Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
December 11, 2019
4:00pm

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – December 11, 2019

DATE: November 26, 2019

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

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

Call to Order

Public Comment Forum – Appendix A

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

Action Item – Maintenance Drug List – Appendix C

Update on Medication Coverage Authorization Unit/Atopic Dermatitis Prescriber Specialty Analysis – Appendix D

Action Item – Vote to Prior Authorize Eticovo™ (Etanercept-ykro), Hadlima™ (Adalimumab-bwwd), Hyrimoz™ (Adalimumab-adaz), Rinvoq™ (Upadacitinib), and Skyrizi™ (Risankizumab-rzaa) – Appendix E

Action Item – Vote to Prior Authorize Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib) – Appendix F

Action Item – Vote to Prior Authorize Aemcolo™ (Rifamycin), Motegrity™ (Prucalopride), Zelnorm™ (Tegaserod), and Ibsrela® (Tenapanor) – Appendix G

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

Action Item – Vote to Prior Authorize Bevyxxa® (Betrixaban) and to Update the Current Xarelto® (Rivaroxaban) Prior Authorization Criteria – Appendix I

Action Item – Vote to Prior Authorize Avaclyr™ (Acyclovir 3% Ophthalmic Ointment) – Appendix J

Action Item – Annual Review of Thrombocytopenia Medications – Appendix K

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

30-Day Notice to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran) – Appendix M

Annual Review of Soliris® (Eculizumab) and 30-Day Notice to Prior Authorize Ultomiris® (Ravulizumab-cwvz) – Appendix N

Action Item – Annual Review of Muscular Dystrophy Medications – Appendix O

Annual Review of Carbaglu® (Carglumic Acid) – Appendix P

Industry News and Updates – Appendix Q

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – December 11, 2019 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Skrepnek

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum – See Appendix A

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

Items to be presented by Dr. Muchmore, Chairman:

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

A. November 13, 2019 DUR Minutes – Vote
B. November 13, 2019 DUR Recommendations Memorandum

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

4. Action Item – Maintenance Drug List – See Appendix C

A. Maintenance Drug List – Vote

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

5. Update on Medication Coverage Authorization Unit/Atopic Dermatitis Prescriber Specialty Analysis – See Appendix D

A. Pharmacy Helpdesk Activity for November 2019
B. Medication Coverage Activity for November 2019
C. Atopic Dermatitis Prescriber Specialty Analysis

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

6. Action Item – Vote to Prior Authorize Eticovo™ (Etanercept-ykro), Hadlima™ (Adalimumab-bwwd), Hyrimoz™ (Adalimumab-adaz), Rinvoq™ (Upadacitinib), and Skyrizi™ (Risankizumab-rzaa) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib) – See Appendix F

A. Introduction
B. Recommendations

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

8. Action Item – Vote to Prior Authorize Aemcolo™ (Rifamycin), Motegrity™ (Prucalopride), Zelnorm™ (Tegaserod), and Ibsrela® (Tenapanor) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Drizalma Sprinkle™ [Duloxetine Delayed-Release (DR) Capsules], Spravato™ (Esketamine Nasal Spray), and Citalopram 20mg/10mL, Escitalopram 10mg/10mL, and Fluoxetine 20mg/5mL (Unit Dose Cups) – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Bevyxxa® (Betrixaban) and to Update the Current Xarelto® (Rivaroxaban) Prior Authorization Criteria – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Avaclyr™ (Acyclovir 3% Ophthalmic Ointment) – See Appendix J

A. Introduction
B. College of Pharmacy Recommendations

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

12. Action Item – Annual Review of Thrombocytopenia Medications – See Appendix K

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

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

13. Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/ Formoterol Fumarate) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Maintenance Asthma and COPD Medications
C. Prior Authorization of Maintenance Asthma and COPD Medications
D. Market News and Updates
E. Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Maintenance Asthma and COPD Medications
H. Utilization Details of Inhaled Corticosteroids

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

14. 30-Day Notice to Prior Authorization Scenesse® (Afamelanotide) and Givlaari™ (Givosiran) – See Appendix M

A. Introduction
B. Market News and Updates
C. Scenesse® (Afamelanotide) Product Summary
D. Givlaari™ (Givosiran) Product Summary
E. College of Pharmacy Recommendations

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

15. Annual Review of Soliris® (Eculizumab) and 30-Day Notice to Prior Authorize Ultomiris® (Ravulizumab-cwvz) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Soliris® (Eculizumab)
C. Prior Authorization of Soliris® (Eculizumab)
D. Market News and Updates

E. Ultomiris® (Ravulizumab-cwvz) Product Summary
F. College of Pharmacy Recommendations

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

16. Action Item – Annual Review of Muscular Dystrophy Medications – See Appendix O
A. Current Prior Authorization Criteria
B. Utilization of Muscular Dystrophy Medications
C. Prior Authorization of Muscular Dystrophy Medications
D. Market News and Updates
E. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

17. Annual Review of Carbaglu® (Carglumic Acid) – See Appendix P
A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Carbaglu® (Carglumic Acid)
D. Prior Authorization of Carbaglu® (Carglumic Acid)
E. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

18. Industry News and Updates – See Appendix Q
A. Introduction
B. News and Updates

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

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

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

20. Future Business* (Upcoming Product and Class Reviews)
No live meeting scheduled for January 2020. January 2020 will be a packet only meeting.
A. Revcovi® (Elapegademase-lvlr)
B. Gamifant® (Emapalumab-lzsg)
C. Glaucoma Medications
D. Insomnia Medications
E. Firdapse® (Amifampridine)
F. Korlym® (Mifepristone)
**Future business subject to change.*

21. Adjournment

Appendix A

Changes to Public Comment Procedure

Oklahoma Health Care Authority
December 2019

Public Comment Procedure

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

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing once the DUR Board agenda has been posted and no later than 24 hours before the meeting. This allows for a 4-day window to sign up.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.
- To sign up for public comment, email DURPublicComment@okhca.org and complete the required information requested (testimony registration form will be posted prior to January 2020).

Appendix B

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

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.		x
Markita Broyles, D.Ph.; MBA	x	
Darlla D. Duniphin, MHS; PA-C		x
Theresa Garton, M.D.	x	
Megan A. Hanner, D.O.	x	
Ashley Huddleston, Pharm.D.; BCOP	x	
Lynn Mitchell, M.D.	x	
John Muchmore, M.D.; Ph.D.; Chairman	x	
Lee Munoz, D.Ph.	x	
James Osborne, Pharm.D.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Thomas Ha, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Grant H. Skrepnek, R.Ph.; 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	
Tri Van, Pharm.D.; Pharmacy Resident	x	
Graduate Students: Matthew Dickson, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Corby Thompson, Pharm.D.		x
Visiting Pharmacy Student(s): Madison Holbrook, Moshood Seidu	x	

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

OTHERS PRESENT:		
Ron Cain, Pfizer	Gia McLean, Celgene	Dave Poskey, UCB
Charlie Collins, Sanofi-Genzyme	Roger Grotzinger, BMS	Jeff Knappen, Spark
Anthony Deleon, BMS	Frances Bauman, Novo Nordisk	D.R. McCale, Akcea
Kimberly Rowsom, UCB	Erica Brumleve, GSK	Shellie Keast, Mercer
Jim Chapman, AbbVie	Burl Beasley, EGID HealthChoice	Cris Valladares, Celgene
Gwendolyn Caldwell, PhRmA	Heather Dehln, Pfizer	Brian Maves, Pfizer
Marc Parker, Sunovion		

PRESENT FOR PUBLIC COMMENT:	
Gia McLean	Celgene
Kimberly Rowsom	UCB

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA ITEM NO. 13 GIA MCLEAN

2B: AGENDA ITEM NO. 13 KIMBERLY ROWSOM

ACTION: NONE REQUIRED

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

3A: OCTOBER 9, 2019 DUR MINUTES – VOTE

3B: OCTOBER 9, 2019 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

Dr. Holderread had 1 correction: Page 16, Agenda Item #1 should say presented by Dr. Mitchell instead of Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: 2020 DRUG UTILIZATION REVIEW BOARD MEETING DATES

4A: 2020 DUR BOARD MEETING DATES – VOTE

Materials included in agenda packet; presented by Dr. Holderread

Dr. Muchmore proposed the November 2020 meeting be discussed via email among the Board members

Dr. Mitchell moved to approve all meeting dates except November 2020; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS

5A: PHARMACY HELPDESK ACTIVITY FOR OCTOBER 2019

5B: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2019

5C: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE HARVONI® (LEDIPASVIR/SOFOSBUVIR ORAL PELLETS) AND SOVALDI® (SOFOSBUVIR ORAL PELLETS)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE VYNDAQEL® (TAFAMIDIS MEGLUMINE) AND VYNDAMAX™ (TAFAMIDIS)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE RECARBRIO™ (IMIPENEM/CILASTATIN/ RELEBACTAM) AND XENLETA™ (LEFAMULIN)

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE TURALIO™ (PEXIDARTINIB)

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Schmidt
Dr. Huddleston moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF SKIN CANCER MEDICATIONS

10A: INTRODUCTION

10B: CURRENT PRIOR AUTHORIZATION CRITERIA

10C: UTILIZATION OF SKIN CANCER MEDICATIONS

10D: PRIOR AUTHORIZATION OF SKIN CANCER MEDICATIONS

10E: MARKET NEWS AND UPDATES

10F: RECOMMENDATIONS

10G: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE ELZONRIS® (TAGRAXOFUSP-ERZS) AND INREBIC® (FEDRATINIB)

11A: INTRODUCTION

11B: MARKET NEWS AND UPDATES

11C: ELZONRIS® (TAGRAXOFUSP-ERZS) PRODUCT SUMMARY

11D: INREBIC® (FEDRATINIB) PRODUCT SUMMARY

11E: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Schmidt

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF ATOPIC DERMATITIS (AD) MEDICATIONS

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF AD MEDICATIONS

12C: PRIOR AUTHORIZATION OF AD MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: COLLEGE OF PHARMACY RECOMMENDATIONS

12F: UTILIZATION DETAILS OF AD MEDICATIONS

Materials included in agenda packet; presented by Dr. Abbott

Dr. Broyles moved to approve; seconded by Dr. Huddleston
ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ETICOVO™ (ETANERCEPT-YKRO), HADLIMA™ (ADALIMUMAB-BWWD), HYRIMOZ™ (ADALIMUMAB-ADAZ), RINVOQ™ (UPADACITINIB), AND SKYRIZI™ (RISANKIZUMAB-RZAA)

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS
13C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS
13D: MARKET NEWS AND UPDATES
13E: RINVOQ™ (UPADACITINIB) PRODUCT SUMMARY
13F: SKYRIZI™ (RISANKIZUMAB-RZAA) PRODUCT SUMMARY
13G: COLLEGE OF PHARMACY RECOMMENDATIONS
13H: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS

Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AEMCOLO™ (RIFAMYCIN), MOTEGRITY™ (PRUCALOPRIDE), ZELNORM™ (TEGASEROD), AND IBSRELA® (TENAPANOR)

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: PRODUCT SUMMARIES
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF CONSTIPATION AND DIARRHEA MEDICATIONS

Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DRIZALMA SPRINKLE™ [DULOXETINE DELAYED-RELEASE (DR) CAPSULES], SPRAVATO™ (ESKETAMINE NASAL SPRAY), AND CITALOPRAM 20MG/10ML, ESCITALOPRAM 10MG/10ML, AND FLUOXETINE 20MG/5ML UNIT DOSE CUPS

15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF ANTIDEPRESSANTS
15C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS
15D: MARKET NEWS AND UPDATES
15E: SPRAVATO™ (ESKETAMINE NASAL SPRAY) PRODUCT SUMMARY
15F: COST COMPARISON
15G: COLLEGE OF PHARMACY RECOMMENDATIONS
15H: UTILIZATION DETAILS OF ANTIDEPRESSANTS

Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BEVYXXA® (BETRIXABAN) AND TO UPDATE THE CURRENT XARELTO® (RIVAROXABAN) PRIOR AUTHORIZATION CRITERIA

16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
16C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
16D: MARKET NEWS AND UPDATES
16E: BEVYXXA® (BETRIXABAN) PRODUCT SUMMARY

16F: COLLEGE OF PHARMACY RECOMMENDATIONS
16G: UTILIZATION DETAILS OF ANTICOAGULANTS
16H: UTILIZATION DETAILS OF PLATELET AGGREGATION INHIBITORS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF ANTIVIRAL MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AVACLYR™ (ACYCLOVIR 3% OPHTHALMIC OINTMENT)
17A: CURRENT PRIOR AUTHORIZATION CRITERIA
17B: UTILIZATION OF ANTIVIRAL MEDICATIONS
17C: PRIOR AUTHORIZATION OF ANTIVIRAL MEDICATIONS
17D: MARKET NEWS AND UPDATES
17E: AVACLYR™ (ACYCLOVIR 3% OPHTHALMIC OINTMENT) PRODUCT SUMMARY
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF ANTIVIRAL MEDICATIONS
Materials included in agenda packet; presented by Dr. Van
ACTION: NONE REQUIRED

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

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

AGENDA ITEM NO. 20: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
20A: MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS
20B: THROMBOCYTOPENIA MEDICATIONS
20C: CARBAGLU® (CARGLUMIC ACID)
20D: SOLIRIS® (ECULIZUMAB) AND ULTOMIRIS® (RAVULIZUMAB-CWVZ)
20E: MUSCULAR DYSTROPHY MEDICATIONS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: ADJOURNMENT
The meeting was adjourned at 5:24PM.

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

Memorandum

Date: November 14, 2019

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

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

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

Recommendation 1: 2020 Drug Utilization Review Board Meeting Dates

MOTION CARRIED by unanimous approval.

January 8, 2020
February 12, 2020
March 11, 2020
April 8, 2020
May 13, 2020
June 10, 2020
July 8, 2020
August 12, 2020
September 9, 2020
October 14, 2020
November 11, 2020 *(Meeting will need to be moved to account for Veterans Day holiday)*
December 9, 2020

Recommendation 2: U.S. Food and Drug Administration (FDA) Safety Alerts

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir Oral Pellets) and Sovaldi® (Sofosbuvir Oral Pellets)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Harvoni® (ledipasvir/ sofosbuvir oral pellets) and Sovaldi® (sofosbuvir oral pellets) with criteria similar to Harvoni® (ledipasvir/sofosbuvir) and Sovaldi® (sofosbuvir) tablet formulations. Additionally, the College of Pharmacy recommends updating the Harvoni® (ledipasvir/sofosbuvir), Sovaldi® (sofosbuvir), and Mavyret™ (glecaprevir/pibrentasvir) prior authorization criteria based on new FDA approvals. The following criteria will apply (changes and additions noted in red):

Harvoni® (Ledipasvir/Sofosbuvir Tablets and Oral Pellets) Approval Criteria:

1. Member must be ~~12~~ 3 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT) 1, GT 4, GT 5, or GT 6; and
3. Request for the generic formulation will require a patient-specific, clinically significant reason the member cannot use the brand formulation; and***
4. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
6. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test ~~that is at least 6 months old~~ and has a recent (within the last 3 months) detectable and quantifiable HCV RNA (>15 IU/mL) ~~test 6 months after date of positive HCV antibody test~~; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1:**
        i. Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA <6 million IU/mL: Harvoni® for 8 weeks
        ii. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA >6 million IU/mL: Harvoni® for 12 weeks
        iii. Treatment-experienced without cirrhosis: Harvoni® for 12 weeks
        iv. Treatment-experienced with compensated cirrhosis:
            1. Harvoni® with ribavirin for 12 weeks; or
            2. Harvoni® for 24 weeks

v. Treatment-naïve or treatment-experienced with decompensated cirrhosis: Harvoni® with ribavirin for 12 weeks

b. **GT-1 or GT-4:**
   i. Treatment-naïve or treatment-experienced liver transplant recipients with or without compensated cirrhosis: Harvoni® with ribavirin for 12 weeks

c. **GT-4, GT-5, or GT-6:**
   i. Treatment-naïve or treatment-experienced with or without compensated cirrhosis: Harvoni® for 12 weeks

d. New regimens will apply as approved by the FDA; and

8. Members who are 6 years of age and older and request the oral pellet formulation of Harvoni® must provide a patient-specific, clinically significant reason for use of the oral pellet formulation in place of the tablet formulation; and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for those on ribavirin); and
15. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/ emtricitabine in combination with tenofovir disoproxil fumarate; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
17. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating hepatitis C virus (HCV), liver transplantation, or another directed therapy; and
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a

month in order to prevent prescription limit issues from affecting the member's compliance.

****The brand formulation of Harvoni® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

Sovaldi® (Sofosbuvir Tablets and Oral Pellets) Approval Criteria:

1. Member must be ~~12~~ 3 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT) 1, GT 2, GT 3, or GT 4; and
3. Requests for the generic formulation will require a patient-specific, clinically significant reason the member cannot use the brand formulation; and***
4. Sovaldi® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Sovaldi® must be used as a component of a combination regimen; and
6. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
7. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test ~~that is at least 6 months old~~ and has a recent (within the last 3 months) detectable and quantifiable HCV RNA (>15 IU/mL) ~~test 6 months after date of positive HCV antibody test~~; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
8. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1:**
        i. Treatment-naïve or experienced, non-cirrhotic or cirrhotic: Sovaldi® with ribavirin and peginterferon alfa for 12 weeks
    b. **GT-2:**
        i. Treatment-naïve, non-cirrhotic: Sovaldi® with ribavirin for 12 weeks
        ii. Treatment-naïve, cirrhotic: Sovaldi® with ribavirin for 12 or 16 weeks
        iii. Treatment-experienced, non-cirrhotic or cirrhotic:
            1. Sovaldi® with ribavirin for 12 or 16 weeks; or
            2. Sovaldi® with ribavirin and peginterferon alfa for 12 weeks
    c. **GT-3:**
        i. Treatment-naïve or experienced, non-cirrhotic and cirrhotic:
            1. Sovaldi® with ribavirin and peginterferon alfa for 12 weeks; or
            2. Sovaldi® with ribavirin for 24 weeks (if interferon ineligible)
    d. **GT-4:**
        i. Treatment-naïve or experienced, non-cirrhotic and cirrhotic:
            1. Sovaldi® with ribavirin and peginterferon alfa for 12 weeks

e. New regimens will apply as approved by the FDA; and

9. Members who are older than 6 years of age and request the oral pellet formulation of Sovaldi® must provide a patient-specific, clinically significant reason for use of the oral pellet formulation in place of the tablet formulation; and
10. Member must sign and submit the Hepatitis C Intent to Treat contract; and
11. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
12. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
13. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
14. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
15. Member must not have decompensated cirrhosis; and
16. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for those on ribavirin); and
17. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, phenytoin, oxcarbazepine, tipranavir/ritonavir, didanosine, or St. John's wort; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
19. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating hepatitis C virus (HCV), liver transplantation, or another directed therapy; and
20. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
21. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
22. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance; and
23. Additionally, due to superior SVR rates and shortened treatment durations with Harvoni®, authorization of Sovaldi® for GT-1 will require a patient-specific, clinically significant reason why Harvoni® is not an option.

****The brand formulation of Sovaldi® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

Mavyret™ (Glecaprevir/Pibrentasvir) Approval Criteria:

1. Member must be ~~18~~ 12 years of age or older or weigh at least 45kg; and

2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT) 1, GT 2, GT 3, GT 4, GT 5, or GT 6; and
3. Mavyret™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
4. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on the prior authorization request; and
5. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test ~~that is at least 6 months old~~ and has a recent (within the last 3 months) detectable and quantifiable HCV RNA (>15 IU/mL) ~~test 6 months after date of positive HCV antibody test~~; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
6. The following regimens and requirements based on cirrhosis status, viral genotype, and treatment history will apply (new regimens will apply as approved by the FDA):

Genotype	Prior Treatment Experience	No Cirrhosis	Compensated Cirrhosis
1, 2, 3, 4, 5, or 6	Treatment-Naïve	8 weeks	~~12~~ 8 weeks
1	NS5A w/o NS3/4A PI	16 weeks	16 weeks
1	NS3/4A PI w/o NS5A	12 weeks	12 weeks
1, 2, 4, 5, or 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks

w/o = without; PI = protease inhibitor; PRS = pegylated interferon, ribavirin, and/or sofsobuvir
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
Examples of NS3/4A PIs include: boceprevir, glecaprevir, grazoprevir, paritaprevir, simeprevir, telaprevir, voxilaprevir
HCV/HIV-1 co-infection and patients with any degree of renal impairment follow the same dosage recommendations in the table above. Mavyret™ is recommended for 12 weeks in adult and pediatric patients 12 years and older or weighing at least 45 kg who are liver or kidney transplant recipients. A 16-week treatment duration is recommended in GT 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A PI or in GT 3-infected patients who are PRS treatment-experienced.

7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
10. Prescriber must agree to counsel members on the potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and

12. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
13. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy; and
15. Member must not be taking the following medications: carbamazepine, rifampin, ethinyl estradiol-containing medications, St. John's wort, atazanavir, darunavir, lopinavir, ritonavir, efavirenz, atorvastatin, lovastatin, simvastatin, rosuvastatin doses greater than 10mg per day, or cyclosporine doses greater than 100mg per day; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Approval of the 8-week carton (in place of the 4-week carton) requires a patient-specific, clinically significant reason why the member requires the 8-week carton in place of the 4-week carton; and
19. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 16 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 4: Vote to Prior Authorize Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Vyndaqel® (tafamidis meglumine) and Vyndamax™ (tafamidis) with the following criteria:

Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis) Approval Criteria:

1. An FDA approved indication for the treatment of cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular (CV) mortality and CV-related hospitalization; and
2. Diagnosis confirmed by:
    a. Genetic confirmation of transthyretin (*TTR*) mutation (e.g., Val122Ile) or wild-type amyloidosis; and
    b. Cardiac imaging (including ultrasound or MRI) confirming cardiac involvement; and
3. Presence of amyloid deposits confirmed by:

   a. Nuclear scintigraphy; or
   b. Endomyocardial biopsy; and
4. Member must have medical history of heart failure (NYHA Class I to III); and
5. Prescriber must confirm light-chain amyloidosis (AL) has been ruled out; and
6. Vyndaqel® or Vyndamax™ must be prescribed by or in consultation with a cardiologist or geneticist (or an advanced care practitioner with a supervising physician who is a cardiologist or geneticist); and
7. Prescriber must verify Vyndaqel® or Vyndamax™ will not be used concomitantly with Onpattro® (patisiran) or Tegsedi™ (inotersen); and
8. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
9. A quantity limit of 4 Vyndaqel® capsules or 1 Vyndamax™ capsule per day will apply.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Onpattro® and Tegsedi™ approval criteria:

Onpattro® (Patisiran) Approval Criteria:

1. An FDA approved indication for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
   a. Tissue (fat pad) biopsy confirming amyloid deposits; and
   b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Onpattro® must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist); and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
5. Prescriber must confirm the member will be pre-medicated with intravenous (IV) corticosteroid, oral acetaminophen, IV histamine-1 (H_1) antagonist, and IV histamine-2 (H_2) antagonist 60 minutes prior to Onpattro® administration to reduce the risk of infusion-related reaction(s); and
6. Onpattro® will not be approved for concomitant use with Tegsedi™ (inotersen), Vyndaqel® (tafamidis meglumine), or Vyndamax™ (tafamidis); and
7. Member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
8. Onpattro® approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Tegsedi™ (Inotersen) Approval Criteria:

1. An FDA approved indication for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
   a. Tissue (fat pad) biopsy confirming amyloid deposits; and
   b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and

3. Tegsedi™ must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist (or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist); and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
5. Prescriber must agree to monitor ALT, AST, and total bilirubin prior to initiation of Tegsedi™ and every 4 months during treatment; and
6. Prescriber must confirm the first injection of Tegsedi™ administered by the member or caregiver will be performed under the guidance of a health care professional; and
7. Prescriber must confirm the member or caregiver has been trained by a health care professional on the subcutaneous (sub-Q) administration and proper storage of Tegsedi™; and
8. Tegsedi™ will not be approved for concomitant use with Onpattro® (patisiran), Vyndaqel® (tafamidis meglumine), or Vyndamax™ (tafamidis); and
9. Prescriber, pharmacy, and member must be enrolled in the Tegsedi™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
10. Tegsedi™ approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
11. A quantity limit of 4 syringes per 28 days will apply.

Recommendation 5: Vote to Prior Authorize Recarbrio™ (Imipenem/Cilastatin/ Relebactam) and Xenleta™ (Lefamulin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Recarbrio™ (imipenem/ cilastatin/relebactam) and Xenleta™ (lefamulin) with the following criteria:

Recarbrio™ (Imipenem/Cilastatin/Relebactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
   a. Complicated intra-abdominal infection (cIAI); or
   b. Complicated urinary tract infection (cUTI), including pyelonephritis; and
2. Member must be 18 years of age or older; and
3. The prescriber must verify that limited or no alternative treatment options are available; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/ tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. A quantity limit of 56 vials per 14 days will apply.

Xenleta™ (Lefamulin) Approval Criteria:

1. An FDA approved diagnosis of community-acquired bacterial pneumonia (CABP) caused by designated susceptible microorganisms; and

2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use an appropriate beta-lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin/sulbactam) in combination with a macrolide (e.g., azithromycin, clarithromycin) or doxycycline, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
4. Approval quantity will be based on Xenleta™ prescribing information and FDA approved dosing regimen(s).

Additionally, the College of Pharmacy recommends updating the current approval criteria for Avycaz® (ceftazidime/avibactam), Zerbaxa® (ceftolozane/tazobactam), and Baxdela® (delafloxacin) based on the new FDA approved indications (changes noted in red):

Avycaz® (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
   a. Complicated intra-abdominal infection (cIAI), used in combination with metronidazole; or
   b. Complicated urinary tract infection (cUTI), including pyelonephritis; or
   c. Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP); and
2. Member must be ~~18 years~~ 3 months of age or older; and
3. For the diagnosis of cIAI, Avycaz® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/ tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. ~~A quantity limit of 42 vials per 14 days will apply.~~ Approval quantity will be based on Avycaz® prescribing information and FDA approved dosing regimen(s).

Zerbaxa® (Ceftolozane/Tazobactam) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following infections caused by designated susceptible microorganisms:
   a. Complicated intra-abdominal infection (cIAI), used in combination with metronidazole; or
   b. Complicated urinary tract infection (cUTI), including pyelonephritis; ~~and~~ or
   c. Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP); and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Zerbaxa® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin/beta lactamase inhibitor combination (e.g., piperacillin/ tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and

5. ~~A quantity limit of 42 vials per 14 days will apply.~~ Approval quantity will be based on Zerbaxa® prescribing information and FDA approved dosing regimen(s).

Baxdela® (Delafloxacin) Tablet and Vial Approval Criteria [Acute Bacterial Skin and Skin Structure Infection (ABSSSI) Diagnosis]:

1. An FDA approved diagnosis of ~~acute bacterial skin and skin structure infection (~~ABSSSI~~)~~ caused by designated susceptible bacteria; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, doxycycline, trimethoprim/sulfamethoxazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. Approval quantity will be based on Baxdela® prescribing information and FDA approved dosing regimen(s); and
    a. For Baxdela® vials, an initial quantity limit of 6 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

Baxdela® (Delafloxacin) Tablet and Vial Approval Criteria [Community-Acquired Bacterial Pneumonia (CABP) Diagnosis]:

1. An FDA approved diagnosis of CABP caused by designated susceptible bacteria; and
2. A patient-specific, clinically significant reason why the member cannot use an appropriate beta-lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin/sulbactam) in combination with a macrolide (e.g., azithromycin, clarithromycin) or doxycycline, monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin, gemifloxacin), or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. Approval quantity will be based on Baxdela® prescribing information and FDA approved dosing regimen(s); and
    a. For Baxdela® vials, an initial quantity limit of 6 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

Lastly, the College of Pharmacy recommends updating the current approval criteria for ciprofloxacin 100mg tablets, ciprofloxacin 500mg and 1,000mg extended-release tablets, and ofloxacin 300mg and 400mg tablets and moxifloxacin 400mg tablets, based on the current low net cost of moxifloxacin 400mg tablets (changes noted in red):

Ciprofloxacin 100mg Tablets Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member cannot use alternative strengths of ciprofloxacin tablets, levofloxacin tablets, moxifloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

Ciprofloxacin 500mg and 1,000mg Extended-Release (ER) Tablets Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member cannot use the immediate-release formulation of ciprofloxacin tablets, levofloxacin tablets, moxifloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

Ofloxacin 300mg and 400mg Tablets ~~and Moxifloxacin 400mg Tablets~~ Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, moxifloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

Recommendation 6: Vote to Prior Authorize Turalio™ (Pexidartinib)

MOTION CARRIED by unanimous approval.

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. Pexidartinib must be used as a single-agent only.

Recommendation 7: Annual Review of Skin Cancer Medications

MOTION CARRIED by unanimous approval.

Update the prior authorization criteria to reflect new FDA approved indications; changes can be seen in the following criteria listed in red (only criteria with updates listed):

Bavencio® (Avelumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of advanced RCC; and
2. Must be used as first-line treatment; and
3. Must be used in combination with axitinib.

Keytruda® (Pembrolizumab) Approval Criteria [Endometrial Cancer Diagnosis]:

1. Diagnosis of advanced endometrial cancer that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
2. Progressive disease following prior systemic therapy; and
3. Member is not a candidate for curative surgery or radiation; and
4. Must be used in combination with lenvatinib; and
5. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Esophageal Cancer Diagnosis]:

1. Diagnosis of locally advanced or metastatic esophageal carcinoma; and
2. Must be used following disease progression after 1 or more prior lines of systemic therapy; and
3. Tumor must be squamous cell histology; and
4. Tumor must have positive PD-L1 expression [Combined Positive Score (CPS) ≥10]; and
5. Pembrolizumab must be used as monotherapy; and
6. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. ~~Diagnosis of recurrent or metastatic disease~~ First-line or recurrent setting; and
2. Squamous cell histology; and
3. ~~Member has received a prior platinum containing regimen (i.e., cisplatin, carboplatin); and~~

4. If used in the recurrent setting, member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
5. Dose does not exceed 200mg every 3 weeks.

Keytruda® (Pembrolizumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of metastatic SCLC; and
2. Progressed on or following a platinum-based regimen and at least 1 other regimen; and
3. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Recommendation 8: 30-Day Notice to Prior Authorize Elzonris® (Tagraxofusp-erzs) and Inrebic® (Fedratinib)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Atopic Dermatitis (AD) Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes and additions, based on recent FDA approvals, to the prior authorization criteria for Dupixent® (dupilumab injection), as shown in red:

Dupixent® (Dupilumab Injection) Approval Criteria [Atopic Dermatitis (AD) Diagnosis]:

1. An FDA approved diagnosis of moderate-to-severe AD not adequately controlled with topical prescription therapies; and
2. Member must be ~~18~~ 12 years of age or older; and
3. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
   a. 1 medium potency to very-high potency Tier-1 topical corticosteroid; and
   b. 1 topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. Dupixent® must be prescribed by a dermatologist, allergist, or immunologist or the member must have been evaluated by a dermatologist, allergist, or immunologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is a dermatologist, allergist, or immunologist); and
5. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use (Dupixent® has not been studied in combination with other biologic therapies); and
6. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Dupixent® (Dupilumab Injection) Approval Criteria [Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment in adult patients with inadequately controlled CRSwNP; and
2. Member must be 18 years of age or older; and
3. Member must have a documented trial with an intranasal corticosteroid that resulted in failure (or have a contraindication or documented intolerance); and
4. Member must meet 1 of the following:
    a. Member has required prior sino-nasal surgery; or
    b. Member has previously been treated with systemic corticosteroids in the past 2 years (or has a contraindication or documented intolerance); and
5. Dupixent® must be prescribed by an otolaryngologist, allergist, immunologist, or pulmonologist or the member must have been evaluated by an otolaryngologist, allergist, immunologist, or pulmonologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an otolaryngologist, allergist, immunologist, or pulmonologist); and
6. Member has symptoms of chronic rhinosinusitis (e.g., facial pain/pressure, reduction or loss of smell, nasal blockade/obstruction/congestion, nasal discharge) for 12 weeks or longer despite attempts at medical management; and
7. Member has evidence of nasal polyposis by direct examination, sinus CT scan, or endoscopy; and
8. Member will continue to receive intranasal corticosteroid therapy, unless contraindicated; and
9. Prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
10. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use; and
11. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval; and
12. A quantity limit of 2 syringes every 28 days will apply.

Recommendation 10: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Eticovo™ (Etanercept-ykro), Hadlima™ (Adalimumab-bwwd), Hyrimoz™ (Adalimumab-adaz), Rinvoq™ (Upadacitinib), and Skyrizi™ (Risankizumab-rzaa)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Aemcolo™ (Rifamycin), Motegrity™ (Prucalopride), Zelnorm™ (Tegaserod), and Ibsrela® (Tenapanor)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Drizalma Sprinkle™ [Duloxetine Delayed-Release (DR) Capsules], Spravato™ (Esketamine Nasal Spray), and Citalopram 20mg/10mL, Escitalopram 10mg/10mL, and Fluoxetine 20mg/5mL Unit Dose Cups

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Bevyxxa® (Betrixaban) and to Update the Current Xarelto® (Rivaroxaban) Prior Authorization Criteria

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Antiviral Medications and 30-Day Notice to Prior Authorize Avaclyr™ (Acyclovir 3% Ophthalmic Ointment)

NO ACTION REQUIRED.

Recommendation 15: Industry News and Updates

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 17: Future Business

NO ACTION REQUIRED.

Appendix C

Maintenance Drug List

Oklahoma Health Care Authority
December 2019

Introduction[1,2,3]

Many Medicaid programs have limitations on medication days' supply in order to control costs. Dispensing a longer days' supply may result in increased wastage as a result of discontinuations or lost medications. Recently, some Medicaid programs have allowed for dispensing of 90-day supply of medications in an effort to reduce spending related to dispensing fees and drug ingredient costs while potentially improving adherence.

Taitel and others conducted a retrospective observational study of California Medicaid claims dispensed from Walgreens in 2010. The purpose of the study was to evaluate whether 90-day supply dispensing could improve adherence, minimize wastage, and control costs. A total of 52,898 patients with claims for statins, antihypertensive medications, selective serotonin reuptake inhibitors (SSRIs), or diabetes medications were reviewed for adherence [assessed via medication possession ratio (MPR)], persistence (defined as <30 day gap in therapy), and wastage (defined as a switch of medication or strength within the same therapeutic class before the expected refill date). Adherence was determined to be 20% higher and persistence was 23% higher for those with 90-day supply in comparison to the 30-day supply group, resulting in an average increase of 0.14 MPR and 44 days of continuous therapy. Wastage was determined to be similar between the comparison groups. After accounting for average wastage, all therapeutic classes reviewed resulted in a per person per year (PPPY) savings as follows: statins $7.70; antihypertensive medications $10.80; SSRIs $18.52; and diabetes medications $26.86.

In November 2019, the Oklahoma Health Care Authority (OHCA) Board voted to update the current policy and rules regarding dispensing limitations. Previously, medications could only be dispensed and reimbursed by SoonerCare up to a 34-day supply or if the quantity did not exceed 100 units. The newly voted OHCA policy and rules state the following regarding dispensing limitations and a maintenance drug list (317:30-5-77.1):

> "Prescription quantities shall be limited to a 34-day supply, except in the following situations:
> 1) The Drug Utilization Review (DUR) Board has recommended a different day supply or quantity limit based on published medical data, including the manufacturer's package insert;
> 2) The product is included on the Maintenance List of medications which are exempted from this limit and may be dispensed up to a 90-day supply;
> 3) The manufacturer of the drug recommends a dispensing quantity less than a 34-day supply…."

> "The DUR Board shall develop a Maintenance List of medications which are used in general practice on a continuing basis. These drugs shall be made available through the Vendor Drug Program in quantities up to a 90-day supply when approved by the prescriber. The DUR Board shall review the Maintenance List at least annually."

The purpose of this report is to recommend categories of medications to the DUR Board for inclusion on the maintenance drug list, which is to be maintained by the DUR Board. Medications included in the maintenance drug list are set up to allow a 90-day supply of medications in the claims processing system without the need for an override.

Recommendations

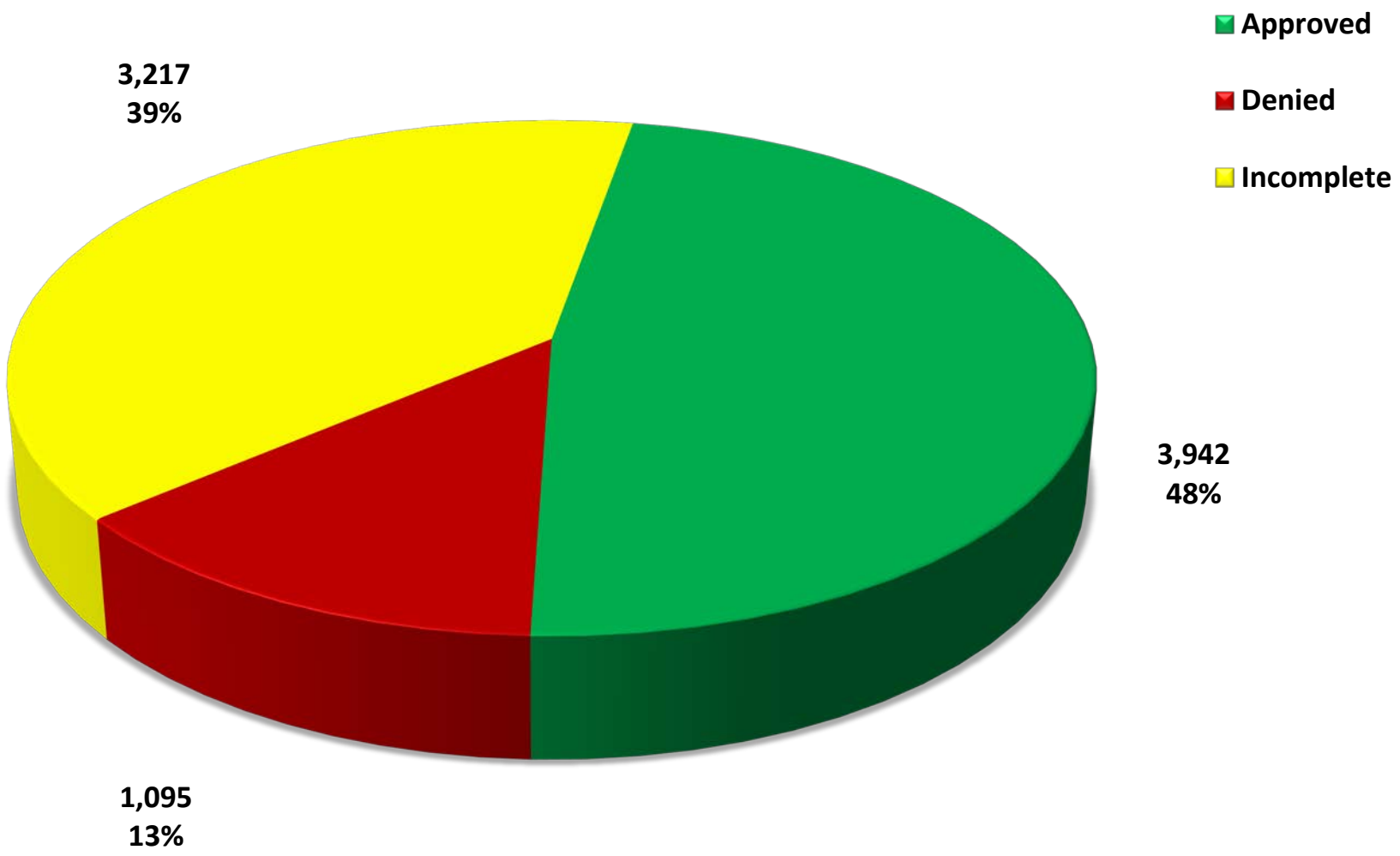
The College of Pharmacy, in partnership with the OHCA, recommends the addition of the following categories of medications to the maintenance drug list:

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

[1] Oklahoma Health Care Authority (OHCA). Provider Billing and Procedures Manual. Available online at: http://www.okhca.org/providers.aspx?id=122. Last revised 11/2017. Last accessed 11/25/2019.
[2] OHCA. OHCA Board Meeting Agenda: November 2019. Available online at: http://www.okhca.org/about.aspx?id=2671. Issued 11/20/2019. Last accessed 11/26/2019.
[3] Taitel M, Fensterheim L, Kirkham H, et al. Medication Days' Supply, Adherence, Wastage, and Cost Among Chronic Patients in Medicaid. *MMRR* 2012; 2(3): E1-E13. doi: dx.doi.org/10.5600/mmrr.002.03.a04.

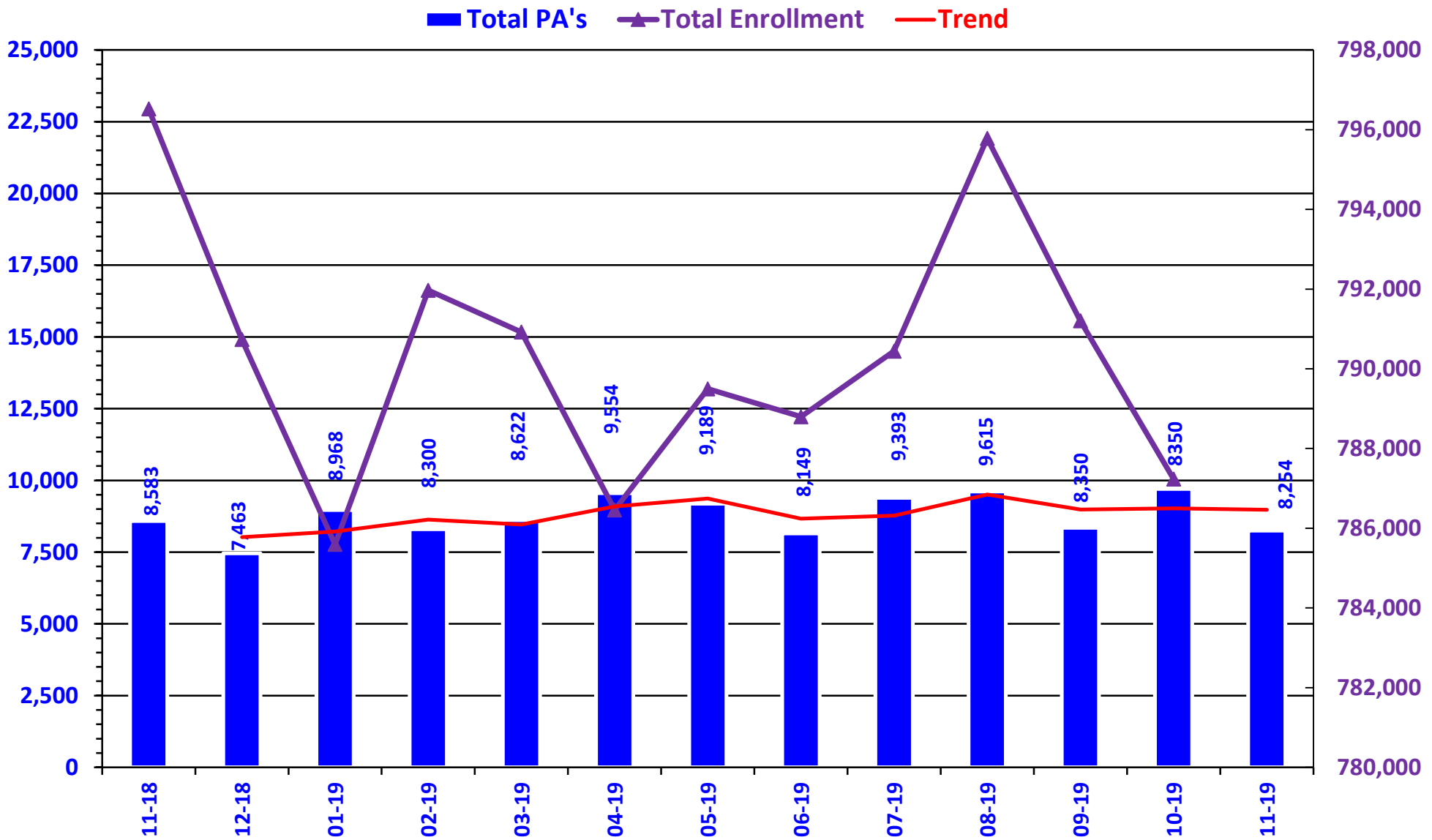
Appendix D

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER 2019



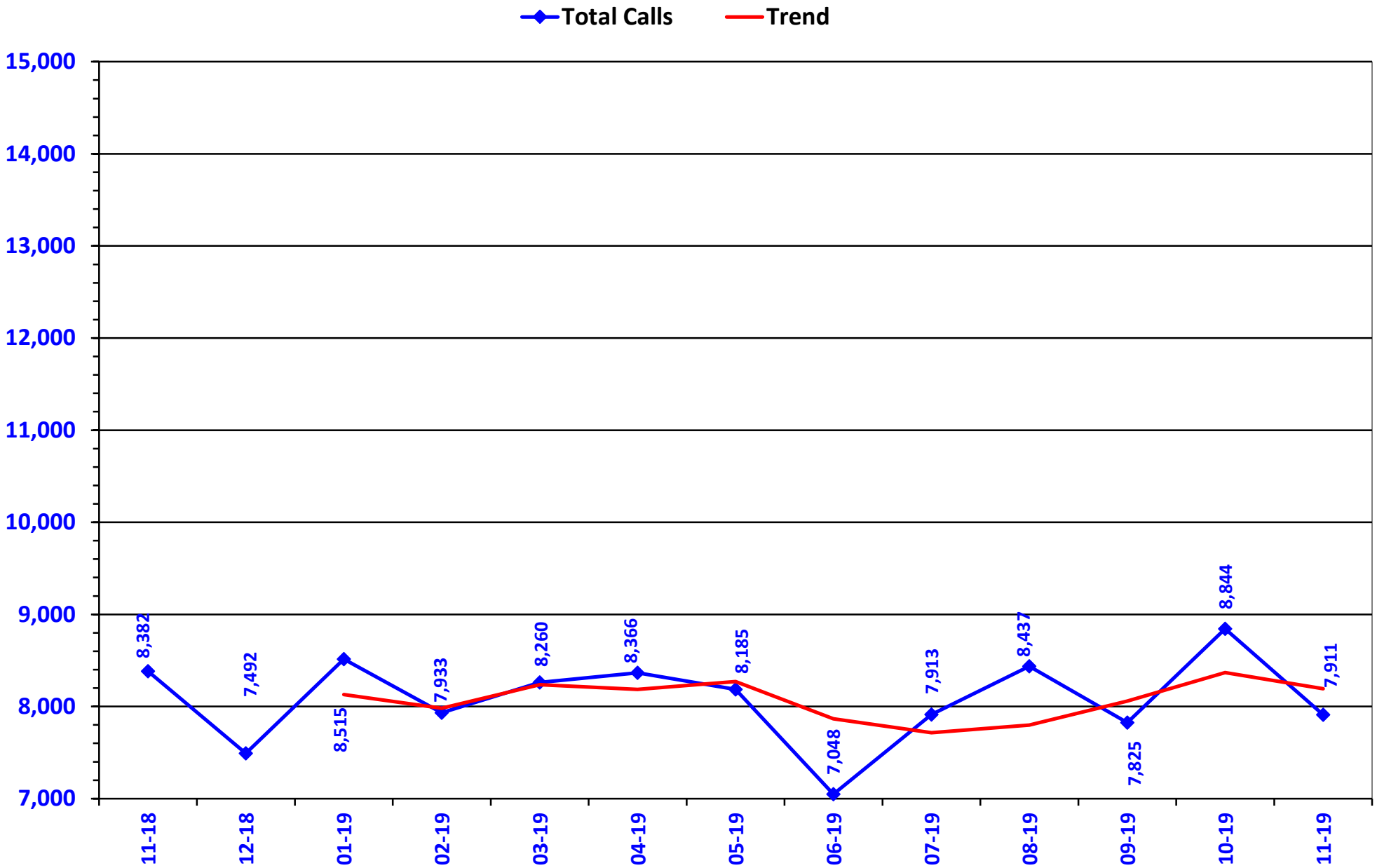
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2018 – NOVEMBER 2019



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
NOVEMBER 2018 – NOVEMBER 2019



Prior Authorization Activity

11/1/2019 Through 11/30/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	62	7	22	33	360
Analgesic - Narcotic	288	145	24	119	162
Antiasthma	91	17	20	54	282
Antibiotic	22	9	3	10	230
Anticonvulsant	157	66	18	73	283
Antidepressant	182	50	34	98	303
Antidiabetic	256	85	37	134	356
Antihistamine	20	5	9	6	296
Antimigraine	136	36	44	56	166
Antineoplastic	73	42	3	28	159
Antiparasitic	11	0	3	8	0
Antiulcers	121	48	22	51	102
Anxiolytic	17	5	2	10	218
Atypical Antipsychotics	271	127	18	126	350
Biologics	168	86	22	60	263
Bladder Control	30	4	9	17	358
Blood Thinners	254	154	10	90	334
Botox	36	24	5	7	304
Buprenorphine Medications	70	9	2	59	67
Calcium Channel Blockers	14	4	3	7	275
Cardiovascular	61	34	4	23	323
Chronic Obstructive Pulmonary Disease	207	44	50	113	335
Constipation/Diarrhea Medications	147	22	52	73	219
Contraceptive	21	3	10	8	138
Dermatological	309	87	94	128	96
Diabetic Supplies	433	250	24	159	199
Endocrine & Metabolic Drugs	98	47	11	40	143
Erythropoietin Stimulating Agents	23	12	5	6	98
Fibromyalgia	98	5	2	91	321
Fish Oils	11	0	6	5	0
Gastrointestinal Agents	92	22	18	52	206
Genitourinary Agents	11	5	1	5	360
Growth Hormones	76	52	5	19	148
Hepatitis C	149	101	10	38	7
HFA Rescue Inhalers	34	2	3	29	181
Insomnia	42	2	10	30	177
Insulin	114	38	18	58	311
Miscellaneous Antibiotics	12	5	0	7	14
Multiple Sclerosis	45	16	6	23	138
Muscle Relaxant	41	3	12	26	74
Nasal Allergy	57	9	19	29	146
Neurological Agents	110	46	14	50	267
NSAIDs	27	2	6	19	52
Ocular Allergy	18	4	6	8	88
Osteoporosis	3	1	1	1	350
Other*	296	78	57	161	261
Otic Antibiotic	24	5	6	13	18
Pediculicide	31	2	2	27	8
Respiratory Agents	69	36	1	32	129
Statins	21	2	11	8	223

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Stimulant	685	316	90	279	345
Synagis	344	147	93	104	142
Testosterone	45	14	10	21	346
Topical Antifungal	27	2	4	21	22
Topical Corticosteroids	62	1	33	28	85
Vitamin	66	26	21	19	167
Pharmacotherapy	79	71	0	8	260
Emergency PAs	0	0	0	0	
Total	**6,267**	**2,435**	**1,025**	**2,807**	
Overrides					
Brand	31	19	0	12	288
Compound	17	11	0	6	143
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	7	6	0	1	74
Dosage Change	368	353	3	12	14
High Dose	7	5	0	2	276
Ingredient Duplication	6	6	0	0	14
Lost/Broken Rx	103	95	3	5	14
MAT Override	276	241	2	33	65
NDC vs Age	342	220	19	103	245
Nursing Home Issue	58	49	4	5	15
Opioid MME Limit	151	87	3	61	89
Opioid Quantity	38	32	1	5	163
Other*	43	38	2	3	8
Prescriber Temp Unlock	1	1	0	0	360
Quantity vs. Days Supply	474	294	31	149	230
STBS/STBSM	9	7	0	2	49
Stolen	21	17	1	3	37
Third Brand Request	33	24	1	8	18
Overrides Total	**1,987**	**1,507**	**70**	**410**	
Total Regular PAs + Overrides	**8,254**	**3,942**	**1,095**	**3,217**	

Denial Reasons	
Unable to verify required trials.	2,584
Does not meet established criteria.	1,113
Lack required information to process request.	594
Other PA Activity	
Duplicate Requests	506
Letters	12,464
No Process	9
Changes to existing PAs	619
Helpdesk Initiated Prior Authorizations	715
PAs Missing Information	19

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

Atopic Dermatitis Prescriber Specialty Analysis

Oklahoma Health Care Authority
December 2019

Introduction

During the November 2019 Drug Utilization Review (DUR) Board presentation of the Annual Review of the Atopic Dermatitis (AD) Medications, the DUR Board requested additional review and analysis of the top prescriber specialties of these medications by number of SoonerCare paid claims. The following report provides additional data and analysis regarding prescriber specialty of AD medications.

AD Medications: Prescriber Specialty Analysis

The following table shows the top 5 prescriber specialites of AD medications by number of claims along with the percentage of all AD claims written by the designated prescriber specialty. Nurse practitioners and physician assistants comprise 44.88% of claims for AD medications in fiscal year 2019.

Prescriber Specialty	Number of AD Claims	Percentage of Total AD Claims
Nurse Practitioner	1,250	26.50%
Physician Assistant	867	18.38%
General Pediatrician	820	17.38%
Dermatologist	572	12.13%
Family Practitioner	541	11.47%

AD = atopic dermatitis
Fiscal Year 2019 = 07/01/2018 to 06/30/2019

For additional comparison, the top prescriber specialties for alternative disease states commonly treated in the pediatric primary care setting were analyzed. The following table shows the top 5 prescriber specialites of pediculocide medications and otic anti-infective medications by percentage of all claims written by the designated prescriber specialty. Nurse practitioners and physician assistants accounted for 52.98% of pediculocide claims and 48.04% of otic anti-infective claims during fiscal year 2019.

Prescriber Specialty	Percentage of Total Pediculocide Claims	Percentage of Total Otic Anti-Infective Claims
Nurse Practitioner	35.45%	29.05%
General Pediatrician	25.48%	14.17%
Physician Assistant	17.53%	18.99%
Family Practitioner	13.78%	10.50%

Fiscal Year 2019 = 07/01/2018 to 06/30/2019

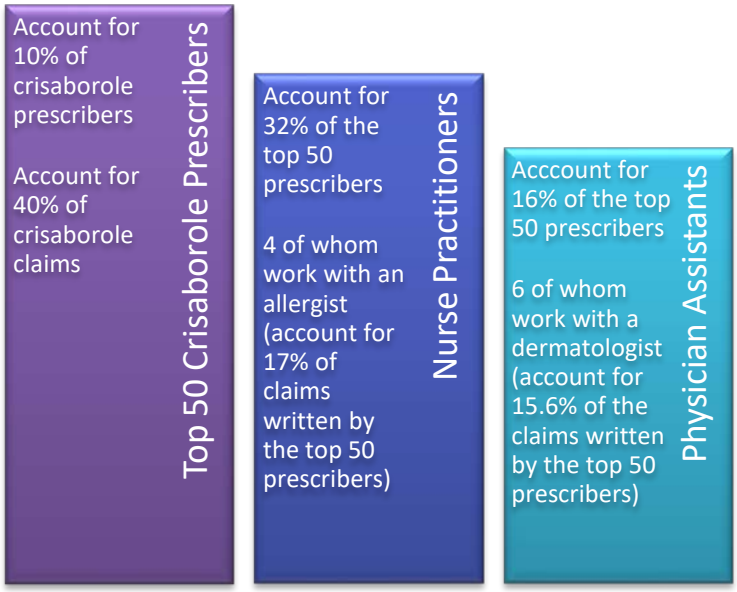
The following table contains data representing the percentage of prescribers within the designated specialty who have paid SoonerCare claims for an AD medication out of the total

number of prescribers within the designated specialty ("per capita rate of AD prescribing") during fiscal year 2019.

Prescriber Specialty	Per Capita Rate of AD Prescribing
Dermatologist	43.28%
General Pediatrician	20.72%
Nurse Practitioner	11.79%
Physician Assistant	10.60%
Family Practice Physician	10.40%

AD = atopic dermatitis
Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Prescribers of Eucrisa® (crisaborole), the most commonly prescribed AD medication, were further evaluated. Nurse practitioners and physician assistants in the top 50 crisaborole prescribers during fiscal year 2019 were further reviewed for association with a specialist (i.e., practicing in a specialty clinic or supervising physician specialty). The following graphic highlights the breakdown of nurse practitioners and physician assistants associated with specialists. A total of 32.6% of the top 50 crisaborole prescribers were nurse practitioners or physician assistants that are assocaited with a specialist (i.e., allergist, dermatologist).



Conclusions

Prescriber specilties associated with prescribing of AD medications appear to be in line with other disease states commonly treated in the pediatric primary care setting. In addition, when evaluated on a per capita prescribing basis, dermatologists have the highest rate of AD prescribing followed by general pediatricians. The College of Pharmacy does not recommend any changes to the current AD criteria based on prescriber specialty. The College of Pharmacy will continue to monitor AD prescriber specialty and present data to the DUR Board where appropriate.

Appendix E

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

Oklahoma Health Care Authority
December 2019

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13]

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

- **Hyrimoz™ (adalimumab-adaz):** In October 2018, Sandoz announced the FDA approval of Hyrimoz™ (adalimumab-adaz), a biosimilar to Humira® (adalimumab), for the treatment of patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), and plaque psoriasis (PsO).
- **Eticovo™ (etanercept-ykro):** In April 2019, Samsung Bioepis announced the FDA approval of Eticovo™ (etanercept-ykro), a biosimilar to Enbrel® (etanercept), for the treatment of patients with AS, PsO, polyarticular JIA, PsA, and RA.
- **Hadlima™ (adalimumab-bwwd):** In July 2019, Samsung Bioepis announced the FDA approval of Hadlima™ (adalimumab-bwwd), a biosimilar to Humira® (adalimumab), for the treatment of RA, JIA, PsA, AS, adult CD, UC, and PsO.

New Molecular Entity FDA Approval(s):

- **Skyrizi™ (risankizumab-rzaa):** In April 2019, AbbVie, Inc. announced the FDA approval of Skyrizi™ (risankizumab-rzaa), an interleukin-23 (IL-23) inhibitor, for the treatment of moderate-to-severe PsO in adults who are candidates for systemic therapy or phototherapy. Skyrizi™ is supplied as 75mg/0.83mL single-dose, prefilled syringes. The recommended dose of risankizumab is 150mg [(2) 75mg injections] administered by subcutaneous (sub-Q) injection at week 0, week 4, and every 12 weeks thereafter. Risankizumab is intended for use under the guidance and supervision of a health care professional. Patients may self-inject risankizumab after training in sub-Q injection technique. Risankizumab may be administered via sub-Q injection into the thighs or abdomen. Administration of risankizumab in the upper, outer arm should only be performed by a health care professional or caregiver. The Wholesale Acquisition Cost (WAC) of Skyrizi™ is $7,375.00 per syringe, resulting in a cost of $29,500.00 for 24 weeks of therapy.
- **Rinvoq™ (upadacitinib):** In August 2019, AbbVie, Inc. announced the FDA approval of Rinvoq™ (upadacitinib), an oral Janus kinase (JAK) inhibitor, for the treatment of adults with moderate-to-severe RA who have had an inadequate response or intolerance to methotrexate (MTX). Use of upadacitinib in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended. Rinvoq™ is supplied as 15mg extended-release (ER) oral tablets, and the recommended dose is 15mg by mouth once daily. Upadacitinib is not recommended for use in patients

with severe hepatic impairment (Child-Pugh C) and upadacitinib has a *Boxed Warning* regarding the risk of serious infections, malignancy, and thrombosis. The WAC of Rinvoq™ is $163.89 per tablet, resulting in a monthly cost of $4,916.70.

Select New FDA Approved Indication(s) and Formulations:

- **Humira® (adalimumab) for Pediatric Uveitis:** In October 2018, the FDA approved Humira® (adalimumab) for the treatment of uveitis in pediatric patients 2 years of age and older. Adalimumab was previously FDA approved for the treatment of adult patients with uveitis in 2016.
- **Benlysta® (belimumab) for Pediatric Lupus:** In April 2019, the FDA approved Benlysta® (belimumab) intravenous (IV) infusion for the treatment of children with systemic lupus erythematosus (SLE). This is the first time that the FDA has approved a treatment for pediatric patients with SLE. Belimumab has been FDA approved for use in adult SLE patients since 2011.
- **Otezla® (apremilast) for Behçet's Disease:** In July 2019, the FDA approved Otezla® (apremilast), an oral phosphodiesterase-4 (PDE-4) inhibitor, for the treatment of adults with oral ulcers associated with Behçet's disease. Behçet's disease affects roughly 5 in 100,000 people in the United States, with oral ulcers being the most common manifestation. Current compendia and practice guidance recommend topical corticosteroids (TCSs) applied topically to the mouth or use of oral colchicine as first-line treatments. Apremilast is the only FDA-approved treatment for oral ulcers associated with Behçet's disease. Apremilast was previously FDA approved for the treatment of patients with PsO and PsA.
- **Rituxan® (rituximab) for Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA):** In September 2019, the FDA approved Rituxan® (rituximab) for the treatment of GPA and MPA, rare vasculitis conditions, in patients 2 years of age and older. When used for GPA and MPA, rituximab must be used in combination with corticosteroids. Rituximab is the first FDA approved therapy for children with GPA and MPA. Characteristics of the disease include inflamed small blood vessels, which reduce the flow of blood and can ultimately damage organs such as the lungs and kidneys. Rituximab was previously FDA approved to treat adult patients with GPA and MPA, non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), RA, and pemphigus vulgaris (PV).

Recommendations

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

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	**adalimumab-adaz (Hyrimoz™)**

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
hydroxychloroquine		adalimumab-adbm (Cyltezo™)
leflunomide		adalimumab-atto (Amjevita™)
mesalamine		**adalimumab-bwwd (Hadlima™)**
methotrexate		alefacept (Amevive®)
minocycline		anakinra (Kineret®)
NSAIDs		apremilast (Otezla®)[β]
oral corticosteroids		baricitinib (Olumiant®)
		brodalumab (Siliq™)
		canakinumab (Ilaris®)[¥]
		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi™)
		etanercept-ykro (Eticovo™)
		golimumab (Simponi® & Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-abda (Renflexis™)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		risankizumab-rzza (Skyrizi™)
		rituximab (Rituxan®)**~**
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®)[Ω]
		tildrakizumab-asmn (Ilumya™)
		tocilizumab (Actemra®)[π]
		tofacitinib (Xeljanz® & Xeljanz® XR)
		upadacitinib (Rinvoq™)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

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

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

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

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

[β]Unique criteria applies for a diagnosis of Behçet's disease (BD).

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

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

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

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

Targeted Immunomodulator Tier-2 Approval Criteria:

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

Targeted Immunomodulator Tier-3 Approval Criteria:

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

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

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

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

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

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

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

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical only benefit while the subcutaneous (sub-Q) formulation will be covered as a pharmacy only benefit; and

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

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

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

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[5] AbbVie, Inc. AbbVie Receives FDA Approval of RINVOQ™ (upadacitinib), an Oral JAK Inhibitor For The Treatment of Moderate to Severe Rheumatoid Arthritis. Available online at: https://news.abbvie.com/news/press-releases/abbvie-receives-fda-approval-rinvoq-upadacitinib-an-oral-jak-inhibitor-for-treatment-moderate-to-severe-rheumatoid-arthritis.htm. Issued 08/16/2019. Last accessed 11/18/2019.

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Appendix F

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

Oklahoma Health Care Authority
December 2019

Introduction[1,2]

Elzonris® (Tagraxofusp-erzs):

- **Therapeutic Class:** CD123-directed cytotoxin
- **Indication(s):** Treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years of age and older
- **Boxed Warning:** Capillary leak syndrome
- **How Supplied:** 1,000mcg/1mL single-dose vial (SDV)
- **Dose:** 12mcg/kg intravenously (IV) over 15 minutes once daily on days 1 to 5 of a 21-day cycle
- **Cost:** Wholesale Acquisition Cost (WAC) of $25,529.35 per 1,000mcg vial; treatment cost will vary depending on patient weight

Inrebic® (Fedratinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with intermediate-2 or high-risk primary or secondary [post-polycythemia vera (PV) or post-essential thrombocytopenia (ET)] myelofibrosis
- **Boxed Warning:** Encephalopathy including Wernicke's
- **How Supplied:** 100mg capsule
- **Dose:** 400mg orally once daily with or without food for patients with a baseline platelet count ≥50 x 10^9/L
- **Cost:** WAC of $175.00 per 100mg capsule, resulting in a monthly cost of $21,000.00

Recommendations

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

1. Diagnosis of BPDCN; and
2. Member must be 2 years of age or older; and
3. Must be used as a single-agent.

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

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

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Appendix G

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

Oklahoma Health Care Authority
December 2019

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

- **Aemcolo™ (rifamycin)** was approved by the U.S. Food and Drug Administration (FDA) in November 2018 for the treatment of adult patients with travelers' diarrhea caused by non-invasive strains of *Escherichia coli* (*E. coli*). Aemcolo™ is an orally administered, minimally absorbed antibiotic that is engineered with Cosmo Pharmaceuticals' Multi Matrix Technology, which allows for delayed release to the colon. Aemcolo™ is supplied as 194mg delayed-release tablets, and the recommended dosage is 388mg (2 tablets) orally twice daily for 3 days. The Wholesale Acquisition Cost (WAC) of Aemcolo™ is $12.00 per 194mg tablet, resulting in a cost per 3-day treatment of $144.00.
- **Motegrity™ (prucalopride)** was approved by the FDA in December 2018 for the treatment of adult patients with chronic idiopathic constipation (CIC). Prucalopride is a selective serotonin-4 (5-HT_4) receptor agonist that improves bowel motility by stimulating colonic peristalsis. Motegrity™ is supplied as 1mg and 2mg oral tablets, and the recommended dosage of prucalopride is 2mg orally once daily, taken with or without food. The National Average Drug Acquisition Cost (NADAC) of Motegrity™ is $13.66 per 2mg tablet, resulting in a monthly cost of $409.80.
- **Zelnorm™ (tegaserod),** a selective 5-HT_4 receptor agonist, was approved by the FDA in March 2019 for the treatment of irritable bowel syndrome with constipation (IBS-C) in adult women younger than 65 years of age. The safety and effectiveness of tegaserod in men with IBS-C have not been established. Zelnorm™ was originally FDA approved in 2002 for the treatment of IBS-C in women but was voluntarily withdrawn from the United States market in 2007 due to a potential safety signal regarding ischemic events including angina and stroke. Stroke, myocardial infarction (MI), and cardiovascular (CV) death [major adverse CV events (MACE)] have been reported in adults taking tegaserod who had an increased risk of developing an adverse CV event based on their medical history. A retrospective analysis of tegaserod found that the rate of MACE for tegaserod-treated patients ranged from 0.03% to 0.06% in the overall population and 0.01% to 0.03% in the female population younger than 65 years of age without a history of CV ischemic disease, compared to no MACE in the placebo-treated group. Zelnorm™ is supplied as 6mg oral tablets, and the recommended dosage of tegaserod is 6mg orally twice daily. Tegaserod should be discontinued in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment. The WAC of Zelnorm™ is $6.48 per 6mg tablet, resulting in a monthly cost of $388.80.

- **Ibsrela® (tenapanor)** was approved by the FDA in September 2019 for the treatment of adult patients with IBS-C. Tenapanor is an oral, minimally-absorbed small molecule that acts locally in the gastrointestinal (GI) tract to inhibit the sodium/hydrogen exchanger 3 (NHE3), which reduces the absorption of sodium from the small intestine and colon, resulting in an increase in water secretion into the intestinal lumen, thereby accelerating intestinal transit time and resulting in a softer stool consistency. Ibsrela® is supplied as 50mg oral tablets, and the recommended dosage of tenapanor is 50mg orally twice daily. Tenapanor has a *Boxed Warning* for the risk of serious dehydration in pediatric patients; the safety and effectiveness of tenapanor have not been established in pediatric patients younger than 18 years of age, and tenapanor is contraindicated in patients younger than 6 years of age. Cost information for Ibsrela® is not yet available.

Recommendations

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

Aemcolo™ (Rifamycin) Approval Criteria:

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

Motegrity™ (Prucalopride) Approval Criteria:

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

Zelnorm™ (Tegaserod) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with constipation (IBS-C) in female members 18 to 64 years of age; and
2. Member must be female for authorization of Zelnorm™ (the safety and effectiveness of Zelnorm™ in men with IBS-C have not been established); and
3. Member must not have any of the contraindications for use of Zelnorm™ [i.e., history of myocardial infarction (MI), stroke, transient ischemic attack (TIA), or angina; history of ischemic colitis or other forms of intestinal ischemia; severe renal impairment (estimated glomerular filtration rate {eGFR} <15mL/min/1.73m^2) or end-stage renal disease (ESRD); moderate or severe hepatic impairment (Child-Pugh B or C); history of bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions; hypersensitivity to tegaserod)]; and
4. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
5. Documented and updated colon screening for members older than 50 years of age; and
6. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
8. Approval will initially be for 6 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment. Zelnorm™ should be discontinued in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment; and
9. A quantity limit of 60 tablets per 30 days will apply.

Ibsrela® (Tenapanor) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least 3 different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and

5. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
7. A quantity limit of 60 tablets per 30 days will apply.

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

Symproic® (Naldemedine) Approval Criteria:

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

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[4] Motegrity™ (Prucalopride) Prescribing Information. Shire. Available online at: https://www.shirecontent.com/PI/PDFs/MOTEGRITY_USA_ENG.pdf. Last revised 12/2018. Last accessed 11/14/2019.

[5] US WorldMeds. FDA Approves the Reintroduction of Zelnorm™ (Tegaserod) for Irritable Bowel Syndrome with Constipation (IBS-C) in Women Under 65. *BioSpace*. Available online at: https://www.biospace.com/article/releases/fda-approves-the-reintroduction-of-zelnorm-tegaserod-for-irritable-bowel-syndrome-with-constipation-ibs-c-in-women-under-65/. Issued 04/01/2019. Last accessed 11/14/2019.

[6] Zelnorm™ (Tegaserod) Prescribing Information. Sloan Pharma. Available online at: https://www.alfasigmausa.com/wp-content/uploads/master/zelnorm-pi.pdf. Last revised 03/2019. Last accessed 11/14/2019.

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Appendix H

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

Oklahoma Health Care Authority
December 2019

Introduction[1,2]

Drizalma Sprinkle™ [duloxetine delayed-release (DR) capsules] is a serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for the treatment of major depressive disorder (MDD) in adults, generalized anxiety disorder (GAD) in adults and pediatric patients 7 to 17 years of age, diabetic peripheral neuropathy in adults, and chronic musculoskeletal pain in adults. It is available in the following dosage strengths: 20mg, 30mg, 40mg, and 60mg. The recommended dosing range is from 30mg/day to 120mg/day depending on diagnosis. Drizalma Sprinkle™ may be swallowed whole or the capsules may be opened and the contents sprinkled over applesauce and swallowed immediately. Additionally, Drizalma Sprinkle™ capsules may be opened and mixed with water for nasogastric (NG) tube administration. Drizalma Sprinkle™ carries a *Boxed Warning* for suicidal thoughts and behaviors. The Wholesale Acquisition Cost (WAC) of Drizalma Sprinkle™ is $5.85 per capsule regardless of strength, resulting in a monthly cost of $175.50 for once daily dosing; dosing may vary based on diagnosis. For comparison, duloxetine 60mg DR capsules (generic Cymbalta®) has a National Average Drug Acquisition Cost (NADAC) of $0.16 per capsule, resulting in monthly cost of $4.80 at a dose of 60mg once daily.

Spravato™ (esketamine nasal spray) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults. Spravato™ is supplied as a 56mg dose kit containing (2) 28mg nasal spray devices or an 84mg dose kit containing (3) 28mg nasal spray devices. It is self-administered by the patient under the direct supervision of a health care provider. A treatment session consists of nasal administration of Spravato™ and post-administration observation. It is recommended to assess the patient's blood pressure (BP) before and after administration. The recommended dosing for the induction phase is twice per week during weeks 1 to 4. The day 1 starting dose is 56mg with subsequent doses of 56mg or 84mg. Dosage adjustments should be made based on efficacy and tolerability. Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine need for continued treatment. The recommended dosing for the maintenance phase is once weekly dosed at 56mg or 84mg for weeks 5 to 8. For week 9 and after, the recommended dosing is 56mg or 84mg every 2 weeks or once weekly. Dosing frequency should be individualized to the least frequent dosing to maintain remission/response. Spravato™ carries a *Boxed Warning* for sedation, dissociation, abuse and misuse, and suicidal thoughts and behaviors. Because of the risks of serious adverse outcomes, Spravato™ is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Spravato™ REMS program.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Dose	Cost Per Month*
Spravato™ (esketamine nasal spray) 56mg kit	**$295.00**	**$590.00**	**$2,360.00**
Spravato™ (esketamine nasal spray) 84mg kit	**$295.00**	**$885.00**	**$3,540.00**
duloxetine 60mg capsule	$0.16	$0.16	$4.80
escitalopram 20mg tablet	$0.07	$0.07	$2.10

Unit = nasal spray device, capsule, or tablet.
*Cost per month for duloxetine and escitalopram based on maximum FDA recommended maintenance dosing for major depressive disorder. Cost per month for Spravato™ based on once weekly dosing (4 doses).
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.

Citalopram 20mg/10mL, escitalopram 10mg/10mL, and fluoxetine 20mg/5mL unit dose cups may provide convenience, but come at a considerably higher cost than the use of bulk stock bottles. The following table shows the cost comparison between the unit dose cups and bulk stock bottles for these medications.

Cost Comparison:

Medication	Cost Per mL (Unit Dose)	Cost Per 30 Days* (Unit Dose)	Cost Per mL (Bulk)	Cost Per 30 Days* (Bulk)
citalopram 20mg/10mL	**$1.12**	**$336.00**	$0.16	$48.00
escitalopram 10mg/10mL	**$0.72**	**$216.00**	$0.33	$99.00
fluoxetine 20mg/5mL	**$1.11**	**$166.50**	$0.49	$73.50

*Cost per 30 days based on FDA recommended dosing for major depressive disorder. Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

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

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

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

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

Spravato™ (Esketamine Nasal Spray) Approval Criteria:

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

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

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

1. An FDA approved indication; and

2. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.

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

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

[1] Drizalma Sprinkle™ Prescribing Information. Sun Pharmaceutical Industries, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212516s000lbl.pdf. Last revised 07/2019. Last accessed 11/11/2019.

[2] Spravato™ Prescribing Information. Janssen Pharmaceutical Companies. Available online at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SPRAVATO-pi.pdf. Last revised 05/2019. Last accessed 11/11/2019.

Appendix I

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

Oklahoma Health Care Authority
December 2019

Introduction[1,2,3,4]

- **Bevyxxa® (betrixaban)** was approved by the U.S. Food and Drug Administration (FDA) in June 2017 for the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE. Bevyxxa® is a factor Xa (FXa) inhibitor available as an oral capsule in 2 strengths: 40mg and 80mg. The recommended dose of betrixaban is an initial single dose of 160mg, followed by 80mg once daily, taken at the same time each day with food for 35 to 42 days of treatment. For patients with severe renal impairment [creatinine clearance (CrCl) ≥15 to <30mL/min], the recommended dose of betrixaban is an initial dose of 80mg followed by 40mg once daily on subsequent days for 35 to 42 days of treatment. The Wholesale Acquisition Cost (WAC) of Bevyxxa® is $15.00 per capsule, regardless of strength, which results in a treatment cost of $645.00, based on the loading dose on day 1 followed by up to a total of 42 days of treatment.
- **Xarelto® (rivaroxaban)** was approved by the FDA in October 2019 for the prevention of VTE in hospitalized, acutely ill medical patients at risk for thromboembolic complications who are not at high-risk of bleeding. Rivaroxaban can now be initiated for these patients during hospitalization and continued after discharge for a total recommended duration of 31 to 39 days. Rivaroxaban was previously approved for the following: nonvalvular atrial fibrillation; treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; prophylaxis of DVT which may lead to PE in patients undergoing knee or hip replacement surgery; and for use in combination with aspirin to reduce the risk of major cardiovascular (CV) events in patients with coronary artery disease (CAD) or peripheral artery disease (PAD).

Recommendations

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

Bevyxxa® (Betrixaban) Approval Criteria:

1. An FDA approved indication for the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE; and

2. If the member started on the medication in the hospital, number of days of treatment with betrixaban in the hospital must be provided; and
3. Approvals will be for a maximum duration of 42 days (including use accounted for while in hospital); and
4. A quantity limit of 43 capsules per 42 days will apply.

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

Xarelto® (Rivaroxaban) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; or
    c. Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery; or
    d. In combination with aspirin, to reduce the risk of major cardiovascular (CV) events [CV death, myocardial infarction (MI), and stroke] in members with chronic coronary artery disease (CAD) or peripheral artery disease (PAD); or
    e. Prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding; and
2. For Xarelto® (rivaroxaban) 15mg and 20mg:
    a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. For Xarelto® (rivaroxaban) 10mg:
    a. One prescription for up to ~~35~~ 39 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis in patients following hip or knee replacement surgery or for prophylaxis of VTE in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding; or
4. For Xarelto® (rivaroxaban) 2.5mg:
    a. Must be used in combination with aspirin 75 to 100mg to reduce the risk of major CV events in members with chronic CAD or PAD.

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[1] FDA. FDA Approved Betrixaban (Bevyxxa®, Portola) for the Prophylaxis of Venous Thromboembolism (VTE) in Adult Patients. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approved-betrixaban-bevyxxa-portola-prophylaxis-venous-thromboembolism-vte-adult-patients. Issued 06/23/2017. Last accessed 11/21/2019.

[2] Bevyxxa® (Betrixaban) Prescribing Information. Portola Pharmaceuticals, Inc. Available online at: https://www.bevyxxa.com/wp-content/uploads/2019/08/PI-V1.5-Clean-Word-30July-2019-linked.pdf. Last revised 07/2019. Last accessed 11/21/2019.

[3] Bevyxxa® (Betrixaban) - New Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_bevyxxa_2017-0623.pdf. Issued 2017. Last accessed 11/21/2019.

[4] Janssen Pharmaceutical Companies of Johnson & Johnson. U.S. FDA Approves Xarelto® (Rivaroxaban) to Help Prevent Blood Clots in Acutely Ill Medical Patients. *PR Newswire*. Available online at: https://markets.businessinsider.com/news/stocks/u-s-fda-approves-xarelto-rivaroxaban-to-help-prevent-blood-clots-in-acutely-ill-medical-patients-1028596385. Issued 10/14/2019. Last accessed 11/21/2019.

Appendix J

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

Oklahoma Health Care Authority
December 2019

Introduction[1]

Avaclyr™ (acyclovir 3% ophthalmic ointment) is a herpes simplex virus (HSV) nucleoside analog DNA polymerase inhibitor indicated for the treatment of acute herpetic keratitis (dendritic ulcers) in patients with HSV-1 and HSV-2. Avaclyr™ is supplied as a topical sterile ointment containing 3% acyclovir. The recommend dosing is to apply a 1cm ribbon of ointment in the lower cul-de-sac of the affected eye(s) 5 times per day until healed, then 3 times per day for 7 days.

Cost Comparison: There are several different formulations of acyclovir available in addition to alternative products for the treatment of acute herpetic keratitis (dendritic ulcers) in patients with HSV. The cost of Avaclyr™ is not yet available.

Medication	Cost Per Unit[+]	Cost Per Treatment*
Avaclyr™ (acyclovir 3% ophthalmic ointment)	**NA**	**NA**
trifluridine 1% ophthalmic solution	$22.70	$170.25
acyclovir 400mg oral tablet	$0.08	$2.80

[+]Unit = milliliter (mL) or tablet; NA = not available
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Cost per treatment for solution = 1 bottle; cost per treatment of tablet = recommended dose of 400mg 5 times daily for 7 days

Recommendations

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

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

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

[1] U.S. Food and Drug Administration (FDA). Drugs@FDA: FDA Approved Drug Products. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/0202408s000lbl.pdf. Last accessed 11/21/2019.

Appendix K

Fiscal Year 2019 Annual Review of Thrombocytopenia Medications

Oklahoma Health Care Authority
December 2019

Current Prior Authorization Criteria

Cablivi® (Caplacizumab-yhdp) Approval Criteria:

1. An FDA approved diagnosis of acquired thrombotic thrombocytopenic purpura (aTTP); and
2. Member must be undergoing plasma exchange therapy; and
    a. Dates of initiation of plasma exchange therapy must be listed on the prior authorization request; and
    b. Authorizations will be for the duration of plasma exchange and for 30 days after discontinuation of plasma exchange; and
3. Member must be utilizing immunosuppressant therapy; and
4. Must be prescribed by, or in consultation with, a hematologist; and
5. A quantity limit of 11mg per day will apply. Initial approvals will be for the duration of plasma exchange plus 30 days. Reauthorization, after completing 30 days post-plasma exchange, may be considered if the prescriber documents sign(s) of persistent underlying disease remain. Reauthorization will be for a maximum of 28 days.

Doptelet® (Avatrombopag) Approval Criteria:

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

Mulpleta® (Lusutrombopag) Approval Criteria:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure; and
2. Date of procedure must be listed on the prior authorization request; and

3. Prescriber must verify the member will have the procedure 2 to 8 days after the member receives the last dose of Mulpleta®; and
4. Member must have a baseline platelet count <50 X 10^9/L (recent baseline platelet count must be provided); and
5. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and
6. Mulpleta® must not be used in an attempt to normalize platelet counts; and
7. A quantity limit of 7 tablets per scheduled procedure will apply.

Tavalisse™ (Fostamatinib) Approval Criteria:

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

Utilization of Thrombocytopenia Medications: Fiscal Year 2019

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	23	125	$1,085,861.96	$8,686.90	$295.07	4,626	3,680
2019	14	62	$735,612.30	$11,864.71	$395.49	2,430	1,860
% Change	**-39.10%**	**-50.40%**	**-32.30%**	**36.60%**	**34.00%**	**-47.50%**	**-49.50%**
Change	**-9**	**-63**	**-$350,249.66**	**$3,177.81**	**$100.42**	**-2,196**	**-1,820**

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

Fiscal Year 2019 Utilization of Nplate® (Romiplostim): Medical Claims

Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	6	68	$327,516.30	$4,816.42	4,711

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

Demographics of Members Utilizing Thrombocytopenia Medications

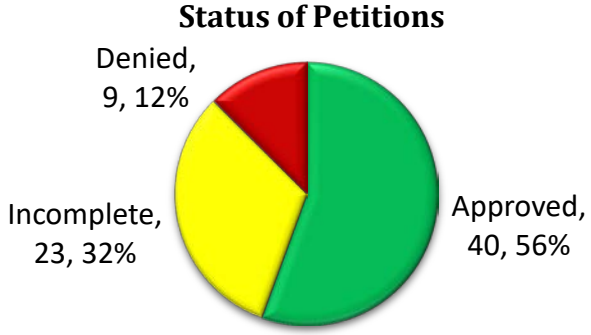
- Due to the limited number of members utilizing thrombocytopenia medications, detailed demographic information could not be provided.

Top Prescriber Specialties of Thrombocytopenia Medications by Number of Claims

- The only prescriber specialties listed on paid pharmacy claims for thrombocytopenia medications during fiscal year 2019 were pediatric hematologist/oncologist and hematologist/oncologist.

Prior Authorization of Thrombocytopenia Medications

There were 72 prior authorization requests submitted for thrombocytopenia medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



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

Anticipated Patent Expiration(s):

- Doptelet® (avatrombopag): May 2025
- Mulpleta® (lusutrombopag): September 2031
- Tavalisse™ (fostamatinib): July 2032

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

- **June 2019:** The FDA approved a supplemental New Drug Application (sNDA) that expands the use of Doptelet® (avatrombopag) to include the treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. In the pivotal Phase 3 study, Doptelet® resulted in a platelet count of at least 50 x 10^9/L at day 8 of therapy in the majority of patients. Efficacy was superior to placebo in maintaining the platelet levels in the target range during the 6-month treatment period. Additional supportive data for the ITP sNDA was provided by 2 Phase 2 ITP clinical trials, as well as 2 Phase 3 trials for the treatment of thrombocytopenia in patients with chronic liver disease (CLD). The safety and tolerability of Doptelet® is supported by safety data for 128 patients with ITP and more than 1,000 patients treated across 24 studies in the Doptelet® clinical development program across multiple indications. Doptelet® is also approved for the treatment of thrombocytopenia in adults with CLD who are scheduled to undergo a procedure.
- **October 2019:** The FDA approved a supplemental Biologics License Application (sBLA) for Nplate® (romiplostim) to include new data in its prescribing information showing sustained platelet responses in adults with ITP. The updated indication expands treatment with Nplate® to newly diagnosed and persistent adult ITP patients who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. The FDA previously approved an sBLA for Nplate® in December 2018 for the treatment of pediatric patients with ITP.

Pipeline:

- **Efgartigimod:** In October 2019, Argenx provided an update on the status of clinical trials for efgartigimod, a human IgG1 Fc fragment that is intended to result in a targeted reduction of IgG autoantibodies. Argenx is evaluating efgartigimod across 4 indications where IgG autoantibodies are directly pathogenic, including generalized myasthenia gravis, ITP, pemphigus vulgaris, and chronic inflammatory demyelinating polyneuropathy. For the treatment of ITP, the global Phase 3 program will include 2 registrational trials which will run concurrently. The first trial is expected to start in the second half of 2019 and will evaluate intravenous (IV) efgartigimod on top of standard of care and the second trial will evaluate IV efgartigimod to induce IgG antibody reduction and clinical response followed by fixed dose subcutaneous efgartigimod to maintain clinical benefit.

Recommendations

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

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

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with CLD who are scheduled to undergo a procedure; and
2. ~~A patient-specific, clinically significant reason why the member cannot use Mulpleta® (lusutrombopag); and~~
3. Date of procedure must be listed on the prior authorization request; and
4. Prescriber must verify the member will have the procedure within 5 to 8 days after the member receives the last dose of Doptelet®; and
5. Member must have a baseline platelet count <50 X 10^9/L; and
6. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and
7. Doptelet® must not be used in an attempt to normalize platelet counts; and
8. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
9. Prescriber must verify member is not breastfeeding; and
10. A quantity limit of 15 tablets per scheduled procedure will apply.

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

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment; and
2. Member must be 18 years of age or older; and
3. Previous insufficient response with at least 1 of the following treatments:
    a. Corticosteroids; or
    b. Immunoglobulins; or
    c. Splenectomy; and
4. A patient-specific, clinically significant reason why the member cannot use an alternative thrombopoietin (TPO) receptor agonist available without a prior authorization must be provided; and
5. Prescriber must verify the degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
6. Prescriber must verify platelet counts will be assessed weekly until a stable platelet count greater than 50 x 10^9/L has been achieved, and then obtained monthly thereafter; and
7. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
8. Doptelet® must not be used in an attempt to normalize platelet counts; and
9. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
10. Prescriber must verify member is not breastfeeding; and

11. A quantity limit of 60 tablets per 30 days will apply.

Utilization Details of Thrombocytopenia Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
PROMACTA TAB 75MG	31	6	$413,795.89	$13,348.25	$444.94	56.25%
PROMACTA TAB 50MG	17	5	$217,119.73	$12,771.75	$425.72	29.52%
PROMACTA TAB 25MG	8	3	$46,065.46	$5,758.18	$191.94	6.26%
TAVALISSE TAB 150MG	4	1	$39,339.48	$9,834.87	$327.83	5.35%
TAVALISSE TAB 100MG	2	1	$19,291.74	$9,645.87	$321.53	2.62%
TOTAL	**62**	**14***	**$735,612.30**	**$11,864.71**	**$395.49**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Promacta® was FDA approved in 2008 and has a significant federal rebate.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Last revised 11/2019. Last accessed 11/15/2019.
[2] Dova Pharmaceuticals, Inc. Dova Pharmaceuticals Announces FDA Approval of Supplemental New Drug Application for Doptelet® (avatrombopag) for Treatment of Chronic Immune Thrombocytopenia (ITP). *Globe Newswire*. Available online at: http://investors.dova.com/news-releases/news-release-details/dova-pharmaceuticals-announces-fda-approval-supplemental-new. Issued 06/27/2019. Last accessed 11/18/2019.
[3] Amgen. Nplate® (romiplostim) Now Approved For Earlier Use In Adults with Immune Thrombocytopenia. *PR Newswire*. Available online at: https://www.amgen.com/media/news-releases/2019/10/nplate-romiplostim-now-approved-for-earlier-use-in-adults-with-immune-thrombocytopenia/. Issued 10/18/2019. Last accessed 11/18/2019.
[4] Argenx. Argenx Reports Third Quarter 2019 Financial Results and Provides Business Update. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/24/1934580/0/en/argenx-reports-third-quarter-2019-financial-results-and-provides-business-update.html. Issued 10/24/2019. Last accessed 11/18/2019.

Appendix L

Fiscal Year 2019 Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate)

Oklahoma Health Care Authority
December 2019

Current Prior Authorization Criteria

Inhaled Corticosteroids 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 (Asmanex®)	
mometasone furoate/formoterol (Dulera® HFA)	

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.

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

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

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

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

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

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

QVAR® RediHaler™ (Beclomethasone Dipropionate HFA) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. 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.

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

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

Long-Acting Beta$_2$ Agonist (LABA) and Long-Acting Muscarinic Antagonist (LAMA) Tier-2 Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), chronic bronchitis, or emphysema; and
3. A 4-week trial of at least 1 long-acting beta$_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days; or

4. A documented adverse effect, drug interaction, or contraindication to all available Tier-1 products; or
5. A clinical exception may apply for members who are unable to effectively use hand-actuated devices, such as Spiriva® Handihaler®, or who are stable on nebulized therapy.

Spiriva® Respimat® (Tiotropium Bromide Soft Mist Inhaler) Approval Criteria [Asthma Diagnosis]:

1. An FDA approved diagnosis of asthma; and
2. Member must be 6 years of age or older; and
3. Member must have used a medium-to-high dose inhaled corticosteroid and long-acting $beta_2$ agonist (ICS/LABA) for at least 1 month immediately prior to request for authorization; and
4. Member must have had a trial of a leukotriene receptor antagonist for at least 1 month in the last 90 days; and
5. Member must have a history of exacerbations despite required trials; and
6. Member must remain on an ICS or ICS/LABA while on tiotropium therapy; and
    a. Member's asthma must be considered uncontrolled by prescriber:
        i. Member requires rescue inhaler >2 days per week for reasons other than prevention of exercise induced bronchospasms; or
        ii. Member requires oral systemic corticosteroids; or
    b. A clinical situation warranting initiation of tiotropium therapy in addition to an ICS/LABA due to severity of asthma; and
7. A patient-specific, clinically significant reason the member is unable to use Spiriva® HandiHaler® (tiotropium) which does not require prior authorization must be provided.

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

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting $beta_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components must be provided.

Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in patients with a history of exacerbations; and
2. A 4 week trial of at least 1 long-acting $beta_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
3. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA must be provided.

Daliresp® (Roflumilast) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD) with history of chronic bronchitis; and
2. Forced expiratory volume (FEV) ≤50% of predicted; and
3. Member is inadequately controlled on long-acting bronchodilator therapy (must have 3 or more claims for long-acting bronchodilators in the previous 6 months).

Cinqair® (Reslizumab) Approval Criteria:

1. An FDA approved indication of add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype; and
2. Member must be 18 years of age or older; and
3. Member must have a blood eosinophil count ≥400cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. Cinqair® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
8. Cinqair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Member's weight should be provided on prior authorization requests. Weights should have been taken within the last 4 weeks to provide accurate weight-based dosing.

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

1. An FDA approved indication for add-on maintenance treatment of patients with moderate-to-severe eosinophilic phenotype asthma or oral corticosteroid-dependent asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count of ≥150cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids

despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. The prescriber must verify the member has been counseled on proper administration and storage of Dupixent®; and
8. Dupixent® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. Quantities approved must not exceed FDA recommended dosing requirements.

Fasenra® (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count ≥150cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. Fasenra® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
8. Fasenra® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. A quantity limit of 1 prefilled syringe per 56 days will apply.

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

1. An FDA approved diagnosis of EGPA; and
2. Member meets 1 of the following:
    a. Member must have a past history of at least 1 confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] within the past 12 months; or
    b. Member must have refractory disease within the last 6 months following induction of a standard treatment regimen administered compliantly for at least 3 months; and
3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite glucocorticoid therapy (oral prednisone equivalent ≥7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. Nucala® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
7. A quantity limit of 3 vials per 28 days will apply; and
8. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by a Birmingham Vasculitis Activity Score (BVAS) of 0 (zero), fewer EGPA relapses from baseline, or a decrease in daily OCS dose regimen from baseline.

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

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

7. Nucala® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
8. Nucala® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
10. A quantity limit of 1 vial per 28 days will apply.

Xolair® (Omalizumab Injection) Approval Criteria [Asthma Diagnosis]:

1. A diagnosis of severe persistent asthma; and
2. Member must be between 6 and 75 years of age; and
3. Member must have a positive skin test to at least 1 perennial aeroallergen. Positive perennial aeroallergens must be listed on the prior authorization request; and
4. Member must have a pretreatment serum IgE level between 30 and 1,300 IU/mL (depending on member age); and
5. Member's weight must be between 20kg and 150kg; and
6. Member must have been on medium-to-high-dose inhaled corticosteroids (ICS) (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose) for at minimum the past 3 months; and
7. Prescribed Xolair® dose must be an FDA approved regimen per Xolair® prescribing information; and
8. Xolair® must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
9. Xolair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the past 12 months, or member must have been determined to be dependent on systemic corticosteroids to prevent serious exacerbations; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval.

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

1. An FDA approved diagnosis of CIU; and
2. Member must be 12 years of age or older; and
3. Other forms of urticaria must be ruled out; and
4. Other potential causes of urticaria must be ruled out; and
5. Member must have an Urticaria Activity Score (UAS) ≥16; and

6. Prescriber must be an allergist, immunologist, or dermatologist (or be an advanced care practitioner with a supervising physician that is an allergist, immunologist, or dermatologist); and
7. A trial of a second generation antihistamine dosed at 4 times the maximum FDA dose within the last 3 months for at least 4 weeks (or less if symptoms are intolerable); and
8. Initial dosing will only be approved for 150mg every 4 weeks. If the member has inadequate results at this dose, then the dose may be increased to 300mg every 4 weeks; and
9. Initial approvals will be for the duration of 3 months at which time compliance will be evaluated for continued approval.

Utilization of Maintenance Asthma and COPD Medications: Fiscal Year 2019[1,2]

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	9,020	38,643	$13,714,489.68	$354.90	$11.58	1,288,031	1,183,906
2019	10,316	43,000	$15,853,739.12	$368.69	$11.95	1,352,902	1,326,414
% Change	**14.40%**	**11.30%**	**15.60%**	**3.90%**	**3.20%**	**5.00%**	**12.00%**
Change	**1,296**	**4,357**	**$2,139,249.44**	**$13.79**	**$0.37**	**64,871**	**142,508**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Please note, the above data does not include asthma-indicated monoclonal antibodies or medications that contain an inhaled corticosteroid alone. Please see the following table and utilization details at the end of this report.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Comparison of Fiscal Years: Asthma-Indicated Monoclonal Antibodies¥

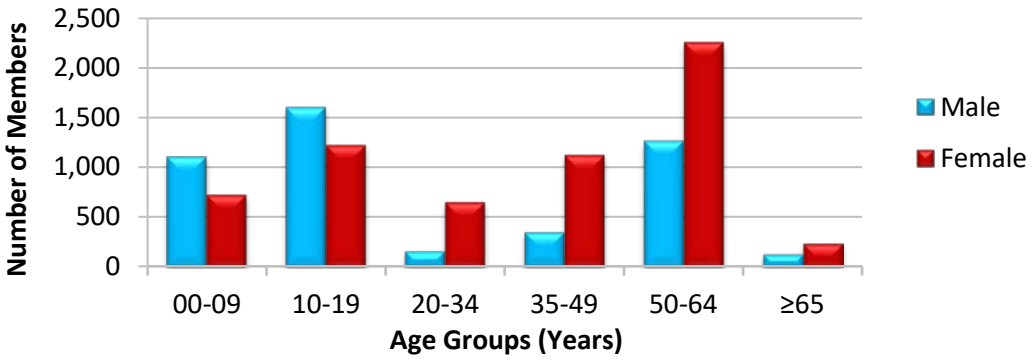
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	45	233	$851,724.81	$3,655.47	$129.13	1,010	6,596
2019	70	470	$1,400,762.99	$2,980.35	$108.87	1,640	12,866
% Change	**55.60%**	**101.70%**	**64.50%**	**-18.50%**	**-15.70%**	**62.40%**	**95.10%**
Change	**25**	**237**	**$549,038.18**	**-$675.12**	**-$20.26**	**630**	**6,270**

¥Pharmacy claims data only.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Utilization data includes Dupixent® used for all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

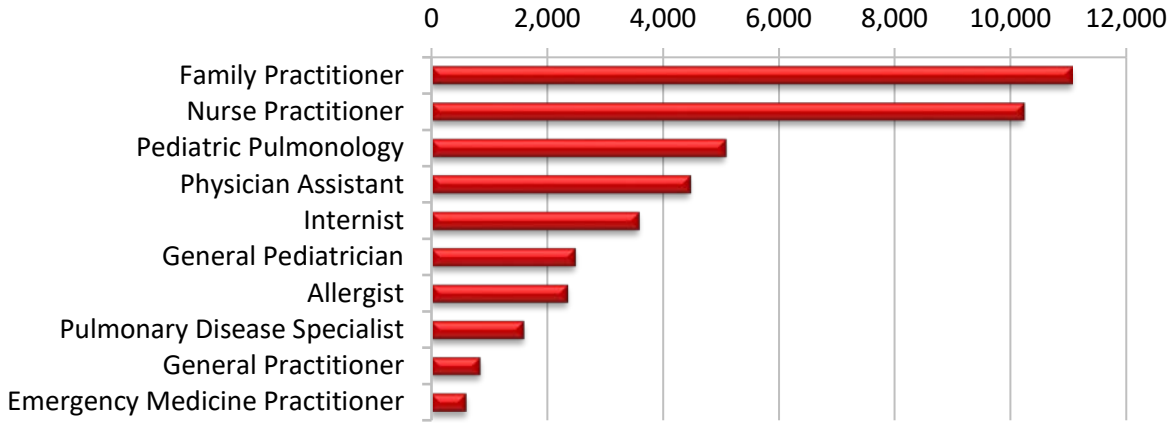
- Please note Cinqair® (reslizumab) is billed by medical claims only and not reflected in the above pharmacy claims data. Xolair® (omalizumab), Cinqair® (reslizumab), and Nucala® (mepolizumab) medical claims utilization details for fiscal year 2019 can be found at the end of this report.
- The U.S. Food and Drug Administration (FDA) approved Dupixent® (dupilumab) as an add-on maintenance therapy for the treatment of moderate-to-severe asthma in patients 12 years of age and older with an eosinophilic phenotype or with oral

corticosteroid (OCS)-dependent asthma in October 2018. Dupilumab was originally FDA approved in March 2017 for the treatment of adults with moderate-to severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable. The comparison of fiscal years utilization data of asthma indicated monoclonal antibodies includes dupilumab which may have been used to treat AD.

Demographics of Members Utilizing Maintenance Asthma and COPD Medications



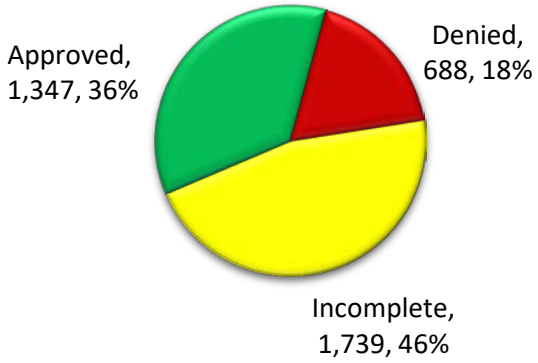
Top Prescriber Specialties of Maintenance Asthma and COPD Medications by Number of Claims



Prior Authorization of Maintenance Asthma and COPD Medications

There were 3,774 prior authorization requests submitted for maintenance asthma and COPD medications during fiscal year 2019. Of those prior authorization requests, 426 were submitted for monoclonal antibody medications. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Dulera® (mometasone/formoterol inhalation aerosol): November 2020
- Perforomist® (formoterol nebulizer solution): June 2021
- Brovana® (arformoterol nebulizer solution): November 2021
- Daliresp® (roflumilast oral tablet): March 2024
- Arcapta® Neohaler® (indacaterol inhalation powder): October 2028
- Seebri® Neohaler® (glycopyrrolate inhalation powder): October 2028
- Utibron® Neohaler® (indacaterol/glycopyrrolate inhalation powder): October 2028
- Tudorza® Pressair® (aclidinium inhalation powder): March 2029
- Duaklir® Pressair® (aclidinium/formoterol inhalation powder): March 2029
- Symbicort® (budesonide/formoterol inhalation aerosol): October 2029
- Spiriva® HandiHaler® (tiotropium inhalation powder): April 2030
- Striverdi® Respimat® (olodaterol inhalation spray): October 2030
- Stiolto® Respimat® (tiotropium/olodaterol inhalation spray): October 2030
- Breo® Ellipta® (fluticasone furoate/vilanterol inhalation powder): October 2030
- Incruse® Ellipta® (umeclidinium inhalation powder): October 2030
- Arnuity® Ellipta® (fluticasone furoate inhalation powder): October 2030
- Anoro® Ellipta® (umeclidinium/vilanterol inhalation powder): November 2030
- Trelegy® Ellipta® (fluticasone furoate/umeclidinium/vilanterol inhalation powder): November 2030
- Bevespi Aerosphere® (glycopyrrolate/formoterol inhalation aerosol): March 2031
- Spiriva® Respimat® (tiotropium soft mist inhaler): April 2031
- QVAR® RediHaler™ (beclomethasone inhalation aerosol): July 2031
- ArmonAir™ RespiClick® (fluticasone propionate inhalation powder): February 2032
- AirDuo RespiClick® (fluticasone propionate/salmeterol inhalation powder): October 2034
- AirDuo® Digihaler™ (fluticasone propionate/salmeterol inhalation powder): August 2035

New FDA Approval(s):

- **April 2019:** Duaklir® Pressair® (aclidinium/formoterol inhalation powder)

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

- **March 2019:** The FDA approved Dupixent® (dupilumab) for the treatment of adolescent patients 12 to 17 years of age with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable. Dupilumab is also approved for the treatment of adult patients with moderate-to-severe AD that is not well controlled with topical prescription therapies; and for use with other asthma medications for the maintenance treatment of moderate-to-severe asthma in patients 12 years of age and older whose asthma is not controlled with their current asthma medications. Sanofi and Regeneron are also studying dupilumab in a broad range of clinical development programs for diseases driven by allergic and other type 2 (T2) inflammation, including pediatric (6 to 11 years of age) AD (Phase 3), pediatric (6 months to 5 years of age) AD (Phase 2/3), pediatric (6 to 11 years of age) asthma (Phase 3), eosinophilic esophagitis (EoE) (Phase 2/3), and food and environmental allergies (Phase 2). Additionally, a future trial is planned for COPD. Criteria for the expanded age approval for the treatment of moderate-to-severe AD was voted on in the November 2019 Drug Utilization Review (DUR) Board meeting.
- **June 2019:** Regeneron and Sanofi announced the FDA approval of Dupixent® (dupilumab) for use with other medications to treat chronic rhinosinusitis with nasal polyposis (CRSwNP) in adults whose disease is not controlled. For patients with CRSwNP, Dupixent® (dupilumab) is supplied as a 300mg pre-filled syringe, and the recommended dose is 300mg every other week as a subcutaneous (subQ) injection. Dupixent® is intended for use under the guidance of a health care professional and can be given in a clinic or at home by self-administration after training by a health care professional. Criteria for Dupixent® for a diagnosis of CRSwNP was voted on in the November 2019 DUR Board meeting.
- **June 2019:** The FDA approved 2 new methods for administering Nucala® (mepolizumab), an autoinjector and a pre-filled safety syringe, for patients or caregivers to administer once every 4 weeks after a health care professional determines at-home administration is appropriate. This is the first anti-interleukin (IL)-5 biologic to be licensed in the United States for at-home administration, and the first respiratory biologic to be approved for administration via an autoinjector. The original lyophilised powder version remains available for subQ administration by a health care professional. The approval is supported by positive patient experience data from 2 open-label, single-arm, Phase 3a studies evaluating the real-world use of Nucala® administered via the new options in-clinic and at-home by patients with severe eosinophilic asthma (SEA), or by their caregivers. Both studies showed patients were able to successfully self-administer treatment with both the autoinjector and pre-filled syringe after appropriate training. In addition, the majority of patients preferred at-home self-administration options compared to in-clinic administration.
- **July 2019:** The FDA approved a supplemental New Drug Application (sNDA) for AirDuo® Digihaler™ (fluticasone propionate/salmeterol) a combination therapy digital inhaler with built-in sensors that connect to a companion mobile application (app) to provide information regarding inhaler use to patients with asthma. AirDuo® Digihaler™ is indicated for the treatment of asthma in patients 12 years of age and older. AirDuo®

Digihaler™ contains built-in sensors that detect when the inhaler is used and measures inspiratory flow rates. This data is then sent to a companion mobile app using Bluetooth® Wireless Technology so that patients can review their data over time, and if desired, share it with their health care providers. Patients can also schedule reminders on their smartphone to take their AirDuo® Digihaler™ as prescribed. AirDuo® Digihaler™ will be available in a small number of Early Experience Programs in partnership with select health care systems in order to gather real-world experience in 2020. Cost information and date of national launch is not yet available.

- **September 2019:** The FDA approved Nucala® (mepolizumab) for use in children as young as 6 years of age who have SEA. Nucala® was first approved in 2015 as an add-on maintenance treatment for patients with SEA who are 12 years of age and older. The expanded FDA approval is supported by an open-label pharmacokinetic (PK) study conducted in children 6 to 11 years of age who were suffering from SEA. The 52-week study showed that the safety profile in pediatric patients 6 to 11 years of age was similar to the known safety profile in patients 12 years of age and older.
- **October 2019:** The FDA approved Fasenra® (benralizumab) in a pre-filled, single-use autoinjector (Fasenra® Pen™) for self-administration. The approval is supported by data from the Phase 3 GRECO trial and the Phase 1 AMES trial, which achieved their primary objective of usability and PK exposure. The safety and tolerability of Fasenra® in these trials were consistent with the established profile of the medicine.

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

- **January 2019:** The FDA approved the first generic formulation of Advair Diskus® (fluticasone propionate/salmeterol) for the treatment of asthma in patients 4 years of age and older and for the maintenance treatment of airflow obstruction and reducing exacerbations in patients with COPD.

News:

- **December 2018:** The Institute for Clinical and Economic Review (ICER) published the final evidence report and meeting summary assessing biologic therapies for treatment of asthma associated with T2 inflammation. The panel found that the evidence demonstrated that Dupixent® (dupilumab) is clinically superior to the standard of care, but that the evidence was insufficient to distinguish between dupilumab and the other 4 biologics in this class [Xolair® (omalizumab), Nucala® (mepolizumab), Cinqair® (reslizumab), and Fasenra® (benrazlizumab)]. Consistent with ICER's value assessment framework, because the incremental cost-effectiveness ratios for all 5 biologics all exceed $175,000 per quality-adjusted life years (QALY), all 5 biologic medications currently approved for uncontrolled moderate-to-severe asthma were deemed "low value" without a formal vote from the panel.

Guideline Update(s):

- **November 2018:** The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has published the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease 2019 Report*. The GOLD 2019 report is a revision of the GOLD 2017 report following systematic literature searches and double-blind

review by the GOLD Science Committee; the GOLD report has been updated to include key peer-reviewed research publications from January 2017 to July 2018. Some updates include a new section on blood eosinophil count, more discussion of the evidence around the use of combination therapies in patients with history of exacerbations, updated algorithms for the initiation of and follow-up management of pharmacological treatment, and new diagrams to improve clarity and to line up with latest evidence. Specific recommendations for the treatment of GOLD groups A, B, C, and D have been revised, and recommendations regarding the follow-up pharmacological management have also been updated and emphasize the need to review, assess, and adjust.

- **April 2019:** The Global Initiative for Asthma (GINA) released the 2019 updates to the Pocket Guide for Asthma Management and Prevention, as well as an updated version of the Pocket Guide on "Diagnosis and Management of Difficult-to-Treat and Severe Asthma in Adolescent and Adult Patients". The 2019 GINA strategy report represents the most significant change in asthma management in over 30 years. GINA no longer recommends starting treatment of asthma with short-acting beta$_2$-agonist (SABA) reliever inhalers on their own. Instead, GINA recommends that all adults and adolescents with asthma should receive either symptom-driven (for mild asthma) or daily inhaled anti-inflammatory controller treatment to reduce their risk of serious exacerbations and to control symptoms. Due to the known dangers of the overuse of SABAs, and current research including evidence that even mild asthma involves inflammation, the GINA guidelines now recommend that adult and adolescent patients with asthma be prescribed a low dose inhaled corticosteroid (ICS)/long-acting beta$_2$ agonist (LABA) to be used for symptom relief, and for asthma that is more than mild, use of this type of medication regularly plus either a SABA or ICS/LABA for quick relief. The only low dose ICS/LABA in the United States with a rapid enough acting LABA component to be included in this new paradigm is Symbicort® 80mcg (budesonide 80mcg/formoterol 4.5mcg), which contains formoterol, a quick-acting and long-lasting bronchodilator. Dulera® (mometasone/formoterol) also contains formoterol, but the corticosteroid doses available are only medium and high dose, without a low dose option.

Pipeline:

- **Benralizumab (Fasenra®):** In November 2018, the FDA granted Orphan Drug designation (ODD) to Fasenra® (benralizumab) for the treatment of EoE. Benralizumab is currently FDA approved as an add-on maintenance treatment of SEA. The FDA also granted benralizumab ODD for the treatment of hypereosinophilic syndrome (HES) in February 2019. Benralizumab is a monoclonal antibody that binds directly to the IL-5 receptor alpha on eosinophils and attracts natural killer cells to induce rapid and near-complete depletion of eosinophils via apoptosis. Additionally, benralizumab is in development for the treatment of severe nasal polyposis and COPD.
- **Ensifentrine/RPL554:** Ensifentrine, also known as RPL554, is a long-acting inhibitor of both phosphodiesterase (PDE)3 and PDE4, 2 enzymes implicated in the development and progression of immunological respiratory diseases, particularly rhinitis and asthma, and this action makes it a potential treatment for respiratory diseases. As a PDE3

inhibitor, the drug is expected to result in bronchodilator actions, whilst the PDE4 component is expected to be anti-inflammatory. Ensifentrine has been administered to more than 730 patients in 12 clinical trials. In March 2018, positive top-line data were reported from a double-blind, placebo-controlled, parallel group, Phase 2b study in the maintenance treatment of COPD. Ensifentrine produced a clinically and statistically significant improvement in peak forced expiratory volume in one second (FEV_1) at 4 weeks in patients with moderate-to-severe COPD compared to placebo. Secondary endpoints measuring 12 hour average FEV_1, COPD symptoms, and quality of life (QOL) were also met. Also in March 2018, positive top-line data were reported from a Phase 2a clinical trial evaluating the PK/pharmacodynamic (PD) profile and tolerability of ensifentrine in cystic fibrosis (CF) patients, with single doses achieving statistically significant ($P<0.05$) increases in average FEV_1. As of October 2019, the last patient was randomized in the Phase 2b dose-ranging study evaluating the effect of nebulized ensifentrine as an add-on treatment with a long-acting bronchodilator in patients with moderate-to-severe COPD, and data is expected around year end of 2019. Commencement of Phase 3 trials is expected in 2020.

- **PT010 (Budesonide/Glycopyrronium/Formoterol Fumarate):** In October 2019, the FDA issued a complete response letter (CRL) regarding the NDA for PT010 (budesonide/ glycopyrronium/formoterol fumarate), an inhaled triple-combination therapy for patients with COPD. The NDA submitted to the FDA included data from the Phase 3 trial, KRONOS. AstraZeneca will now work closely with the FDA regarding next steps, including submitting recent results from the second positive Phase 3 trial, ETHOS, which was not completed at the time the NDA was submitted. PT010 was approved in Japan in June 2019 for the treatment of COPD.
- **SNG001:** SNG001 is an inhaled interferon beta (IFN-beta) currently in Part 2 of a Phase 2 trial aimed at countering the adverse effects of the common cold and influenza viruses in patients with COPD. Part 1 of the trial successfully assessed the safety and antiviral biomarker activity of SNG001 in COPD patients when patients were free of viral infection. The aim of Part 2 is to study the efficacy and safety of inhaled SNG001 in up to 120 COPD patients with a confirmed respiratory viral infection. IFN-beta is a naturally-occurring antiviral protein produced by lung cells upon exposure to a respiratory virus. Lung cells from patients with COPD have been shown to have a poor antiviral response *in vitro.* Treating cells with SNG001 has been shown to orchestrate antiviral defense mechanisms which protect COPD lung cells against respiratory viruses via *in vitro* models. In addition, independent research published by *Nature Communications* suggests that the increased risk of pneumonia associated with the use of ICS to treat exacerbations in COPD could be due to suppression of IFNs and proposes that inhaled IFN-beta therapy could be protective. The trial is being conducted in 15 centers around the United Kingdom and is scheduled to be completed in the winter 2019 to 2020 virus season.
- **Tezepelumab:** In September 2018, the FDA granted Breakthrough Therapy designation (BTD) to tezepelumab for patients with severe asthma, without an eosinophilic phenotype, who are receiving an ICS/LABA with or without oral corticosteroids (OCS)

and additional asthma controllers. The BTD is based on the tezepelumab Phase 2b PATHWAY data that showed a significant reduction in the annual asthma exacerbation rate compared with placebo in a broad population of severe asthma patients irrespective of patient phenotype including T2 biomarker status. Currently available biologic therapies only target T2-driven inflammation. Tezepelumab is a potential first-in-class new therapy that blocks thymic stromal lymphopoietin (TSLP), an upstream modulator of multiple inflammatory pathways. Tezepelumab is currently in development in the Phase 3 PATHFINDER clinical trial program.

Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) Product Summary[22,23,24,25,26]

Indication(s): Duaklir® Pressair® (aclidinium bromide/formoterol fumarate) is a combination of aclidinium bromide, an anticholinergic, and formoterol fumarate, a LABA indicated for the maintenance treatment of patients with COPD.

- **Limitations of Use:** Duaklir® Pressair® is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Dosing:

- Duaklir® Pressair® is supplied as breath-actuated, multi-dose dry powder inhaler metering 400mcg of aclidinium bromide and 12mcg of formoterol fumarate per actuation.
- The recommended dose of Duaklir® Pressair® is 1 oral inhalation twice daily (once in the morning and once in the evening).

Mechanism of Action: Duaklir® Pressair® contains 2 bronchodilators: aclidinium, a long-acting muscarinic antagonist (LAMA; also known as an anticholinergic) and formoterol, a LABA.

- Aclidinium bromide has similar affinity to the subtypes of muscarinic receptors M_1 to M_5. In the airways, it exhibits pharmacological effects through inhibition of M_3 receptors at the smooth muscles leading to bronchodilation.
- Inhaled formoterol fumarate acts locally in the lungs as a bronchodilator. The pharmacologic effects of beta$_2$-adrenoceptor agonist drugs, including formoterol, are at least in part attributable to stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels cause relaxation of bronchial smooth muscle and inhibition of the release of mediators of immediate hypersensitivity from cells, especially from mast cells.

Contraindication(s):

- Use of a LABA, including formoterol fumarate, without an ICS is contraindicated in patients with asthma
- Hypersensitivity to aclidinium bromide or formoterol fumarate or to any component of of Duaklir® Pressair®

Adverse Reactions: The most common adverse reactions experienced during Duaklir® Pressair® clinical studies (incidence ≥3% and more common than placebo) include: upper respiratory tract infection, headache, and back pain.

Efficacy: The efficacy of Duaklir® Pressair® was demonstrated in 1 active-controlled and 2 placebo-controlled studies enrolling 4,977 patients with moderate-to-severe COPD, including chronic bronchitis and emphysema. The 3 studies randomized patients to Duaklir® Pressair® (aclidinium400mcg/formoterol fumarate 12mcg), Tudorza® Pressair® (aclidinium 400mcg), and formoterol fumarate 12mcg. Studies 1 and 2 included a placebo arm, and Study 3 included an active, blinded, control arm. The co-primary endpoints were change from baseline in trough FEV_1 and change from baseline in 1-hour post-dose FEV_1 at week 24 versus formoterol fumarate and Tudorza® Pressair®, respectively. In the 3 trials, Duaklir® Pressair® demonstrated a statistically significant increase in mean change from baseline in trough FEV_1 and change from baseline in 1-hour post-dose FEV_1 at week 24 versus formoterol fumarate 12mcg and Tudorza® Pressair® 400mcg, respectively.

Cost Comparison:

Medication	Cost Per 30 Days	Cost Per Year
Duaklir® Pressair® (aclidinium bromide/formoterol fumarate 400mcg/12mcg)	**$995.00**	**$11,940.00**
Tudorza® Pressair® (aclidinium 400mcg)±	$520.00	$6,240.00
Bevespi Aerosphere® (glycopyrrolate/formoterol fumarate 9mcg/4.8mcg)*	$350.96	$4,211.52
Spiriva® HandiHaler® (tiotropium 18mcg)+	$411.60	$4,939.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Spiriva® HandiHaler® was FDA approved in 2009 and has a significant federal rebate.
±Tudorza® Pressair®: FDA approved regimen is 1 inhalation twice daily and is supplied in a sealed bag in 60 metered doses and 30 metered doses. The cost above is for the 60 metered dose product.
*Bevespi Aerosphere® contains 120 inhalations per 10.7gram canister and the FDA approved regimen is 2 inhalations twice daily.
+Spiriva® HandiHaler® (tiotropium inhalation powder): FDA approved regimen is 2 inhalations of the powder contents from a single Spiriva® capsule (18mcg) once daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Duaklir® Pressair® (aclidinium bromide/formoterol fumarate) with the following criteria:

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

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting $beta_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components must be provided.

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

Fasenra® (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count of ≥150cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Fasenra® prefilled syringe, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Fasenra® prefilled autoinjector pen, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Fasenra®; and
9. Fasenra® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 prefilled syringe or prefilled autoinjector pen per 56 days will apply.

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

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have a blood eosinophil count of 150 cells/mcL can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high-dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and

5. Member must have failed a medium-to-high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
9. Nucala® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 vial, prefilled autoinjector, or prefilled syringe per 28 days will apply.

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

1. An FDA diagnosis of EGPA; and
2. Member meets 1 of the following:
    a. Member must have a past history of at least 1 confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] within the past 12 months; or
    b. Member must have refractory disease within the last 6 months following induction of a standard treatment regimen administered compliantly for at least 3 months; and
3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or

7. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
8. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
9. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by a Birmingham Vasculitis Activity Score (BVAS) of 0 (zero), fewer EGPA relapses from baseline, or a decrease in daily OCS dosing from baseline.

Utilization Details of Maintenance Asthma and COPD Medications: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
COMBINATION LABA/ICS PRODUCTS						
TIER-1						
ADVAIR HFA AER 115/21MCG	6,942	2,030	$2,519,731.33	$11.59	$362.97	15.70%
ADVAIR DISKU AER 250/50MCG	6,578	2,238	$2,478,957.06	$12.47	$376.86	15.44%
SYMBICORT AER 160/4.5MCG	4,482	1,294	$1,454,898.13	$10.31	$324.61	9.06%
DULERA AER 200/5MCG	2,765	803	$835,964.20	$9.89	$302.34	5.21%
ADVAIR DISKU AER 500/50MCG	2,377	675	$1,172,556.84	$16.38	$493.29	7.31%
ADVAIR DISKU AER 100/50MCG	2,134	859	$637,045.27	$9.85	$298.52	3.97%
ADVAIR HFA AER 230/21MCG	1,996	554	$958,441.24	$15.17	$480.18	5.97%
DULERA AER 100/5MCG	1,424	481	$426,901.70	$9.55	$299.79	2.66%
ADVAIR HFA AER 45/21MCG	1,288	439	$363,284.84	$8.86	$282.05	2.26%
FLUTIC/SALME AER 250/50MCG	1,202	659	$331,983.08	$9.07	$276.19	2.07%
SYMBICORT AER 80/4.5MCG	1,133	470	$313,732.92	$8.79	$276.90	1.95%
FLUTIC/SALME AER 500/50MCG	397	205	$141,497.36	$11.85	$356.42	0.88%
FLUTIC/SALME AER 100/50MCG	331	195	$76,039.37	$7.57	$229.73	0.47%
SUBTOTAL	**33,049**	**10,902**	**$11,711,033.34**	**$11.47**	**$354.35**	**72.95%**
TIER-2						
BREO ELLIPTA INH 100/25MCG	114	31	$37,809.65	$11.06	$331.66	0.24%
WIXELA INHUB AER 250/50MCG	6	6	$752.36	$4.18	$125.39	0.00%
WIXELA INHUB AER 100/50MCG	2	2	$209.16	$3.49	$104.58	0.00%
SUBTOTAL	**122**	**39**	**$38,771.17**	**$10.59**	**$317.80**	**0.24%**
INDIVIDUAL COMPONENT LABA PRODUCTS						
TIER-1						
SEREVENT DIS AER 50MCG	702	243	$264,997.00	$12.41	$377.49	1.65%
SUBTOTAL	**702**	**243**	**$264,997.00**	**$12.41**	**$377.49**	**1.65%**
TIER-2						
BROVANA NEB 15MCG	89	27	$70,291.76	$30.74	$789.80	0.44%
PERFOROMIST NEB 20MCG	12	4	$10,458.52	$28.73	$871.54	0.07%
STRIVERDI AER 2.5MCG	3	1	$614.78	$6.83	$204.93	0.00%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SUBTOTAL	**104**	**32**	**$81,365.06**	**$29.68**	**$782.36**	**0.51%**
INDIVIDUAL COMPONENT LAMA PRODUCTS						
TIER-1						
SPIRIVA CAP HANDIHLR 18MCG	7,915	1,993	$3,261,240.88	$13.36	$0.00	20.32%
SUBTOTAL	**7,915**	**1,993**	**$3,261,240.88**	**$13.36**	**$0.00**	**20.32%**
TIER-2						
SPIRIVA SPR 2.5MCG	210	41	$84,391.42	$13.21	$401.86	0.53%
LONHALA MAGN SOL 25MCG	72	18	$79,293.60	$36.71	$1,101.30	0.50%
INCRUSE ELPT INH 62.5MCG	70	16	$22,538.37	$10.73	$321.98	0.14%
SPIRIVA AER 1.25MCG	65	18	$24,460.55	$12.61	37631.62%	0.15%
TUDORZA PRES AER 400MCG	28	7	$9,724.07	$9.82	$347.29	0.06%
YUPELRI SOL 175MCG/3ML	2	2	$2,074.24	$34.54	$1,037.12	0.01%
2SUBTOTAL	**447**	**102**	**$222,482.25**	**$16.31**	**$497.72**	**1.39%**
COMBINATION LABA/LAMA PRODUCTS						
ANORO ELLIPT AER 62.5/25MCG	196	40	$76,969.61	$13.09	$392.70	0.48%
STIOLTO AER 2.5/2.5MCG	91	22	$34,079.02	$12.48	$374.49	0.21%
UTIBRON NEOHALER	1	1	$357.83	$11.93	$357.83	0.00%
SUBTOTAL	**288**	**63**	**$111,406.46**	**$12.89**	**$386.83**	**0.69%**
COMBINATION LABA/LAMA/ICS PRODUCTS						
TRELEGY ELLIPTA 100/62.5/25MCG	179	46	$94,062.70	$17.52	$525.49	0.59%
BEVESPI AER 9/4.8MCG	38	11	$13,214.40	$11.86	$347.75	0.08%
SUBTOTAL	**217**	**57**	**$107,277.10**	**$16.55**	**$494.36**	**0.67%**
PDE4 ENZYME INHIBITOR PRODUCTS						
DALIRESP TAB 500MCG	148	23	$51,460.87	$11.63	$347.71	0.32%
DALIRESP TAB 250MCG	8	4	$3,704.99	$15.97	$463.12	0.02%
SUBTOTAL	**156**	**27**	**$55,165.86**	**$11.85**	**$353.63**	**0.34%**
TOTAL	**43,000**	**10,316***	**$15,853,739.12**	**$11.95**	**$368.69**	**100%**

*Total number of unduplicated members. Costs do not reflect rebated prices or net costs. Fiscal Year 2019 = 07/01/2018 to 06/30/2019; LABA= long-acting beta$_2$ agonist; LAMA= long-acting muscarinic antagonist; ICS= inhaled corticosteroid; PDE4 = phosphodiesterase-4

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: PHARMACY CLAIMS						
DUPIXENT INJ 300/2ML	344	46	$1,026,338.04	$110.22	$2,983.54	73.27%
DUPIXENT INJ 200/1.14ML	41	10	$121,126.84	$116.92	$2,954.31	8.65%
XOLAIR SOL 150MG	38	9	$87,786.94	$82.51	$2,310.18	6.27%
FASENRA INJ 30MG/ML	23	7	$110,401.66	$141.18	$4,800.07	7.88%
NUCALA INJ 100MG	11	2	$32,190.34	$104.51	$2,926.39	2.30%
XOLAIR INJ 150MG/ML	8	2	$17,441.52	$77.86	$2,180.19	1.25%
XOLAIR INJ 75MG/0.5ML	5	1	$5,477.65	$39.13	$1,095.53	0.39%
TOTAL	**470**	**70***	**$1,400,762.99**	**$108.87**	**$2,980.35**	**100%**

*Total number of unduplicated members. Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Costs do not reflect rebated prices or net costs. Utilization data includes Dupixent® used for all diagnoses and does not differentiate between asthma diagnoses and other diagnoses, for which use may be appropriate.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	TOTAL UNITS	COST/ CLAIM	% COST
MONOCLONAL ANTIBODY PRODUCTS: MEDICAL CLAIMS						
OMALIZUMAB INJ (J2357)	150	14	$370,506.60	10,050	$2,470.04	93.82%
MEPOLIZUMAB INJ (J2182)	6	1	$17,724.00	600	$2,954.00	4.49%
RESLIZUMAB INJ (J2786)	1	3	$6,664.32	801	$6,664.32	1.69%
TOTAL	**157**	**18***	**$394,894.92**	**11,451**	**$2,515.25**	**100%**

*Total number of unduplicated members. Fiscal Year 2019 = 07/01/2018 to 06/30/2019
Costs do not reflect rebated prices or net costs. Please note the medical utilization data for omalizumab (J2357) includes all FDA-approved diagnoses. Omalizumab (J2357) medical claims utilization for non-asthma coded diagnoses included 18 paid claims for a total cost of $34,327.20 for Fiscal Year 2019.

Utilization Details of Inhaled Corticosteroids: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
INHALED CORTICOSTEROID PRODUCTS						
TIER-1						
FLOVENT HFA AER 110MCG	20,497	8,299	$4,924,231.06	$6.67	$240.24	42.43%
FLOVENT HFA AER 44MCG	20,206	8,430	$3,685,328.23	$5.59	$182.39	31.75%
BUDESONIDE SUS 0.5MG/2ML	3,404	1,741	$334,001.68	$3.80	$98.12	2.88%
BUDESONIDE SUS 0.25MG/2ML	3,371	2,142	$294,951.46	$3.43	$87.50	2.54%
FLOVENT HFA AER 220MCG	2,625	1,141	$987,774.30	$9.99	$376.29	8.51%
PULMICORT INH 90MCG	1,021	452	$191,516.90	$7.12	$187.58	1.65%
PULMICORT INH 180MCG	794	396	$181,767.47	$5.89	$228.93	1.57%
FLOVENT DISK AER 100MCG	634	277	$123,945.54	$5.84	$195.50	1.07%
ASMANEX HFA AER 100 MCG	559	232	$100,767.13	$4.76	$180.26	0.87%
ALVESCO AER 80MCG	542	219	$142,904.11	$8.69	$263.66	1.23%
FLOVENT DISK AER 250MCG	458	150	$121,087.50	$7.98	$264.38	1.04%
FLOVENT DISK AER 50MCG	372	162	$69,309.09	$5.68	$186.31	0.60%
ASMANEX 30 AER 220MCG	311	105	$55,837.10	$5.94	$179.54	0.48%
ASMANEX 60 AER 220MCG	307	108	$68,251.12	$6.89	$222.32	0.59%
ALVESCO AER 160MCG	280	88	$73,212.33	$8.12	$261.47	0.63%
ASMANEX HFA AER 200 MCG	272	117	$60,552.79	$5.77	$222.62	0.52%
BUDESONIDE SUS 1MG/2ML	252	104	$105,261.44	$15.27	$417.70	0.91%
QVAR AER 40MCG	184	128	$29,962.33	$4.40	$162.84	0.26%
ASMANEX 30 AER 110MCG	99	52	$17,059.19	$5.74	$172.32	0.15%
QVAR AER 80MCG	83	68	$18,588.50	$5.77	$223.96	0.16%
ASMANEX 120 AER 220MCG	67	30	$18,476.53	$5.81	$275.77	0.16%
SUBTOTAL	**56,338**	**24,441**	**$11,604,785.80**	**$6.18**	**$205.99**	**100%**
TIER-2						
QVAR REDIHAL AER 40MCG	10	3	$1,310.24	$3.36	$131.02	0.01%
ARNUITY ELPT INH 100MCG	2	1	$355.66	$5.93	$177.83	0.00%
QVAR REDIHA AER 80MCG	1	1	$220.74	$3.68	$220.74	0.00%
SUBTOTAL	**13**	**5**	**$1,886.64**	**$3.70**	**$145.13**	**0.01%**
TOTAL	**56,351**	**22,163***	**$11,606,672.44**	**$6.18**	**$205.97**	**100%**

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

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Appendix M

30-Day Notice to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran)

Oklahoma Health Care Authority
December 2019

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

Erythropoietic protoporphyria (EPP) is a rare, inherited metabolic disorder caused by a deficiency of the enzyme ferrochelatase (FECH), which results from mutations in the *FECH* gene. Due to abnormally low levels of the FECH enzyme, excessive amounts of protoporphyrin accumulate in the bone marrow, blood plasma, and red blood cells (RBCs). Protoporphyrins also build up in the superficial blood vessels under the skin and are highly sensitive to sunlight; when protoporphyrins absorb sunlight, it results in a reaction that causes severe pain and inflammation. The major symptoms of EPP are related to phototoxicity, which results in severe pain on exposure to sunlight; some patients may also be sensitive to some types of artificial ultraviolet (UV) lights (e.g., fluorescent lights). Upon sun exposure, patients may first experience tingling, itching, and burning of the skin, and the skin may become red and swollen after continued exposure. Some patients may also have edema and persistent erythema of the affected areas, and in rare cases, affected areas of the skin may develop blisters and scar if exposure to sunlight is prolonged. The hands, arms, and face are the most commonly affected areas. The severity and degree of symptoms varies from patient to patient. The diagnosis of EPP is made by a thorough clinical evaluation (of characteristic symptoms) and specialized laboratory tests (to detect increased levels of protoporphyrin in the plasma or RBCs); genetic testing is useful to confirm the diagnosis. EPP is a very rare, inherited disorder that affects males and females in equal numbers. It is estimated that EPP occurs in about 1 in 75,000 to 1 in 200,000 individuals in Europe; the number of patients affected by EPP in the United States is unknown.

There is no cure for EPP; standard treatment for EPP consists of avoidance of sunlight. The use of sun protective clothing will also benefit patients with EPP, and window tinting or films for the vehicle or house may also be beneficial. Sunscreens that contain physical reflecting agents (e.g., zinc oxide, titanium dioxide) or tanning creams that increase skin pigmentation (e.g., creams containing dihydroxyacetone) may be helpful to some patients. A high potency form of oral beta-carotene has been used to try to improve affected patients tolerance of sunlight; however, there is no data to support this treatment. Patients with EPP should take vitamin D supplements, as they are likely to have low vitamin D levels from avoiding sunlight. Other treatments for EPP are symptomatic and supportive. In October 2019, the U.S. Food and Drug Administration (FDA) approved Scenesse® (afamelanotide), the first FDA-approved treatment to help adult patients with EPP increase their light exposure. Scenesse® was first approved in Europe in 2014. Afamelanotide is an α-melanocyte stimulating hormone (α-MSH) analog that functions as a melanocortin-1 receptor (MC1-R) agonist, resulting in increased production of eumelanin in the skin independent of exposure to sunlight or artificial UV light sources.

Melanin, in the form of eumelanin, is photoprotective; eumelanin absorbs, scatters, and quenches UV light, scavenges free radicals, and acts as a neutral density filter that reduces all wavelengths of light equally.

EPP is 1 of a group of disorders known as the porphyrias, which are all characterized by abnormally high levels of porphyrins in the body due to deficiencies of certain enzymes essential to the synthesis of hemoglobin; the symptoms associated with the various types differ, depending on the specific enzyme that is deficient. Acute hepatic porphyria (AHP) refers to a set of metabolic disorders in which the enzyme deficiency occurs in the liver; AHP includes acute intermittent porphyria (AIP), variegate porphyria (VP), aminolevulinic acid (ALA) dehydratase deficiency porphyria (ALAD), and hereditary coproporphyria (HCP). AIP, VP, and HCP are inherited in an autosomal dominant manner, and several mutations have been identified through DNA analysis. ALAD is inherited in an autosomal recessive manner and is very rare. Acute and chronic symptoms due to the effects on the central nervous system (CNS) and peripheral nervous system (PNS) characterize AHPs. The most common presenting symptom is neuropathic abdominal discomfort. The motor, sensory, and autonomic nervous systems are often affected, resulting in autonomic changes (e.g., tachycardia, hypertension), muscle weakness, sensory loss, and pain in the back, chest, and extremities. Three groups of symptoms (abdominal pain, CNS abnormalities, and peripheral neuropathy) are described as a “classic triad” that should suggest acute porphyria. The diagnosis of AHP is made through a thorough clinical evaluation (of characteristic symptoms) and specialized laboratory tests. Urine porphobilinogen (PBG) is the most important first-line screening test, which is both highly sensitive and highly specific. In almost all cases of AHPs, urinary PBG is significantly elevated; however, repeat testing during an acute attack may be needed to diagnosis AHP, as levels may be normal between attacks. Up to 90% of genetic carriers of the more common, autosomal dominantly inherited AHPs (AIP, VP, and HCP) have been discovered, in DNA tests, to be latent for classic symptoms and may need DNA or enzyme testing to make a diagnosis. In the United States, the prevalence of porphyria is estimated to be 1 in 25,000 individuals. The autosomal dominantly inherited AHPs (AIP, VP, and HCP) affect males and females equally. In most regions, AIP is the most common AHP, and ALAD is the least common.

The goal of treatment for an acute attack of AHP is to abate the attack as quickly as possible and to provide supportive and symptomatic care until the acute attack resolves. Hospitalization is usually required; therapy requires confirmation that the patient has AHP, based on the finding of elevated urinary PBG (either at present or previously), but does not require a diagnosis of the exact type of AHP. For patients with an acute attack severe enough to require hospitalization, opioid analgesia, or other intravenous (IV) medication, or that is accompanied by nausea and vomiting, motor neuropathy, paresis, seizures, agitation, delirium, psychosis, ileus that prevents oral intake, or hyponatremia, IV administration of hemin is recommended to prevent progression of symptoms based on the high risk of life-threatening sequelae from a severe acute attack of AHP. Liver transplantation is reserved for patients with life-threatening acute attacks or progression of symptoms despite IV hemin therapy. Though uncommon, frequent attacks may persist for many months or even a few years; this is more common in women, with symptoms occurring monthly, 2 to 4 days before menstruation. In November

2019, the FDA approved Givlaari™ (givosiran), the first FDA-approved treatment for AHP. Givosiran is a small interfering RNA (siRNA) therapeutic targeting ALA synthase 1 (ALAS1), which works by specifically reducing elevated levels of ALAS1 messenger RNA (mRNA), leading to reduction of toxins associated with attacks and other disease manifestations of AHP.

Market News and Updates[10,11,12,13]

Anticipated Exclusivity Expiration(s):

- Scenesse® (afamelanotide): October 2024

New FDA Approval(s):

- **October 2019:** The FDA approved Clinuvel's Scenesse® (afamelanotide) to increase pain-free light exposure in adult patients with a history of phototoxic reactions from EPP. Afamelanotide was granted Priority Review and Orphan Drug designations by the FDA.
- **November 2019:** The FDA approved Alnylam's Givlaari™ (givosiran) for the treatment of adult patients with AHP. Givosiran was granted Priority Review, Breakthrough Therapy, and Orphan Drug designations by the FDA.

Pipeline:

- **Afamelanotide:** Clinuvel is currently evaluating Scenesse® (afamelanotide) in adult patients with vitiligo and with VP. Clinuvel also has another α-MSH analog, CUV9900, in early development.

Scenesse® (Afamelanotide) Product Summary[14]

Indication(s): Scenesse® (afamelanotide) is a MC1-R agonist indicated to increase pain-free light exposure in adult patients with a history of phototoxic reactions from EPP.

Dosing:

- Scenesse® is supplied as a subcutaneous (subQ) implant containing 16mg of afamelanotide. The afamelanotide implant is a bioresorbable and sterile rod approximately 1.7cm in length and 1.45mm in diameter.
- The recommended dosage of afamelanotide is to insert a single 16mg implant subQ above the anterior supra-iliac crest every 2 months.
- The afamelanotide implant should be stored in a refrigerator (between 36 to 46°F) and protected from light prior to implantation.
- The afamelanotide implant should be inserted using an SFM Implantation Cannula or other implantation devices that have been determined by the manufacturer to be suitable for implantation of Scenesse® (*refer to Scenesse® Prescribing Information for specific implantation instructions*).
- Afamelanotide should be administered by a health care professional who is proficient in the subQ implantation procedure and has completed the training program provided by the manufacturer prior to administration of the Scenesse® implant.
- Patients should be monitored for 30 minutes after the implant administration.
- Patients should maintain sun and light protection measures during treatment with afamelanotide to prevent phototoxic reactions related to EPP.

Mechanism of Action: Afamelanotide is a synthetic tridecapeptide and a structural analog of α-MSH. Afamelanotide functions as a melanocortin receptor agonist that binds predominately to MC1-R and increases the production of eumelanin in the skin independently of exposure to sunlight or artificial UV light sources.

Contraindications: None.

Safety:

- Skin Monitoring: Afamelanotide may lead to generalized increased skin pigmentation and darkening of pre-existing nevi and ephelides because of its pharmacologic effect. A full body skin examination is recommended twice yearly to monitor pre-existing and new skin pigmentary lesions.
- Pregnancy: There are no data on afamelanotide use in pregnant women to evaluate for any drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproductive and developmental toxicity studies, no adverse developmental effects were observed with afamelanotide administration during the period of organogenesis to pregnant rats at subQ doses up to 12 times the maximum recommended human dose (MRHD).
- Lactation: There are no data on the presence of afamelanotide or any of its metabolites in human or animal milk, the effects on the breastfed infant, or the effect on milk production.
- Pediatric Use: The safety and effectiveness of afamelanotide have not been established in pediatric patients.
- Geriatric Use: There were 10 patients 65 years of age or older in the clinical studies of afamelanotide for EPP; of the 125 patients treated with afamelanotide, 4 (3%) were 65 years of age or older. Clinical studies of afamelanotide did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently from younger patients.

Drug Interaction(s): No drug interaction studies were conducted with afamelanotide.

Adverse Reactions: In randomized, vehicle-controlled clinical trials involving 244 adult patients with EPP without significant liver involvement, the most common adverse reactions (occurred in ≥2% of patients in the afamelanotide-treated group and more frequently than in the placebo-treated group) following afamelanotide treatment were implant site reaction, nausea, oropharyngeal pain, cough, fatigue, skin hyperpigmentation, dizziness, melanocytic nevus, respiratory tract infection, somnolence, non-acute porphyria, and skin irritation.

Efficacy: The efficacy of afamelanotide in patients with EPP was evaluated in 2 vehicle-controlled, parallel-group clinical trials (CUV039 and CUV029), which were designed to assess exposure to direct sunlight on days with no phototoxic pain. The patients enrolled in the 2 trials were primarily Caucasian (98%), the mean age was 40 years (range 18 to 74 years), and 53% of patients were male. In both trials, quality of life improved with afamelanotide therapy.

- CUV039: Study CUV039 enrolled 93 patients, of whom 48 received afamelanotide (16mg implant administered subQ every 2 months) and 45 received vehicle. Patients

received 3 implants and were followed for 180 days. On each study day, patients recorded the number of hours spent in direct sunlight between 10am and 6pm, the number of hours spent in shade between 10am and 6pm, and whether they experienced any phototoxic pain that day. The primary endpoint was the total number of hours over 180 days spent in direct sunlight between 10am and 6pm with no pain; the median total number of hours was 64.1 hours for patients receiving afamelanotide, compared to 40.5 hours for patients receiving vehicle.

- CUV029: Study CUV029 enrolled 74 patients, of whom 38 received afamelanotide (16mg implant administered subQ every 2 months) and 38 received vehicle. Patients received 5 implants and were followed for 270 days. On each study day, patients recorded the number of hours spent outdoors between 10am and 3pm, whether "most of the day" was spent in direct sunlight, shade, or a combination of both, and whether they experienced any phototoxic pain that day. The primary endpoint was the total number of hours over 270 days spent outdoors between 10am and 3pm on days with no pain for which "most of the day" was spent in direct sunlight; the median total number of hours was 6 hours for patients receiving afamelanotide, compared to 0.75 hours for patients receiving vehicle. The analysis did not include sun exposure on days for which patients reported spending time in a combination of both direct sunlight and shade.

Cost: Cost information for Scenesse® (afamelanotide) is not yet available.

Givlaari™ (Givosiran) Product Summary[15]

Indication(s): Givlaari™ (givosiran) is an ALAS1-directed siRNA therapy indicated for the treatment of adult patients with AHP.

Dosing:

- Givlaari™ is supplied as a 189mg/mL solution for injection in an 11mL single-dose vial (SDV).
- The recommended dosage of givosiran is 2.5mg/kg via subQ injection once monthly. Dosing is based on actual body weight.
- Givosiran is intended for subQ administration by a health care professional only. Medical support to appropriately manage anaphylactic reactions should be available when administering givosiran.
- Doses requiring volumes greater than 1.5mL should be divided equally into multiple syringes. Givosiran injection may be administered subQ into the abdomen, the back or side of the upper arms, or the thighs. Injection sites should be rotated, and if more than 1 injection is needed for a single dose of givosiran, the injection sites should be at least 2cm apart.

Mechanism of Action: Givosiran is an ALAS1-directed siRNA, covalently linked to a ligand containing 3 N-acetylgalactosamine (GalNAc) residues to enable delivery of the siRNA to hepatocytes. Givosiran causes degradation of ALAS1 mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA; this leads to reduced circulating

levels of neurotoxic intermediates ALA and PBG, factors associated with attacks and other disease manifestations of AHP.

Contraindication(s): Givlaari™ is contraindicated in patients with known hypersensitivity to givosiran; reactions have included anaphylaxis.

Safety:

- Anaphylactic Reaction: Anaphylaxis has occurred with givosiran treatment (<1% of patients in clinical trials). Medical support to appropriately manage anaphylactic reactions should be available with administering givosiran. Patients should be monitored for signs and symptoms of anaphylaxis, and if anaphylaxis occurs, the administration of givosiran should be discontinued immediately and appropriate medical treatment should be instituted.
- Hepatic Toxicity: Transaminase elevations [alanine aminotransferase (ALT)] of at least 3 times the upper limit of normal (ULN) were observed in 15% of patients treated with givosiran in clinical trials. Transaminase elevations primarily occurred between 3 to 5 months following initiation of treatment. Liver function tests should be measured prior to initiating treatment with givosiran, every month during the first 6 months of treatment, and as clinically indicated thereafter. Treatment with givosiran should be interrupted or discontinued for severe or clinically significant transaminase elevations; for patients who have dose interruption and subsequent improvement, the givosiran dose should be reduced (*refer to Givlaari™ Prescribing Information for specific dose modification for adverse reactions*).
- Renal Toxicity: Increases in serum creatinine levels and decreases in estimated glomerular filtration rate (eGFR) have been reported during treatment with givosiran. In clinical trials, 15% of givosiran-treated patients experienced a renally-related adverse reaction. Renal function should be monitored during treatment with givosiran as clinically indicated.
- Injection Site Reactions: Injection site reactions have been reported in 25% of patients receiving givosiran in clinical trials. Symptoms included erythema, pain, pruritus, rash, discoloration, or swelling around the injection site. Among 12 patients with reactions, the highest severity of the reaction was mild among 11 (92%) patients and moderate in 1 (8%) patient. One patient experienced a single, transient, recall reaction of erythema at a prior injection site with a subsequent dose administration.
- Immunogenicity: As with all oligonucleotides, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. In clinical studies, 1 of 111 patients with AHP (0.9%) developed treatment-emergent anti-drug antibodies (ADA) during treatment with givosiran. No clinically significant differences in the clinical efficacy, safety, pharmacokinetic, or pharmacodynamics profiles of givosiran were observed in the patient who tested positive for anti-givosiran antibodies.
- Pregnancy: There are no available data with givosiran use in pregnant women to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproduction studies, subQ administration of givosiran to

pregnant rabbits during the period of organogenesis resulted in adverse developmental outcomes at doses that produced maternal toxicity.

- Lactation: There are no data on the presence of givosiran in human milk, the effects on the breastfed infant, or the effect on milk production.
- Pediatric Use: The safety and effectiveness of givosiran have not been established in pediatric patients.
- Geriatric Use: Clinical studies of givosiran did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently from younger patients.

Drug Interactions:

- Sensitive CYP1A2 and CYP2D6 Substrates: Concomitant use of givosiran increases the concentration of CYP1A2 and CYP2D6 substrates, which may increase adverse reactions of these substrates. Concomitant use of givosiran with CYP1A2 and CYP2D6 substrates should be avoided, for which minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, the CYP1A2 or CYP2D6 substrate dosage should be decreased in accordance with approved product labeling. Drug interaction studies with givosiran included caffeine (sensitive CYP1A2 substrate) and dextromethorphan (sensitive CYP2D6 substrate).

Adverse Reactions: In the placebo-controlled, double-blind clinical trial involving 94 adult patients (48 patients received givosiran), the most common adverse reactions (occurred at least 5% more frequently in patients treated with givosiran compared to patients treated with placebo) were nausea, injection site reaction, rash, increased serum creatinine, transaminase elevations, and fatigue. Permanent discontinuation occurred in 1 patient due to elevated transaminases.

Efficacy: The efficacy of givosiran in patients with AHP was evaluated in a randomized, double-blind, placebo-controlled, multinational trial (ENVISION). The trial enrolled 94 patients with AHP (89 patients with AIP, 2 with VP, 1 with HCP, and 2 with no identified mutation). The median age of patients studied was 37.5 years (range 19 to 65 years), 89% of patients were female, and 78% were Caucasian. Inclusion criteria for the trial specified a minimum of 2 porphyria attacks requiring hospitalization, urgent health care visit, or IV hemin administration at home in the 6 months prior to study entry. Eligible patients were randomized 1:1 to receive once monthly subQ injections of givosiran 2.5mg/kg or placebo during the 6-month double-blind period. Hemin use during the trial was permitted for the treatment of acute porphyria attacks. Efficacy in the 6-month double-blind period was measured by the rate of porphyria attacks that required hospitalization, urgent health care visit, or IV hemin administration at home. The following table (Table 1) summarizes the efficacy results for givosiran. On average, patients with AHP treated with givosiran experienced 70% [95% confidence interval (CI): 60%, 80%] fewer porphyria attacks compared to placebo-treated patients. Givosiran also resulted in a reduction in hemin use, urinary ALA, and urinary PBG.

Table 1. Rate of Porphyria Attacks and Days of Hemin Use in Patients with AHP

	Givosiran (N=48)	Placebo (N=46)
Mean Rate (95% CI) of Porphyria Attacks[a]	1.9 (1.3, 2.8)	6.5 (4.5, 9.3)
Rate Ratio[b] (Givosiran/Placebo) (95% CI)	0.3* (0.2, 0.4)	
Mean Days (95% CI) of IV Hemin Use	4.7 (2.8, 7.9)	12.8 (7.6, 21.4)
Ratio[b] (Givosiran/Placebo) (95% CI)	0.3¥ (0.1, 0.5)	

AHP = acute hepatic porphyria; N = number of patients; CI = confidence interval; IV = intravenous
[a]Attacks that require hospitalization, urgent health care visits, or IV hemin administration at home
[b]Adjusted for prior hemin prophylaxis status and historical attack rates; a ratio <1 represents a favorable outcome for givosiran
*p<0.000; ¥p=0.0002

Cost: Cost information for Givlaari™ (givosiran) is not yet available.

Recommendations

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

Scenesse® (Afamelanotide) Approval Criteria:

1. An FDA approved indication to increase pain-free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP); and
   a. The diagnosis of EPP must be confirmed by genetic testing; and
2. Member must be 18 years of age or older; and
3. Scenesse® must be administered by a health care professional who is proficient in the subcutaneous (subQ) implantation procedure and has completed the training program provided by the manufacturer prior to administration of the Scenesse® implant; and
   a. Scenesse® must be shipped via cold chain supply shipping and delivery to the health care setting where the member is scheduled to receive the implant administration; and
   b. Scenesse® must be stored under refrigeration (36 to 46°F) and protected from light prior to implantation; and
4. The Scenesse® implant should be inserted using an SFM Implantation Cannula or other implantation device that has been determined by the manufacturer to be suitable for implantation of Scenesse®; and
5. The prescriber must agree that the member will be monitored by a health care provider for at least 30 minutes after the implant administration; and
6. The prescriber must agree that the member will have a full body skin examination performed at least twice yearly while the member is being treated with Scenesse® to monitor pre-existing and new skin pigmentary lesions; and
7. Documentation that member will maintain sun and light protection measures during treatment with Scenesse® to prevent phototoxic reactions related to EPP; and
8. A quantity limit of 1 implant per 60 days will apply. Initial approvals will be for 2 implants for the duration of 4 months. Further approval may be granted if the prescriber

documents that the member is responding well to treatment as indicated by increased tolerance of sunlight (i.e., less phototoxic reactions).

Givlaari™ (Givosiran) Approval Criteria:

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

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Appendix N

Fiscal Year 2019 Annual Review of Soliris® (Eculizumab) and 30-Day Notice to Prior Authorize Ultomiris® (Ravulizumab-cwvz)

Oklahoma Health Care Authority
December 2019

Current Prior Authorization Criteria

Soliris® (Eculizumab) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria (PNH) or Atypical Hemolytic Uremic Syndrome (aHUS) Diagnosis]:

1. Member must have an established diagnosis of paroxysmal nocturnal hemoglobinuria or atypical hemolytic uremic syndrome via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply for members with a diagnosis of PNH; or
3. For members younger than 18 years of age, approval can be granted with a documented diagnosis of aHUS.

Soliris® (Eculizumab) Approval Criteria [Generalized Myasthenia Gravis (gMG) Diagnosis]:

1. An FDA approved diagnosis of gMG; and
2. Positive serologic test for anti-AChR antibodies; and
3. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV; and
4. MG-Activities of Daily Living (MG-ADL) total score ≥6; and
5. Member must meet 1 of the following:
    a. Failed treatment over 1 year or more with 2 or more immunosuppressive therapies (ISTs) either in combination or as monotherapy; or
    b. Failed at least 1 IST and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIg); and
6. Initial approvals will be for the duration of 6 months at which time an updated MG-ADL score must be provided. Continued authorization requires improvement in the MG-ADL score from baseline. Subsequent approvals will be for the duration of 1 year.

Utilization of Soliris® (Eculizumab): Fiscal Year 2019

Soliris® (Eculizumab) Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	5	80	$1,888,266.53	$23,603.33	$1,800.06	18,100	1,049
2019	6	89	$1,807,970.51	$20,314.28	$1,829.93	19,110	988
% Change	**20.00%**	**11.30%**	**-4.30%**	**-13.90%**	**1.70%**	**5.60%**	**-5.80%**
Change	**1**	**9**	**-$80,296.02**	**-$3,289.05**	**$29.87**	**1,010**	**-61**

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

Soliris® (Eculizumab) Fiscal Year Comparison: Medical Claims

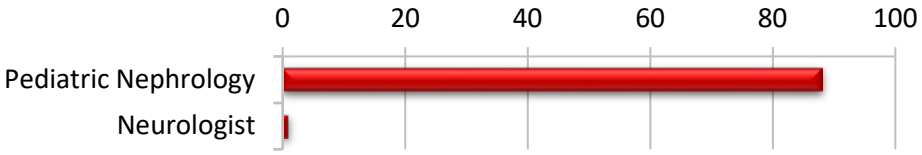
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/Claim	Total Units
2018	7	29	$1,176,895.50	$40,582.60	7,110
2019	4	32	$1,500,424.80	$46,888.28	6,510
% Change	**-42.86%**	**10.34%**	**27.49%**	**15.54%**	**-8.44%**
Change	**-3**	**3**	**$323,529.30**	**$6,305.68**	**-600**

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

Demographics of Members Utilizing Soliris® (Eculizumab): Pharmacy Claims

- Due to the limited number of members utilizing Soliris® (eculizumab) during fiscal year 2019, detailed demographic information could not be provided.

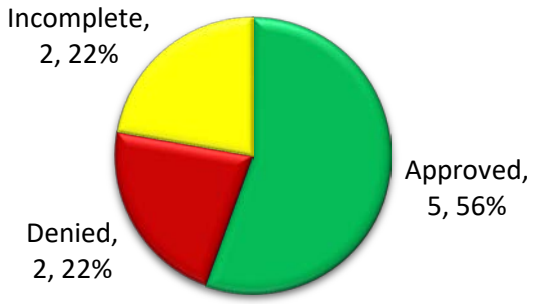
Top Prescriber Specialties of Soliris® (Eculizumab) by Number of Claims: Pharmacy Claims



Prior Authorization of Soliris® (Eculizumab)

There were 9 prior authorization requests submitted for 5 unique members for Soliris® (eculizumab) during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



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

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

- **Ultomiris® (ravulizumab-cwvz) for Paroxysmal Nocturnal Hemoglobinuria (PNH):** In December 2018, the FDA approved Ultomiris® (ravulizumab), the first long-acting complement inhibitor administered every 8 weeks, for the treatment of adult patients with PNH. PNH is a chronic, progressive, debilitating, and life-threatening ultra-rare blood disorder characterized by hemolysis that is mediated by an uncontrolled activation of the complement system. PNH has an average age of onset in the early 30s

and occurs in both men and women. Patients with PNH may experience a wide range of signs and symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine, and anemia. Hallmark symptoms of PNH include thrombosis, which can occur in blood vessels throughout the body, damage vital organs and cause premature death. Despite historical supportive care, including transfusion and anticoagulation management, 20 to 35% of patients with PNH die within 5 to 10 years of diagnosis. Prior to FDA approval of ravulizumab, Soliris® (eculizumab) was the primary treatment for PNH. Eculizumab treatment requires biweekly infusions in contrast to ravulizumab which is dosed every 8 weeks.

- **Soliris® (eculizumab) for Neuromyelitis Optica Spectrum Disorder (NMOSD):** In June 2019, the FDA approved Soliris® (eculizumab), a complement inhibitor, for the treatment of adults with NMOSD who are anti-aquaporin-4 (AQP4) antibody positive. Eculizumab is the first FDA-approved treatment for the treatment of NMOSD. NMOSD is an inflammatory disorder of the central nervous system (CNS) characterized by demyelination and axonal damage predominately targeting the optic nerves and spinal cord. Typical presentation of NMOSD includes attacks of optic neuritis, which result in ocular pain and vision loss; patients also commonly have attacks resulting in transverse myelitis and subsequent numbness, weakness, or paralysis of the arms and legs. Attacks can occur in groupings, followed by partial recovery during periods of remission. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. NMOSD can be associated with antibodies that bind to the AQP4 protein; this binding appears to activate other components of the immune system, causing inflammation and damage to the CNS. NMOSD is believed to affect 4,000 to 8,000 patients in the United States. The effectiveness of eculizumab for the treatment of NMOSD was demonstrated in a study of 143 patients with NMOSD who had AQP4 antibodies who were randomized to receive either eculizumab or placebo. Compared with placebo, treatment with eculizumab reduced the number of NMOSD relapses by 94% over 48 weeks [annualized relapse rates for the eculizumab and placebo groups were 0.02 and 0.35, respectively; absolute risk reduction 33%; rate ratio 0.04; 95% confidence interval (CI) 0.01 to 0.15]. Eculizumab also reduced the need for hospitalizations and the need for treatment of acute attacks with corticosteroids and plasma exchange. Eculizumab was previously FDA approved for the treatment of patients with PNH to reduce hemolysis, for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA), and for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive.
- **Ultomiris® (ravulizumab-cwvz) for aHUS:** In October 2019, the FDA approved Ultomiris® (ravulizumab), a complement inhibitor, for the treatment of aHUS to inhibit complement-mediated TMA for patients 1 month of age and older. aHUS is a rare disease that can affect both children and adults and can lead to potentially irreversible damage to the kidneys and other vital organs, resulting in kidney failure (requiring dialysis or transplant) and premature death. aHUS is characterized by inflammation and the formation of blood clots in small blood vessels throughout the body (TMA) mediated by chronic, uncontrolled activation of the complement system. TMA consists of thrombocytopenia, hemolytic anemia, and acute kidney injury (AKI). If left untreated,

significant proportions of adults (46%) and children (16%) can progress to end-stage renal disease (ESRD) or death. Ravulizumab was previously FDA approved for the treatment of adults with PNH.

Pipeline Update(s):

- **APL-2:** In February 2019, Apellis Pharmaceuticals, Inc. announced that the FDA granted Fast Track designation to APL-2, an inhibitor of complement factor C3, being studied for the treatment of patients with PNH who remain anemic despite treatment with eculizumab. The FDA's Fast Track program expedites the review of drugs to treat serious conditions that fill an unmet medical need. Apellis is currently evaluating APL-2 in PEGASUS, a Phase 3 trial for patients with PNH. Previously reported interim data from 2 Phase 1b trials showed improvements in lactate dehydrogenase and hemoglobin levels in patients who are suboptimal responders to eculizumab and in untreated patients.
- **OMS721 (narsoplimab):** In March 2019, Osmeros Corporation announced the assignment of a generic name, narsoplimab, to OMS721, an investigational monoclonal antibody for the treatment of complement- and inflammation-related disorders. Osmeros is currently evaluating narsoplimab in 3 Phase 3 trials in patients with aHUS, hematopoetic stem cell transplant-associated TMA (HSCT-TMA), and IgA nephropathy. The aHUS trial is currently recruiting patients with confirmed aHUS. Patients will receive a loading dose of narsoplimab intravenously (IV), followed by daily injections.

Ultomiris® (Ravulizumab-cwvz) Product Summary[8]

Indication(s): Ultomiris® (ravulizumab) is complement inhibitor indicated for the treatment of adult patients with PNH or for the treatment of adults and pediatric patients 1 month of age and older with aHUS to inhibit complement-mediated TMA.

Boxed Warning: Serious Meningococcal Infections

- Life-threatening meningococcal infections/sepsis have occurred in patients treated with ravulizumab.
- Prescribers should comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Patients should be immunized with meningococcal vaccines at least 2 weeks prior to administering the first dose of ravulizumab, unless the risks of delaying ravulizumab therapy outweigh the risk of developing a meningococcal infection.
- Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Patients should be monitored for early signs of meningococcal infections and evaluated immediately if infection is suspected.
- Ultomiris® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Ultomiris® REMS, prescribers must enroll in the program and must counsel patients about the risk of meningococcal infection/sepsis, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Dosing:

- Ultomiris® is supplied as 300mg/30mL single-dose vials (SDV) for IV infusion.

- The recommended dose of ravulizumab varies depending on weight and indication. The following tables (Table 1 and Table 2) highlight the recommended regimens.

Table 1: Ravulizumab Dosing Regimen(s) – aHUS Diagnosis

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Interval
≥5 to <10	600	300 every 4 weeks
≥10 to <20	600	600 every 4 weeks
≥20 to <30	900	2,100 every 8 weeks
≥30 to <40	1,200	2,700 every 8 weeks
≥40 to <60	2,400	3,000 every 8 weeks
≥60 to <100	2,700	3,300 every 8 weeks
≥100	3,000	3,600 every 8 weeks

aHUS = atypical hemolytic uremic syndrome; Kg = kilogram; mg = milligram

Table 2: Ravulizumab Dosing Regimen(s) – PNH Diagnosis

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Interval
≥40 to <60	2,400	3,000 every 8 weeks
≥60 to <100	2,700	3,300 every 8 weeks
≥100	3,000	3,600 every 8 weeks

PNH = paroxysmal nocturnal hemoglobinuria; Kg = kilogram; mg = milligram

- For patients switching from eculizumab to ravulizumab, the loading dose of ravulizumab should be administered 2 weeks after the last eculizumab infusion.
- Ravulizumab should be administered via IV infusion following aseptic technique. Infusion rates and infusion times vary based on dose and patient body weight.
- Patients should be vaccinated for meningococcal disease according to current ACIP guidelines to reduce the risk of serious infection. If ravulizumab must be initiated immediately and vaccines are administered less than 2 weeks before starting ravulizumab therapy, patients should be provided 2 weeks of antibacterial drug prophylaxis.
- Health care professionals who prescribe ravulizumab must enroll in the Ultomiris® REMS program.

Mechanism of Action: Ravulizumab is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a (the proinflammatory anaphylatoxin) and C5b [the initiating subunit of the terminal complement complex (C5b-9)] and preventing the generation of the terminal complement complex C5b9. Ravulizumab inhibits terminal complement-mediated intravascular hemolysis in patients with PNH and complement-mediated TMA in patients with aHUS.

Contraindication(s):

- Patients with unresolved *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying ravulizumab treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions:

- Serious Meningococcal Infections: Life-threatening meningococcal infections have occurred in patients treated with ravulizumab. The use of ravulizumab increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.
- Other Infections: Patients may have increased susceptibility to encapsulated bacteria infections, especially infections caused by *Neisseria meningitidis, Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*.
- Monitoring Disease Manifestations after Ravulizumab Discontinuation:
  - PNH Treatment Discontinuation: After discontinuing treatment with ravulizumab, patients should be closely monitored for signs and symptoms of hemolysis, identified by elevated lactic acid dehydrogenase (LDH) along with sudden decreases in PNH clone size or hemoglobin, or a re-appearance of symptoms.
  - aHUS Discontinuation: Ravulizumab treatment for aHUS should be a minimum duration of 6 months. Due to the heterogeneous nature of aHUS events and patient-specific risk factors, treatment duration beyond the initial 6 months should be individualized. After discontinuing treatment with ravulizumab, patients should be monitored for clinical symptoms and laboratory signs of TMA complications for at least 12 months.
- Infusion Reactions: Administration of ravulizumab may result in infusion reactions. In clinical trials, 5 out of 296 patients treated with ravulizumab experienced infusion reactions (lower back pain, drop in blood pressure, infusion-related pain, elevation in blood pressure, and limb discomfort) during ravulizumab administration.

Efficacy: The safety and efficacy of ravulizumab in patients with PNH was assessed in 2 open-label, randomized, active-controlled, non-inferiority Phase 3 studies: PNH Study 301 and PNH Study 302. Study 301 enrolled patients with PNH who were complement inhibitor-naïve and had active hemolysis. Study 302 enrolled patients with PNH who were clinically stable after having been treated with eculizumab for at least the past 6 months.

- Study 301 was a 26-week, multicenter, open-label, randomized, active-controlled, non-inferiority, Phase 3 study conducted in 246 patients naïve to complement inhibitor treatment prior to study entry. Patients with PNH were randomized 1:1 to either ravulizumab or eculizumab. Efficacy was established based upon transfusion avoidance and hemolysis as directly measured by normalization of LDH levels. Transfusion avoidance was defined as patients who did not receive a transfusion and not meet the protocol specified guidelines for transfusion from baseline up to day 183. The transfusion avoidance rate was 73.6% for ravulizumab and 66.1% for eculizumab (treatment effect 6.8; 95% CI -4.66, 18.14); LDH normalization was 53.6% and 49.4% for ravulizumab and eculizumab, respectively (treatment effect 1.19; 95% CI 0.80, 1.77). Study results established non-inferiority of ravulizumab to eculizumab in the complement inhibitor-naïve treatment population.
- Study 302 was as a 26-week, multicenter, open-label, randomized, active-controlled, non-inferiority, Phase 3 study conducted in 195 patients with PNH who were clinically stable after having been treated with eculizumab for at least the past 6 months. Patients were randomized 1:1 to either continue eculizumab or to switch to ravulizumab. Efficacy

was established based on hemolysis as measured by LDH percent change from baseline to day 183 and supportive efficacy data was transfusion avoidance. The transfusion avoidance rate was 87.6% for ravulizumab and 82.7% for eculizumab (treatment effect 5.5%; 95% CI -4.66, 18.14); LDH percentage change was -0.82% and 8.4% for ravulizumab and eculizumab, respectively (treatment effect 9.2; 95% CI -0.42, 18.8).

The efficacy of ravulizumab in patients with aHUS who displayed signs of TMA was assessed in 2 open-label, single-arm studies, Study 311 (adult patients) and Study 312 (pediatric patients).

- Study 311 was a 26-week study conducted in 56 adult patients with aHUS who were naïve to complement inhibitor treatment prior to study entry. Efficacy was based on Complete TMA Response during the 26-week period, as evidenced by normalization of hematological parameters (platelet count and LDH) and ≥25% improvement in serum creatinine from baseline. Patients had to meet each Complete TMA Response criteria at 2 separate assessments obtained at least 4 weeks apart and any measurement in between. Complete TMA Response was observed in 30 of the 56 patients (54%) during the 26-week period. A total of 17 of the 29 patients (59%) who required dialysis at study entry discontinued dialysis by the end of the available follow-up, and 6 of 27 (22%) patients who were off dialysis at baseline were on dialysis at last available follow-up.
- Study 312 was a 26-week, single-arm study conducted in 16 pediatric patients with aHUS. A total of 14 eculizumab-naïve patients with a documented diagnosis of aHUS were enrolled and included in this interim analysis. The median age at the time of first infusion was 5.2 years (range 0.9, 17.3 years). Efficacy was based upon Complete TMA Response during the 26-week period, as evidenced by normalization of hematological parameters (as mentioned in the summary of Study 311). Complete TMA Response was observed in 10 of the 14 patients (71%) during the 26-week period. A total of 4 of the 5 patients who required dialysis at study entry were able to discontinue dialysis after the first month in the study and for the duration of ravulizumab treatment. No patient initiated dialysis during the study.

Cost Comparison:

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

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

Recommendations

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

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

1. An FDA approved diagnosis of NMOSD; and
2. Member is anti-aquaporin-4 (AQP4) antibody positive; and

3. Member must be 18 years of age or older.

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

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

1. Member must have an established diagnosis of paroxysmal nocturnal hemoglobinuria via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply.

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

1. Member must have a documented diagnosis of aHUS.

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Appendix O

Fiscal Year 2019 Annual Review of Muscular Dystrophy Medications

Oklahoma Health Care Authority
December 2019

Current Prior Authorization Criteria

Exondys 51® (Eteplirsen) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping; and
2. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Emflaza® (Deflazacort) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD); and
2. Member must be 5 years of age or older; and
3. Emflaza® must be prescribed by or in consultation with a prescriber who specializes in the treatment of DMD; and
4. Member must have a minimum 6-month trial of prednisone that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with Emflaza®; and
5. A patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed must be provided; and
6. Patients already established on deflazacort via the ACCESS DMD Program must also document a patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed; and
7. For Emflaza® suspension, a patient-specific, clinically significant reason why the member cannot use the tablet formulation in the place of oral suspension even when the tablets are crushed must be provided; and
8. Prescriber must verify the member has had a baseline eye examination; and
9. The member's recent weight must be provided in order to authorize the appropriate amount of drug required according to package labeling; and
10. For the tablets, a quantity limit of 30 tablets per 30 days will apply and for the suspension, a quantity limit of 39mL (3 bottles) per 30 days will apply. Quantity limit requests will be based on the member's recent weight taken within the last 30 days.

Utilization of Muscular Dystrophy Medications: Fiscal Year 2019

Fiscal Year 2019 Utilization

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1	6	$45,584.70	$7,597.45	$253.25	180	180

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

- There was no SoonerCare utilization of muscular dystrophy medications during fiscal year 2018 to allow for a fiscal year comparison.
- There were no medical claims for muscular dystrophy medications during fiscal year 2019.

Demographics of Members Utilizing Muscular Dystrophy Medications

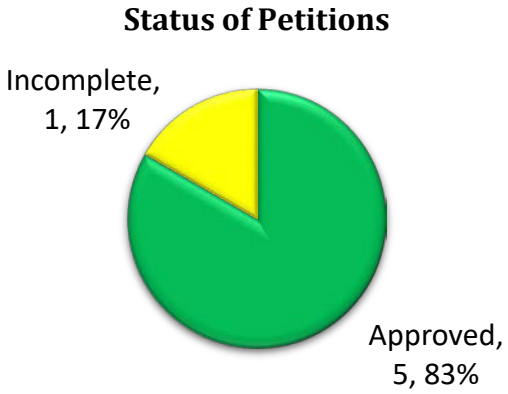
- Due to the small number of members utilizing muscular dystrophy medications during fiscal year 2019, detailed demographic information could not be provided.

Top Prescriber Specialties of Muscular Dystrophy Medications by Number of Claims

- The only prescriber specialty listed on paid claims for muscular dystrophy medications during fiscal year 2019 was general pediatrician. However, upon further review, the member is followed by a neurology specialist.

Prior Authorization of Muscular Dystrophy Medications

There were 6 prior authorization requests submitted for 2 unique members for muscular dystrophy medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



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

Anticipated Patent Expiration(s):

- Emflaza® (deflazacort): Emflaza® has no unexpired patents, but exclusivity expires in February 2022 for New Chemical Entity, in February 2024 for Orphan Drug exclusivity for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older, and in June 2026 for the treatment of DMD in patients 2 years of age to younger than 5 years of age.
- Exondys 51® (eteplirsen): March 2034

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

- **June 2019:** The U.S. Food and Drug Administration (FDA) approved PTC Therapeutics' supplemental New Drug Application (sNDA) for Emflaza® (deflazacort) to expand its labeling to include patients with DMD who are between 2 and 5 years of age. Deflazacort was first approved by the FDA in February 2017 for the treatment of DMD in patients 5 years of age and older. Approval for patients 2 to <5 years of age was

supported by data from a 52-week, Phase 3, double-blind, placebo-controlled study of 196 patients 5 to 15 years of age with DMD. The prescribing information was also updated to include additional information regarding immunizations. The prescribing information recommends that immunizations be administered according to guidelines prior to starting deflazacort. Additionally, the prescribing information indicates that patients taking deflazacort may receive concurrent vaccinations, except for live-attenuated or live vaccines; these should be administered at least 4 to 6 weeks prior to starting treatment with deflazacort.

News:

- **August 2019:** The Institute for Clinical and Economic Review (ICER) released a Final Evidence Report and Report-at-a-Glance assessing the comparative clinical effectiveness and value of the corticosteroid deflazacort (Emflaza®, PTC Therapeutics), and 2 exon-skipping therapies, eteplirsen (Exondys 51®, Sarepta Therapeutics) and golodirsen (Sarepta Therapeutics; not FDA approved at the time of this review; see additional news information for current status). ICER's report on these 3 treatments for DMD was reviewed at the July 2019 public meeting of the New England Comparative Effectiveness Public Advisory Council (NE CEPAC). A majority of the council members voted that the evidence suggests that deflazacort achieves a net health benefit over prednisone. However, the panel did not find sufficient evidence to show a net health benefit of either eteplirsen or golodirsen over supportive care alone. After considering all of the evidence as well as patient input on the non-clinical factors associated with these treatments, an overwhelming majority of the NE CEPAC voted that both deflazacort and eteplirsen represent a low long-term value for money. The NE CEPAC did not vote on golodirsen's long-term value for money because the treatment's price is not yet known. To reach commonly cited cost-effectiveness thresholds of $100,000 to $150,000 per Quality Adjusted Life Year (QALY) gained, ICER's evaluation found that deflazacort's annual net price would need to be between $19,900 and $31,700, requiring a 73 to 83% decrease from the treatment's current Wholesale Acquisition Cost (WAC). No price can be suggested as a fair value-based price for eteplirsen or golodirsen because no persuasive evidence yet exists to demonstrate the clinical effectiveness of either drug. At its current cost of more than $1 million per year, eteplirsen would still far exceed commonly cited cost-effectiveness thresholds even if the most favorable assumptions were granted around the potential efficacy of the treatment. Following the voting session, a policy roundtable of experts convened to discuss the implications of the evidence for policy and practice. Key recommendations stemming from the roundtable discussion include:
    - Patient groups and clinicians should work with manufacturers early in the design of clinical trials to embed the expectation that patient-centered outcomes will be measured in key trials and that the company will bring an effective drug to market at a price that aligns fairly with the demonstrated benefits for patients.
    - To balance early access with the need for fair pricing and ongoing evidence development, drugs granted accelerated approval should be priced closer to the marginal cost of production until clinical benefits are proven.
    - Given the substantial remaining uncertainty regarding the benefits of these treatments in certain subpopulations and their high cost, it is reasonable for

insurers and other payers to develop prior authorization criteria to ensure prudent use.

- **August 2019:** Sarepta Therapeutics received a Complete Response Letter (CRL) from the FDA regarding a New Drug Application (NDA) seeking accelerated approval of golodirsen injection for the treatment of DMD in patients with a confirmed mutation amenable to exon 53 skipping. The CRL cited 2 concerns: the risk of infections related to intravenous (IV) infusion ports and renal toxicity seen in pre-clinical models of golodirsen and observed following administration of other antisense oligonucleotides. Renal toxicity with golodirsen was observed in pre-clinical models at doses that were ten-fold higher than the dose used in clinical studies. Renal toxicity was not observed in Study 4053-101, on which the application for golodirsen was based. Doug Ingram, president and chief executive officer for Sarepta, commented that "Over the entire course of its review, the Agency did not raise any issues suggesting the non-approvability of golodirsen, including the issues that formed the basis of the complete response letter. We will work with the Division to address the issues raised in the letter and, to the fullest extent possible, find an expeditious pathway forward for the approval of golodirsen. We know that the patient community is waiting."
- **November 2019:** The FDA halted a clinical trial involving Solid Biosciences' DMD gene therapy, SGT-001, after a patient suffered serious kidney and blood-related injuries. Solid Biosciences reports the patient became ill soon after being treated, experiencing an over-activation of the immune system, an "acute kidney injury," reductions in platelets and red blood cells, and "cardio-pulmonary insufficiency." All of the toxicities were deemed related to SGT-001 by the patient's treating doctor. The patient is being treated and is recovering. This is the third time that Solid Biosciences has run into a serious safety problem with SGT-001. The FDA placed similar clinical holds on the same clinical trial after each prior incident, but later allowed the company to proceed with patient dosing. In a statement, the company said it "will work with the FDA in an effort to resolve the hold and determine next steps." SGT-001 uses an inactivated virus to deliver a miniaturized but functional version of the dystrophin gene to muscle cells. The gene therapy is designed to be a 1-time and potentially curative treatment for all DMD patients, regardless of the mutation that causes their disease.

Pipeline:

- **Edasalonexent:** In September 2019, Catabasis Pharmaceuticals completed enrollment for the Phase 3 PolarisDMD trial of edasalonexent in DMD. Top-line results from the Phase 3 PolarisDMD trial are expected in the fourth quarter of 2020 and the trial is anticipated to support an NDA filing in 2021. Edasalonexent is an investigational, oral, small molecule designed to inhibit NF-kB. Edasalonexent is being developed as a potential foundational therapy for all patients affected by DMD, regardless of their underlying mutation. In DMD, the loss of dystrophin leads to chronic activation of NF-kB, which is a key driver of skeletal and cardiac muscle disease progression. In MoveDMD, a Phase 2 trial and open-label extension, edasalonexent preserved muscle function and substantially slowed disease progression compared to rates of change in a control period, and significantly improved biomarkers of muscle health and inflammation. The FDA granted Orphan Drug, Fast Track, and Rare Pediatric Disease (RPD) designations to edasalonexent for the treatment of DMD.

- **Vamorolone:** Top-line data were presented on vamorolone in October 2019 at the World Muscle Society (WMS) congress showing continued improvement of muscle function and improved tolerability compared with corticosteroids after 18 months of vamorolone treatment in DMD patients. Data from 23 patients treated with 2 or 6mg/kg/day vamorolone for at least 18 months showed vamorolone consistently and significantly improved standardized motor function outcomes measured as velocity to stand from supine (P=0.012), to run/walk 10 meters (P<0.0001), and to climb 4 stairs (P=0.001) from baseline to month 18. Motor function outcomes for vamorolone-treated patients were also consistently better than outcomes for age-matched, steroid-naïve patients (N=19) from an external natural history study (velocity to stand from supine: P=0.085; run/walk 10 meters: P=0.005; climb 4 stairs: P=0.036; all in favor of vamorolone treatment). Additionally, motor function outcomes of vamorolone-treated DMD boys were compared to age-matched prednisone-treated patients from an external control group. Both vamorolone- and prednisone-treated groups showed similar improvements in these gross motor outcomes, demonstrating that vamorolone exerts therapeutic efficacy similar to standard corticosteroids. Also, vamorolone-treated patients showed normal growth rates, and less physician-reported weight gain and Cushingoid features compared to published studies of prednisone and deflazacort. These findings confirmed earlier data that indicated a better tolerability profile of vamorolone compared to standard corticosteroids.
- **Viltolarsen:** In October 2019, NS Pharma submitted a rolling NDA to the FDA for its exon-skipping therapy under development, viltolarsen, to treat DMD amenable to exon 53 skipping. The NDA submission follows results from a Phase 2 clinical trial evaluating the safety and optimal dosing of viltolarsen. Viltolarsen was administered as an IV infusion once weekly for 6 months, compared to placebo in 8 ambulatory DMD boys, ages 4 to 10 years, with a confirmed exon 53 mutation. Viltolarsen was found to restore dystrophin in the patients' muscles after 20 to 24 weeks of weekly infusions (at doses of 40mg/kg or 80mg/kg). Treatment was also found to be safe and tolerable, with all adverse events said to be mild or moderate, and none causing a patient to discontinue treatment. Preliminary findings suggested clinical improvement in boys with DMD who received the drug compared to natural history study data. Up to 74 ambulant patients are currently being enrolled in a randomized, double-blind, placebo-controlled, Phase 3 study to further assess the efficacy and safety of viltolarsen. Patients will be randomized to once-weekly IV infusions of viltolarsen at 80mg/kg or to placebo for up to 48 weeks. Viltolarsen was previously granted RPD, Orphan Drug, and Fast Track designations by the FDA.

Recommendations

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

Emflaza® (Deflazacort) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD); and
2. Member must be 2 ~~5~~ years of age or older; and
3. Emflaza® must be prescribed by or in consultation with a prescriber who specializes in the treatment of DMD; and

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

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[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 11/2019. Last accessed 11/06/2019.

[2] PTC Therapeutics, Inc. PTC Therapeutics Receives FDA Approval for the Expansion of the EMFLAZA® (deflazacort) Labeling to Include Patients 2-5 Years of Age. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/ptc-therapeutics-receives-fda-approval-for-the-expansion-of-the-emflaza-deflazacort-labeling-to-include-patients-2-5-years-of-age-300863988.html. Issued 06/07/2019. Last accessed 11/06/2019.

[3] Park B. Emflaza Approved for Younger Patients With Duchenne Muscular Dystrophy. *MPR.* Available online at: https://www.empr.com/home/news/emflaza-approved-for-younger-patients-with-duchenne-muscular-dystrophy/. Issued 06/10/2019. Last accessed 11/06/2019.

[4] Institute for Clinical and Economic Review (ICER). ICER Issues Final Report and Policy Recommendations Regarding Treatments for Duchenne Muscular Dystrophy. Available online at: https://icer-review.org/announcements/final_dmd_report/. Issued 08/15/2019. Last accessed 11/11/2019.

[5] Sarepta Therapeutics. Sarepta Therapeutics Receives Complete Response Letter from the US Food and Drug Administration for Golodirsen New Drug Application. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/08/19/1903797/0/en/Sarepta-Therapeutics-Receives-Complete-Response-Letter-from-the-US-Food-and-Drug-Administration-for-Golodirsen-New-Drug-Application.html. Issued 08/19/2019. Last accessed 11/11/2019.

[6] Feuerstein A. Solid Biosciences' Duchenne gene therapy trial halted after patient suffers serious toxicity. *STAT*. Available online at: https://www.statnews.com/2019/11/12/solid-biosciences-duchenne-gene-therapy-trial-halted-after-patient-suffers-serious-toxicity/. Issued 11/12/2019. Last accessed 11/19/2019.

[7] Catabasis Pharmaceuticals, Inc. Catabasis Pharmaceuticals Announces the Phase 3 PolarisDMD Trial of Edasalonexent in Duchenne Muscular Dystrophy has Exceeded Target Enrollment. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20190930005768/en/Catabasis-Pharmaceuticals-Announces-Phase-3-PolarisDMD-Trial. Issued 09/30/2019. Last accessed 11/19/2019.

[8] Santhera Pharmaceuticals. Santhera Announces Presentation by ReveraGen of Positive 18-Month Data with Vamorolone in Duchenne Muscular Dystrophy. Available online at: http://www.santhera.com/assets/files/press-releases/2019-10-07_WMS_Vamorolone_e_final.pdf. Issued 10/07/2019. Last accessed 11/19/2019.

[9] Swanson J. NS Pharma Submits New Drug Application to FDA for Viltolarsen to Treat DMD Amenable to Exon 53 Skipping. *MDA*. Available online at: https://strongly.mda.org/ns-pharma-submits-new-drug-application-to-fda-for-viltolarsen-to-treat-dmd-amenable-to-exon-53-skipping/. Issued 10/07/2019. Last accessed 11/19/2019.

[10] Silva C. Request to Approve Viltolarsen, Exon 53 Skipping Treatment for Duchenne MD, Before FDA. *Muscular Dystrophy News Today*. Available online at: https://musculardystrophynews.com/2019/10/07/request-viltolarsen-approval-duchenne-exon-53-skipping-treatment-before-fda/. Issued 10/07/2019. Last accessed 11/19/2019.

Appendix P

Fiscal Year 2019 Annual Review of Carbaglu® (Carglumic Acid)

Oklahoma Health Care Authority
December 2019

Introduction[1,2]

N-acetylglutamate synthase (NAGS) deficiency is a rare, autosomal recessive genetic disorder caused by mutations of the *NAGS* gene and characterized by complete or partial lack of the enzyme NAGS. NAGS plays an important role in the urea cycle and in the removal of nitrogen from the body. The lack of the NAGS enzyme results in excessive accumulation of nitrogen, in the form of ammonia, resulting in hyperammonemia. Excess ammonia, which is a neurotoxin, travels to the central nervous system (CNS) through the blood, resulting in the symptoms and physical findings of NAGS deficiency, including vomiting, refusal to eat, progressive lethargy, and coma.

Carbaglu® (carglumic acid) was approved by the U.S. Food and Drug Administration (FDA) in March 2010 as an adjunctive therapy for the treatment of acute hyperammonemia and as maintenance therapy for chronic hyperammonemia due to a deficiency of the hepatic enzyme NAGS. Carglumic acid is a synthetic structural analogue of N-acetylglutamate, an essential allosteric activator of carbamoyl phosphate synthetase 1 (CPS 1) in liver mitochondria that converts ammonia into urea.

Carbaglu® is supplied as a tablet for oral administration. Carglumic acid tablets should not be swallowed whole or crushed. The tablets should be dispersed in water immediately before use. For acute hyperammonemia, the recommended dosage is 100 to 250mg/kg/day. Dosing should be titrated based on individual patient plasma ammonia levels and clinical symptoms. The total daily dose should be divided into 2 to 4 doses.

The efficacy of carglumic acid in the treatment of hyperammonemia due to NAGS deficiency was evaluated in a retrospective review of the clinical course of 23 NAGS deficiency patients who received carglumic acid treatment for a median of 7.9 years (range 0.6 to 20.8 years). Short-term efficacy was evaluated using mean and median changes in plasma ammonia levels from baseline to days 1 to 3. Persistence of efficacy was evaluated using long-term mean and median changes in plasma ammonia level. By day 3, normal plasma ammonia levels were attained in patients for whom data were available. Long-term efficacy was measured using the last reported plasma ammonia level for each of the 13 patients analyzed (median length of treatment was 6 years; range 1 to 16 years). The mean and median ammonia levels were 23µmol/L and 24µmol/L, respectively, after a mean treatment duration of 8 years.

Current Prior Authorization Criteria

Carbaglu® (Carglumic Acid) Approval Criteria:

1. An FDA approved diagnosis of N-acetylglutamate synthase (NAGS) deficiency; and
2. Carbaglu® must be prescribed by, or in consultation with, a geneticist; and

3. Documentation of active management with a low protein diet; and
4. Initial approvals will be for the duration of 1 year. After that time, reauthorization will require the prescriber to verify that the member is responding well to therapy.

Utilization of Carbaglu® (Carglumic Acid): Fiscal Year 2019

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	1	11	$684,174.70	$62,197.70	$2,073.26	3,600	330
2019	1	13	$1,031,677.53	$79,359.81	$2,714.94	5,280	380
% Change	**0.0%**	**18.2%**	**50.8%**	**27.6%**	**31.0%**	**46.7%**	**15.2%**
Change	**0**	**2**	**$347,502.83**	**$17,162.11**	**$641.68**	**1,680**	**50**

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

Demographics of Members Utilizing Carbaglu® (Carglumic Acid)

- Due to the limited number of members utilizing Carbaglu® (carglumic acid) during fiscal year 2019, detailed demographic information could not be provided.

Top Prescriber Specialties of Carbaglu® (Carglumic Acid) by Number of Claims

- The only prescriber specialty listed on paid pharmacy claims for Carbaglu® (carglumic acid) during fiscal year 2019 was medical geneticist.

Prior Authorization of Carbaglu® (Carglumic Acid)

There were 2 prior authorization requests for 1 unique member submitted for Carbaglu® (carglumic acid) during fiscal year 2019, both of which were approved.

Recommendations

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

[1] N-Acetylglutamate Synthetase Deficiency. *NORD Natl Organ Rare Disord*. Available online at: https://rarediseases.org/rare-diseases/n-acetylglutamate-synthetase-deficiency/. Last accessed 11/21/2019.
[2] U.S. Food and Drug Administration (FDA). Drugs@FDA: FDA Approved Drug Products. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022562s002lbl.pdf. Last accessed 11/21/2019.

Appendix Q

Industry News and Updates

Oklahoma Health Care Authority
December 2019

Introduction

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

News and Updates[1,2]

News:

- **Drone Delivery:** A major pharmacy retailer announced it made its first prescription drone delivery. Another major pharmacy retailer is also testing drone prescription delivery. According to Ash Shehata, national sector leader for the Healthcare and Life Sciences Practice at KPMG, drones are less expensive than vehicles to operate and provide more flexibility to fly to a particular location. Shehata also stated that "retailers are looking at increasing consumer convenience with home delivery, but they can do it in a much more urgent basis than traditional mail order pharmacy." However, since the Federal Aviation Administration has requirements regarding the commercial use of drones, regulatory changes will be necessary for prescription drone delivery to become broadly adopted. Shehata also pointed out that there's an additional opportunity for drones in delivery and inventory management for physicians and hospitals.
- **Antibiotic-Resistant Infections:** The Centers for Disease Control and Prevention (CDC) released a report that stated antibiotic-resistant bacteria and fungi cause more than 2.8 million infections in the United States and account for 35,000 deaths. According to the CDC Director, Dr. Robert Redfield, "a death from antibiotic-resistant infection occurs about every 15 minutes, and a resistant infection occurs every 11 seconds." Using data sources not previously available, the updated "Antibiotic Resistance Threats in the United States, 2019" groups the top 18 antibiotic-resistant threats based on level of concern to human health: urgent, serious, or concerning. Two new organisms, drug-resistant *Candida auris* and carbapenem-resistant *Acinetobacter*, were added to the list of urgent threats bringing the most serious organism list to 5. Dr. Redfield stated that the response includes:
    - Preventing infections, including by receiving recommended vaccinations;
    - Slowing development of resistance through better use of antibiotics and antifungals; and
    - Stopping the spread of resistance when it develops.

[1] Blank C. First Rx Drone Delivery Completed by CVS, UPS. *Drug Topics*. Available online at: https://www.drugtopics.com/latest/first-rx-drone-delivery-completed-cvs-ups. Issued 11/14/2019. Last accessed 11/15/2019.
[2] Rosenthal M. More Americans Dying From Resistant Infections Than Previously Thought. *Pharmacy Practice News*. Available online at: https://www.pharmacypracticenews.com/Online-First/Article/11-19/More-Americans-Dying-From-Resistant-Infections-Than-Previously-Thought/56569. Issued 11/13/2019. Last accessed 11/15/2019.

Appendix R

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

FDA NEWS RELEASE

For Immediate Release: November 8th, 2019

FDA approves first therapy to treat patients with rare blood disorder

The FDA granted approval to Reblozyl® (luspatercept–aamt) for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions. Beta thalassemia, also called "Cooley's anemia," is an inherited blood disorder that reduces the production of hemoglobin (hb), an iron-containing protein in RBCs that carries oxygen to cells throughout the body. In people with beta thalassemia, low levels of hb lead to a lack of oxygen in many parts of the body and anemia, which can cause pale skin, weakness, fatigue, and more serious complications. Supportive treatment for people with beta thalassemia often consists of lifelong regimens of chronic blood transfusions for survival and treatment for iron overload due to the transfusions. People with beta thalassemia are also at an increased risk of developing abnormal blood clots.

The approval of Reblozyl® was based on the results of a clinical trial of 336 patients with beta thalassemia who required RBC transfusions, of which 112 received placebo. A total of 21% of the patients who received Reblozyl® achieved at least a 33% reduction in transfusions compared to 4.5% of the patients who received placebo. The transfusion reduction meant that the patient needed fewer transfusions over 12 consecutive weeks while taking Reblozyl®.

Common side effects for patients taking Reblozyl® were headache, bone pain, arthralgia, fatigue, cough, abdominal pain, diarrhea, and dizziness. Patients may experience hypertension while using Reblozyl®. Health care professionals are advised to monitor a patient's blood pressure during treatment and to initiate anti-hypertensive treatment if necessary. Patients who receive Reblozyl® should be monitored for thrombosis. The FDA advises health care professionals to tell females of reproductive age to use effective contraception during treatment with Reblozyl®. Women who are pregnant or breastfeeding should not take Reblozyl® because it may cause harm to a developing fetus or newborn baby.

The FDA granted this application Fast Track designation. Reblozyl® also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA granted approval of Reblozyl® to Celegene Corporation.

FDA NEWS RELEASE

For Immediate Release: November 14th, 2019

FDA approves therapy to treat patients with relapsed and refractory mantle cell lymphoma (MCL) supported by clinical trial results showing high response rate of tumor shrinkage

The FDA granted accelerated approval to Brukinsa™ (zanubrutinib) capsules for the treatment of adult patients with MCL who have received at least 1 prior therapy. MCL is a type of non-Hodgkin's lymphoma (NHL) representing 3 to 10% of all NHLs in the United States. By the time it is diagnosed, MCL has usually spread to the lymph nodes, bone marrow, and other organs. In relapsed lymphoma, the disease reappears or grows again after a period of remission, while in refractory lymphoma, the disease does not respond to treatment or responds only briefly.

A single-arm clinical trial of Brukinsa™ included 86 patients with MCL who had received at least 1 prior treatment. The trial measured how many patients experienced complete or partial shrinkage of their tumors after treatment [overall response rate (ORR)]. In the trial, 84% of patients had tumor shrinkage with a median duration of response (time between the initial response to therapy and subsequent disease progression or relapse) of 19.5 months. This trial was supported by an additional single-arm trial that included 32 patients, in which 84% of patients had tumor shrinkage with a median duration of response of 18.5 months.

Common side effects for patients taking Brukinsa™ were decreased neutrophil count, decreased platelet count, upper respiratory tract infection, decreased white blood cell count, decreased hb, rash, bruising, diarrhea, and cough. During treatment, patients should be monitored for hemorrhage, signs and symptoms of infection, cytopenias, and cardiac arrhythmias. Patients are advised to use sun protection if taking this therapy because there is a risk of other malignancies occurring including skin cancers. The FDA advises health care professionals to tell females of reproductive age and males with a female partner of reproductive potential to

use effective contraception during treatment with Brukinsa™. Women who are pregnant or breastfeeding should not take Brukinsa™ because it may cause harm to a developing fetus or newborn baby.
Brukinsa™ was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. Further clinical trials may be required to verify and describe the clinical benefit of Brukinsa™.
The FDA granted this application Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Brukinsa™ also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA granted approval of Brukinsa™ to BeiGene USA, Inc.

FDA NEWS RELEASE

For Immediate Release: November 14th, 2019

FDA approves new antibacterial drug to treat complicated urinary tract infections as part of ongoing efforts to address antimicrobial resistance

The FDA approved Fetroja® (cefiderocol), an antibacterial drug for treatment of patients 18 years of age or older with complicated urinary tract infections (cUTI), including kidney infections caused by susceptible Gram-negative microorganisms, who have limited or no alternative treatment options.
The safety and effectiveness of Fetroja® was demonstrated in a study of 448 patients with cUTIs. Of the patients who were administered Fetroja®, 72.6% had resolution of symptoms and eradication of the bacteria approximately 7 days after completing treatment, compared with 54.6% in patients who received an alternative antibiotic. The clinical response rates were similar between the 2 treatment groups.
Labeling for Fetroja® includes a warning regarding the higher all-cause mortality rate observed in Fetroja®-treated patients compared to those treated with other antibiotics in a trial in critically ill patients with multidrug-resistant Gram-negative bacterial infections. The cause of the increase in mortality has not been established. Some of the deaths were a result of worsening or complications of infection, or underlying co-morbidities. The higher all-cause mortality rate was observed in patients treated for hospital-acquired/ventilator-associated pneumonia (i.e., nosocomial pneumonia), bloodstream infections, or sepsis. The safety and efficacy of Fetroja® has not been established for the treatment of these types of infections.
The most common adverse reactions observed in patients treated with Fetroja® included diarrhea, constipation, nausea, vomiting, elevations in liver tests, rash, infusion site reactions, candidiasis, cough, headache, and hypokalemia. Fetroja® should not be used in individuals with a known history of severe hypersensitivity to beta-lactam antibacterial drugs.
Fetroja® received the FDA's Qualified Infectious Disease Product (QIDP) designation. The QIDP designation is given to antibacterial and antifungal drug products intended to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act. As part of QIDP designation, Fetroja® was granted Priority Review under which the FDA's goal is to take action on an application within an expedited time frame. The FDA granted the approval of Fetroja® to Shionogi & Co., Ltd.

FDA NEWS RELEASE

For Immediate Release: November 15th, 2019

FDA approves first targeted therapy to treat patients with painful complication of sickle cell disease (SCD)

The FDA approved Adakveo® (crizanlizumab-tmca), a treatment to reduce the frequency of vaso-occlusive crisis – a common and painful complication of SCD that occurs when blood circulation is obstructed by sickled RBCs – for patients age 16 years and older.
SCD is an inherited blood disorder in which the RBCs are abnormally shaped (in a crescent or "sickle" shape), which restricts the flow in blood vessels and limits oxygen delivery to the body's tissues, leading to severe pain and organ damage. It is also characterized by severe chronic inflammation that results in vaso-occlusive crisis where patients experience episodes of extreme pain and organ damage. According to the Centers for Disease Control and Prevetion, SCD affects approximately 100,000 Americans. The disease occurs most often in African-Americans, where 1 out of every 365 babies born have the disease.
The Adakveo® approval was based on the results of a randomized clinical trial enrolling 198 patients with SCD with a history of vaso-occlusive crisis. Patients either received Adakveo® or placebo. Patients treated with Adakveo® experienced fewer health care visits for vaso-occlusive crisis annually (median annual rate of 1.63

visits), compared to patients who received placebo (median annual rate of 2.98 visits). In addition, 36% of patients who received Adakveo® did not experience vaso-occlusive crisis during the study, and it delayed the time that patients first experienced vaso-occlusive crisis after starting treatment from 1.4 months to 4.1 months. Common side effects for patients taking Adakveo® were back pain, nausea, pyrexia, and arthralgia. Health care professionals are advised to monitor patients for infusion-related reactions and to discontinue Adakveo® for severe reactions. Patients who receive Adakveo® should be monitored for interference with automated platelet counts or platelet clumping. Health care professionals are advised to run tests as soon as possible or use citrate tubes.

The FDA granted this application Priority Review and Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Adakveo® also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Adakveo® to Novartis.

FDA NEWS RELEASE

For Immediate Release: November 20th, 2019

FDA approves first treatment for inherited rare disease

The FDA approved Givlaari™ (givosiran) for the treatment of adult patients with acute hepatic porphyria, a genetic disorder resulting in the buildup of toxic porphyrin molecules which are formed during the production of heme.

The approval of Givlaari™ was based on the results of a clinical trial of 94 patients with acute hepatic porphyria. Patients received placebo or Givlaari™. Efficacy was measured by the rate of porphyria attacks that required hospitalizations, urgent health care visits, or intravenous infusion of hemin at home. Patients who received Givlaari™ experienced 70% fewer porphyria attacks compared to patients receiving placebo. Common side effects for patients taking Givlaari™ were nausea and injection site reactions. Health care professionals are advised to monitor patients for anaphylactic reactions and renal function. Patients should have their liver function tested before and periodically during treatment.

The FDA granted this application Breakthrough Therapy designation and Priority Review designation. Givlaari™ also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA granted the approval of Givlaari™ to Alnylam Pharmaceuticals.

FDA NEWS RELEASE

For Immediate Release: November 21st, 2019

FDA takes second action under international collaboration, approves new treatment option for patients with chronic lymphocytic leukemia (CLL)

As part of Project Orbis, a collaboration with the Australian Therapeutic Goods Administration (TGA) and Health Canada, the FDA granted supplemental approval to Calquence® (acalabrutinib) for the treatment of adults with CLL or small lymphocytic lymphoma (SLL). This new approved indication for Calquence® provides a new treatment option for patients with CLL or SLL as an initial or subsequent therapy.

CLL and SLL are similar cancers, but they occur in different areas of the body. CLL occurs mainly in the blood and bone marrow, while SLL occurs mainly in the lymph nodes. Both are cancers of lymphocytes. Symptoms of CLL or SLL include low red blood cell counts, low platelet counts, fatigue, enlarged lymph nodes, and a higher risk of infection.

The supplemental approval of Calquence® for patients with CLL or SLL was based on 2 randomized clinical trials that compared Calquence® to other standard treatments. The first clinical trial involved 535 patients with previously untreated CLL. Patients receiving Calquence® had a longer progression-free survival compared to patients receiving other standard treatments. The second clinical trial included 310 patients with previously treated CLL. Patients receiving Calquence® also had a longer progression-free survival than patients receiving other standard treatments.

The most common side effects of Calquence® were anemia, neutropenia, upper respiratory tract infection, thrombocytopenia, headache, diarrhea, and musculoskeletal pain. Patients may experience atrial fibrillation and flutter and should be monitored for symptoms of arrhythmias. Patients may experience serious infections and should be monitored and treated promptly. Patients should also be monitored for bleeding and managed

appropriately. Patients may also experience low blood counts and should have blood work monitored regularly. Patients should be advised to use sun protection as other malignancies, such as skin cancers and other solid tumors, have occurred in patients taking Calquence®.
The FDA advises health care professionals to tell females of reproductive age to use effective contraception during treatment with Calquence®. Women who are pregnant or breastfeeding should not take Calquence® because it may cause harm to a developing fetus or newborn baby, or cause delivery complications.
In addition to the international collaboration with Australia and Canada, this review used the Real-Time Oncology Review (RTOR) pilot program, which can streamline the submission of data prior to the completion and submission of the entire clinical application. RTOR, and its accompanying Assessment Aid, facilitated discussions among the regulatory agencies. These applications were approved 4 months prior to the FDA goal date. The FDA granted this application Priority Review and Breakthrough Therapy designation. The FDA granted approval of Calquence® to AstraZeneca.

FDA NEWS RELEASE

For Immediate Release: November 21st, 2019

FDA approves new treatment for adults with partial-onset seizures (POS)

The FDA approved Xcopri® (cenobamate tablets) to treat POS in adults.The safety and efficacy of Xcopri® to treat POS was established in 2 randomized, double-blind, placebo-controlled studies that enrolled 655 adults. In these studies, patients had POS with or without secondary generalization for an average of approximately 24 years and a median seizure frequency of 8.5 seizures per 28 days during an 8-week baseline period. During the trials, doses of 100, 200, and 400mg daily of Xcopri® reduced the percent of seizures per 28 days compared with the placebo group. The recommended maintenance dose of Xcopri®, following a titration period, is 200mg daily; however, some patients may need an additional titration to 400mg daily, the maximum recommended dose, based on their clinical response and tolerability.
Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as multiorgan hypersensitivity, has been reported among patients taking Xcopri®. In the clinical trials, some patients experienced DRESS, and 1 patient died, when Xcopri® was titrated rapidly (weekly or faster titration). No cases of DRESS were reported in an open-label safety study of 1,339 epilepsy patients when Xcopri® was started at 12.5mg per day and adjusted every 2 weeks; however, this finding does not show that the risk of DRESS is prevented by a slower titration. A higher percentage of patients who took Xcopri® also had a shortening of the QT interval of >20 milliseconds compared to placebo. Xcopri® should not be used in patients with hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri® or Familial Short QT syndrome. QT shortening can be associated with ventricular fibrillation. The most common side effects that patients in the clinical trials reported were somnolence, dizziness, fatigue, diplopia, and headaches.
The FDA granted the approval of Xcopri® to SK Life Science, Inc.

FDA NEWS RELEASE

For Immediate Release: November 25th, 2019

FDA approves novel treatment to target abnormality in SCD

The FDA granted accelerated approval to Oxbryta™ (voxelotor) for the treatment of SCD in adults and pediatric patients 12 years of age and older.
SCD is a lifelong, inherited blood disorder in which RBCs are abnormally shaped (in a crescent, or "sickle" shape), which restricts the flow in blood vessels and limits oxygen delivery to the body's tissues, leading to severe pain and organ damage. It is also characterized by severe and chronic inflammation that worsens vaso-occlusive crises during which patients experience episodes of extreme pain and organ damage. Nonclinical studies have demonstrated that Oxbryta™ inhibits RBC sickling, improves RBC deformability, and improves the blood's ability to flow.
The approval of Oxbryta™ was based on the results of a clinical trial with 274 patients with SCD. In the study, 90 patients received 1,500mg of Oxbryta™, 92 patients received 900mg of Oxbryta™, and 92 patients received placebo. Effectiveness was based on an increase in hb response rate in patients who received 1,500mg of Oxbryta™, which was 51.1% for these patients compared to 6.5% in the placebo group.
Common side effects for patients taking Oxbryta™ were headache, diarrhea, abdominal pain, nausea, fatigue, rash, and pyrexia.
Oxbryta™ was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. Further clinical trials are required to verify and describe the clinical benefit of Oxbryta™.

The FDA granted this application Fast Track designation. Oxbryta™ also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA granted the approval of Oxbryta™ to Global Blood Therapeutics.

Current Drug Shortages Index (as of Nov 25th, 2019):

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

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

Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Eprosartan Mesylate Tablets	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Isocarboxazid Tablets	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Latanoprost Ophthalmic Solution 0.005%	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methocarbamol Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nelarabine (Arranon) Injection	***Currently in Shortage***

Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Primaquine Phosphate Tablet, EQ 15mg Base	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine Transdermal System	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Triamcinolone Acetonide (Triesence) Injection, Suspension	***Currently in Shortage***
Trifluoperazine Hydrochloride Tablets	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***
Vinblastine Sulfate Injection	***Currently in Shortage***
Vincristine Sulfate Injection, USP (Preservative-Free)	***Currently in Shortage***