 epithelial ovarian cancer patients studied [hazard ratio (HR): 0.60; 95% confidence interval (CI): 0.54, 0.66]. There was also a 37% reduction in 5-year mortality reported (HR: 0.63; 95% CI: 0.56, 0.70). Statins inhibit an enzyme in the mevalonate pathway and products of this pathway have been implicated in tumor growth, proliferation, and angiogenesis. The authors caution the results of this observational trial and recommend the result to be validated with a prospective randomized trial.
- **July 2020:** In a large retrospective trial done with Veterans Health Administration data, patients 75 years of age and older who were free from CVD and prescribed a statin for the first time for primary prevention of ASCVD had better clinical outcomes over the years when compared to those who did not take statins. Statin users had a significantly lower risk of events over a mean follow-up of 6.8 years when compared to those that did not use statins (25% less for all-cause mortality, 20% less for CV mortality, and 8% less for composite ASCVD events). Statins are a reasonable choice for patients 75 years of age and older according to the 2018 cholesterol guidelines from the American Heart Association and American College of Cardiology. Since patients older than 75 years of age are one of the fastest-growing population subgroups in health care systems, randomized trials are needed to provide more information on the safety and efficacy of statins in this population.
- **December 2020:** The effect of thyroid hormones in cholesterol control has been documented in multiple studies. One of the pathways shown in pre-clinical studies is the interaction of thyroid hormones with PCSK9

and the destruction of PCSK9. This destruction causes an increase in LDL receptor expression in the cell membrane and decreases LDL-C. Thyroid hormones also potentiate lipoprotein lipase activity that decreases triglycerides. In a systematic review and meta-analysis done by Kotwal and colleagues, the authors found that with overt hypothyroidism, all the lipid panels, including apolipoprotein, were reduced after treatment with levothyroxine. For patients with subclinical hypothyroidism, they found a decrease in the lipid panels, but not to the same extent as overt hypothyroidism. Increases in all lipid panel parameters, except for triglycerides, were also observed in patients with overt hyperthyroidism. There were no significant changes in lipid parameters following treatment of subclinical hyperthyroidism.

Pipeline:

- **Evinacumab:** In August 2020, Regeneron Pharmaceuticals announced the FDA has accepted Priority Review of the company's Biologics License Application (BLA) for evinacumab as an adjunct to other lipid-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH). HoFH is a rare inherited disease that affects approximately 1,300 patients in the United States. Treatment guidelines recommend early and intensive LDL-C lowering, but most of these patients are less responsive to standard therapies such as statins and PCSK9 inhibitors. Evinacumab is the first medication to bind to and block the function of angiopoietin-like 3 (ANGPTL3), an inhibitor of lipoprotein and endothelial lipase that plays a key role in lipid metabolism by increasing levels of triglycerides and other lipids. The Prescription Drug User Fee Act (PDUFA) target action date for the FDA decision is February 11, 2021.
- **Inclisiran (KJX839):** Inclisiran is the only LDL-C lowering therapy to use the small interfering ribonucleic acid (siRNA) mechanism to prevent the production of the target protein in the liver, increasing hepatic uptake of LDL-C and clearing it from the bloodstream. Inclisiran only requires 2 intravenous (IV) infusions per year and works as an adjunct to statin therapy. Inclisiran is currently under review by the FDA for the treatment of primary hyperlipidemia (including HeFH) in adults who have elevated LDL-C while being on a maximally tolerated statin therapy; however, in December 2020, the FDA issued a complete response letter (CRL) to Novartis stating that the agency cannot approve the New Drug Application (NDA) by the PDUFA action date of December 23, 2020 due to unresolved facility inspection-related conditions. The FDA has not raised any concerns related to the safety or efficacy of inclisiran. Novartis will work with the FDA and the third-party manufacturing facility in Europe to complete the inclisiran review, with

hopes to bring this potential first-in-class siRNA medications to patients in the United States as quickly as possible.

Nexletol® (Bempedoic Acid) Product Summary[13,14,15]

Indication(s): Nexletol® (bempedoic acid) is an ACL inhibitor indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C.

Dosing:

- Nexletol® (bempedoic acid) is available as a 180mg oral tablet.
- The recommended dosing of Nexletol® is 180mg once daily with or without food.

Mechanism of Action: Bempedoic acid is an ACL inhibitor that lowers LDL-C by inhibiting cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway.

Warnings and Precautions:

- Hyperuricemia: Bempedoic acid inhibits renal tubular organic anion transporter 2 (OAT2) and may increase blood uric acid levels. In clinical trials, 26% of patients who had normal uric acid levels prior to treatment experienced hyperuricemia 1 or more times while on bempedoic acid. Uric acid level increases usually occurred within the first 4 weeks of treatment and persisted throughout treatment.
- Tendon Rupture: Bempedoic acid has been associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of placebo-treated patients. Tendon rupture occurred within weeks to months of starting bempedoic acid.
- Pregnancy: Based on the mechanism of action, bempedoic acid is not recommended in pregnancy and may cause fetal harm.
- Lactation: Breastfeeding is not recommended when taking bempedoic acid.

Drug Interactions:

- Concomitant use of bempedoic acid with simvastatin >20mg or pravastatin >40mg should be avoided due to an increase in simvastatin and pravastatin concentrations that may lead to myopathy.

Efficacy: The safety and efficacy of bempedoic acid were assessed in 2 multi-center, Phase 3, randomized, double-blind, placebo-controlled trials that enrolled 3,009 adult patients with HeFH or ASCVD who were on maximally tolerated statin therapy.

- CLEAR Harmony: This was a 52-week, Phase 3 trial that included 2,230 patients with HeFH and/or ASCVD who were randomized 2:1 to receive either bempedoic acid (N=1,488) or placebo (N=742) as add-on to a maximally tolerated lipid lowering therapy (LLT). Maximally tolerated LLT was defined as a maximally tolerated statin dose alone or in combination with other lipid-lowering agents.
    - Inclusion Criteria: Enrolled patients included men and non-pregnant, non-lactating women 18 years of age and older with a diagnosis of HeFH and/or ASCVD on maximally tolerated LLT for at least 4 weeks before screening (6 weeks for fibrates) and a fasting LDL-C ≥70mg/dL.
    - Primary Endpoint: The primary endpoint was the overall safety of bempedoic acid, which included the incidence of adverse events (AEs) and changes in safety laboratory variables.
    - Key Secondary Endpoint: Percent change from baseline to week 12 in LDL-C
    - Results: Treatment with bempedoic acid did not lead to a higher overall incidence of AEs when compared to placebo. AEs were reported in 1,167 patients (78.5%) in the treatment group and 587 patients (78.7%) receiving placebo with the majority of the events being graded as mild-to-moderate. The most common AEs seen in both groups were nasopharyngitis, myalgia, upper respiratory tract infection, urinary tract infection, arthralgia, dizziness, muscle spasms, and diarrhea. Serious AEs were reported in 216 patients (14.5%) in the treatment group and 104 patients (14%) in the placebo group. Treatment with bempedoic acid also led to statistically significantly lower LDL-C levels when compared to placebo. The difference between bempedoic acid and placebo in mean percent change in LDL-C from baseline to week 12 was -18% (95% CI: -20%, -16%; P<0.001).
- CLEAR Wisdom: This was a 52-week, Phase 3 trial that included 779 patients with HeFH and/or ASCVD randomized 2:1 to receive either bempedoic acid (N=522) or placebo (N=257) as add-on to a maximally tolerated LLT.
    - Inclusion criteria: The trial included men and non-pregnant, non-lactating women 18 years of age and older with a diagnosis of HeFH and/or ASCVD. Patients had to be on a maximally tolerated statin dose alone or in combination with other approved lipid-lowering agents at stable doses for at least 4 weeks prior to screening (6 weeks for fibrates). A fasting LDL-C level of ≥100mg/dL at the first screening and ≥70mg/dL 1 week before randomization were required for trial inclusion.
    - Primary Endpoint: Percent change from baseline to week 12 in LDL-C

- Results: The difference between bempedoic acid and placebo in mean percent change in LDL-C from baseline to week 12 was -17% (95% CI: -21%, -14%; P<0.001).

Nexlizet™ (Bempedoic Acid/Ezetimibe) Product Summary[16,17]

Indication(s): Nexlizet™ (bempedoic acid/ezetimibe) is a combination ACL inhibitor and cholesterol absorption inhibitor indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C.

Dosing:

- Nexlizet™ (bempedoic acid/ezetimibe) is supplied as an oral tablet containing 180mg bempedoic acid and 10mg ezetimibe.
- The recommended dosing of Nexlizet™ is 1 tablet (180mg bempedoic acid/10mg ezetimibe) once daily with or without food.

Mechanism of Action: Bempedoic acid is an ACL inhibitor that lowers LDL-C by inhibiting cholesterol synthesis in the liver. The molecular target for ezetimibe has been shown to be Niemann-Pick C1-Like 1 (NPC1L1), a sterol transporter. Ezetimibe localizes at the brush border of the small intestines and inhibits the absorption of cholesterol.

Contraindications: Known hypersensitivity to ezetimibe tablets

Drug Interactions:

- Concomitant use of bempedoic acid/ezetimibe with simvastatin >20mg or pravastatin >40mg should be avoided due to an increase in simvastatin and pravastatin concentrations that may lead to myopathy.
- Cyclosporine levels should be monitored in patients using bempedoic acid/ezetimibe with cyclosporine.
- If cholelithiasis is suspected in a patient receiving bempedoic acid/ ezetimibe and fenofibrate, alternative LLT should be considered.

Efficacy: The safety and efficacy of bempedoic acid/ezetimibe as a FCDP were assessed in a 12-week, randomized, double-blind, 4-arm, parallel-group, Phase 3 trial in 301 patients with HeFH, ASCVD, or multiple risk factors for CVD on maximally tolerated statin therapy. Patients were randomized in a 2:2:2:1 ratio to either bempedoic acid 180mg/ezetimibe 10mg FCDP, bempedoic acid 180mg, ezetimibe 10mg, or placebo. Of the 301 patients in the trial, 86 patients were randomized to receive bempedoic acid/ezetimibe FCDP, 88 patients to bempedoic acid, 86 patients to ezetimibe, and 41 patients to placebo.

- Inclusion Criteria: Eligible patients were 18 years of age and older who required lipid-modifying therapy for primary or secondary prevention of CVD. A fasting LDL-C ≥130mg/dL was required for primary prevention or

LDL-C ≥100mg/dL for secondary prevention with a history of HeFH and/or ASCVD. Patients also had to be on maximally tolerated statin therapy at a stable dose for at least 4 weeks prior to screening.

- Primary Endpoint: The primary endpoint was the percent change from baseline to week 12 in LDL-C.
- Results: Treatment with the bempedoic acid/ezetimibe FCDP resulted in statistically significant (P<0.001 for all comparisons) reductions from baseline for least squares (LS) mean LDL-C (-36%) compared with bempedoic acid alone (-17%), ezetimibe alone (-23%), and placebo (2%).

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

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

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

Recommendations

The College of Pharmacy recommends the prior authorization of Nexletol® (bempedoic acid) and Nexlizet™ (bempedoic acid/ezetimibe) with the following criteria in red:

Nexletol® (Bempedoic Acid) and Nexlizet™ (Bempedoic Acid/Ezetimibe) Approval Criteria:

1. An FDA approved indication as an adjunct to diet and maximally tolerated statin therapy for the treatment of 1 of the following:
    a. Heterozygous familial hypercholesterolemia (HeFH); and
        i. Documentation of definite HeFH using the Simon Broome Register criteria, the Dutch Lipid Network criteria, or via genetic testing; or
    b. Established atherosclerotic cardiovascular disease (ASCVD); and
        i. Supporting diagnoses/conditions and dates of occurrence signifying established ASCVD; and
2. Member must be 18 years of age or older; and
3. Member must be on high dose statin therapy [low-density lipoprotein (LDL) reduction capability equivalent to rosuvastatin 40mg] or on maximally tolerated statin therapy; and

a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
c. Member must not be taking simvastatin at doses >20mg or pravastatin at doses >40mg due to drug interactions with Nexletol® and Nexlizet™; and
d. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
e. Tier structure rules still apply; and

4. Member requires additional lowering of LDL-cholesterol (LDL-C) (baseline, current, and goal LDL-C levels must be provided); and
5. A quantity limit of 30 tablets per 30 days will apply; and
6. Initial approvals will be for the duration of 3 months, after which time compliance and recent LDL-C levels to demonstrate the effectiveness of this medication will be required for continued approval. Subsequent approvals will be for the duration of 1 year.

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

Omega-3 Fatty Acids Approval Criteria:

1. An FDA approved indication of 1 of the following:
   a. Severe hypertriglyceridemia; and
      i. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL) and controlled diabetes mellitus [fasting glucose <150mg/dL at the time of triglycerides measurement and hemoglobin A1c (HgA1c) <7.5%]; and
      ii. Previous failure with fibric acid medications; and
      iii. Use of Vascepa® or Epanova® requires a previous failure of or a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®), which is available without prior authorization; or
   b. For the use of Vascepa® as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride levels; and
      i. Member must be on a stable dose of maximally tolerated statin therapy for at least 4 weeks (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and

ii. Laboratory documentation of fasting triglycerides ≥150mg/dL; and
iii. Member must have 1 of the following:
    1. Established cardiovascular disease (CVD); or
    2. Diabetes mellitus and ≥2 additional risk factors for CVD; and

2. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Utilization Details of Antihyperlipidemics: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
COLESEVELAM MEDICATIONS						
COLESEVELAM TAB 625MG	216	57	$22,767.26	$105.40	3.8	2.10%
WELCHOL TAB 625MG	10	3	$5,128.05	$512.81	3.3	0.47%
COLESEVELAM PAK 3.75GM	6	3	$8,686.07	$1,447.68	2.0	0.80%
COLESEVELAM MEDICATIONS TOTAL	**232**	**60***	**$36,581.38**	**$157.68**	**3.9**	**3.37%**
FIBRIC ACID DERIVATIVE MEDICATIONS						
TIER-1 MEDICATIONS						
GEMFIBROZIL TAB 600MG	1,980	413	$28,265.10	$14.28	4.8	2.60%
FENOFIBRATE TAB 145MG	1,566	432	$26,727.53	$17.07	3.6	2.46%
FENOFIBRATE TAB 160MG	1,317	352	$29,765.58	$22.60	3.7	2.74%
FENOFIBRATE TAB 48MG	527	132	$9,845.57	$18.68	4.0	0.91%
FENOFIBRATE TAB 54MG	366	93	$6,955.69	$19.00	3.9	0.64%
FENOFIBRATE CAP 134MG	284	80	$7,194.69	$25.33	3.6	0.66%
FENOFIBRIC CAP 45MG DR	140	21	$4,053.04	$28.95	6.7	0.37%
FENOFIBRATE CAP 67MG	40	9	$888.34	$22.21	4.4	0.08%
TIER-1 SUBTOTAL	**6,220**	**1,493***	**$113,695.54**	**$18.28**	**4.2**	**10.47%**
TIER-2 MEDICATIONS						
FENOFIBRIC CAP 135MG DR	184	44	$12,905.92	$70.14	4.2	1.19%
FENOFIBRATE CAP 200MG	68	13	$2,378.08	$34.97	5.2	0.22%
FENOFIBRATE TAB 120MG	40	8	$24,268.10	$606.70	5.0	2.23%
FENOFIBRATE CAP 150MG	17	3	$4,496.05	$264.47	5.7	0.41%
FENOFIBRATE CAP 43MG	2	1	$63.10	$31.55	2	0.01%
FENOFIBRATE TAB 40MG	1	1	$763.67	$763.67	1.0	0.07%
TIER-2 SUBTOTAL	**312**	**70***	**$44,874.92**	**$143.83**	**4.5**	**4.13%**
FIBRIC ACID DERIVATIVE MEDICATIONS TOTAL	**6,532**	**1,547***	**$158,570.46**	**$24.28**	**4.2**	**14.60%**
OMEGA-3 FATTY ACIDS						
OMEGA-3-ACID CAP 1GM	914	278	$30,792.52	$33.69	3.3	2.84%
VASCEPA CAP 1GM	39	11	$11,476.47	$294.27	4	1.06%
OMEGA-3 FATTY ACIDS TOTAL	**953**	**289***	**$42,268.99**	**$44.35**	**3.3**	**3.89%**
PCSK9 INHIBITORS						
REPATHA SURE INJ 140MG/ML	37	8	$20,916.60	$565.31	4.6	1.93%
PRALUENT INJ 75MG/ML	12	3	$7,247.76	$603.98	4.0	0.67%
REPATHA INJ 140MG/ML	10	1	$5,031.44	$503.14	10.0	0.46%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
REPATHA PUSH INJ 420/3.5ML	6	1	$6,394.89	$1,065.82	6	0.59%
PRALUENT INJ 150MG/ML	3	2	$1,986.31	$662.10	2	0.18%
PCSK9 INHIBITORS TOTAL	**68**	**15***	**$41,577.00**	**$611.43**	**4.5**	**3.83%**
STATIN MEDICATIONS AND EZETIMIBE						
TIER-1 MEDICATIONS						
ATORVASTATIN TAB 40MG	15,235	4,743	$214,975.82	$14.11	3.2	19.79%
ATORVASTATIN TAB 20MG	10,492	3,451	$134,983.99	$12.87	3.0	12.43%
ATORVASTATIN TAB 10MG	6,952	1,973	$83,375.67	$11.99	3.5	7.68%
ATORVASTATIN TAB 80MG	5,319	1,650	$86,632.58	$16.29	3.2	7.98%
SIMVASTATIN TAB 20MG	3,727	1,047	$38,481.32	$10.33	3.6	3.54%
PRAVASTATIN TAB 40MG	2,999	820	$44,355.24	$14.79	3.7	4.08%
SIMVASTATIN TAB 40MG	2,670	730	$28,883.32	$10.82	3.7	2.66%
PRAVASTATIN TAB 20MG	2,059	573	$28,003.43	$13.60	3.6	2.58%
LOVASTATIN TAB 20MG	1,499	475	$17,434.84	$11.63	3.2	1.61%
ROSUVASTATIN TAB 20MG	1,478	491	$20,843.88	$14.10	3.0	1.92%
SIMVASTATIN TAB 10MG	1,246	358	$12,763.07	$10.24	3.5	1.18%
ROSUVASTATIN TAB 10MG	1,161	410	$16,137.84	$13.90	2.8	1.49%
ROSUVASTATIN TAB 40MG	1,086	357	$16,960.13	$15.62	3.0	1.56%
EZETIMIBE TAB 10MG	1,066	314	$18,795.86	$17.63	3.4	1.73%
LOVASTATIN TAB 40MG	755	219	$9,411.95	$12.47	3.4	0.87%
PRAVASTATIN TAB 10MG	722	190	$10,188.26	$14.11	3.8	0.94%
PRAVASTATIN TAB 80MG	564	157	$10,726.32	$19.02	3.6	0.99%
ROSUVASTATIN TAB 5MG	506	176	$6,575.35	$12.99	2.9	0.61%
LOVASTATIN TAB 10MG	294	93	$3,497.17	$11.90	3.2	0.32%
SIMVASTATIN TAB 80MG	236	67	$3,130.96	$13.27	3.5	0.29%
SIMVASTATIN TAB 5MG	78	22	$904.20	$11.59	3.5	0.08%
TIER-1 SUBTOTAL	**60,144**	**16,506***	**$807,061.20**	**$13.42**	**3.6**	**74.31%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
LIVALO TAB 4MG	26	6	$14,131.43	$543.52	4.3	1.30%
LIVALO TAB 2MG	24	5	$13,624.05	$567.67	4.8	1.25%
EZETIM/SIMVA TAB 10/40MG	12	4	$1,753.44	$146.12	3.0	0.16%
LIVALO TAB 1MG	10	2	$2,932.38	$293.24	5	0.27%
VYTORIN TAB 10/80MG	4	1	$3,789.80	$947.45	4	0.35%
EZETIM/SIMVA TAB 10/80MG	2	1	$313.86	$156.93	2	0.03%
SPECIAL PA SUBTOTAL	**78**	**18***	**$36,544.96**	**$468.53**	**4.3**	**3.37%**
STATINS AND EZETIMIBE TOTAL	**60,222**	**16,517***	**$843,606.16**	**$14.01**	**3.6**	**77.68%**
TOTAL	**68,007**	**17,464***	**$1,122,603.99**	**$16.51**	**3.9**	**100%**

CAP = Capsule; DR= Delayed-Release; INJ = Injection; TAB = Tablet; PAK = Packet;
EZETIM/SIMVA = ezetimibe/simvastatin
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix E

Fiscal Year 2020 Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Durysta™ (Bimatoprost Implant)

Oklahoma Health Care Authority
January 2021

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%)		

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

*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

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.

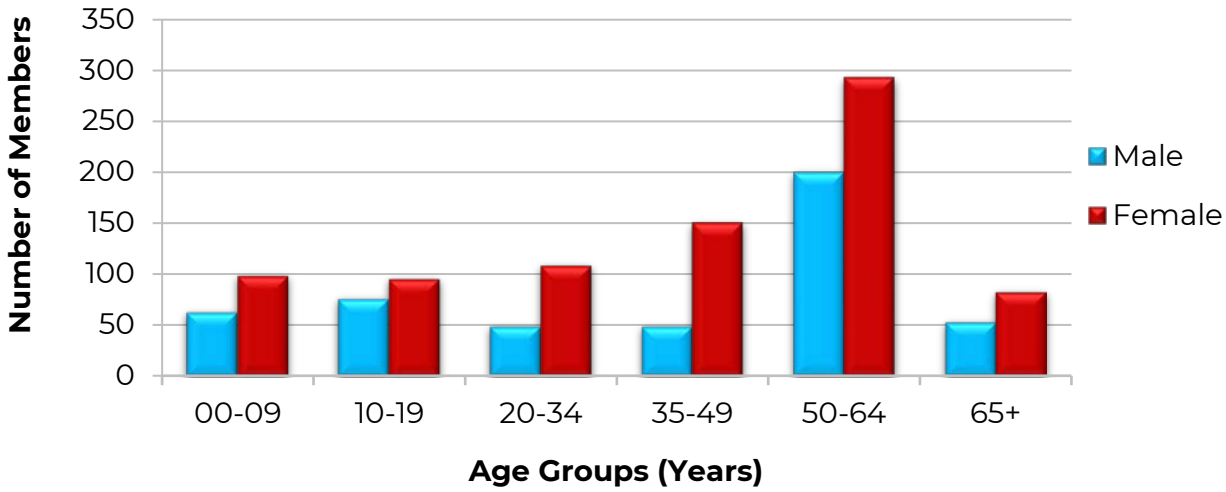
Utilization of Glaucoma Medications: Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

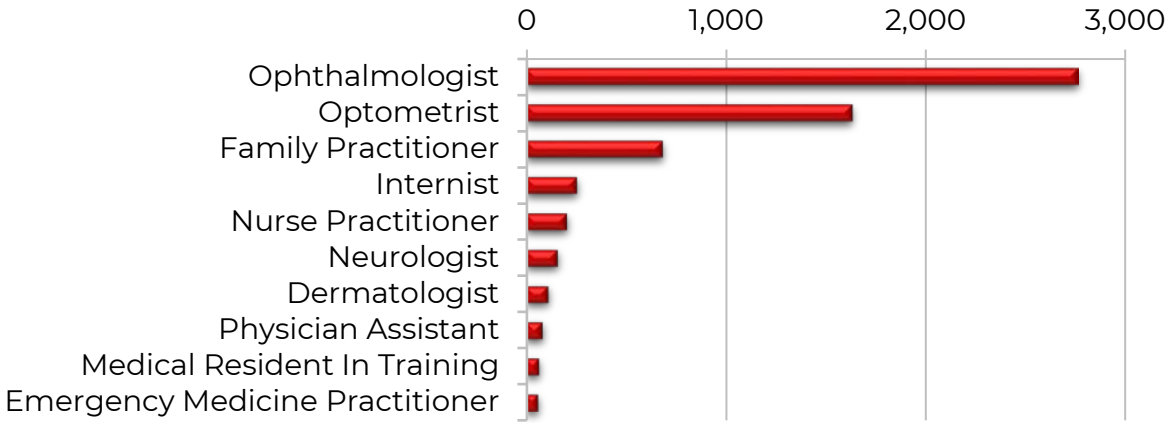
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1,293	6,197	$586,039.51	$94.57	$2.68	81,843	218,970
2020	1,321	6,419	$599,804.54	$93.44	$2.55	81,558	234,967
% Change	**2.20%**	**3.60%**	**2.30%**	**-1.20%**	**-4.90%**	**-0.30%**	**7.30%**
Change	**28**	**222**	**$13,765.03**	**-$1.13**	**-$0.13**	**-285**	**15,997**

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

Demographics of Members Utilizing Glaucoma Medications



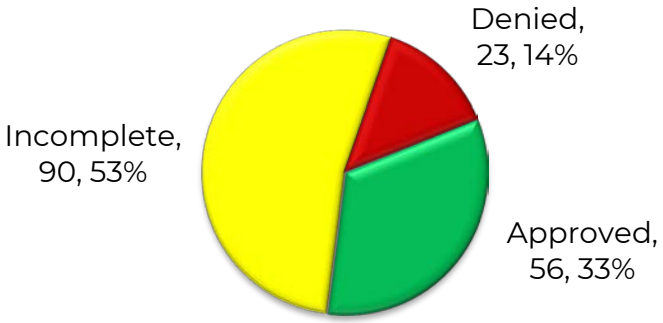
Top Prescriber Specialties of Glaucoma Medications by Number of Claims



Prior Authorization of Glaucoma Medications

There were 169 prior authorization requests submitted for glaucoma medications during fiscal year 2020. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

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

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

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

Pipeline:

- **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 studies 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 studies to have a sustained lowering of IOP, supporting development as a drug. In October 2019, Emerald Bioscience announced data demonstrating the superiority of its formulation of NB1111 in lowering IOP 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, announced data validating the 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 by enhancing drainage of ocular fluid over the trabecular meshwork, 1 of the major tissues for

regulating IOP. 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 study. This study is evaluating the safety, efficacy, durability, and tolerability of OTX-TIC in patients with primary OAG or OHT.

Durysta™ (Bimatoprost Implant) Product Summary[5]

Indication(s): Durysta™ (bimatoprost implant) is a prostaglandin analog indicated for the reduction of IOP in patients with OAG or OHT.

Dosing:

- Durysta™ (bimatoprost implant) is supplied as a biodegradable, intracameral implant containing bimatoprost 10mcg in a drug delivery system for a single administration.
- Durysta™ should not be administered into an eye that has received a prior Durysta™ implant.
- The intracameral injection procedure must be performed under magnification that allows clear visualization of the anterior chamber structures and should be carried out using standard aseptic conditions for intracameral procedures, with the patient's head in a stabilized position. The eye should not be dilated prior to the procedure.

Mechanism of Action: Bimatoprost, a prostaglandin analog, is a synthetic structural analog of prostaglandin with ocular hypotensive activity. Bimatoprost is thought to lower IOP in humans by increasing outflow of aqueous humor through both the trabecular meshwork (conventional) and uveoscleral routes (unconventional). Elevated IOP presents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss.

Contraindication(s):

- Patients with active or suspected ocular or periocular infections
- Patients with corneal endothelial cell dystrophy (e.g., Fuchs' Dystrophy) as the presence of Durysta™ implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss; administration of Durysta™ should be limited to a single implant per eye without retreatment and caution should be used when prescribing Durysta™ in patients with limited corneal endothelial cell reserve
- Patients with prior corneal transplantation or endothelial cell transplantation [e.g., Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK)]
- Patients with absent or ruptured posterior lens capsule due to the risk of implant migration into the posterior segment; laser posterior capsulotomy in pseudophakic patients is not a contraindication for Durysta™ use if the intraocular lens fully covers the opening in the posterior capsule
- Patients with hypersensitivity to bimatoprost or to any other components of the product

Warnings and Precautions:

- Endothelial Cell Loss: Due to possible corneal endothelial cell loss, administration of Durysta™ should be limited to a single implant per eye without retreatment.
- Corneal Adverse Reactions: Durysta™ has been associated with corneal adverse reactions and risks are increased with multiple implants. Durysta™ should be used with caution in patients with limited corneal endothelial cell reserve.
- Iridocorneal Angle: Durysta™ should be used with caution in patients with narrow angles or anatomical angle obstruction.

Adverse Reactions: In controlled studies, the most common ocular adverse reaction reported by 27% of patients treated with Durysta™ was conjunctival hyperemia. Other common adverse reactions reported in 5-10% of patients treated with Durysta™ were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, increased IOP, corneal endothelial cell loss, blurred vision, iritis, and headache.

Efficacy: The efficacy of Durysta™ was evaluated in 2 multicenter, randomized, parallel-group, controlled 20-month (including 8-month extended follow-up) studies of Durysta™ compared to twice daily topical timolol 0.5% ophthalmic drops, in patients with OAG or OHT. Durysta™ demonstrated an IOP reduction of approximately 5-8mmHg in patients with a mean baseline IOP of 24.5mmHg.

Cost Comparison:

Medication	Cost Per Unit
Durysta™ (bimatoprost implant) 10mcg	**$1,950.00/implant**
bimatoprost 0.03% ophthalmic drops	$24.09/mL
latanoprost 0.005% ophthalmic drops	$2.04/mL
timolol maleate 0.05% ophthalmic drops	$0.83/mL

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

Recommendations

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

Durysta™ (Bimatoprost Implant) Approval Criteria:

1. An FDA approved indication to reduce intraocular pressure (IOP) in members with open-angle glaucoma (OAG) or ocular hypertension (OHT); and
2. Member must be 18 years of age or older; and
3. Durysta™ must be prescribed by, or in consultation with, an ophthalmologist; and
4. A patient-specific, clinically significant reason why the member requires Durysta™ and cannot utilize ophthalmic preparations, such as solution or suspension, to treat OAG or OHT must be provided; and
5. The affected eye has not received prior treatment with Durysta™; and
6. The member has no contraindications to Durysta™; and
7. A quantity limit of (1) Durysta™ 10mcg implant per eye per lifetime will apply.

Utilization Details of Glaucoma Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
LATANOPROST SOL 0.005%	1,993	515	$31,963.67	$0.50	$16.04
TIMOLOL MAL SOL 0.5%	666	263	$9,033.26	$0.32	$13.56
TRAVATAN Z DRO 0.004%	640	167	$168,440.70	$7.51	$263.19
DORZ/TIMOL SOL 22.3-6.8MG/ML	509	157	$11,642.72	$0.47	$22.87
COMBIGAN SOL 0.2/0.5%	476	114	$117,880.15	$6.59	$247.65
ACETAZOLAMIDE TAB 250MG	353	108	$23,205.11	$2.13	$65.74
BRIMONIDINE SOL 0.2%	320	113	$5,191.97	$0.43	$16.22
ACETAZOLAMIDE CAP 500MG	240	88	$13,786.21	$1.83	$57.44
DORZOLAMIDE SOL 2%	202	67	$4,862.78	$0.53	$24.07
SIMBRINZA SUS 1/0.2%	193	52	$32,506.26	$4.84	$168.43
ALPHAGAN-P SOL 0.1%	183	49	$47,393.57	$6.09	$258.98

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
AZOPT SUS 1%	88	28	$29,301.86	$7.62	$332.98
ACETAZOLAMIDE TAB 125MG	76	28	$4,187.44	$1.92	$55.10
TIMOLOL MAL SOL 0.25%	70	34	$937.88	$0.28	$13.40
RHOPRESSA SOL 0.02%	49	12	$13,076.91	$8.17	$266.88
ROCKLATAN DRO 0.02/0.005%	28	7	$7,907.40	$9.88	$282.41
TIMOLOL MALE SOL 0.5%	16	10	$2,154.00	$4.67	$134.63
TRAVOPROST DRO 0.004%	3	3	$607.48	$4.78	$202.49
LEVOBUNOLOL SOL 0.5%	2	1	$36.38	$0.61	$18.19
CARTEOLOL SOL 1%	1	1	$23.76	$0.79	$23.76
TIER-1 SUBTOTAL	**6,108**	**1,817**	**$524,139.51**	**$2.34**	**$85.81**
TIER-2 PRODUCTS					
LUMIGAN SOL 0.01%	145	29	$45,610.21	$8.64	$314.55
BIMATOPROST SOL 0.03%	11	2	$1,226.08	$2.15	$111.46
ZIOPTAN DRO 0.0015%	8	1	$1,693.68	$7.06	$211.71
PILOCARPINE SOL 4%	6	1	$488.69	$1.36	$81.45
BETOPTIC-S SUS 0.25%	1	1	$308.96	$10.30	$308.96
TIER-2 SUBTOTAL	**171**	**34**	**$49,327.62**	**$7.61**	**$288.47**
SPECIAL PA PRODUCTS					
TIMOLOL GEL SOL 0.5%	52	28	$5,778.81	$3.74	$111.13
DORZ/TIMOL SOL 2%/0.5%	24	6	$2,492.92	$3.46	$103.87
METHAZOLAMIDE TAB 50MG	23	5	$7,850.59	$10.78	$341.33
VYZULTA SOL 0.024%	15	2	$3,824.36	$9.47	$254.96
ALPHAGAN-P SOL 0.15%	9	2	$3,047.37	$10.88	$338.60
BRIMONIDINE SOL 0.15%	9	4	$2,207.18	$8.03	$245.24
TIMOLOL GEL SOL 0.25%	4	3	$464.32	$3.36	$116.08
COSOPT PF SOL 2%/0.5%	4	2	$671.86	$5.60	$167.97
SPECIAL PA SUBTOTAL	**140**	**52**	**$26,337.41**	**$6.25**	**$188.12**
TOTAL	**6,419**	**1,321***	**$599,804.54**	**$2.55**	**$93.44**

SOL = solution; DRO = drop; MAL = maleate; DORZ = dorzolamide; TIMOL = timolol; TAB = tablet; CAP = capsule; ER = extended-release; SUS = suspension; PA = prior authorization
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/2020. Last accessed 12/11/2020.

[2] Allergan. Allergan Receives FDA Approval for Durysta™ (Bimatoprost Implant) the First and Only Intracameral Biodegradable Sustained-Release Implant to Lower Intraocular Pressure in Open-Angle Glaucoma or Ocular Hypertension Patients. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/allergan-receives-fda-approval-for-durysta-bimatoprost-implant-the-first-and-only-intracameral-biodegradable-sustained-release-implant-to-lower-intraocular-pressure-in-open-angle-glaucoma-or-ocular-hypertension-patients-301017349.html. Issued 03/05/2020. Last accessed 12/11/2020.

[3] 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 12/14/2020.

[4] Ocular Therapeutix. OTX-TIC (Travoprost Implant). Available online at: https://www.ocutx.com/research/otx-tic/. Last accessed 12/14/2020.

[5] Durysta™ Prescribing Information. Allergan. Available online at: https://media.allergan.com/products/durysta_pi.pdf. Last revised 11/2020. Last accessed 12/14/2020.

Appendix F

Fiscal Year 2020 Annual Review of Antiviral Medications

Oklahoma Health Care Authority
January 2021

Current Prior Authorization Criteria

Acyclovir 5% Cream (Generic Zovirax®) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the brand formulation must be provided.

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

1. An FDA approved diagnosis of acute herpetic keratitis (dendritic ulcers) in members 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.

Denavir® (Penciclovir Cream), Sitavig® (Acyclovir Buccal Tablet), and Xerese® (Acyclovir/Hydrocortisone Cream) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets must be provided; and
3. A patient-specific, clinically significant reason why the member cannot use acyclovir cream must be provided.

Prevymis™ (Letermovir Tablet and Injection) Approval Criteria:

1. An FDA approved indication of prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogenic hematopoietic stem cell transplant (HSCT); and
2. Member must be CMV R+; and
3. Member must have received a HSCT within the last 28 days; and
4. Members taking concomitant cyclosporine will only be approved for the 240mg dose; and
5. Members must not be taking the following medications:
    a. Pimozide; or
    b. Ergot alkaloids (e.g., ergotamine, dihydroergotamine); or
    c. Rifampin; or
    d. Atorvastatin, lovastatin, pitavastatin, simvastatin, or repaglinide when co-administered with cyclosporine; and

6. Prevymis™ must be prescribed by an oncology, hematology, infectious disease, or transplant specialist (or an advanced care practitioner with a supervising physician who is an oncology, hematology, infectious disease, or transplant specialist); and
7. Prescriber must verify the member will be monitored for CMV reactivation while on therapy; and
8. Approvals will be for the duration of 100 days post-transplant; and
    a. For Prevymis™ vials, authorization will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
    b. Approval length for the vial formulation will be based on duration of need; and
9. A quantity limit of 1 tablet or vial per day will apply.

Rebetol® (Ribavirin Solution), RibaPak® (Ribavirin Dose Pack), and Ribasphere® (Ribavirin 400mg and 600mg Tablet) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the 200mg tablets or 200mg capsules in place of the unique dosage formulations must be provided.

Zovirax® (Acyclovir Ointment) Approval Criteria:

1. An FDA approved indication of management of initial genital herpes or in limited non-life-threatening mucocutaneous herpes simplex virus (HSV) infection in immunocompromised members; and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets must be provided.

Zovirax® (Acyclovir Suspension) Approval Criteria:

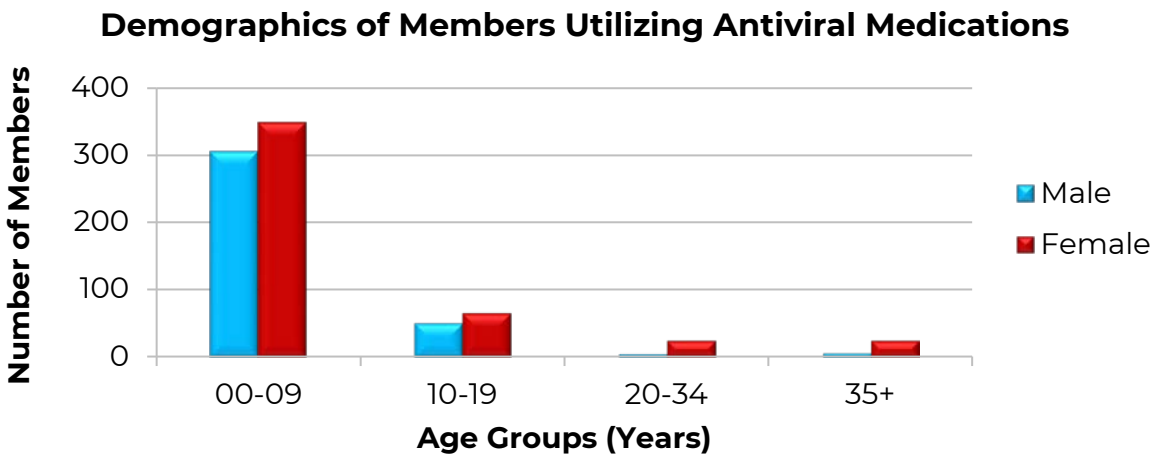
1. An age restriction of 7 years of age and younger will apply. Members older than 7 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

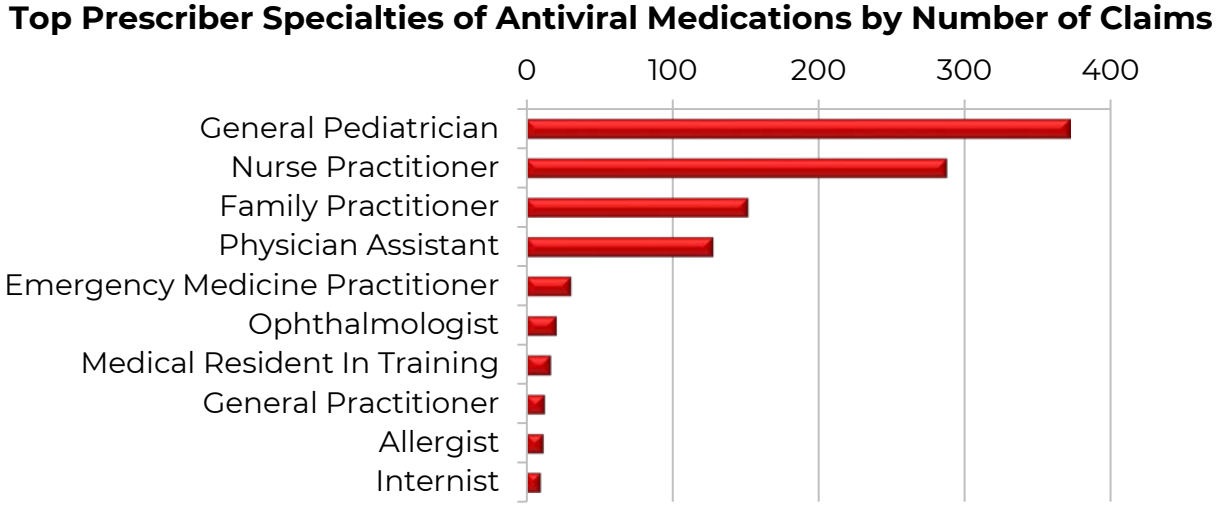
Utilization of Antiviral Medications: Fiscal Year 2020

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1,052	1,405	$453,406.74	$322.71	$19.91	161,435	22,777
2020	833	1,115	$302,447.14	$271.25	$17.58	146,050	17,202
% Change	**-22.80%**	**-20.60%**	**-33.30%**	**-15.90%**	**-11.70%**	**-9.50%**	**-24.50%**
Change	**-219**	**-290**	**-$150,959.60**	**-$51.46**	**-$2.33**	**-15,385**	**-5,575**

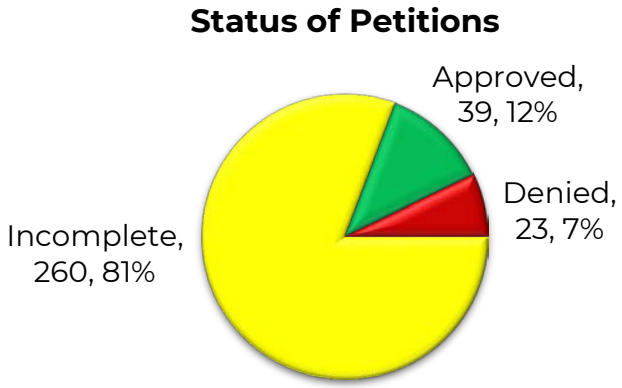
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020





Prior Authorization of Antiviral Medications

There were 322 prior authorization requests submitted for antiviral medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



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

Anticipated Patent Expiration(s):

- Xerese® (acyclovir/hydrocortisone 5%/1% cream): November 2022
- Rebetol® (ribavirin oral solution): October 2023
- Avaclyr™ (acyclovir 3% ophthalmic ointment): March 2026
- Sitavig® (acyclovir buccal tablet): June 2030
- Prevymis™ (letermovir oral tablet and injection): February 2033

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

- **October 2020:** The FDA approved the antiviral drug Veklury® (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40kg for the treatment of COVID-19 requiring hospitalization. Veklury® should only be administered in a hospital or health care setting capable of providing acute care comparable to inpatient hospital care. Veklury® was the first treatment for COVID-19 to receive FDA approval. An Emergency Use Authorization (EUA) for Veklury® was initially issued on May 1, 2020 that included the pediatric population, as well. While this FDA approval is not indicated for pediatric patients, the EUA still allows hospitalized pediatric patients with suspected or confirmed COVID-19 weighing 3.5kg to <40kg to use Veklury®. Clinical trials assessing the safety and efficacy of Veklury® in the pediatric patient population are ongoing. The approval of Veklury® was based on 3 randomized, controlled clinical trials in patients hospitalized with mild-to-severe COVID-19. One double-blind, placebo-controlled trial (ACTT-1) found that the median time to recovery, defined as discharge from the hospital or as hospitalized and no longer requiring supplemental oxygen, was 10 days for the Veklury® group compared to 15 days for the placebo group. The second and third study compared Veklury® for 5 days versus 10 days. Results showed that the odds of a patient's COVID-19 symptoms improving were similar for those in the 5-day group compared to those in the 10-day group, with no statistically significant differences in recovery rates or mortality rates between the 2 groups.
- **November 2020:** The FDA expanded the approved indication for Xofluza® (baloxavir marboxil) to include post-exposure prevention of influenza (flu) for patients 12 years of age and older after contact with an individual who has the flu. Additionally, Xofluza® was previously only available in tablet form and is now also available as granules for mixing in water. It was originally FDA approved in 2018 for the treatment of uncomplicated flu in patients 12 years of age and older who have been symptomatic for no more than 48 hours. The safety and efficacy of Xofluza® for post-flu exposure prevention were supported by 1 randomized, double-blind, controlled trial in which 607 patients, 12

years of age and older, who were exposed to a person with the flu in their household received either a single dose of Xofluza® or a single dose of placebo. The trial's primary endpoint was the proportion of patients who became infected with the flu virus and presented with fever and at least 1 respiratory symptoms from day 1 to day 10. Of those who received Xofluza®, 1% of patients met these criteria, compared to 13% of patients who received a placebo.

News:

- **July 2020:** The virus that causes COVID-19, SARS-CoV-2, cannot grow and spread through the body without the help of the polymerase protein. Therefore, researchers have begun looking at several molecules that interfere with the polymerase reaction, with some of them already approved to treat other viruses. Researchers identified 5 existing drugs that stop the polymerase reaction which include medications used to treat human immunodeficiency virus (HIV), cytomegalovirus (CMV), and hepatitis B (HBV). The 5 FDA approved drugs that could work against COVID-19 include Ziagen® (abacavir) and Zerit® (stavudine) (both used to treat HIV), Valcyte® (valganciclovir) and Vistide® (cidofovir) (both used to treat CMV), and Baraclude® (entecavir) (used to treat HBV). Researchers have drawn their inspiration from previous studies of the first severe acute respiratory syndrome (SARS) virus.
- **November 2020:** TaiGen Biotechnology Company announced that the FDA has approved the Investigational New Drug (IND) application for TG-1000, a novel treatment for flu-A and flu-B. TG-1000 is a novel pan-influenza antiviral, which interrupts viral replication and transmission via a cap-snatching mechanism effective against flu-A, flu-B, avian flu H7N9, and Tamiflu®-resistant viruses.

Guideline Update(s):

- **November 2020:** The National Institutes of Health (NIH) has developed COVID-19 Treatment Guidelines to provide recommendations in the treatment and management of COVID-19. A section of the guidelines provides recommendations for antiviral therapeutic management. Currently remdesivir is the only FDA-approved drug for the treatment of COVID-19. In hospitalized patients that require supplemental oxygen, remdesivir alone is recommended if minimal supplemental oxygen is needed (BIIa*) and remdesivir plus dexamethasone is recommended for patients who require increasing amounts of supplemental oxygen (BIII*). For hospitalized patients that require oxygen delivery through a high-flow device or noninvasive ventilation, remdesivir plus dexamethasone or dexamethasone alone is recommended (BIII*). The guidelines also recommend against the use of chloroquine or hydroxychloroquine with or without azithromycin for the treatment of

COVID-19 in hospitalized patients, except in a clinical trial setting. They also recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors and ivermectin to treat COVID-19, except in a clinical trial setting.
*BIIa = Moderate recommendation with other randomized trials or subgroup analyses of randomized trials; BIII = Moderate recommendation with expert opinion

Pipeline:

- **DAS181:** Ansun Biopharma announced the start of a Phase 3 randomized, placebo-controlled, multicenter clinical trial evaluating the safety and efficacy of DAS181 for the treatment of hospitalized, immunocompromised patients with lower respiratory tract parainfluenza virus infection. The Phase 3 clinical trial (STOP PIV) is being conducted in multiple study centers throughout the United States, Europe, and Asia. DAS181 is a recombinant sialidase protein that can cleave sialic acid, which the virus uses as a receptor, located on the surface of epithelial cells lining the human respiratory tract. DAS181 can block virus entry into respiratory epithelial cells, thus preventing viral infection and spreading. DAS181 has anti-viral activity against parainfluenza, metapneumovirus, enterovirus, and the flu, including strains of the flu that have developed resistance to other drugs and pandemic strains, such as H7N9, H5N1, and H1N1.

Recommendations

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

Utilization Details of Antiviral Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
ACYCLOVIR PRODUCTS						
ACYCLOVIR SUS 200/5ML	836	627	$69,255.01	$82.84	1.33	22.90%
ZOVIRAX CRE 5%	199	147	$159,662.80	$802.33	1.35	52.79%
ACYCLOVIR CRE 5%	74	71	$56,135.49	$758.59	1.04	18.56%
ACYCLOVIR OIN 5%	3	3	$171.65	$57.22	1.00	0.06%
SUBTOTAL	**1,112**	**848**	**$285,224.95**	**$256.50**	**1.31**	**94.31%**
LETERMOVIR PRODUCTS						
PREVYMIS TAB 480MG	3	1	$17,222.19	$5,740.73	3.00	5.69%
SUBTOTAL	**3**	**1**	**$17,222.19**	**$5,740.73**	**3.00**	**5.69%**
TOTAL	**1,115**	**833***	**$302,447.14**	**$271.25**	**1.34**	**100%**

TAB = tablet; SUS = suspension; CRE = cream; OIN = ointment
*Total number of unduplicated utilizing members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/2020. Last accessed 12/11/2020.
[2] U.S. FDA. FDA Approves First Treatment for COVID-19. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19. Issued 10/22/2020. Last accessed 12/11/2020.
[3] U.S. FDA. FDA Expands Approval of Influenza Treatment to Post-Exposure Prevention. Available online at: https://www.fda.gov/news-events/press-announcements/fda-expands-approval-influenza-treatment-post-exposure-prevention. Issued 11/23/2020. Last accessed 12/11/2020.
[4] TaiGen Biotechnology Company. TaiGen Announces FDA Approval of IND for Its Flu Antiviral TG-1000. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/taigen-announces-fda-approval-of-ind-for-its-flu-antiviral-tg-1000-301164444.html. Issued 11/01/2020. Last accessed 12/11/2020.
[5] Weintraub A. 5 FDA-Approved Antivirals Could Target COVID-19: Study. *Fierce Biotech*. Available online at: https://www.fiercebiotech.com/research/five-fda-approved-antivirals-could-target-covid-19-study. Last revised 07/01/2020. Last accessed 12/11/2020.
[6] COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. *National Institutes of Health*. Available online at: http://www.covid19treatmentguidelines.nih.gov/. Last revised 11/03/2020. Last accessed 12/11/2020.
[7] Ansun BioPharma. Ansun Biopharma Announces First Patient Enrolled in Phase 3 Clinical Trial Evaluating DAS181 in Hospitalized, Immunocompromised Patients with Lower Respiratory Tract Parainfluenza Virus Infection. *PR Newswire*. Available online at: https://www.biospace.com/article/releases/ansun-biopharma-announces-first-patient-enrolled-in-phase-3-clinical-trial-evaluating-das181-in-hospitalized-immunocompromised-patients-with-lower-respiratory-tract-parainfluenza-virus-infection/. Issued 05/28/2019. Last accessed 12/11/2020.

Appendix G

Fiscal Year 2020 Annual Review of Korlym® (Mifepristone)

Oklahoma Health Care Authority
January 2021

Current Prior Authorization Criteria

Korlym® (Mifepristone) Approval Criteria:

1. An FDA approved indication to control hyperglycemia secondary to hypercortisolism in adult members 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 an advanced care practitioner with a supervising physician who is an endocrinologist); and
5. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
6. Female members of reproductive potential must use a non-hormonal, medically acceptable method of contraception (unless member has undergone surgical sterilization) during treatment with Korlym® and for at least 1 month after discontinuing treatment; and
7. Member must not have any contraindications to taking Korlym® including the following:
    a. Taking drugs metabolized by CYP3A4 (e.g., simvastatin, lovastatin) and/or CYP3A substrates with narrow therapeutic ranges (e.g., cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, 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.

Utilization of Korlym® (Mifepristone): Fiscal Year 2020

Comparison of Fiscal Years

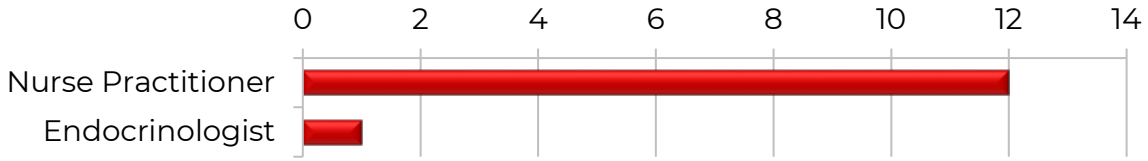
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1	11	$206,048.79	$18,731.71	$624.39	450	330
2020	2	13	$192,668.27	$14,820.64	$529.31	378	364
% Change	**100.00%**	**18.20%**	**-6.50%**	**-20.90%**	**-15.20%**	**-16.00%**	**10.30%**
Change	**1**	**2**	**-$13,380.52**	**-$3,911.07**	**-$95.08**	**-72**	**34**

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

Demographics of Members Utilizing Korlym® (Mifepristone)

- There were 2 unique members utilizing Korlym® (mifepristone) during fiscal year 2020. Due to the limited number of utilizing members, detailed demographic information could not be provided.

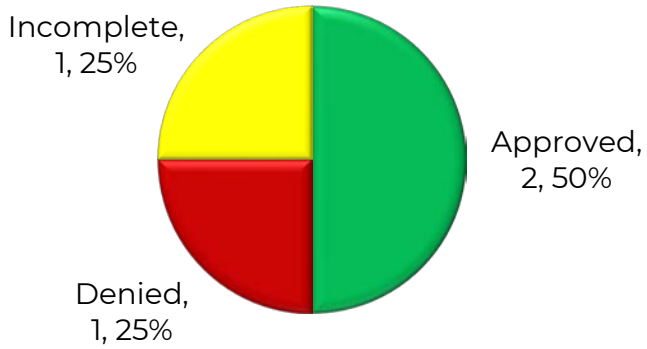
Top Prescriber Specialties of Korlym® (Mifepristone) by Number of Claims



Prior Authorization of Korlym® (Mifepristone)

There were 4 prior authorization requests submitted for Korlym® (mifepristone) during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[1]

Anticipated Patent Expiration(s):

- Korlym® (mifepristone): August 2038

Recommendations

The College of Pharmacy does not recommend any changes to the current Korlym® (mifepristone) prior authorization criteria at this time.

Utilization Details of Korlym® (Mifepristone): Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
KORLYM TAB 300MG	13	2	$192,668.27	$14,820.64	6.5
TOTAL	**13**	**2***	**$192,668.27**	**$14,820.64**	**6.5**

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

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/2020. Last accessed 12/10/2020.

Appendix H

Fiscal Year 2020 Annual Review of Turalio® (Pexidartinib)

Oklahoma Health Care Authority
January 2021

Introduction[1]

Tenosynovial giant cell tumor (TGCT), also referred to as pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), is a rare, non-malignant tumor that can be locally aggressive. TGCT affects the synovium-lined joints, bursae, and tendon sheaths, resulting in reduced mobility in the affected limb or joint. The exact incidence of TGCT is not known; however, it is estimated to be 11 to 50 cases per 1 million person-years, based on studies from 3 countries. TGCT is subcategorized into 2 types, localized and diffuse. Localized TGCT is more common and accounts for 80 to 90% of cases. TGCT affects all age groups. The localized type is more common between 30 and 50 years of age, and the diffuse type occurs most often in individuals younger than 40 years of age.

The current standard of care for TGCT is surgical resection. In patients with recurrent, difficult-to-treat, or diffuse forms of TGCT, the tumor may wrap around ligaments, tendons, bone, or other parts of the joint. In these cases, the tumor may not be amenable to improvement with surgery or may be difficult to remove with surgery. Multiple surgeries for more severe cases may lead to significant joint damage, debilitating functional impairments, reduced quality of life, and amputation. Following complete resection, recurrence rates for localized TGCT are estimated to be up to 15%. Diffuse TGCT recurrence rates are estimated to be approximately 20 to 50% following complete resection. In August 2019, the U.S. Food and Drug Administration (FDA) approved Turalio® (pexidartinib) as the first and only treatment for adult patients with symptomatic TGCT associated with severe morbidity or functional limitations not amenable to improvement with surgery. Prior to FDA approval in January 2019, the American Society of Clinical Oncology (ASCO) selected pexidartinib as 1 of 5 significant advances in rare disease treatment, calling it the first promising investigational therapy for TGCT.

Current Prior Authorization Criteria

Turalio® (Pexidartinib) Approval Criteria [Soft Tissue Sarcoma – Pigmented Villonodular Synovitis (PVNS)/Tenosynovial Giant Cell Tumor (TGCT) Diagnosis]:

1. Member must not be a candidate for surgery; and
2. Used as a single-agent.

Utilization of Turalio® (Pexidartinib): Fiscal Year 2020

There was no SoonerCare utilization of Turalio® (pexidartinib) during fiscal year 2020 (fiscal year 2020 = 07/01/2019 to 06/30/2020).

Prior Authorization of Turalio® (Pexidartinib)

There were no prior authorization requests submitted for Turalio® (pexidartinib) during fiscal year 2020.

Recommendations

The College of Pharmacy does not recommend any changes to the current Turalio® (pexidartinib) prior authorization criteria at this time.

[1] Daiichi-Sankyo. Press Release: FDA Approves Daiichi Sankyo's Turalio® (Pexidartinib) for the Treatment of Select Patients with TGCT, a Rare and Debilitating Tumor. Available online at: https://dsi.com/press-releases/-/article/364091/10481984. Issued 08/02/2019. Last accessed 12/13/2020.

Appendix I

Fiscal Year 2020 Annual Review of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)

Oklahoma Health Care Authority
January 2021

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

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, clinically aggressive hematologic malignancy arising from precursors of myeloid-derived plasmacytoid dendritic cells (type 2 dendritic cells). The nomenclature used to describe BPDCN has evolved over the years along with the understanding of the underlying biology. The exact incidence of BPDCN is unknown due to constantly changing nomenclature and lack of precise defining criteria prior to the 2008 World Health Organization classification system. BPDCN represents 0.7% of primary cutaneous skin lymphomas; however, cutaneous lymphoma registries likely underestimate the true incidence of BPDCN because some patients present without skin lesions. BPDCN is most common in adults and the majority of patients are older adults, but it has been described in all age groups. There is a male to female ratio of approximately 2.5:1. Optimal management of BPDCN is not well defined; however, treatment suggestions are stratified by age because outcomes are generally more favorable in children than in adults. In December 2018, the U.S. Food and Drug Administration (FDA) approved Elzonris® (tagraxofusp-erzs) for the treatment of BPDCN in adults and pediatric patients 2 years of age and older. Prior to this approval, there were no FDA approved therapies for BPDCN, and treatment consisted of intensive chemotherapy followed by bone marrow transplantation.

Myelofibrosis is a type of chronic leukemia. It belongs to a group of related blood cancers known as “myeloproliferative neoplasms (MPNs)” in which bone marrow cells that produce blood cells function abnormally. The result is excessive fibrous tissue formation in the bone marrow, which can lead to severe anemia, weakness, fatigue, splenomegaly, and hepatomegaly. Myelofibrosis can occur on its own (primary myelofibrosis) or as a result of another bone marrow disorder, such as polycythemia vera (PV) or essential thrombocythemia (ET). Between 15 to 20% of myelofibrosis cases begin as either PV or ET. Myelofibrosis occurs in approximately 1.5 out of 100,000 individuals in the United States each year. The disease affects both men and women and is usually diagnosed in patients older than 60 years of age, but can occur at any age. In August 2019, the FDA approved Inrebic® (fedratinib) for the treatment of adult patients with certain types of myelofibrosis. Prior to

this approval, Jakafi® (ruxolitinib) was the only FDA approved treatment for myelofibrosis. Jakafi® entered the marketplace in 2011.

Current Prior Authorization Criteria

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. 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 disease (post-polycythemia vera or post-essential thrombocythemia).

Utilization of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib): Fiscal Year 2020

There was no pharmacy or medical SoonerCare utilization of Elzonris® (tagraxofusp-erzs) or Inrebic® (fedratinib) during fiscal year 2020 (fiscal year 2020 = 07/01/2019 to 06/30/2020).

Prior Authorization of Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)

There were no prior authorization requests submitted for Elzonris® (tagraxofusp-erzs) or Inrebic® (fedratinib) during fiscal year 2020.

Recommendations

The College of Pharmacy does not recommend any changes to the current Elzonris® (tagraxofusp-erzs) or Inrebic® (fedratinib) prior authorization criteria at this time.

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[1] Gurbuxani S. Blastic Plasmacytoid Dendritic Cell Neoplasm. *UpToDate*. Available online at: https://www.uptodate.com/contents/blastic-plasmacytoid-dendritic-cell-neoplasm. Last revised 09/12/2019. Last accessed 12/14/2020.
[2] Elzonris® (Tagraxofusp-erzs) – BPDCN Overview. Stemline Therapeutics, Inc. Available online at: https://www.elzonris.com/hcp/what-is-bpdcn. Last accessed 12/14/2020.
[3] Elzonris® (Tagraxofusp-erzs) – New Orphan Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_elzonris_2018-1224.pdf. Last accessed 12/14/2020.
[4] Myelofibrosis Facts. *Leukemia and Lymphoma Society*. Available online at: https://www.lls.org/sites/default/files/file_assets/FS14_Myelofibrosis%20Fact%20Sheet.pdf. Last revised 11/2015. Last accessed 12/14/2020.
[5] Nelson R. FDA Approves Fedratinib for the Treatment of Myelofibrosis. *Medscape*. Available online at: https://www.medscape.com/viewarticle/916928. Issued 08/16/2019. Last accessed 12/14/2020.

Appendix J

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

Oklahoma Health Care Authority
January 2021

Introduction[1,2,3,4]

Proopiomelanocortin (POMC) deficiency is caused by mutations in the *POMC* gene and is characterized by severe obesity that begins at an early age. These *POMC* gene mutations result in production of an abnormally short version of the POMC protein or no protein at all. As a result, there is a shortage of adrenocorticotropic hormone (ACTH), alpha-melanocyte stimulating hormone (α-MSH), and beta-melanocyte stimulating hormone (β-MSH). Without ACTH, there is a reduction in cortisol production, leading to adrenal insufficiency. Loss of α-MSH and β-MSH in the brain dysregulates the body's energy balance, leading to overeating and severe obesity. Affected infants are usually a normal weight at birth, but are constantly hungry, leading to excessive feeding and ultimately obesity by 1 year of age which continues throughout life. This condition is inherited in an autosomal recessive pattern. POMC deficiency is a rare condition with approximately 50 cases reported in the medical literature.

Leptin receptor (LEPR) deficiency is caused by mutations in the *LEPR* gene. This gene provides instructions for making the LEPR, which is involved in the regulation of body weight. LEPRs are found on the surface of cells in many organs and tissues of the body including the hypothalamus which controls hunger. *LEPR* gene mutations that cause LEPR deficiency prevent the receptor from responding to leptin (a hormone that binds to LEPR in the hypothalamus to signal satiety), leading to excessive hunger and weight gain associated with this disorder. Affected infants are of normal weight at birth, but are constantly hungry and quickly gain weight. The extreme hunger leads to chronic excessive eating and obesity beginning in the first few months of life. Individuals with LEPR deficiency also have hypogonadotropic hypogonadism, caused by reduced production of hormones that direct sexual development. LEPR deficiency is a rare cause of obesity, and its prevalence is unknown.

Proprotein convertase subtilisin/kexin type 1 (PCSK1) deficiency is caused by mutations in the *PCSK1* gene. Individuals with mutations in the *PCSK1* gene exhibit a variable syndrome consisting of obesity, malabsorptive diarrhea, hypogonadotropic hypogonadism, altered thyroid and adrenal function, and impaired regulation of plasma glucose levels in association with

elevated circulating proinsulin-to-insulin ratio. Some variants in the *PCSK1* gene have been found to be associated with alterations in body mass index (BMI), increased circulating proinsulin levels, and defects in glucose homeostasis. PCSK1 deficiency is rare, and its prevalence is unknown.

The melanocortin pathway consists of neurons in the hypothalamus that activate the melanocortin 4 (MC4) receptor. Leptin binds to LEPRs on POMC-expressing neurons in the hypothalamus. In the fed state, leptin stimulates POMC production, which is processed by PCSK1 into α-MSH and β-MSH that bind to and activate MC4, reducing food intake. In November 2020, the U.S. Food and Drug Administration (FDA) approved Imcivree™ (setmelanotide), an MC4 agonist, for chronic weight management in patients with obesity due to POMC, PCSK1, or LEPR deficiency.

Imcivree™ (Setmelanotide) Product Summary[4,5]

Indication(s): Imcivree™ (setmelanotide) is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1, or LEPR deficiency confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance.

Limitation(s) of Use: Imcivree™ is not indicated for the treatment of patients with the following conditions as it would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with *POMC, PCSK1, or LEPR* variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general obesity

Dosing and Administration:

- Imcivree™ is supplied as a 10mg/mL solution in a 1mL multiple-dose vial (MDV).
- Unopened Imcivree™ MDVs should be stored refrigerated at 2°C to 8°C (36°F to 46°F).
- Unopened or opened MDVs can be stored at room temperature [up to 25°C (77°F)] for up to 30 days. Once opened, MDVs should be discarded after 30 days.
- Imcivree™ is administered subcutaneously (sub-Q) in the abdomen, thigh, or arm; injection sites should be rotated daily.
- Prior to initiation of Imcivree™, patients or caregivers should be trained on proper sub-Q injection technique.
- Imcivree™ should be administered at the beginning of the day without regard to meals.

- The recommended dosing of Imcivree™ varies based on patient age and tolerance, as follows:
  - Adults and pediatric patients 12 years of age and older:
    - *Starting dose:* 2mg given sub-Q once daily for 2 weeks
    - *If starting dose is not tolerated:* Reduce dose to 1mg once daily
    - *If 2mg is tolerated and additional weight loss is desired:* Increase dose to 3mg once daily
  - Pediatric patients 6 years to younger than 12 years of age:
    - *Starting dose:* 1mg given sub-Q once daily for 2 weeks
    - *If starting dose is not tolerated:* Reduce dose to 0.5mg once daily
    - *If 1mg is tolerated:* Increase dose to 2mg once daily
    - *If 2mg is tolerated and additional weight loss is desired:* Increase dose to 3mg once daily
- Weight loss should be evaluated after 12 to 16 weeks of treatment; if weight loss of ≥5% of baseline body weight or ≥5% of baseline BMI (for patients with growth potential) has not been achieved, Imcivree™ should be discontinued.

Mechanism of Action: Setmelanotide is an MC4 receptor agonist. MC4 receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure. In patients with obesity due to POMC, PCSK1, and LEPR deficiency associated with insufficient activation of the MC4 receptor, setmelanotide may re-establish MC4 receptor pathway activity to reduce hunger and promote weight loss through decreased caloric intake and increased energy expenditure.

Contraindication(s): None

Safety:
- **Disturbance in Sexual Arousal:** Sexual adverse reactions may occur in patients treated with setmelanotide. Spontaneous penile erections in males (23%) and sexual adverse reactions in females (7%) occurred in clinical studies. Patients should be informed that these adverse reactions may occur. Male patients should be instructed to seek emergency medical attention for an erection lasting >4 hours.
- **Depression and Suicidal Ideation:** Setmelanotide may cause depression or suicidal ideation. Patients with a history of severe depression were excluded from the clinical studies; however, depression (26%) and suicidal ideation (11%) occurred in the clinical studies. Monitoring patients for new onset or worsening depression is recommended. Discontinuing setmelanotide should be considered if patients experience suicidal thoughts or behaviors.

- **Skin Pigmentation and Darkening of Pre-Existing Nevi:** Setmelanotide may cause generalized increased skin pigmentation and darkening of pre-existing nevi. Skin hyperpigmentation occurred in 78% of patients treated with setmelanotide in the clinical studies. This effect is reversible upon discontinuation of the drug.
- **Immunogenicity:** Approximately 61% of adult and pediatric patients with POMC or LEPR deficiency who received setmelanotide (N=28) screened positive for antibodies to setmelanotide; however, all patients who screened positive for antibodies were inconclusive for antibodies to setmelanotide in the confirmatory assay. There was no observation of a rapid decline in setmelanotide concentrations to suggest the presence of anti-drug antibodies.
- **Pregnancy:** Discontinuation of setmelanotide is recommended when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus. Setmelanotide MDVs contain the preservative benzyl alcohol. Because benzyl alcohol is rapidly metabolized by a pregnant woman, its exposure in the fetus is unlikely. However, adverse reactions have occurred in premature neonates and low birth weight infants who received intravenously (IV) administered benzyl alcohol-containing drugs. There are no available data for the use of setmelanotide in pregnant women to inform a drug-associated risk for major birth defects and miscarriage or adverse maternal or fetal outcomes.
- **Lactation:** Treatment with setmelanotide is not recommended for use while breastfeeding due to the preservative benzyl alcohol contained in the MDVs. There is no information on the presence of setmelanotide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. However, setmelanotide is present in the milk of rats.
- **Pediatric Use:** The safety and effectiveness of setmelanotide for obesity due to POMC, PCSK1, or LEPR deficiency have been established in pediatric patients 6 years of age and older. Use of setmelanotide for this indication is supported by evidence from 2 open-label studies that included 9 pediatric patients. The safety and effectiveness of setmelanotide have not been established in pediatric patients younger than 6 years of age. Setmelanotide is not approved for use in neonates or infants. Serious adverse reactions including fatal reactions and “gasping syndrome” occurred in premature neonates and low birth weight infants in the neonatal intensive care unit who received drugs containing benzyl alcohol as a preservative.
- **Geriatric Use:** Clinical studies of setmelanotide did not include patients 65 years of age and older; therefore, it is not known whether they respond differently from younger patients.

- **Renal Impairment:** Population pharmacokinetic analysis of setmelanotide suggests decreased clearance in patients with renal impairment. The majority of patients in the clinical studies of setmelanotide had normal renal function. No dose adjustments of setmelanotide for patients with mild renal impairment [estimated glomerular filtration rate (eGFR) of 60 to 89mL/min/1.73m^2] are needed. Setmelanotide is not recommended for use in patients with moderate (eGFR 30 to 59mL/min/1.73m^2) or severe (eGFR 15 to 29mL/min/1.73m^2) renal impairment or end stage renal disease (eGFR<15mL/min/1.73m^2).

Adverse Reactions: The most common adverse reactions, occurring in ≥20% of patients treated with setmelanotide in the 52-week open-label clinical study, were injection site reaction, skin hyperpigmentation, nausea, headache, diarrhea, abdominal pain, back pain, fatigue, vomiting, depression, upper respiratory tract infection, and spontaneous penile erection.

Efficacy: The safety and efficacy of setmelanotide for chronic weight management in 21 patients with obesity due to POMC, PCSK1, and LEPR deficiency were evaluated in 2 identically designed, 1-year, open-label studies, each with an 8-week, double-blind withdrawal period. In both studies, adult patients had a BMI of ≥30kg/m^2 and pediatric patients had a weight ≥95th percentile using growth chart assessments. Dose titration occurred over a 2- to 12-week period, followed by a 10-week, open-label treatment period. Patients who achieved ≥5kg weight loss (or ≥5% weight loss if baseline body weight was <100kg) at the end of the open-label treatment period continued into a double-blind withdrawal period lasting 8 weeks, including 4 weeks of setmelanotide followed by 4 weeks of placebo. Following the withdrawal sequence, patients re-initiated active treatment with setmelanotide at the therapeutic dose for up to 32 weeks. The primary endpoint was the proportion of patients with ≥10% weight loss compared with baseline at approximately 1 year. A key secondary endpoint, for patients 12 years of age and older, was the mean percentage change in the most hunger score on the 11-point Likert-type scale (0 = not hungry at all to 10 = hungriest possible) at approximately 1 year on the therapeutic dose. The most hunger score was captured using the question, “In the last 24 hours, how hungry did you feel when you were the most hungry?”

- Study 1 Results: Study 1 included patients 6 years of age and older with obesity and genetically confirmed or suspected POMC (N=9) or PCSK1 (N=1) deficiency. The mean BMI at baseline was 40.4kg/m^2 for the adult patients and mean BMI Z-score was 3.4 for the pediatric patients. The mean most hunger score at baseline was 8. In this study, 8 of the 10 patients achieved ≥10% weight loss compared to baseline at 1 year (P<0.0001 compared with historical data). Additionally, the mean percent change in body weight compared with baseline at 1 year for

the designated use set (defined as all patients who received at least 1 dose of study medication and had a baseline assessment, N=10) was -25.6% (P<0.0001). The most hunger score decreased to 5.8 (-27.1%; P=0.0005) at 1 year in 7 patients. Additional parameters with a statistically significant favorable change from baseline after 1 year of treatment with a therapeutic dose of setmelanotide included: waist circumference, non-bone lean mass, total fat mass, fasting glucose, high-density lipoprotein (HDL) cholesterol, and triglycerides.

- Study 2 Results: Study 2 included 11 patients, 6 years of age and older, with obesity and genetically confirmed or suspected LEPR deficiency. The mean BMI at baseline was 48.2kg/m^2 for the adult patients and mean BMI Z-score was 3.5 for the pediatric patients. The mean most hunger score at baseline was 7.1. In this study, 5 of the 11 patients achieved ≥10% weight loss compared to baseline at 1 year (P=0.0001 compared with historical data). Additionally, the mean percent change in body weight compared with baseline at 1 year for the designated use set (N=9) was -12.5% (P<0.0001). The most hunger score decreased to 4.1 (-43.7%; P<0.0001) at 1 year in 7 patients. Additional parameters with a statistically significant favorable change from baseline after 1 year of treatment with a therapeutic dose of setmelanotide included: waist circumference, non-bone lean mass, total fat mass, HDL cholesterol, and low-density lipoprotein (LDL) cholesterol.

Cost: Cost information for Imcivree™ (setmelanotide) is not yet available.

Recommendations

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

Imcivree™ (Setmelanotide) Approval Criteria:

1. An FDA approved indication of chronic weight management in adult and pediatric members 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency; and
2. Molecular genetic testing to confirm variants in the *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance; and
3. Requests for Imcivree™ for obesity due to suspected POMC-, PCSK1-, or LEPR-deficiency with *POMC, PCSK1, or LEPR* variants classified as benign or likely benign, obesity associated with other genetic syndromes, or general obesity will not be approved; and
4. Member's baseline weight and body mass index (BMI) must be provided; and

5. Baseline BMI must be ≥30kg/m^2 for adults or ≥95th percentile on BMI-for-age growth chart assessment for children; and
6. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Imcivree™ therapy and throughout treatment; and
7. Prescriber must verify member has been counseled on potential sexual adverse reactions and when to seek emergency medical care; and
8. Prescriber must verify member does not have moderate, severe, or end stage renal disease [estimated glomerular filtration rate (eGFR) 59 to <15mL/min/1.73m^2]; and
9. Prescriber must verify female member is not pregnant or breastfeeding; and
10. Prescriber must confirm member or caregiver has been trained on the proper storage and administration of Imcivree™ prior to the first dose; and
11. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member's current weight or BMI and member has achieved weight loss of ≥5% of baseline body weight or ≥5% of BMI; and
12. A quantity limit of 9mL per 30 days will apply.

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Appendix K

U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: December 11, 2020

FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine

The FDA issued the first emergency use authorization (EUA) for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The EUA allows the Pfizer-BioNTech COVID-19 Vaccine to be distributed in the United States.

"The FDA's authorization for emergency use of the first COVID-19 vaccine is a significant milestone in battling this devastating pandemic that has affected so many families in the United States and around the world," said FDA Commissioner Stephen M. Hahn, M.D. "Today's action follows an open and transparent review process that included input from independent scientific and public health experts and a thorough evaluation by the agency's career scientists to ensure this vaccine met FDA's rigorous, scientific standards for safety, effectiveness, and manufacturing quality needed to support emergency use authorization. The tireless work to develop a new vaccine to prevent this novel, serious, and life-threatening disease in an expedited timeframe after its emergence is a true testament to scientific innovation and public-private collaboration worldwide."

The FDA has determined that Pfizer-BioNTech COVID-19 Vaccine has met the statutory criteria for issuance of an EUA. The totality of the available data provides clear evidence that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19. The data also support that the known and potential benefits outweigh the known and potential risks, supporting the vaccine's use in millions of people 16 years of age and older, including healthy individuals. By making this determination, the FDA is assuring the public and medical community that it has conducted a thorough evaluation of the available safety, effectiveness, and manufacturing quality information.

The Pfizer-BioNTech COVID-19 Vaccine contains a small piece of the SARS-CoV-2 virus' messenger ribonucleic acid (mRNA) that instructs cells in the body to make the virus' distinctive "spike" protein. When a person receives this vaccine, their body produces copies of the spike protein, which does not cause disease, but triggers the immune system to learn to react defensively, producing an immune response against SARS-CoV-2.

"While not an FDA approval, today's emergency use authorization of the Pfizer-BioNTech COVID-19 Vaccine holds the promise to alter the course of this pandemic in the United States," said Peter Marks, M.D., Ph.D., Director of the FDA's Center for Biologics Evaluation and Research. "With science guiding our decision-making, the available safety and effectiveness data support the authorization of the Pfizer-BioNTech COVID-19 Vaccine because the vaccine's known and potential benefits clearly outweigh its known and potential risks. The data provided by the sponsor have met the FDA's expectations as conveyed in our June and October guidance documents. Efforts to speed vaccine development have not sacrificed scientific standards or the integrity of our vaccine evaluation process. The FDA's review process also included public and independent review from members of the agency's Vaccines and Related Biological Products Advisory Committee. Today's achievement is ultimately a testament to the commitment of our career scientists and physicians, who worked tirelessly to thoroughly evaluate the data and information for this vaccine."

FDA Evaluation of Available Safety Data:

Pfizer BioNTech COVID-19 Vaccine is administered as a series of 2 doses, 3 weeks apart. The available safety data to support the EUA include 37,586 of the patients enrolled in an ongoing randomized, placebo-controlled international study, the majority of whom are from the United States. These patients, 18,801 of whom received the vaccine and 18,785 of whom received saline placebo, were followed for a median of 2 months after receiving the second dose. The most commonly reported side effects, which typically lasted several days, were pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, and fever. Of note, more people experienced these side effects after the second dose than after the first dose, so it is important for vaccination providers and recipients to expect that there may be some side effects after either dose, but may be more likely after the second dose.

It is mandatory for Pfizer and vaccination providers to report the following to the Vaccine Adverse Event Reporting System (VAERS) for Pfizer-BioNTech COVID-19 Vaccine: all vaccine administration errors, serious adverse events, cases of multisystem inflammatory syndrome (MIS), and cases of COVID-19 that result in hospitalization or death.

FDA Evaluation of Available Effectiveness Data:

The effectiveness data to support the EUA include an analysis of 36,523 patients in the ongoing randomized, placebo-controlled international study, the majority of whom are from the United States, who did not have evidence of SARS-CoV-2 infection through 7 days after the second dose. Among these patients, 18,198 received the vaccine and 18,325 received placebo. The vaccine was 95% effective in preventing COVID-19 disease among these clinical trial patients with 8 COVID-19 cases in the vaccine group and 162 in the placebo group. Of these 170 COVID-19 cases, 1 in the vaccine group and 3 in the placebo group were classified as severe. At this time, data are not available to

make a determination about how long the vaccine will provide protection, nor is there evidence that the vaccine prevents transmission of SARS-CoV-2 from person to person.

The EUA Process:

On the basis of the determination by the Secretary of the Department of Health and Human Services on February 4, 2020, that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and who then issued declarations that circumstances exist justifying the authorization of emergency use of unapproved products, the FDA may issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent COVID-19 when there are no adequate, approved, and available alternatives.

The issuance of an EUA is different than an FDA approval of a vaccine. In determining whether to issue an EUA for a product, the FDA evaluates the available evidence and assesses any known or potential risks and any known or potential benefits, and if the benefit-risk assessment is favorable, the product is made available during the emergency. Once a manufacturer submits an EUA request for a COVID-19 vaccine to the FDA, the agency then evaluates the request and determines whether the relevant statutory criteria are met, taking into account the totality of the scientific evidence about the vaccine that is available to the FDA.

The EUA also requires fact sheets that provide important information, including dosing instructions and information about the benefits and risks of the Pfizer-BioNTech COVID-19 Vaccine, be made available to vaccination providers and vaccine recipients.

The company has submitted a pharmacovigilance plan to the FDA to monitor the safety of Pfizer-BioNTech COVID-19 Vaccine. The pharmacovigilance plan includes a plan to complete longer-term safety follow-up for patients enrolled in ongoing clinical trials. The pharmacovigilance plan also includes other activities aimed at monitoring the safety profile of the Pfizer-BioNTech COVID-19 vaccine and ensuring that any safety concerns are identified and evaluated in a timely manner.

The FDA also expects manufacturers whose COVID-19 vaccines are authorized under an EUA to continue their clinical trials to obtain additional safety and effectiveness information and pursue approval.

The EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated, and may be revised or revoked if it is determined the EUA no longer meets the statutory criteria for issuance.

FDA NEWS RELEASE

For Immediate Release: December 09, 2020

Coronavirus (COVID-19) Update: FDA Authorizes First Direct-to-Consumer COVID-19 Test System

The FDA authorized LabCorp's Pixel COVID-19 Test Home Collection Kit for use by any individual 18 years of age and older without a prescription. This product, which is authorized as the first COVID-19 direct-to-consumer (non-prescription) test system, allows an individual to self-collect a nasal swab sample at home and then send that sample for testing to LabCorp. Positive or invalid test results are then delivered to the user via phone call from a health care provider. Negative test results are delivered via email or online portal.

This home sample collection kit can be purchased online or in a store without a prescription. It is intended to enable users to access information about their COVID-19 infection status that could aid with determining if self-isolation is appropriate and to assist with health care decisions after discussion with a health care professional. "This is the first kit for consumers to self-collect a nasal sample for COVID-19 in their home that does not require a prescription," said Jeff Shuren, M.D., J.D., director of FDA's Center for Devices and Radiological Health. "While many home collection kits can be prescribed with a simple online questionnaire, this newly authorized direct-to-consumer collection kit removes that step from the process, allowing anyone to collect their sample and send it to the lab for processing."

FDA NEWS RELEASE

For Immediate Release: November 23, 2020

FDA Approves First Drug to Treat Rare Metabolic Disorder

The FDA approved Oxlumo™ (lumasiran) as the first treatment for primary hyperoxaluria type 1 (PH1), a rare genetic disorder. This approval is a cumulation of the work of experts and community members coordinated by the Oxalosis & Hyperoxaluria Foundation and the Kidney Health Initiative.

"The approval of Oxlumo™ represents a great triumph of community involvement to address a rare disease. It is a result of input from patients, treating physicians, experts and sponsors at a patient-focused drug development meeting and through other collaborative efforts," said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiology and Nephrology in the FDA's Center for Drug Evaluation and Research.

Primary hyperoxalurias (PHs) are caused by excess production of oxalate, a substance consumed in food and also produced by the body. PH1 is the most common and severe type. PH1 affects an estimated 1 to 3 individuals per million in North America and Europe and accounts for approximately 80% of PH cases.

Patients with PH1 produce too much oxalate, which can combine with calcium to cause kidney stones and deposits in the kidneys. Patients can experience progressive kidney damage, which can lead to kidney failure and

the need for dialysis. As kidney function worsens, oxalate can build up and damage other organs, including the heart, bones, and eyes.

Oxlumo™ works to decrease oxalate production. It was evaluated in 2 studies in patients with PH1: a randomized, placebo-controlled study in patients 6 years of age and older and an open-label study in patients younger than 6 years of age. Patients ranged in age from 4 months to 61 years at the first dose. In the first study, 26 patients received a monthly injection of Oxlumo™ followed by a maintenance dose every 3 months; 13 patients received placebo injections. The primary endpoint was the amount of oxalate measured in the urine over 24 hours. In the Oxlumo™ group, patients had, on average, a 65% reduction of oxalate in the urine, compared to an average 12% reduction in the placebo group. By the sixth month of the study, 52% of patients treated with Oxlumo™ reached a normal 24-hour urinary oxalate level; patients treated with the placebo did not reach a normal level.

In the second study, 16 patients younger than 6 years of age all received Oxlumo™. Using another measure of oxalate in the urine, the study showed, on average, a 71% decrease in urinary oxalate by the sixth month of the study. The most common side effects of Oxlumo™ include injection site reaction and abdominal pain.

Oxlumo™ received Orphan Drug and Breakthrough Therapy designations, as well as a Rare Pediatric Disease Priority Review voucher. The FDA granted the approval of Oxlumo™ to Alnylam Pharmaceuticals, Inc.

FDA NEWS RELEASE

For Immediate Release: November 23, 2020

FDA Expands Approval of Influenza Treatment to Post-Exposure Prevention

The FDA expanded the approved indication for Xofluza® (baloxavir marboxil) to include post-exposure prevention of influenza (flu) for patients 12 years of age and older after contact with an individual who has the flu. Xofluza®, previously available only in tablet form, is now available as granules for mixing in water. Xofluza® was originally approved in 2018 for treating uncomplicated flu in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

“This expanded indication for Xofluza® will provide an important option to help prevent influenza just in time for a flu season that is anticipated to be unlike any other because it will coincide with the coronavirus pandemic,” said Debra Birnkrant, M.D., director of the Division of Antiviral Products in the FDA’s Center for Drug Evaluation and Research. “Americans will have to be more vigilant than ever as these viruses spread concurrently.”

Xofluza®’s safety and efficacy for post-flu exposure prevention is supported by 1 randomized, double-blind, placebo-controlled trial in which 607 patients, 12 years of age and older who were exposed to a person with flu in their household, received either a single dose of Xofluza® or a single dose of

a placebo. Of these 607 patients, 303 received Xofluza® and 304 received the placebo. The trial's primary endpoint was the proportion of patients who were infected with flu virus and presented with fever and at least 1 respiratory symptom from day 1 to day 10. Of those who received Xofluza®, 1% of patients met these criteria, compared to 13% of patients who received a placebo for the clinical trial.

The most common side effects of Xofluza® include diarrhea, bronchitis, nausea, sinusitis, and headache. Hypersensitivity, including anaphylaxis, can occur in patients taking Xofluza®. Patients should not take Xofluza® if they have had a known hypersensitivity reaction to Xofluza®. Xofluza® should not be co-administered with dairy products, calcium-fortified beverages, or laxatives, antacids, or oral supplements containing calcium, iron, magnesium, selenium, aluminum, or zinc. The FDA granted the approval of Xofluza® to Genentech USA, Inc.

FDA NEWS RELEASE

For Immediate Release: November 21, 2020

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19

The FDA issued an EUA for casirivimab and imdevimab to be administered together for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age or older weighing at least 40kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19. This includes those who are 65 years of age or older or who have certain chronic medical conditions.

In a clinical trial of patients with COVID-19, casirivimab and imdevimab, administered together, were shown to reduce COVID-19-related hospitalization or emergency room (ER) visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Casirivimab and imdevimab must be administered together by intravenous (IV) infusion.

Casirivimab and imdevimab are not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of casirivimab and imdevimab treatment has not been shown in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

"The FDA remains committed to advancing the nation's public health during this unprecedented pandemic. Authorizing these monoclonal antibody therapies may help outpatients avoid hospitalization and alleviate the burden on our health care system," said FDA Commissioner Stephen M. Hahn, M.D. "As part of our Coronavirus Treatment Acceleration Program, the

FDA uses every possible pathway to make new treatments available to patients as quickly as possible while continuing to study the safety and effectiveness of these treatments."

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses. Casirivimab and imdevimab are monoclonal antibodies that are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells.

"The emergency authorization of these monoclonal antibodies administered together offers health care providers another tool in combating the pandemic," said Patrizia Cavazzoni, M.D., acting director of the FDA's Center for Drug Evaluation and Research. "We will continue to facilitate the development, evaluation, and availability of COVID-19 therapies."

Based on the FDA's review of the totality of the scientific evidence available, the agency has determined that it is reasonable to believe that casirivimab and imdevimab administered together may be effective in treating patients with mild-to-moderate COVID-19. When used to treat COVID-19 for the authorized population, the known and potential benefits of these antibodies outweigh the known and potential risks. There are no adequate, approved and available alternative treatments to casirivimab and imdevimab administered together for the authorized population.

The data supporting this EUA for casirivimab and imdevimab are based on a randomized, double-blind, placebo-controlled clinical trial in 799 non-hospitalized adults with mild-to-moderate COVID-19 symptoms. Of these patients, 266 received a single IV infusion of 2,400mg casirivimab and imdevimab (1,200mg of each), 267 received 8,000mg casirivimab and imdevimab (4,000mg of each), and 266 received a placebo, within 3 days of obtaining a positive SARS-CoV-2 viral test.

The prespecified primary endpoint for the trial was time-weighted average change in viral load from baseline. Viral load reduction in patients treated with casirivimab and imdevimab was larger than in patients treated with placebo at day 7. However, the most important evidence that casirivimab and imdevimab administered together may be effective came from the predefined secondary endpoint of medically attended visits related to COVID-19, particularly hospitalizations and ER visits within 28 days after treatment. For patients at high risk for disease progression, hospitalizations and ER visits occurred in 3% of casirivimab and imdevimab-treated patients on average compared to 9% in placebo-treated patients. The effects on viral load, reduction in hospitalizations and ER visits were similar in patients receiving either of the 2 casirivimab and imdevimab doses.

Under the EUA, fact sheets that provide important information about using casirivimab and imdevimab administered together in treating COVID-19 as authorized must be made available to health care providers and to patients and caregivers. These fact sheets include dosing instructions,

potential side effects and drug interactions. Possible side effects of casirivimab and imdevimab include anaphylaxis and infusion-related reactions, fever, chills, hives, itching, and flushing. The EUA was issued to Regeneron Pharmaceuticals Inc.

FDA NEWS RELEASE

For Immediate Release: November 19, 2020

Coronavirus (COVID-19) Update: FDA Authorizes Drug Combination for Treatment of COVID-19

The FDA issued an EUA for the drug baricitinib, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

In a clinical trial of hospitalized patients with COVID-19, baricitinib, in combination with remdesivir, was shown to reduce time to recovery within 29 days after initiating treatment compared to patients who received a placebo with remdesivir. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Baricitinib is not authorized or approved as a stand-alone treatment for COVID-19.

"Today's action demonstrates the FDA's steadfast efforts to make potential COVID-19 treatments available in a timely manner, where appropriate, while continuing to support research to further evaluate whether they are safe and effective," said FDA Commissioner Stephen M. Hahn, M.D. "As part of our Coronavirus Treatment Acceleration Program, the FDA continues to use every possible avenue to facilitate new treatments for patients as quickly as possible to combat COVID-19."

Baricitinib is a Janus kinase inhibitor, which blocks the activity of 1 or more of a specific family of enzymes, interfering with the pathway that leads to inflammation. Baricitinib (Olumiant®) is a prescription oral tablet medication that is FDA-approved for the treatment of moderately to severely active rheumatoid arthritis. Under this EUA, the FDA is authorizing the emergency use of baricitinib, in combination with remdesivir, for the treatment of certain hospitalized patients with suspected or laboratory-confirmed COVID-19.

Remdesivir (Veklury®) is an FDA-approved IV antiviral drug for use in adult and pediatric patients 12 years of age and older and weighing at least 40kg for the treatment of COVID-19 requiring hospitalization. Remdesivir also remains authorized for emergency use for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5kg to <40kg or hospitalized pediatric patients younger than 12 years of age weighing at least 3.5kg.

"The FDA's emergency authorization of this combination therapy represents an incremental step forward in the treatment of COVID-19 in

hospitalized patients, and FDA's first authorization of a drug that acts on the inflammation pathway," said Patrizia Cavazzoni, M.D., acting director of the FDA's Center for Drug Evaluation and Research. "Despite advances in the management of COVID-19 infection since the onset of the pandemic, we need more therapies to accelerate recovery and additional clinical research will be essential to identifying therapies that slow disease progression and lower mortality in the sicker patients."

Based on the FDA's review of the totality of the scientific evidence available, the agency has determined that it is reasonable to believe that baricitinib, in combination with remdesivir, may be effective in treating COVID-19 for the authorized population. Additionally, when used under the conditions described in the EUA to treat COVID-19, the known and potential benefits of baricitinib outweigh the known and potential risks for the drug. There are no adequate, approved, and available alternative treatments to baricitinib, when used in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.

The data supporting this EUA for baricitinib combined with remdesivir are based on a randomized, double-blind, placebo-controlled clinical trial (ACTT-2), which was conducted by the National Institute of Allergy and Infectious Diseases (NIAID). This clinical trial evaluated whether baricitinib impacted the time it took for patients who were also taking remdesivir to recover from COVID-19. The trial followed patients for 29 days and included 1,033 patients with moderate or severe COVID-19; 515 patients received baricitinib plus remdesivir, and 518 patients received placebo plus remdesivir. Recovery was defined as either being discharged from the hospital or being hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care. The median time to recovery from COVID-19 was 7 days for baricitinib plus remdesivir and 8 days for placebo plus remdesivir. The odds of a patient's condition progressing to death or being ventilated at day 29 was lower in the baricitinib plus remdesivir group versus the placebo plus remdesivir group. The odds of clinical improvement at day 15 was higher in the baricitinib plus remdesivir group versus the placebo plus remdesivir group. For all of these endpoints, the effects were statistically significant.

Under the EUA, fact sheets that provide important information about using baricitinib in combination with remdesivir in treating COVID-19 as authorized must be made available to health care providers and to patients and caregivers. These fact sheets include dosing instructions, potential side effects and drug interactions. Possible side effects of baricitinib in combination with remdesivir include serious infections, blood clots, changes in certain lab test results, and allergic reactions. The EUA was issued to Eli Lilly and Company.

Current Drug Shortages Index (as of December 17, 2020):

The information provided in this section is provided voluntarily to the FDA by manufacturers and is not specific to Oklahoma.

Acetazolamide Injection	***Currently in Shortage***
Amifostine Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze®)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Avycaz® (ceftazidime and avibactam) for Injection, 2 grams/ 0.5 grams	***Currently in Shortage***
Azithromycin Tablets	***Currently in Shortage***
Belatacept (Nulojix®) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1mcg/mL	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Chlorothiazide (Diuril®) Oral Suspension	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***
Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***

Diltiazem Hydrochloride	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt®) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Doxycycline Hyclate Injection	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide®) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze®) Injection	***Currently in Shortage***
Floxuridine for Injection, USP	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***Currently in Shortage***
Gemifloxacin Mesylate (Factive®) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydralazine Hydrochloride Injection, USP	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxypropyl (Lacrisert®) Cellulose Ophthalmic Insert	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Letermovir (Prevymis™) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***

Leuprolide Acetate (Lupron Depot®; Lupron Depot-Ped®) Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine®) Injection with Epinephrine	***Currently in Shortage***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara®) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan®) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sertraline Hydrochloride Oral Solution, USP	***Currently in Shortage***
Sertraline Hydrochloride Tablets	***Currently in Shortage***

Sincalide (Kinevac®) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Timolol Maleate Ophthalmic Solution	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Tobramycin Lyophilized Powder for Injection	***Currently in Shortage***
Triamcinolone Acetonide (Triesence®) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***
Zinc Acetate Capsules	***Currently in Shortage***