Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
October 9, 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 – October 9, 2019

DATE: September 30, 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 October 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

Update on Medication Coverage Authorization Unit/Fall 2019 Pipeline Update – Appendix C

Action Item – Vote to Prior Authorize Ezallor™ Sprinkle (Rosuvastatin Capsule) and Welchol® (Colesevelam Chewable Bar) – Appendix D

Action Item – Vote to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam) – Appendix E

Action Item – Vote to Prior Authorize Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp) – Appendix F

Action Item – Vote to Prior Authorize Nubeqa® (Darolutamide) – Appendix G

Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications – Appendix H

30-Day Notice to Prior Authorize Turalio™ (Pexidartinib) – Appendix I

Action Item – Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators – Appendix J

Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis) – Appendix K

Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Recarbrio™ (Imipenem/Cilastatin/Relebactam) and Xenleta™ (Lefamulin) – Appendix L

Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/ Sofosbuvir Oral Pellets) and Sovaldi® (Sofosbuvir Oral Pellets) – Appendix M

Annual Review of Signifor® LAR (Pasireotide) – Appendix N

Industry News and Updates – Appendix O

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – October 9, 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. Cothran

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. September 11, 2019 DUR Minutes – Vote
B. September 11, 2019 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/Fall 2019 Pipeline Update – See Appendix C

A. Pharmacy Helpdesk Activity for September 2019
B. Medication Coverage Activity for September 2019
C. Fall 2019 Pipeline Update

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

5. Action Item – Vote to Prior Authorize Ezallor™ Sprinkle (Rosuvastatin Capsule) and Welchol® (Colesevelam Chewable Bar) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam) – 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 Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp) – See Appendix F

A. Introduction
B. Product Summaries
C. Recommendations

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

8. Action Item – Vote to Prior Authorize Nubeqa® (Darolutamide) – See Appendix G

A. Introduction
B. Nubeqa® (Darolutamide) Product Summary
C. Recommendations

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

9. Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of ALL/CML Medications
D. Prior Authorization of ALL/CML Medications
E. Market News and Updates
F. Recommendations
G. Utilization Details of ALL/CML Medications

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

10. 30-Day Notice to Prior Authorize Turalio™ (Pexidartinib) – See Appendix I

A. Introduction
B. Turalio™ (Pexidartinib) Product Summary
C. Recommendations

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

11. Action Item – Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators – See Appendix J

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

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

12. Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Amyloidosis Medications
C. Prior Authorization of Amyloidosis Medications
D. Market News and Updates
E. Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis) Product Summaries
F. College of Pharmacy Recommendations

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

13. Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Recarbrio™ (Imipenem/Cilastatin/Relebactam) and Xenleta™ (Lefamulin) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Various Systemic Antibiotics
C. Prior Authorization of Various Systemic Antibiotics
D. Market News and Updates
E. Recarbrio™ (Imipenem/Cilastatin/Relebactam) Product Summary
F. Xenleta™ (Lefamulin) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Various Systemic Antibiotics

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

14. Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir Oral Pellets) and Sovaldi® (Sofosbuvir Oral Pellets) – See Appendix M

A. Introduction
B. Current Prior Authorization Criteria
C. Trends of Hepatitis C Medication Utilization
D. Hepatitis C Summary Statistics for Treated Members
E. Utilization of Hepatitis C Medications
F. Prior Authorization of Hepatitis C Medications

G. Market News and Updates
H. Regimen Comparison
I. College of Pharmacy Recommendations
J. Utilization Details of Hepatitis C Medications

Non-Presentation; Questions Only:

15. Annual Review of Signifor® LAR (Pasireotide) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Signifor® LAR (Pasireotide)
C. Prior Authorization of Signifor® LAR (Pasireotide)
D. Market News and Updates
E. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

16. Industry News and Updates – See Appendix O

A. Introduction
B. News and Updates

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

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

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

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

A. Skin Cancer Medications
B. Targeted Immunomodulator Agents
C. Inrebic® (Fedratinib)
D. Elzonris® (Tagraxofusp-erzs)
E. Constipation and Diarrhea Medications
F. Antidepressants
G. Atopic Dermatitis Medications
H. Antiviral Medications
I. Anticoagulants and Platelet Aggregation Inhibitors

**Future business subject to change.*

19. Adjournment

Appendix A

Changes to Public Comment Procedure

Oklahoma Health Care Authority
October 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 Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each person 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 SEPTEMBER 11, 2019

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.		x
Markita Broyles, D.Ph.; MBA	x	
Darlla D. Duniphin, MHS; PA-C	x	
Theresa Garton, M.D.	x	
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, 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	
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): Justin Wilson, Nicholas Beecher, Kennedy Sounders		

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
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Sr. Director of Pharmacy	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
Thomas Nunn, D.O.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist		x
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Jay Mehta, Jazz Pharmaceuticals	Adam Bloomfield, Sobi	Amy Stanford, Pfizer
Carrie Schaack, Pfizer	Andi Stratton, AveXis	Robert Katz, OUHSC
Tami Sova, Biogen	Dave Poskey, UCB	Frances Bauman, Novo Nordisk
Rhonda Clark, Indivior	Matt Forney, Merck	Jim Chapman, AbbVie
Marc Parker, Sunovion	Cris Valladares, Celgene	
Bruce Christian, Lilly	Amber Schrantz, Lilly	

PRESENT FOR PUBLIC COMMENT:	
Jay Mehta	Jazz Pharmaceuticals
Adam Bloomfield	Sobi
Amy Stanford	Pfizer
Robert Katz	OUHSC

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: NO AGENDA ITEM JAY MEHTA
2B: AGENDA ITEM NO. 6 DR. ROBERT KATZ
2C: AGENDA ITEM NO. 8 AMY STANFORD
2D: AGENDA ITEM NO. 13 ADAM BLOOMFIELD

ACTION: NONE REQUIRED

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

3A: JULY 10, 2019 DUR MINUTES – VOTE
3B: JULY 10, 2019 DUR RECOMMENDATIONS MEMORANDUM
3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Muchmore
Dr. Munoz moved to approve; seconded by Dr. Broyles

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **NOMINATION OF DRUG UTILIZATION REVIEW (DUR) BOARD OFFICERS**

4A: NOMINATIONS OF DRUG UTILIZATION REVIEW (DUR) BOARD OFFICERS

Materials included in agenda packet; presented by Dr. Muchmore
Dr. Muchmore was nominated for chairman by Dr. Broyles; seconded by Dr. Munoz
Dr. Mitchell was nominated for vice chairwoman by Dr. Munoz; seconded by Dr. Broyles

ACTION(S): MOTIONS CARRIED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE**

5A: MEDICATION COVERAGE ACTIVITY FOR JULY 2019
5B: PHARMACY HELPDESK ACTIVITY FOR JULY 2019
5C: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2019
5D: PHARMACY HELPDESK ACTIVITY FOR AUGUST 2019
5E: CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ZOLGENSMA® (ONASEMNOGENE ABEPARVOVEC-XIOI)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
Dr. Broyles moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE BRYHALI™ (HALOBETASOL PROPIONATE 0.01% LOTION), DUOBRII™ (HALOBETASOL PROPIONATE/TAZAROTENE 0.01%/0.045% LOTION), AND LEXETTE™ (HALOBETASOL PROPIONATE 0.05% FOAM) AND TO UPDATE THE TOPICAL CORTICOSTEROIDS PRODUCT BASED PRIOR AUTHORIZATION TIER CHART AND CRITERIA
7A: INTRODUCTION
7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Munoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF BREAST CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE HERZUMA® (TRASTUZUMAB-PKRB), KANJINTI™ (TRASTUZUMAB-ANNS), ONTRUZANT® (TRASTUZUMAB-DTTB), PIQRAY® (ALPELISIB), TALZENNA® (TALAZOPARIB), AND TRAZIMERA™ (TRASTUZUMAB-QYYP)
8A: INTRODUCTION
8B: CURRENT PRIOR AUTHORIZATION CRITERIA
8C: UTILIZATION OF BREAST CANCER MEDICATIONS
8D: PRIOR AUTHORIZATION OF BREAST CANCER MEDICATIONS
8E: MARKET NEWS AND UPDATES
8F: PRODUCT SUMMARIES
8G: RECOMMENDATIONS
8H: UTILIZATION DETAILS OF BREAST CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF PROSTATE CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NUBEQA™ (DAROLUTAMIDE)
9A: INTRODUCTION
9B: CURRENT PRIOR AUTHORIZATION CRITERIA
9C: UTILIZATION OF PROSTATE CANCER MEDICATIONS
9D: PRIOR AUTHORIZATION OF PROSTATE CANCER MEDICATIONS
9E: MARKET NEWS AND UPDATES
9F: NUBEQA™ (DAROLUTAMIDE) PRODUCT SUMMARY
9G: RECOMMENDATIONS
9H: UTILIZATION DETAILS OF PROSTATE CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF CRYSVITA® (BUROSUMAB-TWZA)
10A: INTRODUCTION
10B: CURRENT PRIOR AUTHORIZATION CRITERIA
10C: UTILIZATION OF CRYSVITA® (BUROSUMAB-TWZA)
10D: PRIOR AUTHORIZATION OF CRYSVITA® (BUROSUMAB-TWZA)
10E: MARKET NEWS AND UPDATES
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ANTIHYPERLIPIDEMICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE WELCHOL® (COLESEVELAM CHEWABLE BAR) AND EZALLOR™ SPRINKLE (ROSUVASTATIN CAPSULE)**

11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF ANTIHYPERLIPIDEMICS
11C: PRIOR AUTHORIZATION OF ANTIHYPERLIPIDEMICS
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
11F: UTILIZATION DETAILS OF ANTIHYPERLIPIDEMICS

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

AGENDA ITEM NO. 12: **30-DAY NOTICE TO PRIOR AUTHORIZE SORILUX® (CALCIPOTRIENE 0.005% FOAM)**

12A: INTRODUCTION
12B: SORILUX® (CALCIPOTRIENE 0.005% FOAM) PRODUCT SUMMARY
12C: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF SYNAGIS® (PALIVIZUMAB)
13C: PRIOR AUTHORIZATION OF SYNAGIS® (PALIVIZUMAB)
13D: SEASON COMPARISON
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 14: **ANNUAL REVIEW OF SICKLE CELL DISEASE (SCD) MEDICATIONS**

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF SCD MEDICATIONS
14C: PRIOR AUTHORIZATION OF SCD MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF SCD MEDICATIONS

Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **INDUSTRY NEWS AND UPDATES**

15A: INTRODUCTION
15B: NEWS AND UPDATES

Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

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

AGENDA ITEM NO. 17: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

17A: TURALIO™ (PEXIDARTINIB)
17B: HEPATITIS C MEDICATIONS
17C: ACUTE LYMPHOBLASTIC LEUKEMIA AND CHRONIC MYELOID LEUKEMIA MEDICATIONS

17D: CYSTIC FIBROSIS MEDICATIONS
17E: SIGNIFOR® LAR (PASIREOTIDE)
17F: AMYLOIDOSIS MEDICATIONS
17G: VARIOUS ANTIBIOTICS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ADJOURNMENT
The meeting was adjourned at 5:08pm.

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

Memorandum

Date: September 12, 2019

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

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

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

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

Recommendation 1: Chronic Medication Adherence Program Update

NO ACTION REQUIRED.

Item of Business: Nomination of DUR Board Officers

MOTION(s) CARRIED by unanimous approval.

- Dr. Muchmore nominated and confirmed as chairman.
- Dr. Mitchell nominated and confirmed as vice-chairwoman.

Recommendation 2: Vote to Prior Authorize Zolgensma® (Onasemnogene Abeparvovec-xioi)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Zolgensma® (onasemnogene abeparvovec-xioi) with the following criteria:

Zolgensma® (Onasemnogene Abeparvovec-xioi) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in pediatric patients younger than 2 years of age; and
2. Member must have reached full-term gestational age prior to Zolgensma® infusion; and
3. Molecular genetic testing to confirm bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene; and
4. Member is not currently dependent on permanent invasive ventilation (defined as at least 16 hours of respiratory assistance per day continuously for more than 21 days in the absence of an acute, reversible illness or a perioperative state); and
5. Zolgensma® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or be an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
6. Member must have baseline anti-AAV9 antibody titers ≤1:50; and
7. Prescriber must agree to monitor liver function tests, platelet counts, and troponin-I at baseline and as directed by the Zolgensma® prescribing information; and
8. Prescriber must agree to administer systemic corticosteroids starting 1 day prior to the Zolgensma® infusion and continuing as recommended in the prescribing information based on member's liver function; and
9. Zolgensma® must be shipped to the facility where the member is scheduled to receive treatment and must adhere to the storage and handling requirements in the Zolgensma® prescribing information; and
10. Member will not be approved for concomitant treatment with nusinersen following Zolgensma® infusion (current authorizations for nusinersen will be discontinued upon Zolgensma® approval); and
11. Member's recent weight must be provided to ensure accurate dosing in accordance with Zolgensma® prescribing information; and
12. Only 1 Zolgensma® infusion will be approved per member per lifetime.

In addition, the College of Pharmacy recommends the following changes shown in red to the current Spinraza® (nusinersen) approval criteria:

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
    a. Type 1; or
    b. Type 2; or
    c. Type 3 with symptoms; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as at least 16 hours of respiratory assistance per day continuously for more than 21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or be an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and

5. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
6. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
7. Spinraza® must be administered in a health care facility by a specialist experienced in performing lumbar punctures; and
    a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
8. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
    a. Hammersmith Infant Neurological Exam (HINE); or
    b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
    c. Upper Limb Module (ULM) Test; or
    d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
9. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically-significant improvement or maintenance of function from pre-treatment baseline status using the same exam as performed at baseline assessment:
    a. HINE; or
    b. CHOP-INTEND; or
    c. ULM Test; or
    d. HFMSE; and
10. Approval quantity will be based on Spinraza® prescribing information and FDA approved dosing regimen(s); and
    a. Only one 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

Recommendation 3: Vote to Prior Authorize Bryhali™ (Halobetasol Propionate 0.01% Lotion), Duobrii™ (Halobetasol Propionate/Tazarotene 0.01%/0.045% Lotion), and Lexette™ (Halobetasol Propionate 0.05% Foam) and to Update the Topical Corticosteroids Product Based Prior Authorization Tier Chart and Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Topical Corticosteroids (TCS) Product Based Prior Authorization (PBPA) category based on net costs:

1. Move Diprosone® (betamethasone dipropionate 0.05% ointment) from Tier-1 to Tier-2 of the Ultra-High to High Potency category of the TCS PBPA Tier Chart. Current Tier-2 criteria will apply.
2. Move Temovate® (clobetasol propionate 0.05% ointment) from Tier-3 to Tier-1 of the Ultra-High to High Potency category of the TCS PBPA Tier Chart.
3. Move Apexicon® (diflorasone diacetate 0.05% cream and ointment) and Apexicon E® (diflorasone diacetate/emollient 0.05% cream) from Tier-2 to Tier-3 of the Ultra-High to High Potency category of the TCS PBPA Tier Chart. Current Tier-3 criteria will apply.

4. Move Trianex® (triamcinolone acetonide 0.05% ointment) from Tier-1 to Tier-2 of the Medium-High to Medium Potency category of the TCS PBPA Tier Chart. Current Tier-2 criteria will apply.

Additionally, the College of Pharmacy recommends the following:

1. The placement of Bryhali™ (halobetasol propionate 0.01% lotion) and Lexette™ (halobetasol propionate 0.05% foam) into Tier-3 of the Ultra-High to High Potency category of the TCS PBPA Tier Chart. Current Tier-3 criteria will apply.
2. The prior authorization of Duobrii™ (halobetasol propionate/tazarotene 0.01%/0.045% lotion) with the following criteria:

Duobrii™ (Halobetasol Propionate/Tazarotene 0.01%/0.045% Lotion) Approval Criteria:

1. An FDA approved indication of plaque psoriasis in adults; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. A patient-specific, clinically significant reason why the member cannot use individual components of tazarotene and a topical corticosteroid separately must be provided; and
4. A quantity limit of 100 grams per 30 days will apply.

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

Tier-2 Topical Corticosteroids (TCS) Approval Criteria:

1. Documented trials of all Tier-1 TCS of similar potency in the past 30 days that did not yield adequate relief; and
2. If Tier-1 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-2 TCS in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (e.g., foams, shampoos, sprays, kits); and
4. TCS kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Tier-3 Topical Corticosteroids (TCS) Approval Criteria:

1. Documented trials of all Tier-1 and Tier-2 TCS of similar potency in the past 90 days that did not yield adequate relief; and
2. If Tier-1 and Tier-2 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-3 TCS in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-3 (e.g., foams, shampoos, sprays, kits); and
4. TCS kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% (**Diprolene AF®**)	**C,G**	amcinonide 0.1%	**C,L**	clobetasol propionate 0.025% (**Impoyz™**)	**C**
clobetasol propionate 0.05% (**Temovate®**)	**C,L,O, So**	augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**L,O**	clobetasol propionate 0.05% (**Clobex®**)	**Sh,Spr**
fluocinonide 0.05%	**C,O,So**	betamethasone dipropionate 0.05% (**Diprosone®**)	**C,O**	clobetasol propionate 0.05% (**Olux®, Olux-E®**)	**F**
halobetasol propionate 0.05% (**Ultravate®**)	**C**	clobetasol propionate 0.05% (**Clobex®**)	**L**	desoximetasone 0.25% (**Topicort®**)	**C,O,Spr**
		clobetasol propionate 0.05% (**Temovate®**)	**G**	diflorasone diacetate 0.05% (**Apexicon®**)	**C,O**
		desoximetasone 0.05% (**Topicort®**)	**G**	diflorasone diacetate/emollient 0.05% (**Apexicon E®**)	**C**
		fluocinonide 0.05%	**G**	halobetasol propionate 0.01% (**Bryhali™**)	**L**
		fluocinonide 0.1% (**Vanos®**)	**C**	halobetasol propionate 0.05% (**Lexette™**)	**F**
		flurandrenolide 0.05% (**Cordran®**)	**Tape**		
		halcinonide 0.1% (**Halog®**)	**C,O**		
		halobetasol propionate 0.05% (**Ultravate®**)	**L,O**		
		halobetasol propionate/lactic acid 0.05%/10% (**Ultravate X®**)	**C**		
Medium-High to Medium Potency					
betamethasone dipropionate 0.05%	**L**	betamethasone dipropionate/calcipotriene 0.064%/0.005% (**Taclonex®**)	**O,Spr, Sus**	betamethasone dipropionate 0.05% (**Sernivo®**)	**Spr**
betamethasone valerate 0.1% (**Beta-Val®**)	**C,L,O**	betamethasone valerate 0.12% (**Luxiq®**)	**F**	hydrocortisone valerate 0.2% (**Westcort®**)	**C,O**
fluticasone propionate 0.05% (**Cutivate®**)	**C,O**	calcipotriene/betamethasone dipropionate 0.064%/0.005% (**Enstilar®**)	**F**		
mometasone furoate 0.1% (**Elocon®**)	**C,L,O, So**	clocortolone pivalate 0.1% (**Cloderm®**)	**C**		
triamcinolone acetonide 0.025%	**O**	desoximetasone 0.05% (**Topicort LP®**)	**C,O**		

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
triamcinolone acetonide 0.1%	**C,L,O**	fluocinolone acetonide 0.025% (**Synalar®**)	**C,O**		
triamcinolone acetonide 0.5%	**C,O**	fluocinonide emollient 0.05% (**Lidex E®**)	**C**		
		flurandrenolide 0.05%	**C,L,O**		
		fluticasone propionate 0.05% (**Cutivate®**)	**L**		
		hydrocortisone butyrate 0.1%	**C,L,O, So**		
		hydrocortisone probutate 0.1% (**Pandel®**)	**C**		
		prednicarbate 0.1% (**Dermatop®**)	**C,O**		
		triamcinolone acetonide 0.147mg/g (**Kenalog®**)	**Spr**		
		triamcinolone acetonide 0.05% (**Trianex®**)	**O**		
Low Potency					
desonide 0.05% (**Desonate®**)	**G**	alclometasone dipropionate 0.05% (**Aclovate®**)	**C,O**	fluocinolone acetonide 0.01% (**Derma-Smoothe®; Derma-Smoothe FS®**)	**Oil**
fluocinolone acetonide 0.01% (**Capex®**)	**Sh**	desonide 0.05% (**Verdeso®**)	**F**	desonide 0.05%	**L**
hydrocortisone acetate 1%	**C,O**	fluocinolone acetonide 0.01% (**Synalar®**)	**C,So**	desonide emollient 0.05%	**C,O**
hydrocortisone acetate 2.5%	**C,L,O**	hydrocortisone 2.5% (**Texacort®**)	**So**		
hydrocortisone/urea 1%/10% (**U-Cort®**)	**C**	hydrocortisone/pramoxine 1%/1% (**Pramosone®**)	**C,L**		
triamcinolone acetonide 0.025%	**C,L**				

C = Cream; F = Foam; G = Gel; L = Lotion; O = Ointment; Sh = Shampoo; So = Solution; Spr = Spray; Sus = Suspension
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendation 4: Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Nubeqa™ (Darolutamide)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Crysvita® (Burosumab-twza)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Crysvita® (burosumab-twza) approval criteria based on the results of a randomized clinical trial comparing burosumab to conventional therapy of oral phosphate and active vitamin D therapy:

Crysvita® (Burosumab-twza) Approval Criteria:

1. An FDA approved indication for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric members 1 year of age and older. Diagnosis of XLH must be confirmed by 1 of the following:
    a. Genetic testing; or
    b. Elevated serum fibroblast growth factor 23 (FGF23) level; and
2. Member's serum phosphorus level must be below the normal range for member age; and
3. ~~Member's XLH symptoms must not be adequately controlled on phosphate and calcitriol supplements. Members experiencing adverse effects related to these treatments may also be considered for approval. Detailed information regarding adverse effects must be documented on the prior authorization request; and~~
4. Member must not have any contraindications to taking Crysvita® including the following:
    a. Concomitant use with oral phosphate and active vitamin D analogs; and
    b. Serum phosphorus within or above the normal range for member age; and
    c. Severe renal impairment or end-stage renal disease; and
5. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
    a. Crysvita® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Crysvita® must be shipped via cold chain supply to the member's home and administered by a home health care provider, and the member's caregiver must be trained on the proper storage of Crysvita®; and
6. Member must have clinical signs and symptoms of XLH (symptoms beyond hypophosphatemia alone); and
7. Every 2 week dosing will not be approved for members 18 years of age or older; and
8. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment, and thereafter as appropriate; and
9. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or be an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and

10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; and
11. 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.

Recommendation 7: Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Welchol® (Colesevelam Chewable Bar) and Ezallor™ Sprinkle (Rosuvastatin Capsule)

NO ACTION REQUIRED.

Recommendation 8: 30-Day Notice to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Synagis® (Palivizumab)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Sickle Cell Disease (SCD) Medications

NO ACTION REQUIRED.

Recommendation 11: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 12: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

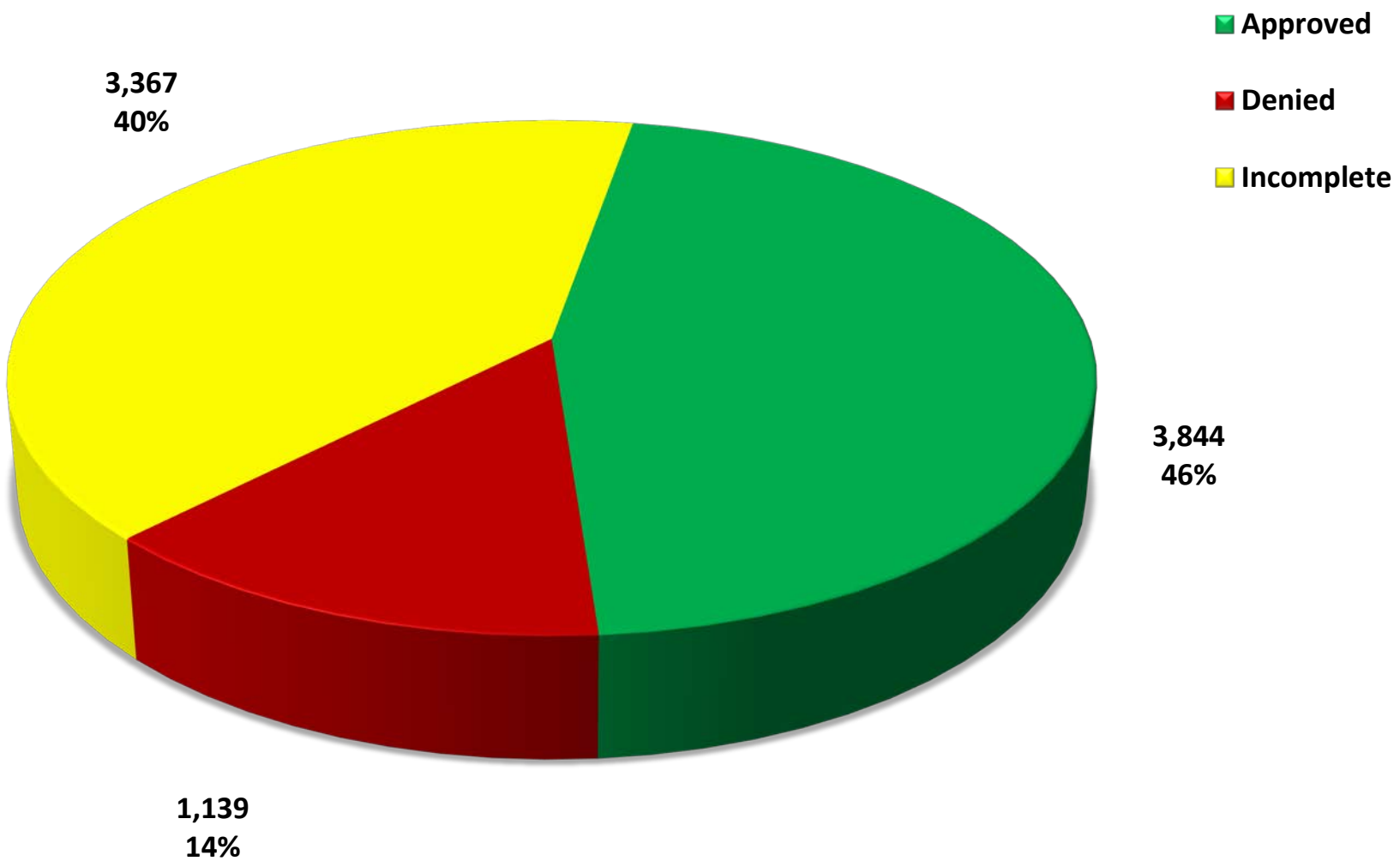
NO ACTION REQUIRED.

Recommendation 13: Future Business

NO ACTION REQUIRED.

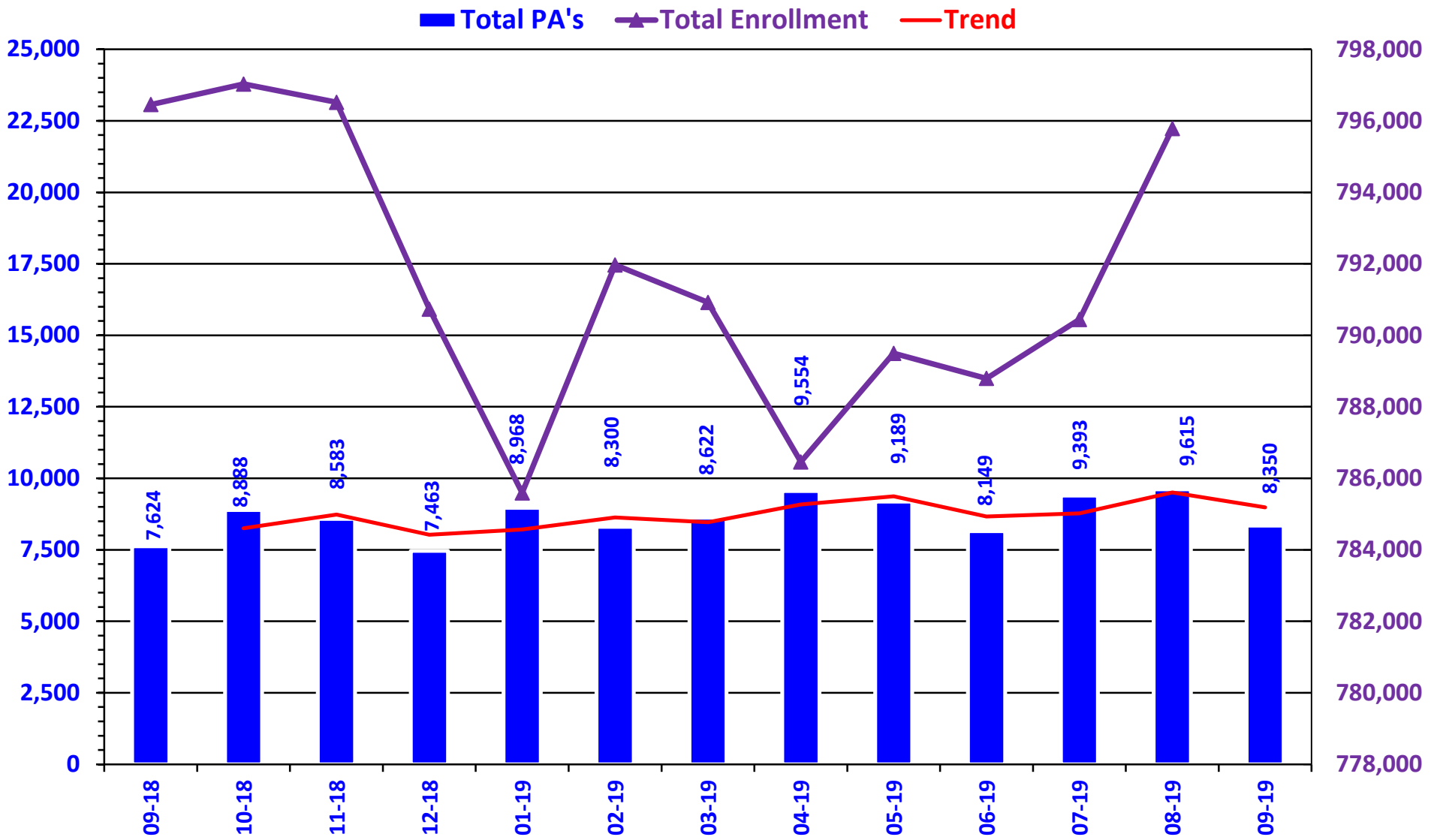
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER 2019



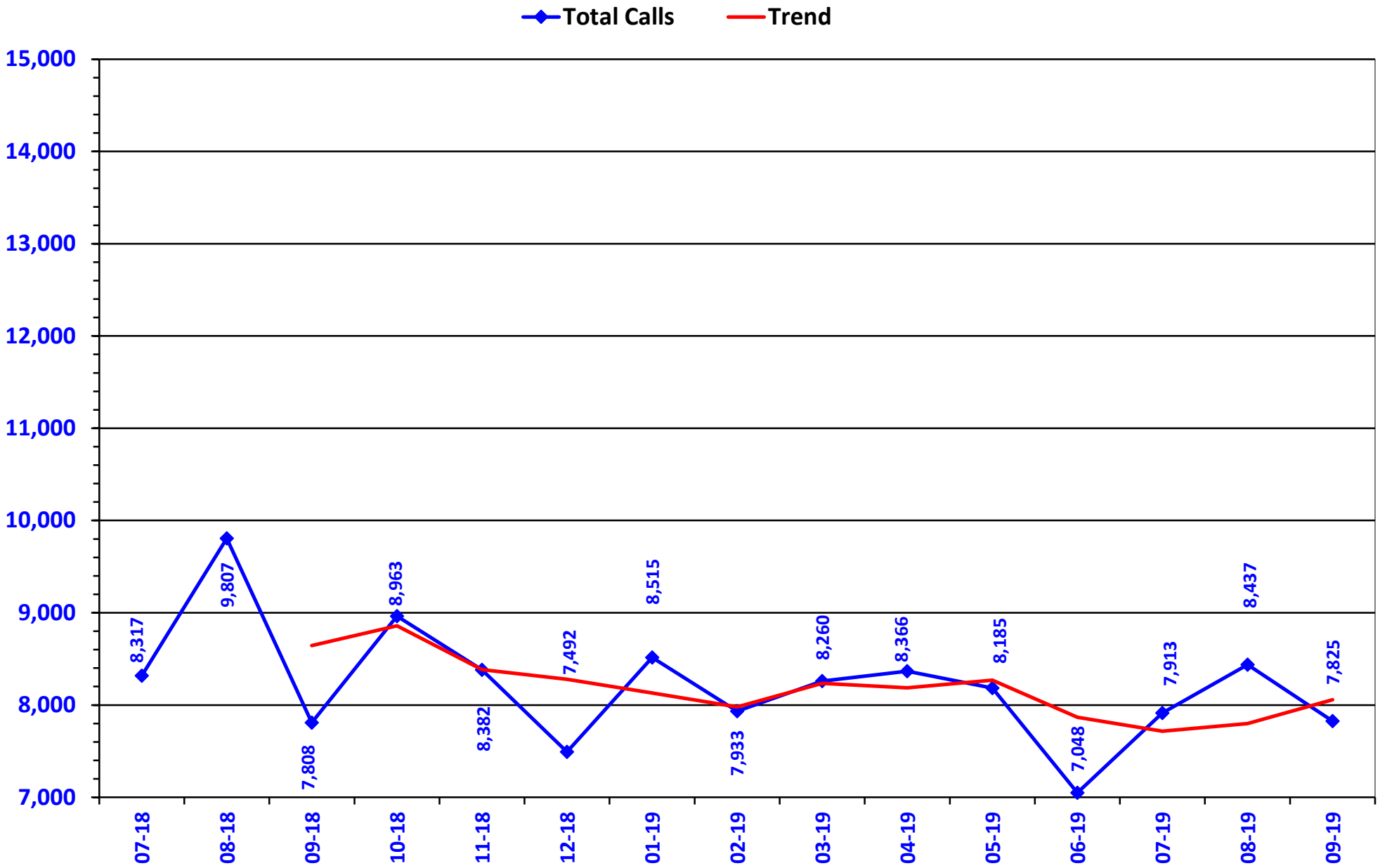
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2018 – SEPTEMBER 2019



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
SEPTEMBER 2018 – SEPTEMBER 2019



Prior Authorization Activity

9/1/2019 Through 9/30/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	76	14	19	43	359
Analgesic - NonNarcotic	18	0	2	16	0
Analgesic - Narcotic	319	151	30	138	161
Angiotensin Receptor Antagonist	18	4	6	8	290
Antiasthma	93	31	20	42	231
Antibiotic	31	21	1	9	300
Anticonvulsant	142	63	10	69	310
Antidepressant	153	38	16	99	334
Antidiabetic	267	74	53	140	347
Antihemophilic Factor	10	8	0	2	202
Antihistamine	28	4	13	11	153
Antimigraine	162	34	48	80	186
Antineoplastic	86	53	11	22	168
Antiparasitic	18	3	5	10	6
Antiulcers	136	34	56	46	84
Anxiolytic	21	3	8	10	133
Atypical Antipsychotics	241	121	33	87	354
Biologics	131	50	26	55	262
Bladder Control	35	7	9	19	324
Blood Thinners	240	138	10	92	332
Botox	41	25	14	2	334
Buprenorphine Medications	103	19	4	80	52
Calcium Channel Blockers	10	2	1	7	26
Cardiovascular	64	30	6	28	303
Chronic Obstructive Pulmonary Disease	154	34	41	79	448
Constipation/Diarrhea Medications	157	26	56	75	242
Contraceptive	31	26	1	4	296
Corticosteroid	19	1	5	13	19
Dermatological	274	78	73	123	136
Diabetic Supplies	536	307	21	208	198
Endocrine & Metabolic Drugs	135	77	16	42	163
Erythropoietin Stimulating Agents	22	9	3	10	111
Fibromyalgia	128	17	9	102	289
Fish Oils	14	1	5	8	361
Gastrointestinal Agents	102	23	27	52	165
Glaucoma	13	5	2	6	213
Growth Hormones	144	92	12	40	142
Hepatitis C	153	93	26	34	9
HFA Rescue Inhalers	47	2	2	43	84
Insomnia	43	6	11	26	160
Insulin	150	57	20	73	319
Multiple Sclerosis	48	17	6	25	215
Muscle Relaxant	43	5	12	26	122
Nasal Allergy	78	14	26	38	107
Neurological Agents	80	25	19	36	187
NSAIDs	25	1	6	18	361
Ocular Allergy	35	7	6	22	84
Ophthalmic Anti-infectives	14	2	1	11	10
Osteoporosis	16	8	2	6	358
Other*	328	73	63	192	270

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Otic Antibiotic	22	5	4	13	10
Pediculicide	26	2	8	16	4
Respiratory Agents	29	17	3	9	213
Statins	22	3	6	13	112
Stimulant	764	363	82	319	343
Synagis	16	0	8	8	0
Testosterone	88	25	22	41	297
Topical Antifungal	20	5	2	13	41
Topical Corticosteroids	59	2	29	28	33
Vitamin	71	25	20	26	190
Pharmacotherapy	58	47	0	11	305
Emergency PAs	0	0	0	0	
Total	**6,407**	**2,427**	**1,056**	**2,924**	
Overrides					
Brand	34	28	2	4	285
Compound	25	17	3	5	62
Diabetic Supplies	6	5	0	1	111
Dosage Change	393	363	5	25	12
High Dose	6	5	1	0	357
IHS-Brand	2	2	0	0	363
Ingredient Duplication	5	4	0	1	7
Lost/Broken Rx	83	73	3	7	15
MAT Override	59	50	0	9	62
NDC vs Age	303	190	26	87	267
Nursing Home Issue	56	55	0	1	11
Opioid MME Limit	189	102	7	80	90
Opioid Quantity	37	25	0	12	161
Other*	42	39	1	2	17
Quantity vs. Days Supply	653	423	33	197	194
STBS/STBSM	19	9	2	8	42
Stolen	2	2	0	0	15
Third Brand Request	29	25	0	4	58
Overrides Total	**1,943**	**1,417**	**83**	**443**	
Total Regular PAs + Overrides	**8,350**	**3,844**	**1,139**	**3,367**	

Denial Reasons	
Unable to verify required trials.	2,632
Does not meet established criteria.	1,162
Lack required information to process request.	704

Other PA Activity	
Duplicate Requests	590
Letters	12,645
No Process	9
Changes to existing PAs	705
Helpdesk Initiated Prior Authorizations	675
PAs Missing Information	28

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

Fall 2019 Pipeline Update

Oklahoma Health Care Authority
October 2019

Introduction

The following report is a pipeline review compiled by the University of Oklahoma College of Pharmacy. Information in this report is focused on medications not yet approved by the U.S. Food and Drug Administration (FDA). The pipeline report is not an all-inclusive list, and medications expected to be highly utilized or have a particular impact in the SoonerCare population have been included for review. Pipeline data is collected from a variety of sources and is subject to change; dates listed are projections and all data presented are for informational purposes only. Costs listed in the following report do not reflect rebated prices or net costs.

Lasmiditan[1,2]

Anticipated Indication(s): Orally administered selective serotonin 5-HT_{1F} agonist for the treatment of acute migraines with or without aura in adults.

Clinical Trial(s): Lasmiditan was evaluated in a double-blind, Phase 3 study of 2,586 patients for the acute treatment of migraine. Patients with migraine, with and without aura, were randomized in a 1:1:1:1 ratio to oral lasmiditan 200mg (N=528), 100mg (N=532), 50mg (N=556), or placebo (N=645). Patients were instructed to dose at home within 4 hours of onset of migraine attack of at least moderate intensity. The primary endpoint was the proportion of patients who were migraine pain-free 2 hours following the dose of lasmiditan as compared to placebo. Most patients (79.2%) had ≥1 cardiovascular (CV) risk factor at baseline, in addition to migraine. The percentage of patients treated with lasmiditan and who were migraine pain-free 2 hours post-dose was significantly greater compared to placebo [lasmiditan 200mg: 38.8%, odds ratio (OR) 2.3, 95% confidence interval (CI) 1.8 to 3.1, P<0.001; 100mg: 31.4%, OR 1.7, CI 1.3 to 2.2, P<0.001; 50mg: 28.6%, OR 1.5, CI 1.1 to 1.9, P=0.003 vs. placebo 21.3%]. Lasmiditan also met the key secondary endpoint, with a significantly greater percentage of patients free of their most bothersome symptom (MBS) compared with placebo at 2 hours following the first dose. In these studies, patients chose their MBS from sensitivity to light, sensitivity to sound, or nausea. Treatment-emergent adverse events (AEs) were reported in 39.0%, 36.1%, and 25.4% of patients on lasmiditan 200mg, 100mg, and 50mg, respectively, versus 11.6% on placebo. The most commonly reported AEs after lasmiditan dosing were dizziness, paresthesia, somnolence, fatigue, nausea, muscle weakness, and numbness.

Place in Therapy: Lasmiditan is a first-in-class, selective serotonin 5-HT_{1F} agonist. Triptans, the current standard of care for the treatment of acute migraine attacks, target 5-$HT_{1B/1D}$ receptors, which can lead to adverse CV events including vasoconstriction. Lasmiditan lacks vasoconstrictor activity.

Projected FDA Decision: December 24, 2019

SoonerCare Impact: During fiscal year 2019, a total of 5,011 members had paid pharmacy claims for triptan medications, accounting for 11,137 claims totaling $308,201.72 in drug spending and an average cost per claim of $27.67.

RVT-802[1,3]

Anticipated Indication(s): Allogenic, cultured, postnatal, thymus tissue-derived, regenerative therapy for the treatment of pediatric congenital athymia. RVT-802 is obtained from unrelated donors younger than 9 months of age.

Clinical Trial(s): RVT-802 was evaluated in a total of 93 patients across multiple clinical studies, including 85 patients who met the criteria for inclusion in the efficacy analysis. The Kaplan-Meier estimates of survival at year 1 and year 2 following treatment were 76% (66% to 84%) and 75% (66% to 83%), respectively. For patients surviving 12 months post-treatment, there was a 93% probability of surviving 10 years post-treatment. During clinical development, the most commonly (≥5%) reported RVT-802 related AEs included thrombocytopenia (11%), neutropenia (8%), pyrexia (5%), and proteinuria (5%).

Place in Therapy: Congenital athymia is a rare and deadly condition associated with complete DiGeorge Anomaly (cDGA). Around 20 infants are born each year in the United States with congenital athymia, which is fatal if untreated. Death typically occurs in the first 24 months of life due to susceptibility to infection. Currently, there are no FDA-approved therapies for this condition and the standard of care has been investigational thymic tissue transplantation or hematopoietic stem cell transplantation (HSCT). RVT-802 is designed to replicate this process in the absence of a thymus. RVT-802 stimulates and facilitates the body's production of naïve, immunocompetent T cells, with the goal of bolstering the immune system and restoring the body's ability to fight infection. Investigational RVT-802 is designed to be administered as a single treatment via implantation into the quadriceps muscles.

Projected FDA Decision: December 2019

SoonerCare Impact: An estimated 20 infants are born each year in the United States with congenital athymia. There is no specific International Classification of Disease 10th Revision (ICD-10) diagnosis code; therefore, SoonerCare specific data could not be provided.

Luspatercept[1,4]

Anticipated Indication(s): Subcutaneous (sub-Q) erythroid maturation agent for the treatment of adult patients with beta-thalassemia-associated anemia who require red blood cell (RBC) transfusions.

Clinical Trial(s): Luspatercept was evaluated in a double-blind, placebo-controlled trial in 332 adult patients with beta-thalassemia who required transfusions of 6 to 20 RBC units in the 24 weeks prior to randomization with no transfusion-free period ≥35 days during that time. The primary endpoint was a ≥33% reduction in transfusion burden with a reduction of ≥2 RBC units

during weeks 13 to 24 when compared with a 12-week baseline period. A total of 21.4% of patients in the luspatercept arm achieved the primary endpoint compared with 4.5% of those receiving placebo (OR 5.79; P<0.0001). Specifically, 19.6% of patients on luspatercept achieved a ≥33% reduction in RBC transfusion burden during weeks 37 to 48 compared with 3.6% of those receiving placebo (P<0.0001). The most common AEs with luspatercept use were thromboembolic events (deep venous thrombosis, pulmonary embolism, portal vein thrombosis, ischemic stroke, thrombophlebitis, and superficial phlebitis), bone pain, hypertension, diarrhea, and nausea.

Place in Therapy: Beta-thalassemia is a rare, hereditary blood disorder characterized by reduced levels of functional hemoglobin. Symptomatic cases occur in approximately 1 in 100,000 individuals. HSCT can be curative but is limited by availability of donors and risks associated with the procedure. The current standard of care for management of severe beta-thalassemia is life-long RBC transfusions and iron chelation. Luspatercept is a novel, first-in-class, erythroid maturation agent. Luspatercept inhibits members of the transforming growth factor (TGF)-beta superfamily which are involved in late stages of erythropoiesis and which inhibit RBC maturation. Luspatercept attempts to restore RBC production. Luspatercept requires sub-Q administration by a health care provider and requires chronic treatment. Another treatment, LentiGlobin/Zynteglo is a 1-time gene therapy treatment for beta-thalassemia that is preparing to file with the FDA and could become available in mid-to-late 2020.

Projected FDA Decision: December 4, 2019

SoonerCare Impact: During fiscal year 2019, there were 11 adult SoonerCare members with at least 2 diagnosis claims for beta-thalassemia for which SoonerCare is the primary payer.

Pipeline Table[1,5]

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
afamelanotide	Clinuvel	Erythropoietic porphyria	SC	Filed NDA	10/06/2019
teriparatide recombinant	Pfenex	Osteoporosis	SC	Filed NDA	10/07/2019
diroximel fumarate	Biogen	Relapsing MS	PO	Filed NDA	10/17/2019
asenapine maleate	Hisamitsu	Schizophrenia	TOP	Filed NDA	10/17/2019
romiplostim (Nplate®)	Amgen	Resistant ITP	SC	Filed sBLA	10/18/2019
ustekinumab (Stelara®)	Janssen	UC	IV; SC	Filed sBLA	10/18/2019
ravulizumab (Ultomiris®)	Alexion	HUS	IV	Filed sBLA	10/19/2019
triamcinolone acetonide	Clearside	Macular edema uveitis	IO	Filed NDA	10/19/2019
synthetic ACTH depot	Assertio	Adrenocortical insufficiency	IM	Filed NDA	10/19/2019
phenylephrine	Eton	Hypotension	IV	Filed NDA	10/21/2019
cetirizine	JDP Therapeutics	Urticaria	IV	Filed NDA	10/30/2019
naloxone	Adamis	Opioid dependence	IM	Filed NDA	10/31/2019
methotrexate	Cumberland	Psoriasis; arthritis	SC	Filed NDA	11/01/2019
rifabutin/amoxicillin/ pantoprazole	RedHill	*H. Pylori* infection	PO	Filed NDA	11/02/2019

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
testosterone undecanoate	Lipocine	Hypogonadism	PO	Filed NDA	11/09/2019
lasmiditan	Eli Lilly	Acute migraines	PO	Filed NDA	11/14/2019
brolucizumab	Novartis	Wet AMD	IO	Filed NDA	11/15/2019
ethinyl estradiol/ levonorgestrel	Agile Therapeutics	Pregnancy prevention	TOP	Filed NDA	11/17/2019
cenobamate	SK Biopharm	Partial-onset seizures	PO	Filed NDA	11/21/2019
riluzole	Aquestive	ALS	SL	Filed NDA	11/30/2019
RVT-802	Enzyvant	Congenital athymia	Implant	Filed NDA	12/2019
luspatercept	Celgene	Beta-thalassemia	SC	Filed BLA	12/04/2019
ubrogepant	Allergan	Acute migraines	PO	Filed NDA	12/15/2019
vernakalant	Correvio	Atrial fibrillation	IV	Filed NDA	12/24/2019
bupivacaine ER	Durect	Postsurgical pain	SC	Filed NDA	12/27/2019
cabotegravir	ViiV	HIV	PO	Filed NDA	12/27/2019
cabotegravir/rilpivirine	ViiV	HIV	IM	Filed NDA	12/27/2019
lemborexant	Eisai	Insomnia	PO	Filed NDA	12/27/2019
lumateperone	Intra-Cellular	Schizophrenia	PO	Filed NDA	12/27/2019
AR-101	Aimmune	Peanut allergy	PO	Filed BLA	01/2020
vedolizumab (Entyvio®)	Takeda	UC/CD	SC	Filed sBLA	01/01/2020
Insulin aspart (Fiasp®)	Novo Nordisk	T1DM (pediatrics)	SC	Filed sNDA	01/01/2020
crizanlizumab	Novartis	SCD	IV	Filed BLA	01/15/2020
semaglutide (Ozempic®, Rybelsus®)	Novo Nordisk	CV risk reduction	PO; SC	Filed sNDA	01/20/2020
risperidone ER	Luye	Schizophrenia	IM	Filed NDA	01/28/2020
empagliflozin/linagliptin/ metformin ER	Boehringer Ingelheim	T2DM	PO	Filed NDA	02/2020
givosiran	Alnylam	Porphyria	SC	Filed NDA	02/04/2020
rimegepant	Biohaven	Acute migraines	PO	Filed NDA	02/20/2020
bempedoic acid	Esperion	Dyslipidemia	PO	Filed NDA	02/21/2020
eptinezumab	Alder	Migraine prevention	IV; SC	Filed BLA	02/22/2020
bempedoic acid/ezetemibe	Esperion	Dyslipidemia	PO	Filed NDA	02/26/2020
teprotumumab	Horizon	Thyroid eye disease	IV	Filed BLA	03/06/2020
naloxone nasal	Insys	Opioid dependence	IN	Filed NDA	03/15/2020
lamotrigine liquid	Eton	Epilepsy	PO	Filed NDA	03/17/2020
elexacaftor	Vertex	CF	PO	Filed NDA	03/20/2020
ozanimod	Celgene	Relapsing MS	PO	Filed NDA	03/25/2020
oailodrostat	Novartis	Cushing's syndrome	PO	Filed NDA	Q1 2020
bimatoprost SR	Allergan	Glaucoma	Implant	Filed NDA	04/01/2020
triheptanoin	Ultragenyx	G1DS	PO	Filed NDA	04/01/2020
viaskin peanut	DBV Technologies	Peanut allergy	TOP	Filed BLA	04/07/2020
opicapone	Neurocrine	PD	PO	Filed NDA	04/26/2020
treprostinil	SteadyMed	PAH	SC	Filed NDA	04/27/2020
dasotraline	Sumitomo	BED	PO	Filed NDA	05/14/2020

NDA = New Drug Application; BLA = Biologic License Application; sBLA = supplemental Biologic License Application; sNDA = supplemental New Drug Application; Admin = administration; SC = subcutaneous; PO = oral; TOP = topical; IV = intravenous; IO = intraocular; IM = intramuscular; SL = sublingual; IN = intranasal; Q1 = quarter 1; ACTH = adrenocorticotropic hormone; ER = extended-release; SR = sustained-release; MS = multiple sclerosis; ITP = immune thrombocytopenic purpura; UC = ulcerative colitis; HUS = hemolytic uremic syndrome; *H. Pylori* = *Helicobacter pylori*; AMD = age-related macular degeneration; ALS = amyotrophic lateral sclerosis; HIV = human immunodeficiency virus; CD = Crohn's disease; T1DM = type 1 diabetes mellitus; SCD = sickle cell disease; CV = cardiovascular; T2DM = type 2 diabetes mellitus; CF = cystic fibrosis; G1DS = glucose transporter type 1 deficiency; PD = Parkinson's disease; PAH = pulmonary arterial hypertension; BED = binge eating disorder

*Most biosimilars and oncology medications excluded from table. Medications known to have received a Complete Response Letter from the FDA that have not resubmitted were also excluded.

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[2] Eli Lilly and Company. Lilly Submits New Drug Application to the FDA for Lasmiditan for Acute Treatment of Migraine, Receives Breakthrough Therapy Designation for Emgality™ (galcanezumab-gnlm) for Prevention of Episodic Cluster Headache. *PR Newswire*. Available online at: https://investor.lilly.com/news-releases/news-release-details/lilly-submits-new-drug-application-fda-lasmiditan-acute. Issued 11/14/2019. Last accessed 09/20/2019.

[3] FDA accepts BLA for Enzyvant's regenerative therapy RVT-802. *The Pharma Letter*. Available online at: https://www.thepharmaletter.com/article/fda-accepts-bla-for-enzyvant-s-regenerative-therapy-rvt-802. Issued 05/06/2019. Last accessed 09/20/2019.

[4] Astor L. FDA Accepts BLA for Luspatercept in MDS and Beta-Thalassemia-Associated Anemias. *Targeted Oncology*. Available online at: https://www.targetedonc.com/news/fda-accepts-bla-for-luspatercept-in-mds-and-betathalassemiaassociated-anemias. Issued 06/04/2019. Last accessed 09/20/2019.

[5] MagellanRx Management. MRx Pipeline. Available online at: https://www1.magellanrx.com/documents/2019/07/mrx-pipeline_q3_july-2019.pdf/. Issued 07/2019. Last accessed 09/23/2019.

Appendix D

Vote to Prior Authorize Ezallor™ Sprinkle (Rosuvastatin Capsule) and Welchol® (Colesevelam Chewable Bar)

Oklahoma Health Care Authority
October 2019

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

- **Ezallor™ Sprinkle (rosuvastatin capsule)** was approved by the U.S. Food and Drug Administration (FDA) in December 2018 for the treatment of adult patients with hypertriglyceridemia as an adjunct to diet; primary dysbetalipoproteinemia (Type III hyperlipoproteinemia) as an adjunct to diet; and homozygous familial hypercholesterolemia (HoFH) to reduce low-density lipoprotein-cholesterol (LDL-C), total cholesterol, and apolipoprotein B (ApoB). Ezallor™ Sprinkle is available as 5mg, 10mg, 20mg, and 40mg capsules, and the recommended dosing range is 5mg to 40mg once daily. The capsules may be swallowed whole, may be opened and the contents (granules) sprinkled onto 1 teaspoon of applesauce to be swallowed immediately without chewing, or may be opened and the contents mixed with water for administration through a nasogastric (NG) tube (*please refer to Ezallor™ Sprinkle prescribing information for specific details regarding administration*). The Wholesale Acquisition Cost (WAC) of Ezallor™ Sprinkle, regardless of strength, is $2.85 per capsule, which results in a monthly cost of $85.50, based on once daily dosing. In comparison, the State Maximum Allowable Cost (SMAC) of rosuvastatin 40mg tablets (generic Crestor®) is $0.12 per tablet, resulting in a monthly cost of $3.60 at a dose of 40mg once daily.
- **Welchol® (colesevelam chewable bar)** was approved by the FDA in April 2019 as an adjunct to diet and exercise to reduce elevated LDL-C in adults with primary hyperlipidemia; to reduce LDL-C levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH); and to improve glycemic control in adults with type 2 diabetes mellitus (DM). Colesevelam is a bile acid sequestrant, and the recommended dosage is 3.75 grams daily, taken with a meal. Welchol® chewable bar formulation will be available as a 3.75g chewable bar in 3 flavors: chocolate, strawberry, and caramel; the chewable bars contain approximately 80 calories per bar. The launch plans for Welchol® chewable bar are pending, and cost information for Welchol® chewable bar is not yet available. Welchol® is also available in brand and generic formulations, as a 625mg tablet and 3.75g packet for oral suspension, both of which are currently available without a prior authorization.
- **Praluent® (alirocumab)** was approved by the FDA in April 2019 to reduce the risk of myocardial infarction (MI), stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease (CVD). This approval was based on data from the ODYSSEY OUTCOMES trial, which was published in the *New England Journal of Medicine (NEJM)* in November 2018, assessing the effect of adding alirocumab to maximally-tolerated statins on cardiovascular (CV) outcomes in 18,924 patients who had acute coronary syndrome (ACS) within 1 year of enrolling in the trial. Patients were eligible for

enrollment in the trial if they were 40 years of age or older, had been hospitalized with ACS (MI or unstable angina) 1 to 12 months before randomization, and had an LDL-C level of ≥70mg/dL, a high-density lipoprotein-cholesterol (HDL-C) level of ≥100mg/dL, or an ApoB level of ≥80mg/dL. Patients who received alirocumab in the trial experienced a 15% reduced risk for major CV events; the primary endpoint included time to first MI, stroke, death from coronary heart disease (CHD), or unstable angina requiring hospitalization (P=0.0003). The FDA also approved alirocumab as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including HeFH) to reduce LDL-C. Alirocumab is a proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor, was first FDA approved in 2015, and is available in a single-dose pre-filled syringe or pen in 2 strengths: 75mg/mL and 150mg/mL. The recommended dosage of alirocumab is 75mg administered subcutaneously (sub-Q) every 2 weeks, up to a maximum dosage of 150mg sub-Q every 2 weeks or 300mg sub-Q every 4 weeks. The WAC for Praluent® is approximately $540 per single-dose pen or syringe, regardless of strength, resulting in an annual cost of roughly $14,000.

Recommendations

The College of Pharmacy recommends the placement of Ezallor™ Sprinkle (rosuvastatin capsule) into the Special Prior Authorization (PA) Tier of the Statin Medications and Ezetimibe Product Based Prior Authorization (PBPA) category. In addition to the current Special PA criteria, the following criteria will apply (changes noted in red):

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

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

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

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

3. Use of Ezallor™ Sprinkle (rosuvastatin capsule) will require a patient-specific, clinically significant reason why the member cannot use rosuvastatin oral tablets, even when the tablets are crushed.

Additionally, the College of Pharmacy recommends the prior authorization of Welchol® (colesevelam) chewable bar with the following criteria:

Welchol® (Colesevelam) Chewable Bar Approval Criteria:

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

Lastly, the College of Pharmacy recommends the following updates to the current PCSK9 Inhibitors Approval Criteria, based on the new FDA approved indications for Praluent® (changes noted in red):

PCSK9 Inhibitors Approval Criteria:

1. **For Repatha® (evolocumab):**
    a. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following:
        i. Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
        ii. An untreated total cholesterol >500mg/dL and at least 1 of the following:
            1. Documented evidence of definite heterozygous familial hypercholesterolemia (HeFH) in both parents; or
            2. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
    b. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or
    c. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and
        i. Documentation of established CVD; and
            1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or
2. **For Praluent® (alirocumab):**
    ~~a. An FDA approved diagnosis of HeFH defined by the presence of 1 of the following criteria:~~
        ~~i. Documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or~~
        ~~ii. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or~~
    ~~b. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of 1 of the following criteria:~~
        ~~i. High cardiovascular risk confirmed by Framingham risk score; and~~

~~1. Supporting diagnoses/conditions signifying this risk level; or~~

~~ii. Documented history of Coronary Heart Disease (CHD); and~~

~~1. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; or~~

c. An FDA approved diagnosis of primary hyperlipidemia (including HeFH); or
d. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established CVD; and
    i. Documentation of established CVD; and
        1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; and

3. Member must be 13 years of age or older for the diagnosis of HoFH or must be 18 years of age or older for all other FDA-approved diagnoses or indications; and
4. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
    a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
    b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
    c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
    d. Tier structure rules still apply; and
5. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
6. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
7. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent®. A quantity limit of 2 syringes or auto-injectors per 28 days will apply for Repatha® 140mg and a quantity limit of 1 auto-injector per 28 days will apply for Repatha® 420mg. Requests for the Repatha® 420mg dose will not be approved for multiple 140mg syringes or auto-injectors but instead should use (1) 420mg auto-injector; and
8. Initial approvals will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every 6 months thereafter for continued approval.

[1] Sun Pharmaceutical Industries Ltd. Sun Pharma Launches Ezallor™ Sprinkle (Rosuvastatin) in the U.S. for People Who Have Difficulty Swallowing. *BioSpace.* Available online at: https://www.biospace.com/article/releases/sun-pharma-launches-ezallor-sprinkle-rosuvastatin-in-the-u-s-for-people-who-have-difficulty-swallowing/. Issued 07/15/2019. Last accessed 09/16/2019.
[2] Ezallor™ Sprinkle (Rosuvastatin) Prescribing Information. Sun Pharmaceutical Industries Ltd. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208647s001lbl.pdf. Last revised 03/2019. Last accessed 09/16/2019.
[3] OptumRx. Welchol® (Colesevelam) – New Formulation Approval. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_welchol_2019-0405.pdf. Issued 04/03/2019. Last accessed 09/16/2019.
[4] Welchol® (Colesevelam) Prescribing Information. Daiichi Sankyo, Inc. Available online at: https://dsi.com/prescribing-information-portlet/getDocument?product=WC&inline=true. Last revised 04/2019. Last accessed 09/16/2019.
[5] Sanofi. FDA Approves Praluent® (Alirocumab) to Prevent Heart Attack, Stroke, and Unstable Angina Requiring Hospitalization. Available online at: http://www.news.sanofi.us/2019-04-26-FDA-approves-Praluent-R-alirocumab-to-prevent-heart-attack-stroke-and-unstable-angina-requiring-hospitalization. Issued 04/26/2019. Last accessed 09/16/2019.
[6] Praluent® (Alirocumab) Prescribing Information. Sanofi. Available online at: http://products.sanofi.us/Praluent/Praluent.pdf. Last revised 04/2019. Last accessed 09/16/2019.

Appendix E

Vote to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam)

Oklahoma Health Care Authority
October 2019

Introduction[1]

Sorilux® (calcipotriene 0.005% foam) is a vitamin-D analog indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 12 years of age and older. Sorilux® is supplied as a white, 0.005% calcipotriene topical foam available in 60g and 120g aluminum cans. The recommended dosing is to apply a thin layer twice daily to the affected areas. Calcipotriene 0.005% foam should not be used by patients with known hypercalcemia.

Cost Comparison: There are several formulations of topical calcipotriene available for the treatment of plaque psoriasis of the scalp and body. The cost of Sorilux® differs greatly from the other available formulations. The Wholesale Acquisition Cost (WAC) of Sorilux® is $12.28 per gram for the 120g canister resulting in a total cost of $1,473.60. For the 60g canister, the National Average Drug Acquisition Cost (NADAC) is $12.24 per gram resulting in a total cost of $734.40. As shown in the following table, an equivalent amount of generic calcipotriene in other formulations is significantly less costly. Sorilux® is not available as a generic product.

Medication	Cost Per Unit	Cost Per Treatment*
Sorilux® (calcipotriene 0.005% foam)	**$12.28**	**$1,473.60**
calcipotriene 0.005% ointment (Calcitrene®)	$2.60	$312.00
calcipotriene 0.005% cream (Dovonex®)	$1.73	$207.60
calcipotriene 0.005% solution (Dovonex®)	$1.60	$192.00

Unit = gram or milliliter (mL)
*Cost per treatment based on 120g or 120mL.
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Sorilux® (calcipotriene 0.005% foam) based on net cost with the following criteria:

Sorilux® (Calcipotriene 0.005% Foam) Approval Criteria:

1. An FDA approved indication for the topical treatment of plaque psoriasis of the scalp and body in patients 12 years of age and older; and
2. A patient-specific, clinically significant reason why the member cannot use the generic formulations of topical calcipotriene, which are available without a prior authorization, must be provided; and
3. A quantity limit of 120g per 30 days will apply.

[1] Sorilux® Prescribing Information. U.S. National Library of Medicine: *DailyMed*. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=51f208d0-7b3f-44cc-8bed-92fa3d2e7bbe. Last revised 5/2019. Last accessed 09/09/2019.

Appendix F

Vote to Prior Authorize Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp)

Oklahoma Health Care Authority
October 2019

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

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

- **October 2018:** The FDA approved Talzenna® (talazoparib), a poly-ADP ribose polymerase (PARP) inhibitor, for the treatment of patients with deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), human epidermal receptor type 2 (HER2)-negative, locally advanced or metastatic breast cancer.
- **December 2018:** The FDA approved Herzuma® (trastuzumab-pkrb) as a biosimilar to Herceptin® (trastuzumab) for the treatment of patients with HER2-overexpressing breast cancer.
- **December 2018:** The FDA approved Lynparza® (olaparib) for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (*gBRCAm* or *sBRCAm*) advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.
- **January 2019:** The FDA approved Ontruzant® (trastuzumab-dttb), a biosimilar to Herceptin® (trastuzumab), across all eligible indications, namely adjuvant treatment of HER2-overexpressing breast cancer, metastatic breast cancer, and metastatic gastric cancer or gastroesophageal junction adenocarcinoma in patients who have not received prior treatment for metastatic disease.
- **February 2019:** The FDA approved Herceptin Hylecta™ (trastuzumab/hyaluronidase-oysk injection) for the treatment of HER2-overexpressing breast cancer. Herceptin Hylecta™ is a combination of trastuzumab, a HER2/neu receptor antagonist, and hyaluronidase, an endoglycosidase.
- **March 2019:** The FDA approved Tecentriq® (atezolizumab) for the treatment of programmed death-ligand 1 (PD-L1)-positive, unresectable, locally advanced or metastatic triple-negative breast cancer. Criteria for this indication was voted on in the June 2019 Drug Utilization Review (DUR) Board meeting.
- **March 2019:** The FDA approved Trazimera™ (trastuzumab-qyyp), a biosimilar to Herceptin® (trastuzumab), for the treatment of HER2-overexpressing breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.
- **April 2019:** The FDA approved a supplemental New Drug Application (sNDA) to expand the indications for Ibrance® (palbociclib) in combination with an aromatase inhibitor or

fulvestrant to include men with hormone receptor-positive (HR+), HER2 advanced or metastatic breast cancer.

- **May 2019:** The FDA approved Kadcyla® (ado-trastuzumab) for the adjuvant treatment of patients with HER2-positive early breast cancer who have residual, invasive disease after neoadjuvant taxane and trastuzumab-based treatment.
- **May 2019:** The FDA approved Piqray® (alpelisib) in combination with fulvestrant for the treatment of men and postmenopausal women with HR+, HER2-negative, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA)-mutated, advanced or metastatic breast cancer following progression on or after an endocrine-based regimen.
- **June 2019:** The FDA approved Kanjinti™ (trastuzumab-anns) a biosimilar to Herceptin® (trastuzumab) for all approved indications of the reference product. These indications include the treatment of HER2-overexpressing adjuvant and metastatic breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.
- **September 2019:** The FDA issued a safety announcement for Ibrance® (palbociclib), Kisqali® (ribociclib), and Verzenio® (abemaciclib) warning that these medications may cause rare but severe inflammation of the lungs. The FDA approved new warnings about this risk to be included in the *Prescribing Information* and *Patient Package Insert* for the entire class of these cyclin-dependent kinase 4/6 (CDK 4/6) inhibitor medications, which are used to treat some patients with advanced breast cancers. Patients taking these medications are being advised to notify their health care professionals if any new or worsening symptoms involving the lungs occur.

Product Summaries[7,8,9,10,11,12]

Piqray® (Alpelisib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** In combination with fulvestrant for the treatment of men and postmenopausal women with HR+, HER2-negative, PIK3CA-mutated, advanced or metastatic breast cancer
- **How Supplied:** 50mg, 150mg, and 200mg oral tablets
- **Dose:** Recommended dose is 300mg [(2) 150mg tablets] once daily
- **Cost:** $276.79 per 150mg tablet; $15,500.24 per 28 days based on the recommended dose of 300mg once daily

Talzenna® (Talazoparib):

- **Therapeutic Class:** PARP inhibitor
- **Indication(s):** Treatment of adult patients with deleterious or suspected deleterious *gBRCAm,* HER2-negative, locally advanced or metastatic breast cancer
- **How Supplied:** 0.25mg and 1mg oral capsules
- **Dose:**
    - Recommended dose is 1mg once daily, with or without food; the 0.25mg capsule is available for dose reduction

- Treatment is recommended until disease progression or unacceptable toxicity occurs
- **Cost:** $486.00 per 1mg capsule; $14,580.00 per month based on the recommended dose of 1mg once daily

Kanjinti™ (Trastuzumab-anns):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)
- **Indication(s):**
  - Treatment of HER2-overexpressing breast cancer
  - Treatment of HER2-overexpressing, metastatic gastric or gastroesophageal junction adenocarcinoma
- **How Supplied:** 420mg lyophilized powder in a multiple-dose vial (MDV) for reconstitution
- **Dose:**
  - Adjuvant Treatment of HER2-Overexpressing Breast Cancer:
    - Recommended initial dose of 4mg/kg over 90 minutes via intravenous (IV) infusion, then 2mg/kg over 30 minutes weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin); 1 week after the last weekly dose of trastuzumab-anns, 6mg/kg should be administered as an IV infusion over 30 to 90 minutes every 3 weeks to complete a total of 52 weeks of therapy; or
    - Recommended initial dose of 8mg/kg over 90 minutes via IV infusion, then 6mg/kg over 30 to 90 minutes via IV infusion every 3 weeks for 52 weeks
  - Metastatic HER2-Overexpressing Breast Cancer:
    - Initial dose of 4mg/kg as a 90 minute IV infusion followed by subsequent weekly doses of 2mg/kg as 30 minute IV infusions until disease progression
  - Metastatic HER2-Overexpressing Gastric Cancer:
    - Initial dose of 8mg/kg over 90 minutes via IV infusion, followed by 6mg/kg over 30 to 90 minutes via IV infusion every 3 weeks until disease progression
- **Cost:** $3,697.26 per vial; cost will vary due to weight-based dosing and duration variability

Ontruzant® (Trastuzumab-dttb):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)
- **Indication(s):**
  - Treatment of HER2-overexpressing breast cancer
  - Treatment of HER2-overexpressing, metastatic gastric or gastroesophageal junction adenocarcinoma
- **How Supplied:** 150mg lyophilized powder in a single-dose vial (SDV) for reconstitution
- **Dose:** Refer to dosing in the Kanjinti™ (trastuzumab-anns) product summary of this report; similar dosing applies for Ontruzant®
- **Cost:** Cost information for Ontruzant® is not yet available

Herzuma® (Trastuzumab-pkrb):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)
- **Indication(s):** Treatment of HER2-overexpressing breast cancer
- **How Supplied:** 420mg lyophilized powder in a MDV for reconstitution
- **Dose:** Refer to dosing in the Kanjinti™ (trastuzumab-anns) product summary of this report; similar dosing applies for Herzuma®
- **Cost:** Cost information for Herzuma® is not yet available

Trazimera™ (Trastuzumab-qyyp):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)
- **Indication(s):**
  - Treatment of HER2-overexpressing breast cancer
  - Treatment of HER2-overexpressing, metastatic gastric or gastroesophageal junction adenocarcinoma
- **How Supplied:** 420mg lyophilized powder in a MDV for reconstitution
- **Dose:** Refer to dosing in the Kanjinti™ (trastuzumab-anns) product summary of this report; similar dosing applies for Trazimera™
- **Cost:** Cost information for Trazimera™ is not yet available

Recommendations

Halaven® (Eribulin) Approval Criteria [Recurrent or Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Previously received at least 2 chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting; or
3. In combination with trastuzumab for human epidermal growth factor receptor 2 (HER2)-positive disease that is:
   a. Hormone receptor (HR)-negative; or
   b. HR-positive with or without endocrine therapy; or
4. As a single-agent for HER2-negative disease that is:
   a. HR-negative; or
   b. HR-positive with visceral crisis or endocrine therapy refractory.

Ibrance® (Palbociclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced, metastatic, hormone receptor positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer; and
2. In combination with:
   a. Letrozole as initial endocrine-based therapy in postmenopausal women; or
   b. Fulvestrant in women with disease progression following endocrine therapy; or
   c. An aromatase inhibitor or fulvestrant in male patients.

Kadcyla® (Ado-Trastuzumab) Approval Criteria [Early Stage or Locally Advanced Breast Cancer Diagnosis]:

1. Diagnosis of early stage or locally advanced breast cancer; and
2. Positive expression of human epidermal growth factor receptor 2 (HER2); and
3. Used as adjuvant treatment in members with residual invasive disease after neoadjuvant therapy with taxane and trastuzumab-based treatment; and
4. Maximum duration of a total of 14 cycles.

Lynparza® (Olaparib) Approval Criteria [Ovarian Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Ovarian Cancer:**
    a. Diagnosis of deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), advanced ovarian cancer; and
    b. Previous treatment with 3 or more prior lines of chemotherapy. Prior chemotherapy regimens should be documented on the prior authorization request; and
    c. A quantity limit based on FDA approved dosing will apply; or
2. **Maintenance Treatment of Advanced Ovarian Cancer:**
    a. Member must be in complete or partial response to first-line platinum based chemotherapy; and
        i. Diagnosis of deleterious or suspected deleterious *gBRCAm* or somatic BRCA-mutated *(sBRCAm)*, advanced ovarian cancer; or
    b. Complete or partial response to second-line or greater platinum-based based chemotherapy (no mutation required); and
    c. A quantity limit based on FDA approved dosing will apply.

Piqray® (Alpelisib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer that has progressed on or after an endocrine-based regimen in men and postmenopausal women; and
2. Disease is hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative; and
3. Presence of PIK3CA-mutated disease; and
4. Must be used in combination with fulvestrant.

Talzenna® (Talazoparib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Disease is human epidermal growth factor receptor 2 (HER2)-negative; and
3. Presence of BRCA 1/2-germline-mutated disease; and
4. Disease is hormone receptor (HR)-negative or HR-positive and endocrine therapy refractory; and
5. Member has symptomatic visceral disease; and
6. Must be used as a single-agent.

Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ogivri™ (Trastuzumab-dkst), Ontruzant® (Trastuzumab-dttb), and Trazimera™ (Trastuzumab-qyyp) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing breast cancer; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab) must be provided.

Kanjinti™ (Trastuzumab-anns), Ogivri™ (Trastuzumab-dkst), Ontruzant® (Trastuzumab-dttb), and Trazimera™ (Trastuzumab-qyyp) Approval Criteria [Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Diagnosis]:

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab) must be provided.

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[5] Amgen. FDA Approves Amgen And Allergan's Kanjinti™ (trastuzumab-anns), A Biosimilar To Herceptin® (trastuzumab). *PR Newswire*. Available online at: https://www.amgen.com/media/news-releases/2019/06/fda-approves-amgen-and-allergans-kanjinti-trastuzumabanns-a-biosimilar-to-herceptin-trastuzumab/. Issued 06/13/2019. Last accessed 09/09/2019.

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Appendix G

Vote to Prior Authorize Nubeqa® (Darolutamide)

Oklahoma Health Care Authority
October 2019

Introduction[1,2]

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

- **July 2018:** The FDA approved Xtandi® (enzalutamide), for the treatment of patients with castration-resistant prostate cancer (CRPC). This approval broadened the indicated patient population to include patients with both non-metastatic CRPC (NM-CRPC) and metastatic CRPC. Enzalutamide was previously FDA approved for the treatment of patients with metastatic CRPC.
- **July 2019:** The FDA approved Nubeqa® (darolutamide) for the treatment of NM-CRPC.
- **September 2019:** The FDA approved Erleada® (apalutamide) for the treatment of metastatic castration-sensitive prostate cancer (CSPC). Apalutamide was initially approved in 2018 for the treatment of NM-CRPC.

Nubeqa® (Darolutamide) Product Summary[3]

Nubeqa® (Darolutamide):

- **Therapeutic Class:** Androgen receptor inhibitor
- **Indication(s):** Treatment of patients with NM-CRPC
- **How Supplied:** 300mg oral tablets
- **Dose:** 600mg [(2) 300mg tablets] by mouth twice daily
  - Tablets should be swallowed whole and taken with food
  - Patients should also receive a concomitant gonadotropin-releasing hormone (GnRH) analog or should have a prior history of bilateral orchiectomy
- **Cost:** Wholesale Acquisition Cost (WAC) for darolutamide 300mg tablet is $96.25, resulting in a daily cost of $385.00 and a monthly cost of $11,550

Recommendations

Erleada® (Apalutamide) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of non-metastatic CRPC; or
2. Diagnosis of non-metastatic prostate cancer with disease progression while on androgen deprivation therapy; and
3. Prostate specific antigen doubling time of ≤10 months; and
4. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy.

Erleada® (Apalutamide) Approval Criteria [Castration-Sensitive Prostate Cancer (CSPC) Diagnosis]:

1. Diagnosis of metastatic CSPC; and
2. Concomitant treatment with a luteinizing hormone-releasing hormone (LHRH) agonist/antagonist or prior history of bilateral orchiectomy.

Nubeqa® (Darolutamide) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of non-metastatic CRPC; and
2. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy.

Xtandi® (Enzalutamide) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of ~~metastatic,~~ CRPC.

Zytiga® (Abiraterone) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Abiraterone must be used in combination with a corticosteroid; and
3. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy.

Zytiga® (Abiraterone) Approval Criteria [Castration-Sensitive Prostate Cancer (CSPC) Diagnosis]:

1. Diagnosis of metastatic, high-risk CSPC; and
2. ~~High-risk disease defined as having at least 2 of the following risk factors:~~
   a. ~~Total Gleason score of ≥8; or~~
   b. ~~Presence of ≥3 lesions on bone scan; or~~
   c. ~~Evidence of measurable visceral metastases; and~~
3. Abiraterone must be used in combination with a corticosteroid.

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[1] U.S. Food and Drug Administration (FDA). FDA approves enzalutamide for castration-resistant prostate cancer. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-enzalutamide-castration-resistant-prostate-cancer. Last revised 07/16/2018. Last accessed 09/09/2019.

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[3] Nubeqa® Prescribing Information. Bayer HealthCare Pharmaceuticals, Inc. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Nubeqa_PI.pdf. Last revised 07/2019. Last accessed 09/05/2019.

Appendix H

Fiscal Year 2019 Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications

Oklahoma Health Care Authority
October 2019

Introduction[1,2,3,4]

Leukemia is an abnormal and autonomous proliferation of 1 or more blood-forming elements with infiltrations of the bone marrow and other organs. Leukemia is a heterogeneous group of neoplasms arising from the malignant transformation of hematopoietic cells that eventually replace the normal marrow, leading to the signs and symptoms of leukemia. Approximately 61,780 new cases of leukemia are expected to be diagnosed in 2019 and approximately 22,840 deaths from leukemia are expected in 2019.

Chronic myeloid leukemia (CML) is a slowly progressing blood and bone marrow disease that usually occurs during or after middle age and rarely occurs in children. CML occurs due to a genetic mutation called the Philadelphia chromosome (Ph) resulting in the bone marrow making an enzyme called tyrosine kinase that causes too many stem cells to become white blood cells (blasts). A piece of chromosome 9 and a piece of chromosome 22 break off and trade places forming the BCR-ABL gene. CML treatment changed dramatically with the approval of imatinib in 2001, a targeted therapy that inhibits the BCR-ABL tyrosine kinase. Currently there are several tyrosine kinase inhibitors (TKIs) approved to treat CML including imatinib, nilotinib, dasatinib, and ponatinib; these are the mainstays of treatment for CML.

Acute lymphoblastic leukemia (ALL) is the most common type of cancer diagnosed in children, but can also be seen in adults. It is estimated that there will be 5,930 new cases of ALL in 2019 and 1,500 estimated deaths from ALL in 2019. The majority of patients with ALL are between 15 and 39 years of age. Adolescent and young adult (AYA) patients are treated similar to pediatric patients receiving aggressive chemotherapy including induction, consolidation, and maintenance for 1 to 3 years. Adults can be treated similar to AYA patients or with multi-agent chemotherapy. Some patients with ALL, typically adults, have Philadelphia chromosome positive (Ph+) disease and can be treated with BCR-ABL TKIs in addition to chemotherapy.

Current Prior Authorization Criteria

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

1. Must be used as a single-agent only; and
2. Member must have 1 of the following:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) ALL; or
    b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL after failure of 2 tyrosine kinase inhibitors (TKIs); or

c. Ph- ALL as consolidation in adolescent/young adult or members younger than 65 years of age without substantial comorbidity with persistent or late clearance minimal residual disease positive (MRD+) following a complete response to induction.

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

1. Must be used as a single-agent only; and
2. Member must have 1 of the following:
   a. Relapsed/refractory Philadelphia chromosome negative (Ph-) ALL; or
   b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL who are intolerant/refractory to 2 or more tyrosine kinase inhibitors (TKIs).

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

1. Chronic, accelerated, or blast phase CML; and
2. Newly diagnosed or resistant/intolerant to other tyrosine kinase inhibitors (TKIs).

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

1. May be authorized for relapsed/refractory ALL either as:
   a. Single-agent; or
   b. In combination with an induction regimen not previously given; and
2. Must be used only in members with E255K/V, F317L/VI/C, F359V/C/I, T315A, or Y253H mutations.

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

1. T315I mutation; or
2. Intolerant or resistant to all other tyrosine kinase inhibitors (TKIs); or
3. Post-hematopoietic stem cell transplantation in members with prior accelerated or blast phase prior to transplant or who have relapsed.

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

1. Induction/consolidation with Hyper-CVAD (cyclophosphamide/vincristine/doxorubicin/ dexamethasone); or
2. Maintenance therapy in combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
3. Maintenance therapy post-hematopoietic stem cell transplant; or
4. Relapsed/refractory disease either as a single-agent, in combination with chemotherapy not previously given, or in members with T315I mutations.

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

1. B-cell precursor ALL; and
2. Member must be 25 years of age or younger; and
3. Refractory or in second or later relapse:

a. Philadelphia chromosome negative (Ph-) ALL: must be refractory or with ≥2 relapses; or
b. Philadelphia chromosome positive (Ph+) ALL: must have failed ≥2 tyrosine kinase inhibitors (TKIs); and

4. Therapies to consider prior to tisagenlecleucel if appropriate: clinical trial, multi-agent chemotherapy with or without hematopoietic cell transplantation (HCT), blinatumomab (category 1 recommendation), and inotuzumab (category 1 recommendation); and
5. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategies (REMS) requirements.

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

1. Large B-cell lymphoma [including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Relapsed or refractory disease; and
3. Member must be 18 years of age or older; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had ≥2 lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategies (REMS) requirements.

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

1. Must be used as a single-agent only; and
2. Member must have 1 of the following:
   a. Primary treatment of advanced phase CML with disease progression to accelerated phase; or
   b. Post-hematopoietic stem cell transplant in members who have relapsed; or
   c. Members with a T315I mutation; or
   d. Members who are intolerant or resistant to ≥2 tyrosine kinase inhibitors (TKIs).

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

1. Newly diagnosed chronic, accelerated, or blast phase CML; or
2. Post-hematopoietic stem cell transplant.

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

1. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
2. Maintenance therapy including:
   a. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
   b. Post-hematopoietic stem cell transplant; or

3. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

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

1. Progressive disease and failed imatinib, sunitinib, or regorafenib; and
2. PDGFRA D842V mutation.

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

1. Newly diagnosed chronic, accelerated, or blast phase CML; or
2. Post-hematopoietic stem cell transplant.

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

1. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
2. Maintenance therapy including:
    a. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
    b. Post-hematopoietic stem cell transplant; or
3. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

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

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

Yescarta® (Axicabtagene) Approval Criteria [Lymphoma Diagnosis]:

1. Large B-cell lymphoma [including diffuse large B cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Member must be 18 years of age or older; and
3. Relapsed or refractory disease; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had ≥2 lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the risk evaluation and mitigation strategies (REMS) requirements.

Utilization of ALL/CML 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	50	347	$2,729,784.31	$7,866.81	$261.60	18,771	10,435
2019	50	314	$2,420,318.04	$7,708.02	$267.56	19,584	9,046
% Change	**0.00%**	**-9.50%**	**-11.30%**	**-2.00%**	**2.30%**	**4.30%**	**-13.30%**
Change	**0**	**-33**	**-$309,466.27**	**-$158.79**	**$5.96**	**813**	**-1,389**

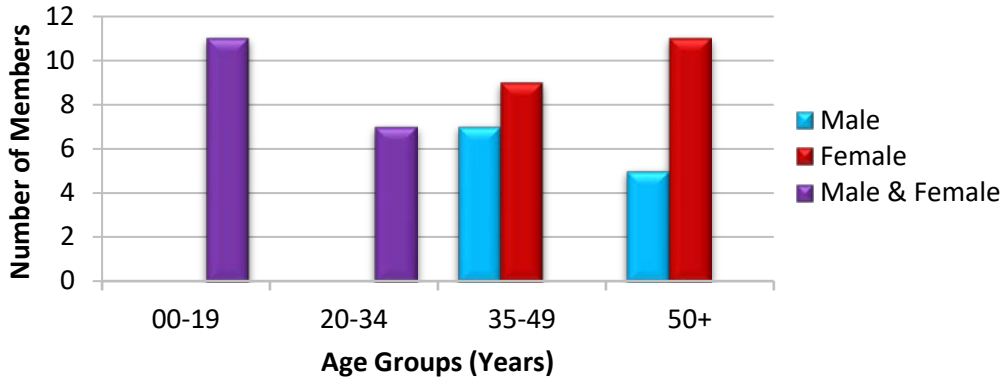
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Fiscal Year 2019 Utilization: Medical Claims

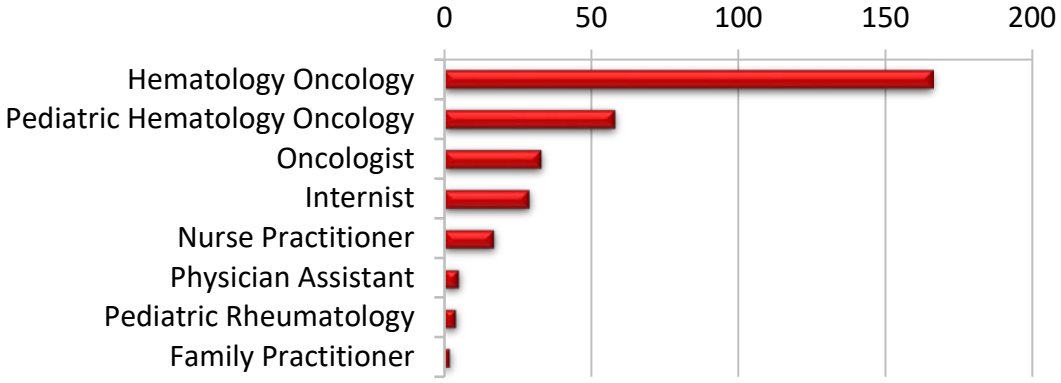
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units
2019	2	3	$484,266.04	$161,422.01	85

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

Demographics of Members Utilizing ALL/CML Medications: Pharmacy Claims



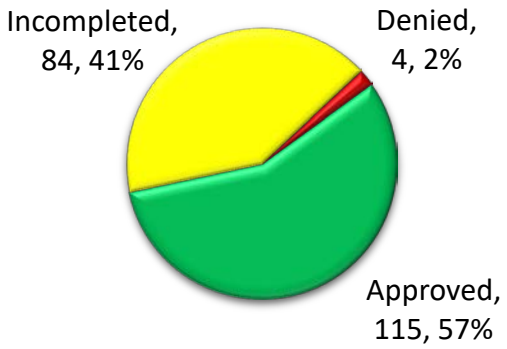
Top Prescriber Specialties of ALL/CML Medications By Number of Claims: Pharmacy Claims



Prior Authorization of ALL/CML Medications

There were 203 prior authorization requests submitted for 54 unique members for ALL/CML medications 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[5]

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

- **January 2019:** The U.S. Food and Drug Administration (FDA) approved dasatinib (Sprycel®) in combination with chemotherapy for the treatment of pediatric patients 1 year of age and older with newly diagnosed Philadelphia chromosome positive (Ph+) ALL. This indication is already included in the current prior authorization criteria for Sprycel®.

Recommendations

There are no recommended changes to the current prior authorization criteria for ALL/CML medications at this time.

Utilization Details of ALL/CML Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
IMATINIB PRODUCTS					
IMATINIB MES TAB 400MG	85	16	$49,597.01	5.31	$583.49
IMATINIB MES TAB 100MG	33	7	$23,970.38	4.71	$726.38
SUBTOTAL	**118**	**20**	**$73,567.39**	**5.9**	**$623.45**
DASATINIB PRODUCTS					
SPRYCEL TAB 100MG	101	17	$1,300,253.92	5.94	$12,873.80
SPRYCEL TAB 70MG	17	4	$126,235.26	4.25	$7,425.60
SPRYCEL TAB 50MG	15	2	$106,047.35	7.5	$7,069.82
SPRYCEL TAB 20MG	7	2	$70,068.71	3.5	$10,009.82
SPRYCEL TAB 140MG	2	1	$27,387.32	2	$13,693.66
SUBTOTAL	**142**	**22**	**$1,629,992.56**	**6.45**	**$11,478.82**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
NILOTINIB PRODUCTS					
TASIGNA CAP 200MG	14	2	$163,386.91	7	$11,670.49
TASIGNA CAP 150MG	11	3	$145,248.24	3.67	$13,204.39
SUBTOTAL	**25**	**5**	**$308,635.15**	**5**	**$12,345.41**
BLINATUMOMAB PRODUCTS					
BLINCYTO INJ 35MCG	10	2	$92,820.13	5	$9,282.01
SUBTOTAL	**10**	**2**	**$92,820.13**	**5**	**$9,282.01**
PONATINIB PRODUCTS					
ICLUSIG TAB 45MG	11	2	$182,289.93	5.5	$16,571.81
ICLUSIG TAB 15MG	5	2	$99,407.39	2.5	$19,881.48
SUBTOTAL	**16**	**3**	**$281,697.32**	**5.33**	**$17,606.08**
BOSUTINIB PRODUCTS					
BOSULIF TAB 100MG	3	1	$33,605.49	3	$11,201.83
SUBTOTAL	**3**	**1**	**$33,605.49**	**3**	**$11,201.83**
TOTAL	**314**	**50***	**$2,420,318.04**	**6.28**	**$7,708.02**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
BLINCYTO (J9039)	2	1	$9,266.04	2	$4,633.02
KYMRIAH (Q2042)	1	1	$475,000.00	1	$475,000.00
TOTAL	**3**	**2***	**$484,266.04**	**1.5**	**$161,422.01**

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

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Appendix I

30-Day Notice to Prior Authorize Turalio™ (Pexidartinib)

Oklahoma Health Care Authority
October 2019

Introduction[1]

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

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

Turalio™ (Pexidartinib) Product Summary[2]

Turalio™ (Pexidartinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery
- **How Supplied:** 200mg capsule
- **Dose:** 400mg orally twice daily
- **Cost:** Wholesale Acquisition Cost (WAC) of $165 per 200mg capsule; resulting in a monthly cost of $19,800

Recommendations

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.

[1] Daiichi-Sankyo. Press Release: FDA Approves Daiichi Sankyo's Turalio™ (pexidartinib) for the Treatment of Select Patients with TGCT, a Rare and Debilitating Tumor. Available online at: https://dsi.com/press-releases/-/article/364091/10481984. Issued 08/02/2019. Last accessed 08/28/2019.

[2] Turalio™ Prescribing Information. Daiichi Sankyo Company, Limited. Available online at: https://dsi.com/prescribing-information-portlet/getPIContent?productName=Turalio&inline=true. Last revised 08/2019. Last accessed 08/28/2019.

Appendix J

Fiscal Year 2019 Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators

Oklahoma Health Care Authority
October 2019

Current Prior Authorization Criteria

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved indication of cystic fibrosis (CF) with a mutation in the *CFTR* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
2. Documentation must be submitted with results of *CFTR* genetic testing; and
3. Member must be 1 year of age or older; and
4. A quantity limit of 2 tablets or 2 granule packets per day (56 per 28 days) will apply; and
5. An age restriction of 2 years to younger than 6 years of age will apply to Kalydeco® oral granule packets. Members 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
6. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene; and
3. Orkambi® will not be approved for members with CF other than those homozygous for the *F508del* mutation; and
4. Member must be 2 years of age or older; and
5. Members using Orkambi® must be supervised by a pulmonary specialist; and
6. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi®, every 3 months during the first year of treatment, and annually thereafter; and
7. Member must not be taking any of the following medications concomitantly with Orkambi®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
8. A quantity limit of 4 tablets per day or 112 tablets per 28 days will apply or a quantity limit of 2 packets per day or 56 packets per 28 days will apply; and

9. An age restriction of 2 years to younger than 6 years of age will apply to Orkambi® oral granule packets. Members age 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
10. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation or who have at least 1 mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Symdeko® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) and experiencing adverse effects associated with Orkambi® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify that member has been counseled on proper administration of Symdeko® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter; and
8. Member must not be taking any of the following medications concomitantly with Symdeko®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
9. A quantity limit of 2 tablets per day or 56 tablets per 28 days will apply; and
10. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events must be provided for members who switched from Orkambi® to Symdeko®.

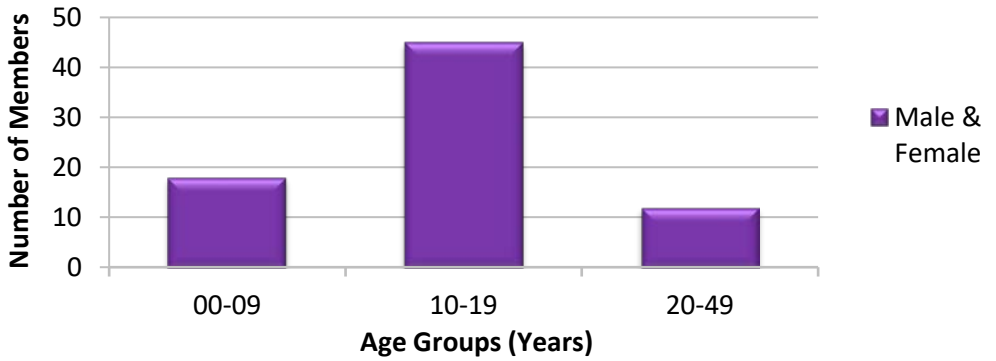
Utilization of CFTR Modulators: Fiscal Year 2019

Comparison of Fiscal Years

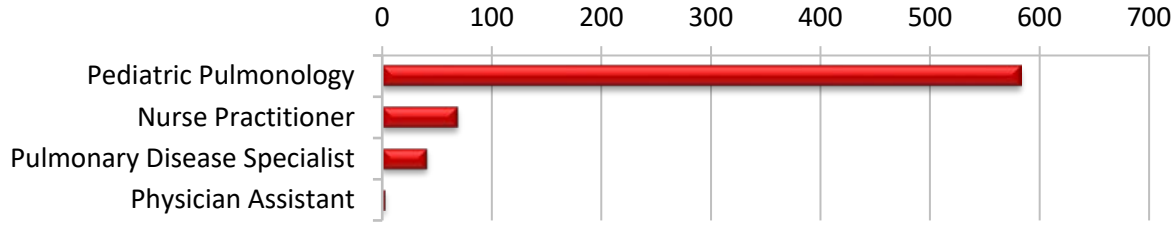
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	57	472	$10,081,544.76	$21,359.20	$762.83	44,968	13,216
2019	77	696	$14,646,144.00	$21,043.31	$751.55	49,952	19,488
% Change	**35.10%**	**47.50%**	**45.30%**	**-1.50%**	**-1.50%**	**11.10%**	**47.50%**
Change	**20**	**224**	**$4,564,599.24**	**-$315.89**	**-$11.28**	**4,984**	**6,272**

*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 CFTR Modulators



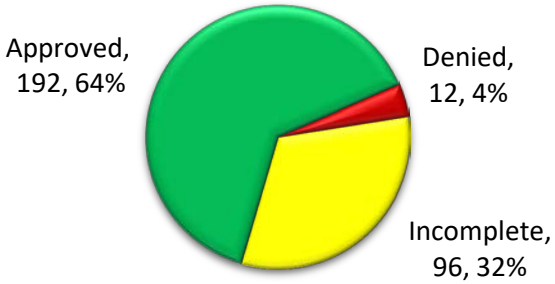
Top Prescriber Specialties of CFTR Modulators by Number of Claims



Prior Authorization of CFTR Modulators

There were 300 prior authorization requests submitted for CFTR modulators during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Orkambi® (lumacaftor/ivacaftor tablets and granules): December 2030
- Kalydeco® (ivacaftor granules): February 2033
- Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets): July 2033

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

- **April 2019:** The FDA approved Kalydeco® (ivacaftor) for use in children with CF 6 months to younger than 12 months of age who have at least 1 mutation in their *CFTR* gene that is responsive to Kalydeco® based on clinical and/or *in vitro* assay data. Kalydeco® is already approved in the United States, Canada, and European Union for the treatment of cystic fibrosis (CF) in patients 12 months of age and older. This FDA approval is based on data from a 24-week, Phase 3, open-label, safety cohort (ARRIVAL) of 11 children with CF 6 months to younger than 12 months of age who have 1 of 10 mutations in the *CFTR* gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D,* or *R117H*). The study demonstrated a safety profile similar to that observed in previous Phase 3 studies of older children and adults; most adverse events were mild or moderate in severity, and no patient discontinued therapy due to adverse events.
- **June 2019:** The FDA approved Symdeko® (tezacaftor/ivacaftor and ivacaftor) for use in children with CF 6 through 11 years of age who have 2 copies of the *F508del* CFTR mutation or who have at least 1 mutation in the *CFTR* gene that is responsive to Symdeko®. Symdeko® was previously approved by the FDA for use in patients with CF 12 years of age and older with 2 copies of the *F508del* mutation or 1 copy of a responsive mutation. An additional dosage strength of Symdeko® tablets is now available (tezacaftor 50mg/ivacaftor 75mg and ivacaftor 75mg) in connection with this approval.

News:

- **September 2019:** The Institute for Clinical and Economic Review (ICER) initiated an assessment of the comparative clinical effectiveness and value of CF therapies. The report will focus on elexacaftor/tezacaftor/ivacaftor (VX-445), the triple-combination therapy currently under review by the FDA. Throughout the 8-month development of their evaluation, ICER invites stakeholders to participate in the process to help inform and shape their final report. The CF Foundation will provide feedback to ICER throughout the process to help them understand CF and the complexities of the disease. The final ICER report will be released in April 2020.

Pipeline:

- **Lenabasum:** In October 2018, Corbus Pharmaceuticals Holdings, Inc. presented new data demonstrating lenabasum's effect on airway macrophages harvested from human CF lungs at the 2018 North American CF Conference held in Denver, Colorado. Lenabasum (formerly known as anabasum, resunab, and JBT-101) is a novel, oral, synthetic, investigational compound being developed to resolve chronic inflammation in patients with CF, systemic sclerosis, dermatomyositis, and systemic lupus erythematosus (SLE). Lenabasum mimics the effects of endocannabinoids, which are

naturally-occurring chemicals in the body that are involved in regulating appetite, metabolism, mood, pain, and inflammation. Lenabasum preferentially binds to cannabinoid receptor type 2 (CB2), which is found primarily on the surfaces of activated immune cells. Upon binding to the CB2 receptors, lenabasum triggers the production of pro-inflammatory mediators, which reduce inflammation. Ultimately, lenabasum acts to "turn off" chronic inflammation and halt tissue thickening and scarring (fibrosis) without suppressing the activity of the immune system. It is thought that reducing inflammation could help prevent permanent tissue damage in the lungs of people with CF. Lenabasum is currently being evaluated in a study evaluating airway macrophages (AMs) that were recovered from surgically removed lungs from CF patients undergoing lung transplants to determine the effect of lenabasum on the production and secretion of inflammatory cytokines and other biomarkers of inflammation and resolution. Adherent AMs were treated with endotoxin from *Pseudomonas aeruginosa*. A treatment of 6 hours was selected based on maximal messenger RNA (mRNA) transcript expression and detection of protein secretion in 3-day-old cultured AMs. Treatment with vehicle did not affect the expression of inflammatory biomarkers, whereas lenabasum did. Corbus is currently evaluating lenabasum for the treatment of CF in a Phase 2b multicenter, double-blinded, randomized, placebo-controlled study. The study will enroll approximately 415 subjects with CF who are at least 12 years of age and at increased risk for pulmonary exacerbations. The primary efficacy outcome is the event rate of pulmonary exacerbations, defined as the average number of pulmonary exacerbations per subject per time period. Secondary efficacy outcomes include other measures of pulmonary exacerbations, change in CF Questionnaire-Revised Respiratory domain score, and change in forced expiratory volume in 1 second, percent predicted (FEV_1pp). The study will be conducted in approximately 100 sites across North America, Europe, and Australia. Subjects will be centrally randomized to 1 of 3 cohorts to receive lenabasum 20mg twice per day, lenabasum 5mg twice per day, or placebo twice per day for 28 weeks in a 2:1:2 ratio. This Phase 2b CF study was designed with input from the CF Therapeutics Development Network and the European CF Society Clinical Trials Network and is funded in part by a Development Award for up to $25 million from the CF Foundation. Corbus expects to report topline results for the Phase 2b CF study in 2020.

- **Acebilustat:** In October 2018, Celtaxsys, Inc. announced results of the Phase 2 EMPIRE-CF trial evaluating their once-daily anti-inflammatory molecule, acebilustat, for the treatment of CF, irrespective of the causative genotype at the North American CF Conference (NACFC). In the 200 patient, double-blind, placebo controlled study, acebilustat demonstrated clinically meaningful improvements in pulmonary exacerbations, both reducing the frequency of pulmonary exacerbations and increasing time to next exacerbation over 48 weeks of therapy. These results showed that acebilustat-treated patients (N=133) exhibited a 19% reduction in pulmonary exacerbations and a 22% reduced risk in progressing to first pulmonary exacerbation versus placebo on a per-protocol basis. Patients with less severe impairment of lung function (FEV_1pp >75, N=47) achieved the largest benefit from acebilustat treatment, achieving a 35% reduction in pulmonary exacerbation rate, a 43% reduction in risk of

experiencing their first exacerbation, and a 96% increased likelihood of being free of exacerbations after 48 weeks of treatment versus placebo. Furthermore, patients concomitantly treated with CFTR modulator therapy (N=43) exhibited a clinically meaningful 20% reduction in pulmonary exacerbations, a 29% increased time to first exacerbation, and a 47% higher likelihood of no exacerbations compared to patients treated with CFTR modulators and placebo. Celtaxsys, with continued support from the CF Foundation, has commenced preparations for designing and executing the Phase 3 clinical program of acebilustat.

- **LUNAR-CF:** In August 2019, it was reported that the CF Foundation has increased its commitment to $15 million in conjunction with an amended agreement to advance LUNAR-CF, a novel mRNA therapeutic formulated with Arcturus' LUNAR® delivery technology. The goal of the multi-year program is to create mRNA therapies to treat people with CF, develop methods to deliver RNA components to cells in the lung, and file an Investigational New Drug (IND) application for a therapeutic candidate. LUNAR-CF is an mRNA replacement therapy designed to enable CFTR-deficient patients to naturally produce healthy functional CFTR in their own lung cells. Arcturus plans to submit an IND application to the FDA in the second half of 2020. Preclinical proof-of-concept data demonstrated that LUNAR® technology can deliver mRNA to bronchial epithelial cells and resulted in expression of the CFTR protein in animal models.
- **VX-445:** In August 2019, the FDA accepted a New Drug Application (NDA) for VX-445, a triple combination regimen containing elexacaftor, tezacaftor and ivacaftor. The FDA has granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) target action date of March 19, 2020. The submission was supported by previously disclosed positive results of 2 global Phase 3 studies in patients with CF: a 24-week Phase 3 study in patients with 1 *F508del* mutation and 1 minimal function mutation and a 4-week Phase 3 study in patients with 2 *F508del* mutations. Both Phase 3 studies showed statistically significant improvements in lung function (FEV_{1pp}), which was the primary endpoint, and in all key secondary endpoints. In these studies, the triple combination regimen was generally well tolerated.

Recommendations

The College of Pharmacy recommends updating the current Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets) and Kalydeco® (ivacaftor) prior authorization criteria with the following changes noted in red:

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) with a mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
2. Documentation must be submitted with results of *CFTR* genetic testing; and
3. Member must be 6 months ~~1 year~~ of age or older; and
4. A quantity limit of 2 tablets or 2 granule packets per day (56 per 28 days) will apply; and
5. An age restriction of 6 months ~~1 years~~ to younger than 6 years of age will apply to Kalydeco® oral granule packets. Members 6 years of age or older will require a patient-

specific, clinically significant reason why the member cannot use the oral tablet formulation; and

6. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who are homozygous for the *F508del* mutation or who have at least 1 mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use; and
3. Member must be 6 ~~12~~ years of age or older; and
4. Members using Symdeko® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) and experiencing adverse effects associated with Orkambi® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify that member has been counseled on proper administration of Symdeko® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter; and
8. Member must not be taking any of the following medications concomitantly with Symdeko®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
9. A quantity limit of 2 tablets per day or 56 tablets per 28 days will apply; and
10. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events must be provided for members who switched from Orkambi® to Symdeko®.

Utilization Details of CFTR Modulators: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
IVACAFTOR PRODUCTS						
KALYDECO TAB 150MG	117	11	$2,752,404.42	$840.17	$23,524.82	18.79%
KALYDECO PAK 50MG	3	1	$71,721.00	$853.82	$23,907.00	0.49%
SUBTOTAL	**120**	**12**	**$2,824,125.42**	**$840.51**	**$23,534.38**	**19.28%**
TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SYMDEKO TAB 100-150MG	321	38	$7,036,713.78	$782.90	$21,921.23	48.04%
SUBTOTAL	**321**	**38**	**$7,036,713.78**	**$782.90**	**$21,921.23**	**48.04%**
LUMACAFTOR/IVACAFTOR PRODUCTS						
ORKAMBI TAB 100-125MG	171	22	$3,069,040.12	$640.99	$17,947.60	20.95%
ORKAMBI GRA 150-188MG	59	10	$1,234,874.62	$747.50	$20,930.08	8.43%
ORKAMBI TAB 200-125MG	25	6	$481,390.06	$687.70	$19,255.60	3.29%
SUBTOTAL	**255**	**38**	**$4,785,304.80**	**$670.21**	**$189.47**	**32.67%**
TOTAL	**696**	**77***	**$14,646,144.00**	**$751.55**	**$21,043.31**	**100%**

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

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm?resetfields=1/. Last revised 09/2019. Last accessed 09/17/2019.

[2] Vertex Pharmaceuticals, Inc. FDA Approves Kalydeco® (ivacaftor) as First and Only CFTR Modulator to Treat Eligible Infants with CF as Early as Six Months of Age. *Business Wire*. Available online at: https://investors.vrtx.com/news-releases/news-release-details/fda-approves-kalydecor-ivacaftor-first-and-only-cftr-modulator. Issued 04/30/2019. Last accessed 09/17/2019.

[3] Vertex Pharmaceuticals, Inc. FDA Approves Symdeko® (tezacaftor/ivacaftor and ivacaftor) to Treat the Underlying Cause of CF in Children Age 6-11 Years with Certain Mutations in the CFTR Gene. *Business Wire*. Available online at: https://investors.vrtx.com/news-releases/news-release-details/fda-approves-symdekor-tezacaftorivacaftor-and-ivacaftor-treat. Issued 06/21/2019. Last accessed 09/17/2019.

[4] Cystic Fibrosis Foundation. ICER Announces Assessment of Triple-Combination Therapy. Available online at: https://www.cff.org/News/News-Archive/2019/ICER-Announces-Assessment-of-Triple-Combination-Therapy/. Issued 09/13/2019. Last accessed 09/17/2019.

[5] Corbus Pharmaceuticals Holdings, Inc. Corbus Pharmaceuticals Presents Data on Impact of Lenabasum on Inflammation of Airway Macrophages from Cystic Fibrosis Lungs at the 2018 North American Cystic Fibrosis Conference. *Globe Newswire*. Available online at: https://www.corbuspharma.com/press-releases/detail/285/corbus-pharmaceuticals-presents-data-on-impact-of-lenabasum. Issued 10/18/2018. Last accessed 09/17/2019.

[6] Celtaxsys, Inc. Acebilustat Phase 2 Trial Highlights Presented at the Annual North American CF Conference by Dr. Felix Ratjen. Available online at: https://celtaxsys.com/2019/01/09/acebilustat-phase-2-trial-highlights-presented-at-the-annual-north-american-cf-conference-by-dr-felix-ratjen/. Issued 01/09/2019. Last accessed 09/17/2019.

[7] Celtaxsys, Inc. Results from Celtaxsys' Acebilustat Phase 2 Trial in Cystic Fibrosis Patients Showing Clinically Meaningful Improvement in Pulmonary Exacerbations Presented at the North American Cystic Fibrosis Conference. Available online at: http://www.celtaxsys.com/2018/10/22/results-from-celtaxsys-acebilustat-phase-2-trial-in-cystic-fibrosis-patients-showing-clinically-meaningful-improvement-in-pulmonary-exacerbations-presented-at-the-north-american-cystic-fibros/. Issued 10/22/2018. Last accessed 09/17/2019.

[8] Kalydeco® (ivacaftor) Prescribing Information. Vertex Pharmaceuticals, Inc. Available online at: https://pi.vrtx.com/files/uspi_ivacaftor.pdf. Last revised 08/2018. Last accessed 09/17/2019.

[9] Arcturus Therapeutics. Arcturus Therapeutics Receives up to $15 Million Commitment from the Cystic Fibrosis Foundation to create mRNA Therapies to Treat Cystic Fibrosis Patients. *Globe Newswire*. Available online at: http://ir.arcturusrx.com/news-releases/news-release-details/arcturus-therapeutics-receives-15-million-commitment-cystic. Issued 08/01/2019. Last accessed 09/17/2019.

[10] Vertex Pharmaceuticals, Inc. FDA Accepts New Drug Application for VX-445 (Elexacaftor), Tezacaftor and Ivacaftor Combination Treatment. *Business Wire*. Available online at: https://investors.vrtx.com/news-releases/news-release-details/fda-accepts-new-drug-application-vx-445-elexacaftor-tezacaftor. Issued 08/20/2019. Last accessed 09/17/2019.

Appendix K

Fiscal Year 2019 Annual Review of Amyloidosis Medications and 30-Day Notice to Prior Authorize Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis)

Oklahoma Health Care Authority
October 2019

Current Prior Authorization 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™; 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®; 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.

Utilization of Amyloidosis Medications: Fiscal Year 2019

There was no SoonerCare utilization of amyloidosis medications during fiscal year 2019 (fiscal year 2019 = 07/01/2018 to 06/30/2019).

Prior Authorization of Amyloidosis Medications

There were no prior authorization requests submitted for amyloidosis medications during fiscal year 2019.

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

Anticipated Patent Expiration(s):

- Vyndaqel® (tafamidis meglumine): April 2024
- Onpattro® (patisiran): October 2030
- Tegsedi™ (inotersen): April 2031
- Vyndamax™ (tafamidis): August 2035

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

- **May 2019:** Pfizer announced that the FDA approved both Vyndaqel® (tafamidis meglumine) and Vyndamax™ (tafamidis) 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. Vyndaqel® and Vyndamax™ are 2 oral formulations of the first-in-class transthyretin stabilizer tafamidis, and the first and only medications approved by the FDA to treat ATTR-CM**.**

Pipeline:

- **AG10:** AG10 is an investigational, orally-administered small molecule designed to potently stabilize tetrameric transthyretin (TTR), stopping the molecular events that give rise to transthyretin amyloidosis (ATTR). In a Phase 2 clinical trial in patients with symptomatic ATTR-CM, AG10 was generally well tolerated, demonstrated >90% average

TTR stabilization at day 28, and in a dose-dependent manner increased serum TTR concentrations, an indicator predicting survival in a retrospective study of ATTR-CM patients. AG10 is being studied in an open-label extension of a Phase 2 clinical trial in patients with ATTR-CM. Additionally, a Phase 3 clinical trial (ATTRibute-CM) in patients with ATTR-CM is being initiated.

- **CAEL-101:** CAEL-101 is a fibril-reactive monoclonal antibody (mAb) that has completed a Phase 1a/1b study for the treatment of patients with amyloid light chain (AL) amyloidosis. Phase 1a/1b data presented at the American Society of Hematology's 59th Annual Meeting in December 2017, the 16th International Symposium on Amyloidosis in March 2018, the American Society of Echocardiography 29th Annual Scientific Sessions in June 2018, and the American Society of Hematology's 60th Annual Meeting in December 2018 support CAEL-101's potential to be a safe and well-tolerated therapy that promotes amyloid resolution. The data also demonstrated a correlation between a sustained decrease in N-terminal pro-brain natriuretic peptide levels and an improvement in global longitudinal strain (GLS) following CAEL-101 treatment in patients with cardiac AL amyloidosis.
- **PRX004:** PRX004 is an investigational mAb designed to specifically target and clear the misfolded forms of the TTR amyloid protein found in ATTR. PRX004 is currently in a Phase 1 study in patients with ATTR.

Vyndaqel® (Tafamidis Meglumine) and Vyndamax™ (Tafamidis) Product Summaries[6,7,8]

Indication(s): Vyndaqel® (tafamidis meglumine) and Vyndamax™ (tafamidis) are TTR stabilizers indicated for the treatment of wild type or hereditary ATTR-CM in adults to reduce CV mortality and CV-related hospitalization.

Dosing:

- Vyndaqel® is supplied as a 20mg oral capsule and Vyndamax™ is supplied as a 61mg oral capsule.
- Vyndaqel® is available in a box containing 4 cartons and each carton contains 3 blister cards. Each blister card contains 10 capsules for a total of 120 capsules per box.
- Vyndamax™ is available in a carton of 3 blister cards, and each blister card contains 10 capsules for a total of 30 capsules per box.
- Vyndamax™ was developed for patient convenience and is not substitutable with Vyndaqel® on a per milligram basis.
- The recommended dosage is either Vyndaqel® 80mg [(4) 20mg tafamidis meglumine capsules] once daily or Vyndamax™ 61mg once daily.
- The capsules should be swallowed whole and not crushed or cut.

Mechanism of Action: Tafamidis is a selective stabilizer of TTR. Tafamidis binds to TTR at the thyroxine binding sites, stabilizing the tetramer and slowing dissociation into monomers, the rate-limiting step in the amyloidogenic process.

Contraindication(s): None.

Adverse Reactions: The frequency of adverse events in patients treated with tafamidis meglumine 20mg (N=88) or 80mg [N=176; administered as (4) 20mg capsules] was similar to that of placebo (N=177). Adverse events that emerged during treatment were generally mild-to-moderate in severity, and permanent discontinuation of tafamidis meglumine or placebo as a result of adverse events was less common in the tafamidis meglumine groups than in the placebo group.

Use in Specific Populations:

- Pregnancy: Based on findings from animal studies, tafamidis may cause fetal harm when administered to a pregnant woman. However, limited available human data with tafamidis meglumine use in pregnant women (at a dose of 20mg per day) have not identified any drug-associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproductive studies, oral administration of tafamidis meglumine to pregnant rabbits during organogenesis resulted in adverse effects on development at a dosage providing approximately 9 times the area under the curve (AUC) in humans at the maximum recommended human dose (MRHD) of tafamidis meglumine (80mg), and increased incidence of fetal skeletal variation at a dosage providing equivalent human exposure (AUC) at the MRHD. Postnatal mortality, growth retardation, and impaired learning and memory were observed in offspring of pregnant rats administered tafamidis meglumine during gestation and lactation at a dosage approximately 2 times the MRHD based on body surface area (mg/m^2).
- Lactation: There are no available data on the presence of tafamidis in human milk, the effect on the breastfed infant, or the effect on milk production. Tafamidis is present in rat milk. When a drug is present in animal milk, it is likely the drug will be present in human milk. Based on findings from animal studies which suggest the potential for serious adverse reactions in the breastfed infant, patients should be advised that breastfeeding is not recommended during treatment with tafamidis.
- Females and Males of Reproductive Potential: Based on findings from animal studies, tafamidis may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should consider pregnancy planning and prevention when taking these medications.
- Pediatric Use: The safety and effectiveness of tafamidis have not been established in pediatric patients.
- Geriatric Use: No dosage adjustment is required for tafamidis in patients 65 years of age or older. Of the total number of patients in the clinical study (N=441), 90.5% were 65 years of age or older, with a median age of 75 years.

Efficacy: Efficacy of tafamidis was demonstrated in a multicenter, international, randomized, double-blind, placebo-controlled study in 441 patients with wild type or hereditary ATTR-CM. Patients were randomized in a 1:2:2 ratio to receive tafamidis meglumine 20mg (N=88), tafamidis meglumine 80mg (N=176), or matching placebo (N=177) once daily for 30 months, in addition to standard of care (e.g., diuretics). Treatment assignment was stratified by the presence or absence of a variant *TTR* genotype as well as baseline disease severity [New York Heart Association (NYHA) Class I to III]. In the primary analysis, all-cause mortality, followed by

frequency of CV-related hospitalizations were assessed. Key secondary endpoints were the change from baseline to month 30 for the 6-minute walk test (6MWT) and the Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS), in which higher scores indicate better health status. In the primary analysis, all-cause mortality and rates of CV-related hospitalizations were lower among the 264 patients who received tafamidis meglumine than the 177 patients who received placebo (P<0.001). Tafamidis meglumine was associated with lower all-cause mortality than placebo [78 of 264 (29.5%) vs. 76 of 177 (42.9%); hazard ratio (HR), 0.70; 95% confidence interval (CI), 0.51 to 0.96] and a lower rate of CV-related hospitalizations, with a relative risk ratio of 0.68 (0.48 per year vs. 0.70 per year; 95% CI, 0.56 to 0.81). At month 30, tafamidis meglumine was also associated with a lower rate of decline in distance for the 6MWT (P<0.001) and a lower rate of decline in KCCQ-OS score (P<0.001).

Cost: The Wholesale Acquisition Cost (WAC) of Vyndaqel® (tafamidis meglumine) is $156.25 per 20mg capsule, and the WAC of Vyndamax™ (tafamidis) is $625.00 per 61mg capsule. This results in a cost per 30 days, based on recommended dosing, of $18,750.00 for either product.

Recommendations

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 the 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. 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
6. Prescriber must verify Vyndaqel® or Vyndamax™ will not be used concomitantly with Onpattro® (patisiran) or Tegsedi™ (inotersen); and
7. 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
8. 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.

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Appendix L

Fiscal Year 2019 Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Recarbrio™ (Imipenem/Cilastatin/Relebactam) and Xenleta™ (Lefamulin)

Oklahoma Health Care Authority
October 2019

Current Prior Authorization Criteria

Oral Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the immediate-release formulation and/or other cost-effective therapeutic equivalent alternative(s) cannot be used.
2. The following oral antibiotics currently require prior authorization and the special formulation approval criteria will apply:
   - Amoxicillin 500mg tablets
   - Amoxicillin/clavulanate potassium extended-release (ER) tablets (Augmentin XR®)
   - Cephalexin 250mg and 500mg tablets
   - Cephalexin 750mg capsules
   - Doxycycline hyclate 75mg and 150mg tablets (Acticlate®)
   - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
   - Doxycycline monohydrate 75mg capsules
   - Doxycycline monohydrate 150mg capsules and tablets
   - Doxycycline monohydrate 40mg DR capsules (Oracea®)
   - Minocycline ER capsules (Ximino™)
   - Minocycline ER tablets (Minolira™)
   - Minocycline ER tablets (Solodyn®)

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 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.

Baxdela™ (Delafloxacin) Tablet and Vial Approval Criteria:

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).
    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.

Ciprofloxacin 100mg Tablet Approval Criteria:

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

Dalvance® (Dalbavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. A quantity limit of 3 vials per 7 days will apply.

Levofloxacin 25mg/mL Oral Solution, Ciprofloxacin 250mg/5mL Oral Suspension, and Ciprofloxacin 500mg/5mL Oral Suspension Approval Criteria:

1. Members older than 6 years of age require a patient-specific, clinically significant reason why the oral tablet formulation(s) cannot be used.

Minocycline Immediate-Release Tablets Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member requires the immediate-release tablet formulation and cannot use the immediate-release capsule formulation or other cost-effective therapeutic equivalent alternative(s).

Nuzyra™ (Omadacycline) Approval Criteria [Community-Acquired Bacterial Pneumonia (CABP) Diagnosis]:

1. An FDA approved diagnosis of 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 Nuzyra™ prescribing information and FDA approved dosing regimen(s).
    a. For Nuzyra™ vials, an initial quantity limit of 4 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 tablet formulation for the remainder of therapy.

Nuzyra™ (Omadacycline) Approval Criteria [Acute Bacterial Skin and Skin Structure Infections (ABSSSI) Diagnosis]:

1. An FDA approved diagnosis of ABSSSI 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 vancomycin, linezolid, doxycycline, trimethoprim/sulfamethoxazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
4. Use of Nuzyra™ vials will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
5. Approval quantity will be based on Nuzyra™ prescribing information and FDA approved dosing regimen(s).

Ofloxacin 300mg and 400mg Tablet and Moxifloxacin 400mg Tablet Approval Criteria:

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

Seysara™ (Sarecycline) Approval Criteria:

1. An FDA approved diagnosis of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris; and
2. Member must be 9 years of age or older; and
3. Seysara™ is not covered for members older than 20 years of age; and
4. A patient-specific, clinically significant reason why the member cannot use minocycline, doxycycline, tetracycline, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate strength according to package labeling; and

6. A quantity limit of 30 tablets per 30 days will apply.

Sivextro® (Tedizolid) Tablet and Vial Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use linezolid or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. A quantity limit of 6 tablets or vials per 6 days will apply.

Solosec™ (Secnidazole) Oral Granules Approval Criteria:

1. An FDA approved diagnosis of bacterial vaginosis; and
2. A patient-specific, clinically significant reason why the member cannot use metronidazole, tinidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. A quantity limit of 1 packet per 30 days will apply.

Suprax® (Cefixime) and Cedax® (Ceftibuten) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent; and
2. A patient-specific, clinically significant reason why the member cannot use cephalexin, cefdinir, or other cost-effective therapeutic equivalent alternative(s) must be provided.

Tetracycline 250mg and 500mg Capsule Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the member requires tetracycline and cannot use doxycycline, minocycline capsules, or other cost-effective therapeutic equivalent alternative(s).

Vabomere™ (Meropenem/Vaborbactam) Approval Criteria:

1. An FDA approved diagnosis of complicated urinary tract infection (cUTI) including pyelonephritis caused by designated susceptible microorganisms; and
2. A patient-specific, clinically significant reason why the member cannot use piperacillin/tazobactam or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. Approval quantity will be based on Vabomere™ prescribing information and FDA approved dosing regimen(s).

Xerava™ (Eravacycline) Approval Criteria:

1. An FDA approved diagnosis of complicated intra-abdominal infection (cIAI) 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 penicillin/beta lactamase inhibitor combination (e.g., piperacillin/ tazobactam), a carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), or a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s) must be provided; and

4. 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.

Zemdri™ (Plazomicin) Approval Criteria:

1. An FDA approved diagnosis of complicated urinary tract infection (cUTI), including pyelonephritis, caused by designated susceptible microorganisms; and
2. A patient-specific, clinically significant reason why the member cannot use an appropriate alternative aminoglycoside (e.g., gentamicin, tobramycin) or other cost-effective therapeutic equivalent alternative(s) must be provided; and
3. 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.

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
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), or 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.

Utilization of Various Systemic Antibiotics: Fiscal Year 2019

Please note, the following utilization data only includes systemic antibiotics that currently require prior authorization; systemic antibiotics available without prior authorization are not included in the data.

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	278	377	$81,439.98	$216.02	$17.64	38,791	4,618
2019	237	334	$126,243.70	$377.98	$29.80	35,679	4,237
% Change	**-14.7%**	**-11.4%**	**55.0%**	**75.0%**	**68.9%**	**-8.0%**	**-8.3%**
Change	**-41**	**-43**	**$44,803.72**	**$161.96**	**$12.16**	**-3,112**	**-381**

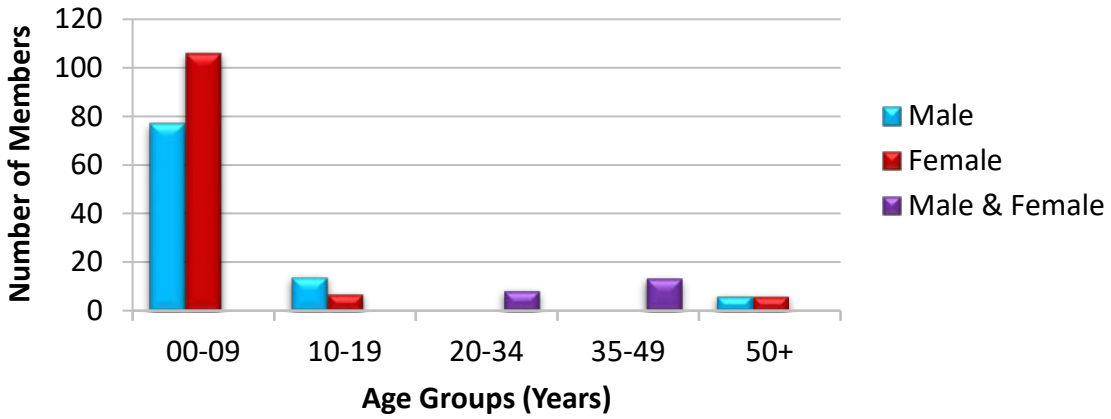
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Fiscal Year 2019 Utilization of Various Systemic Antibiotics: Medical Claims

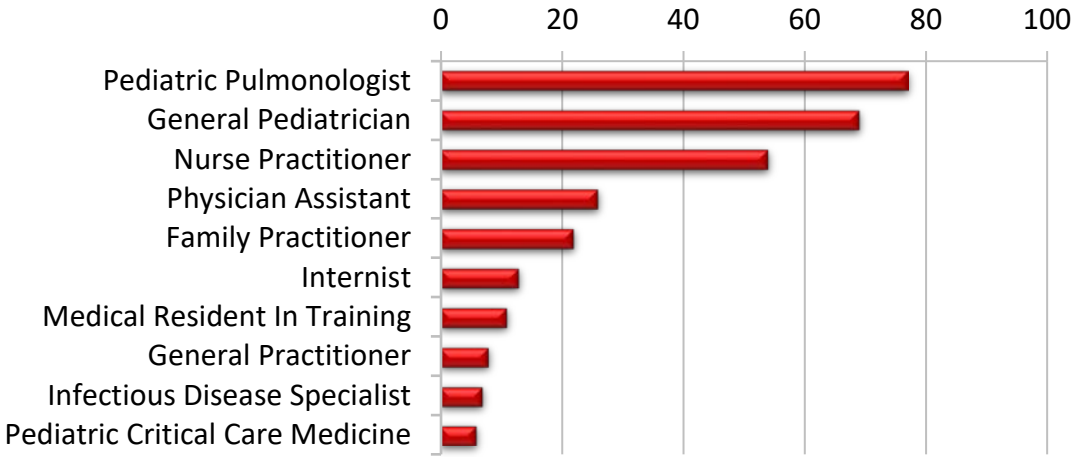
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2019	12	12	$36,369.60	$3,030.80	1

*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 Various Systemic Antibiotics: Pharmacy Claims

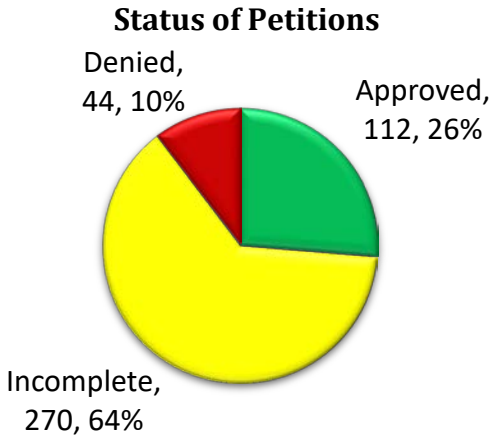


Top Prescriber Specialties of Various Systemic Antibiotics by Number of Claims: Pharmacy Claims



Prior Authorization of Various Systemic Antibiotics

There were 426 prior authorization requests submitted for various systemic antibiotics during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



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

Anticipated Patent Expiration(s):

- Augmentin XR® [amoxicillin/clavulanate potassium extended-release (ER) tablet]: April 2020
- Dalvance® [dalbavancin vial for intravenous (IV) infusion]: December 2023
- Solodyn® (minocycline ER tablet): March 2027
- Ximino™ (minocycline ER capsule): April 2027
- Doryx® [doxycycline hyclate delayed-release (DR) tablet]: February 2028
- Suprax® (cefixime 500mg/5mL oral suspension): December 2028
- Nuzyra™ (omadacycline vial for IV infusion): March 2029
- Baxdela™ (delafloxacin tablet): December 2029
- Nuzyra™ (omadacycline tablet): September 2030
- Sivextro® (tedizolid tablet and vial for IV infusion): December 2030
- Xerava™ (eravacycline vial for IV infusion): December 2030
- Zemdri™ (plazomicin vial for IV infusion): June 2031
- Vabomere® (meropenem/vaborbactam vial for IV infusion): August 2031
- Avycaz® (ceftazidime/avibactam vial for IV infusion): June 2032
- Baxdela™ (delafloxacin vial for IV infusion): February 2033
- Seysara™ (sarecycline tablet): February 2033
- Orbactiv® (oritavancin vial for IV infusion): July 2035
- Zerbaxa® (ceftolozane/tazobactam vial for IV infusion): August 2035

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

- **March 2019:** The FDA approved a label expansion for Avycaz® (ceftazidime/avibactam) to include the treatment of pediatric patients 3 months of age and older with complicated intra-abdominal infections (cIAI) including pyelonephritis, used in combination with metronidazole, or complicated urinary tract infections (cUTI), caused by designated susceptible microorganisms. This is the first FDA approval of a pediatric indication for cUTI and cIAI in more than a decade. Ceftazidime/avibactam was first FDA approved in 2015 for the treatment of adult patients with the aforementioned indications. Ceftazidime/ avibactam was subsequently approved in 2018 for the

treatment of adult patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by designated susceptible microorganisms. Avycaz® is supplied as a 2.5g vial for IV infusion (ceftazidime/avibactam 2g/0.5g), and the recommended dosage of ceftazidime/avibactam and duration of treatment varies based on indication. The recommended dosage of ceftazidime/avibactam and duration of treatment for pediatric patients varies based on patient weight and indication. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftazidime/avibactam and other antibacterial drugs, ceftazidime/avibactam should be used only to treat indicated infections that are proven or strongly suspected to be caused by susceptible bacteria (*refer to Avycaz® prescribing information for specific microbiology information)*.

- **June 2019:** The FDA approved Zerbaxa® (ceftolozane/tazobactam) for the treatment of adult patients with HABP/VABP caused by designated susceptible gram-negative microorganisms. Ceftolozane/tazobactam was first FDA approved in 2014 for the treatment of adult patients with cIAI, used in combination with metronidazole, or cUTI, including pyelonephritis, caused by designated susceptible microorganisms. Zerbaxa® is supplied as a 1.5g vial for IV infusion (ceftolozane/tazobactam 1g/0.5g), and the recommended dosage of ceftolozane/tazobactam and duration of treatment varies based on indication. The recommended dosage of ceftolozane/tazobactam for HABP/VABP is 3g every 8 hours by IV infusion over 1 hour for 8 to 14 days. For all FDA-approved indications, the duration of treatment is dependent on severity and site of infection and on clinical and bacteriological progress. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftolozane/tazobactam and other antibacterial drugs, ceftolozane/tazobactam should be used only to treat indicated infections that are proven or strongly suspected to be caused by susceptible bacteria (*refer to Zerbaxa® prescribing information for specific microbiology information)*.
- **July 2019:** The FDA approved Merck's Recarbrio™ (imipenem/cilastatin/relebactam), a new combination antibacterial, for use in adult patients who have limited or no alternative treatment options for the treatment of cIAI or cUTI, including pyelonephritis, caused by designated susceptible microorganisms. Merck anticipates making Recarbrio™ available later this year.
- **August 2019:** The FDA approved Nabriva Therapeutics' Xenleta™ (lefamulin), a pleuromutilin antibacterial, for the treatment of adult patients with community-acquired bacterial pneumonia (CABP) caused by designated susceptible microorganisms. Lefamulin is the first IV and oral antibiotic with a novel mechanism of action approved by the FDA for CABP in nearly 2 decades. Nabriva is also currently developing lefamulin for pediatric indications and is investigating lefamulin to expand to additional indications, such as acute bacterial skin and skin structure infections (ABSSSI), HABP/VABP, sexually transmitted infections (STIs), osteomyelitis, and prosthetic joint infections.

News:

- **FDA Drug Safety Communication (Fluoroquinolones):** An FDA review found that fluoroquinolone antibiotics can increase the occurrence of rare but serious events of ruptures or tears in the aorta. These tears, called aortic dissections, or ruptures of an aortic aneurysm can lead to dangerous bleeding or even death and can occur with fluoroquinolones for systemic use, either given orally or through an injection. Fluoroquinolones should not be used in patients who have an aortic aneurysm or are at risk for an aortic aneurysm, such as patients with peripheral atherosclerotic vascular diseases, hypertension, certain genetic conditions (e.g., Marfan syndrome, Ehlers-Danlos syndrome), and elderly patients. Fluoroquinolones should be prescribed to these patients only when no other treatment options are available. The FDA is requiring that a new warning about this risk be added to the prescribing information and patient *Medication Guide* for all fluoroquinolones.
- **Fluoroquinolones Associated with Heart Valve Problems:** Analysis of the FDA Adverse Events Reporting Systems (FAERS) data from 2004 to 2018 showed that fluoroquinolones overall had a significant 45% higher likelihood of valvular regurgitation events than other drugs. Patients on fluoroquinolone antibiotics carried a 2.4 times and 1.75 times greater risk of developing mitral and aortic regurgitation compared to patients on amoxicillin and azithromycin, respectively. The authors concluded that patients with aortic regurgitation should not be prescribed a fluoroquinolone antibiotic unless absolutely necessary where the benefits outweigh the risks and that further studies are needed to fully characterize the incremental risk of valvular heart disease and other adverse events in patients treated with fluoroquinolones.
- **2019 Guideline on Recurrent Uncomplicated Urinary Tract Infections (UTIs) in Women:** The American Urological Association (AUA) released a new joint clinical guideline with the Canadian Urological Association (CUA) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) on the diagnosis and treatment of recurrent UTIs (rUTIs) in women. Some key recommendations from the guideline include:
    - Clinicians should not treat asymptomatic bacteriuria (Strong Recommendation; Evidence Level: Grade B)
    - Clinicians should use first-line therapy (i.e., nitrofurantoin, trimethoprim/sulfamethoxazole, fosfomycin) dependent on the local antibiogram for the treatment of symptomatic UTIs in women (Strong Recommendation; Evidence Level: Grade B)
    - Clinicians should treat rUTI patients experiencing acute cystitis episodes with as short a duration of antibiotics as reasonable, generally no longer than 7 days (Moderate Recommendation; Evidence Level: Grade B)
    - Following discussion of risks, benefits, and alternatives, clinicians may prescribe antibiotic prophylaxis to decrease the risk of future UTIs in women of all ages previously diagnosed with UTIs (Moderate Recommendation; Evidence Level: Grade B)
    - In peri- and post-menopausal women with rUTIs, clinicians should recommend vaginal estrogen therapy to reduce the risk of future UTIs if there is no

contraindication to estrogen therapy (Moderate Recommendation; Evidence Level: Grade B)

Pipeline:

- **Zoliflodacin:** Entasis Therapeutics, in partnership with the National Institutes of Health (NIH) and the Global Antibiotic Research and Development Partnership (GARDP), is currently developing zoliflodacin for the treatment of uncomplicated gonorrhea. Zoliflodacin, a novel oral antibiotic that inhibits DNA synthesis in a different way than currently approved antibiotics, was well-tolerated and successfully cured most cases of uncomplicated gonorrhea in a Phase 2 multicenter clinical trial. Zoliflodacin has been granted Qualified Infectious Disease Product (QIDP) and Fast Track designations by the FDA.
- **Talicia®:** RedHill Biopharma submitted a New Drug Application (NDA) to the FDA for Talicia® (RHB-105) for the treatment of *Helicobacter pylori (H. pylori)* infection. Talicia® is a novel and proprietary fixed-dose, all-in-one oral capsule combination of 2 antibiotics, rifabutin and amoxicillin, and a proton pump inhibitor (PPI), omeprazole. Talicia® has been granted QIDP and Fast Track designations by the FDA and has been assigned a target Prescription Drug User Fee Act (PDUFA) action date of November 3, 2019.

Recarbrio™ (Imipenem/Cilastatin/Relebactam) Product Summary[15]

Indication(s): Recarbrio™ (imipenem/cilastatin/relebactam) is indicated in patients 18 years of age or older who have limited or no alternative treatment options for the treatment of cUTI, including pyelonephritis, or cIAI caused by designated susceptible microorganism(s).

- Approval of these indications is based on limited clinical safety and efficacy data for imipenem/cilastatin/relebactam.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of imipenem/cilastatin/relebactam and other antibacterial drugs, imipenem/cilastatin/ relebactam should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

Microbiology: Imipenem/cilastatin/relebactam is indicated for the treatment of the following infections caused by the listed susceptible microorganisms:

- **cUTI, including pyelonephritis:** *Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa.*
- **cIAI:** *Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Fusobacterium nucleatum, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Parabacteroides distasonis,* and *Pseudomonas aeruginosa.*

Dosing:

- Recarbrio™ is supplied as a dry powder in a 1.25g single-dose vial (SDV) that must be constituted and further diluted prior to IV infusion. Each 1.25g Recarbrio™ SDV contains imipenem 500mg, cilastatin 500mg, and relebactam 250mg.
- The recommended dosage of imipenem/cilastatin/relebactam for patients with creatinine clearance (CrCl) ≥90mL/min is 1.25g administered every 6 hours by IV infusion over 30 minutes.
- The duration of therapy should be guided by the severity and location of the infection. The recommended duration of imipenem/cilastatin/relebactam therapy is 4 to 14 days.
- Imipenem/cilastatin/relebactam dosage should be adjusted in patients with renal impairment. Patients with CrCl <90mL/min require dosage reduction of imipenem/ cilastatin/relebactam, and CrCl should be monitored for patients with fluctuating renal function (*refer to Recarbrio™ prescribing information for recommended dosing in patients with renal impairment*). Patients with CrCl <15mL/min should not receive imipenem/cilastatin/relebactam unless hemodialysis is instituted within 48 hours. There is inadequate information to recommend usage of imipenem/cilastatin/relebactam for patients undergoing peritoneal dialysis.
- Based on case reports in the literature, concomitant use of carbapenems, including imipenem/cilastatin, with valproic acid or divalproex sodium may decrease valproic acid concentrations, which may increase the risk of breakthrough seizures. Concomitant use of imipenem/cilastatin/relebactam with valproic acid or divalproex sodium should be avoided, and alternative antibacterials other than carbapenems should be considered to treat infections in patients whose seizures are well controlled on valproic acid or divalproex sodium.

Mechanism of Action: Recarbrio™ is an antibacterial combination product consisting of imipenem (a carbapenem antibacterial drug), cilastatin (a renal dehydropeptidase inhibitor), and relebactam (a diazabicyclooctane beta lactamase inhibitor). Imipenem is bactericidal and inhibits bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs); imipenem is stable in the presence of some beta lactamases. Cilastatin limits the renal metabolism of imipenem and does not have antibacterial activity. Relebactam protects imipenem from degradation by certain serine beta lactamases and has no intrinsic antibacterial activity.

Efficacy: The determination of efficacy and safety of imipenem/cilastatin/relebactam was supported in part by the previous findings of the efficacy and safety of imipenem/cilastatin for the treatment of cIAI and cUTI, which was first FDA approved under brand name Primaxin® in 1985. The contribution of relebactam to Recarbrio™ was primarily established *in vitro* and in animal models of infection.

Cost: Cost information for Recarbrio™ is not yet available.

Xenleta™ (Lefamulin) Product Summary[16]

Indication(s): Xenleta™ (lefamulin) is indicated in patients 18 years of age or older for the treatment of CABP caused by designated susceptible microorganism(s).

- To reduce the development of drug-resistant bacteria and maintain the effectiveness of lefamulin and other antibacterial drugs, lefamulin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

Microbiology: Lefamulin is indicated for the treatment of CABP caused by the following susceptible microorganisms: *Streptococcus pneumoniae, Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae,* and *Chlamydophila pneumoniae.*

Dosing:

- Xenleta™ is supplied as 600mg oral tablet and as a 150mg/15mL SDV that requires further dilution prior to IV infusion.
- Lefamulin dosage should be adjusted in patients with severe hepatic impairment (*refer to Xenleta™ prescribing information for recommended dosing in patients with severe hepatic impairment*).
- Lefamulin IV infusion should be administered over 60 minutes.
- For oral dosing, patients should take lefamulin tablets at least 1 hour before a meal or 2 hours after a meal. Tablets should be taken whole with 6 to 8 ounces of water; tablets should not be crushed or divided.
- Lefamulin tablets are contraindicated with sensitive CYP3A4 substrates that prolong the QT interval (e.g., pimozide). Concomitant administration of oral lefamulin with sensitive CYP3A4 substrates may result in increased plasma concentrations of these drugs, leading to QT prolongation and cases of torsades de pointes.
- Lefamulin has the potential to prolong the QT interval in some patients and should be avoided in patients with known prolongation of the QT interval; those with ventricular arrhythmias including torsades de pointes; those receiving Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic agents; or those receiving other drugs that prolong the QT interval, such as antipsychotics, erythromycin, pimozide, moxifloxacin, and tricyclic antidepressants.
- The recommended dosage of lefamulin is included in the following table (Table 1).

Table 1. Recommended Dosage of Lefamulin in Adult Patients with CABP

Lefamulin Dosage	Treatment Duration
150mg IV[+] every 12 hours*	5 to 7 days
600mg PO every 12 hours	5 days

CABP = community-acquired bacterial pneumonia; IV = intravenous; PO = orally

[+]IV infusion administered over 60 minutes

*With the option to switch to lefamulin tablets (600mg every 12 hours) to complete the treatment course

Mechanism of Action: Lefamulin is a semi-synthetic, systemic pleuromutilin antibacterial that inhibits bacterial protein synthesis through interactions with the A- and P-sites of the peptidyl transferase center (PTC) in domain V of the 23s rRNA of the 50S subunit. The binding pocket of the bacterial ribosome closes around the mutilin core for an induced fit that prevents correct positioning of the tRNA. Lefamulin is bactericidal *in vitro* against *Streptococcus pneumoniae,*

Haemophilus influenzae, and *Mycoplasma pneumoniae* (including macrolide-resistant strains) and is bacteriostatic against *Staphylococcus aureus* and *Streptococcus pyogenes* at clinically relevant concentrations.

Efficacy: A total of 1,289 adults with CABP were randomized in 2 multicenter, multinational, double-blind, double-dummy, non-inferiority trials (Trial 1 and Trial 2).

- Trial 1 compared lefamulin (5 to 10 days of treatment) to moxifloxacin ± linezolid (7 to 10 days of treatment). In Trial 1, 276 patients were randomized to lefamulin (150mg IV every 12 hours, with the option to switch to 600mg orally every 12 hours after at least 3 days of IV treatment) and 275 patients were randomized to moxifloxacin (400mg IV every 24 hours, with the option to switch to 400mg orally every 24 hours after at least 3 days of IV treatment). If methicillin-resistant *Staphylococcus aureus* (MRSA) was suspected at screening, patients randomized to moxifloxacin were to receive adjunct linezolid (600mg IV every 12 hours, with the option to switch to 600mg orally every 12 hours after at least 3 days of IV treatment), and patients randomized to receive lefamulin were to receive linezolid placebo.
- Trial 2 compared lefamulin (5 days of treatment) to moxifloxacin (7 days of treatment). In Trial 2, 370 patients were randomized to lefamulin (600mg orally every 12 hours for 5 days) and 368 patients were randomized to moxifloxacin (400mg orally every 24 hours for 7 days).

In both trials, efficacy was determined by Early Clinical Response (ECR) at 72 to 120 hours after the first dose in the Intent-to-treat (ITT) analysis set, which was comprised of all randomized patients. Patients entered the trials with at least 3 of 4 symptoms consistent with CABP (cough, sputum production, chest pain, and/or dyspnea). Response was defined as survival with improvement of at least 2 symptoms, no worsening of any symptom, and no receipt of non-study antibacterial treatment for CABP. The following table (Table 2) summarizes the ECR rates in the 2 trials.

Table 2. ECR Rates in Trial 1 and Trial 2 (ITT Analysis Set)

	Lefamulin n/N (%)	Moxifloxacin[+] n/N (%)	Treatment Difference (95% CI)[¥]
Trial 1*	241/276 (87.3)	248/275 (90.2)	-2.9 (-8.5, 2.8)
Trial 2	336/370 (90.8)	334/368 (90.8)	0.1 (-4.4, 4.5)

ECR = early clinical response; ITT = intent-to-treat; n = number of patients achieving ECR; N = number of patients in the ITT analysis set; % = percentage; CI = confidence interval

[+]Trial 1 compared lefamulin to moxifloxacin ± linezolid

[¥]Treatment difference = % lefamulin – % moxifloxacin

*Compared IV treatment, with the option to switch to oral treatment to complete the treatment course after at least 3 days of IV treatment

Cost: The Wholesale Acquisition Cost (WAC) of Xenleta™ is $137.50 per 600mg tablet or $102.45 per 150mg/15mL SDV for IV infusion, resulting in an estimated cost of lefamulin therapy of $1,375.00 for 5 days of oral therapy or $1,024.50 to $1,434.30 for 5 to 7 days of IV therapy.

Recommendations

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) and Zerbaxa® (ceftolozane/tazobactam) 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).

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 Tablet 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 Tablet ~~and Moxifloxacin 400mg Tablet~~ 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).

Utilization Details of Various Systemic Antibiotics: Fiscal Year 2019

Please note, the following utilization data only includes systemic antibiotics that currently require prior authorization; systemic antibiotics available without prior authorization are not included in the data.

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	UNITS/ CLAIM	% COST
LEVOFLOXACIN PRODUCTS							
LEVOFLOXACIN SOL 25MG/ML	162	105	$21,628.14	$133.51	1.5	129.7	17.13%
SUBTOTAL	**162**	**105**	**$21,628.14**	**$133.51**	**1.5**	**129.7**	**17.13%**
CIPROFLOXACIN PRODUCTS							
CIPRO (5%) SUS 250MG/5ML	74	64	$11,054.41	$149.38	1.2	112.2	8.76%
CIPRO (10%) SUS 500MG/5ML	36	31	$6,493.61	$180.38	1.2	119.4	5.14%
CIPROFLOXACIN SUS 500MG/5ML	1	1	$124.71	$124.71	1	100	0.10%
SUBTOTAL	**111**	**96**	**$17,672.73**	**$159.21**	**1.2**	**114.4**	**14.00%**
MOXIFLOXACIN PRODUCTS							
MOXIFLOXACIN TAB 400MG	14	11	$451.53	$32.25	1.3	8.3	0.36%
SUBTOTAL	**14**	**11**	**$451.53**	**$32.25**	**1.3**	**8.3**	**0.36%**
TETRACYCLINE PRODUCTS							
TETRACYCLINE CAP 500MG	11	11	$2,108.05	$191.64	1	52.7	1.67%
TETRACYCLINE CAP 250MG	3	3	$1,110.66	$370.22	1	110.3	0.88%
SUBTOTAL	**14**	**14**	**$3,218.71**	**$229.91**	**1**	**65.1**	**2.55%**
CEFIXIME PRODUCTS							
CEFIXIME SUS 100MG/5ML	6	3	$1,219.10	$203.18	2	66.7	0.97%
SUPRAX CAP 400MG	2	2	$61.50	$30.75	1	1	0.05%
CEFIXIME CAP 400MG	1	1	$22.29	$22.29	1	1	0.02%
SUPRAX CHW TAB 200MG	1	1	$537.97	$537.97	1	14	0.43%
CEFIXIME SUS 200MG/5ML	1	1	$292.38	$292.38	1	50	0.23%
SUBTOTAL	**11**	**8**	**$2,133.24**	**$193.93**	**1.4**	**42.5**	**1.69%**
CEFTAZIDIME/AVIBACTAM PRODUCTS							
AVYCAZ INJ 2.5GM	7	2	$52,821.02	$7,545.86	3.5	21	41.84%
SUBTOTAL	**7**	**2**	**$52,821.02**	**$7,545.86**	**3.5**	**21**	**41.84%**
CEFTOLOZANE/TAZOBACTAM PRODUCTS							
ZERBAXA INJ 1.5GM	6	2	$18,955.36	$3,159.23	3	29	15.01%
SUBTOTAL	**6**	**2**	**$18,955.36**	**$3,159.23**	**3**	**29**	**15.01%**
SECNIDAZOLE PRODUCTS							
SOLOSEC GRAN 2GM	3	2	$802.24	$267.41	1.5	1	0.64%
SUBTOTAL	**3**	**2**	**$802.24**	**$267.41**	**1.5**	**1**	**0.64%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	UNITS/ CLAIM	% COST
MINOCYCLINE PRODUCTS							
MINOCYCLINE TAB 65MG ER	3	1	$3,191.55	$1,063.85	3	30	2.53%
SUBTOTAL	**3**	**1**	**$3,191.55**	**$1,063.85**	**3**	**30**	**2.53%**
DELAFLOXACIN PRODUCTS							
BAXDELA TAB 450MG	2	2	$3,273.99	$1,637.00	1	23	2.59%
SUBTOTAL	**2**	**2**	**$3,273.99**	**$1,637.00**	**1**	**23**	**2.59%**
TEDIZOLID PRODUCTS							
SIVEXTRO TAB 200MG	1	1	$2,095.19	$2,095.19	1	6	1.66%
SUBTOTAL	**1**	**1**	**$2,095.19**	**$2,095.19**	**1**	**6**	**1.66%**
TOTAL	**334**	**237***	**$126,243.70**	**$377.98**	**1.4**	**106.8**	**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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
ORITAVANCIN PRODUCTS						
ORBACTIV J2407	10	10	$28,239.60	$2,823.96	1	77.65%
SUBTOTAL	**10**	**10**	**$28,239.60**	**$2,823.96**	**1**	**77.65%**
DALBAVANCIN PRODUCTS						
DALVANCE J0875	2	2	$8,130.00	$4,065.00	1	22.35%
SUBTOTAL	**2**	**2**	**$8,130.00**	**$4,065.00**	**1**	**22.35%**
TOTAL	**12⁺**	**12***	**$36,369.60**	**$3,030.80**	**1**	**100%**

*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
Please note: Orbactiv® (oritavancin) is currently available without prior authorization as a result of a value-based contract (VBC) with the manufacturer of Orbactiv®; however, Orbactiv® will follow the original prior authorization criteria if the manufacturer chooses not to participate in the VBC.

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Appendix M

Fiscal Year 2019 Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/ Sofosbuvir Oral Pellets) and Sovaldi® (Sofosbuvir Oral Pellets)

Oklahoma Health Care Authority
October 2019

Introduction[1,2]

Sovaldi® (sofosbuvir) and Olysio® (simeprevir), both approved by the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2013, were previously restricted under Oklahoma law, preventing prior authorization management by the Oklahoma Health Care Authority. The state law was changed in May 2014 allowing for prior authorization implementation of the hepatitis C virus (HCV) medications effective July 1, 2014.

As new direct-acting antivirals (DAAs) were FDA approved, they were subsequently reviewed and recommended to be prior authorized by the Drug Utilization Review (DUR) Board. Harvoni® (ledipasvir/sofosbuvir) was reviewed in November 2014, Viekira Pak® (dasabuvir/ombitasvir/ paritaprevir/ritonavir) was reviewed in January 2015, Daklinza™ (daclatasvir) and Technivie™ (ombitasvir/paritaprevir/ritonavir) were reviewed in December 2015, Zepatier® (elbasvir/ grazoprevir) was reviewed in April 2016, Epclusa® (sofosbuvir/velpatasvir) and Viekira XR® [dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release (ER)] were reviewed in December 2016, and Mavyret™ (glecaprevir/pibrentasvir) and Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) were reviewed in December 2017.

In February 2017, the DUR Board voted to remove the minimum fibrosis score requirement with a full implementation date of January 1, 2018. The minimum fibrosis score was lowered from F2 to F1 effective July 1, 2017 and from F1 to F0 effective January 1, 2018. In April 2018, the DUR Board voted to update the viral load requirements to ensure treated members have chronic HCV; the viral load requirements were implemented in May 2018 and are reflected in the current prior authorization criteria section of this report.

	Fiscal Year 2015	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018	Fiscal Year 2019
Total HCV Drug Spending	$21,863,385.60	$32,105,818.63	$26,475,372.50	$36,248,488.07	$24,798,344.80

HCV = hepatitis C virus
Costs do not reflect rebated prices or net costs.
State fiscal year = July 1st to June 30th.
Minimum fibrosis score lowered to F1 on 07/01/2017 and to F0 on 01/01/2018.

Current Prior Authorization Criteria

Harvoni® (ledipasvir/sofosbuvir), Zepatier® (elbasvir/grazoprevir), Epclusa® (sofosbuvir/ velpatasvir), Mavyret™ (glecaprevir/pibrentasvir), and Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) are the preferred DAAs. Use of an alternative HCV DAA regimen requires patient-specific, clinically significant reasoning why the preferred DAAs are not appropriate for the

member. The following is a template for standard prior authorization criteria for the preferred HCV medications. The criteria for each medication is based on FDA approved regimens and American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) guidance-recommended regimens. Specific HCV medication criteria will vary based on product labeling, FDA approved indications, guidance recommendations, drug interaction potential, and use in specific populations.

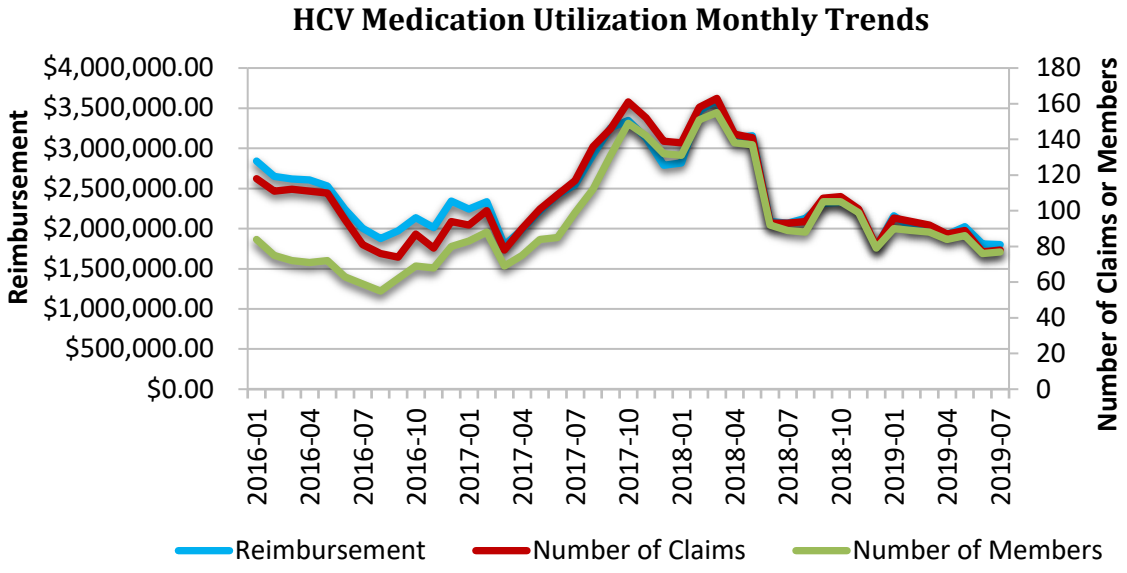
Hepatitis C Medication Approval Criteria:

1. FDA approved age appropriate to the requested medication; and
2. An FDA approved diagnosis of chronic hepatitis C (CHC) and an FDA-indicated genotype (GT) appropriate to the requested medication; and
3. Requested hepatitis C medication 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) GT 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 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. FDA approved regimens and requirements based on cirrhosis status, viral GT, treatment history, and viral load thresholds will apply; and
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. 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. Decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C) restrictions based on FDA approvals and safety recommendations will apply; and
13. Member must not have a limited life expectancy (less than 12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and

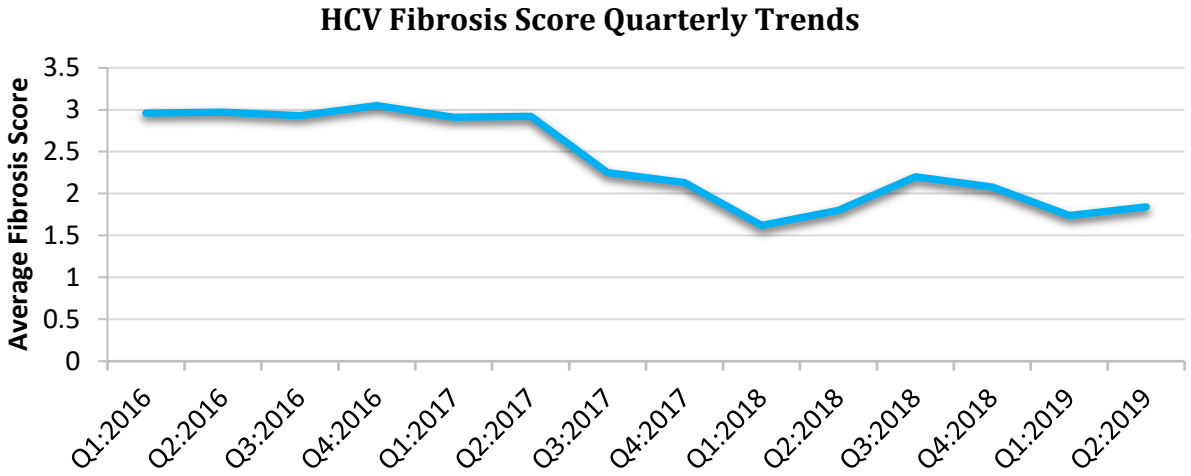
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy; and
15. Member must not be taking any medications not recommended for use with the requested hepatitis C medication; 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. 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
19. 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.

Trends of Hepatitis C Medication Utilization: Trends 2016 to 2019

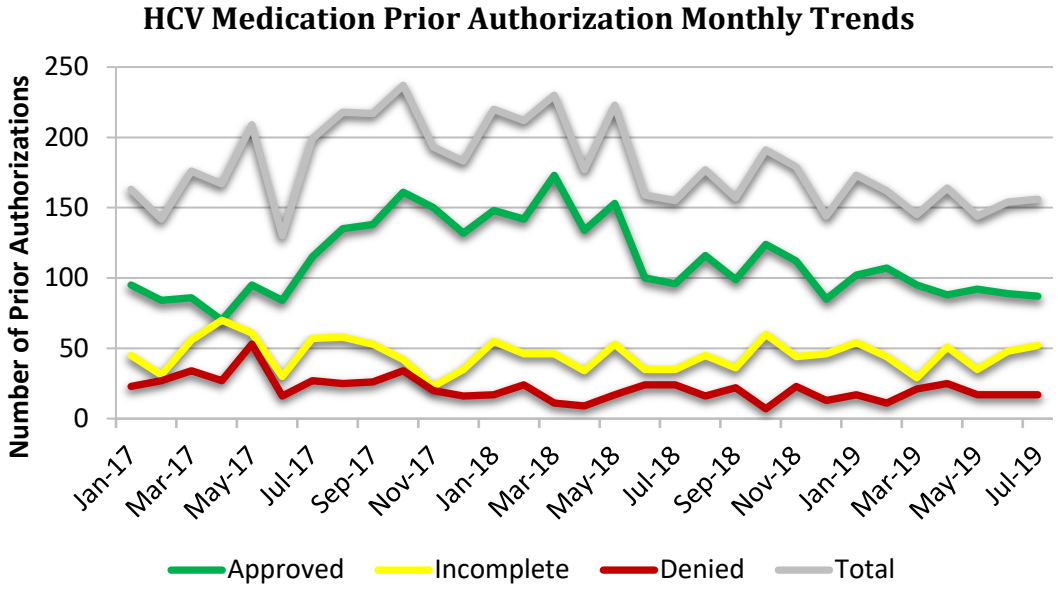
The following is a line graph representing the monthly trend in reimbursement, number of claims, and number of members utilizing HCV medications since January 2016. A steep increase can be seen following the minimum METAVIR fibrosis score change of F2 to F1 (July 1, 2017), and again following the change to F0 (January 1, 2018). Recently, in 2019, total reimbursement, the number of claims, and the number of members utilizing HCV medications have since declined to similar totals experienced prior to the removal of the minimum fibrosis score.



The following graph outlines the trends in average METAVIR equivalent fibrosis score by quarter. An immediate decline in average fibrosis score can be seen following the change to F1 in July 2017. The average fibrosis score dropped by 37.8% from quarter (1) 2016 (Q1:2016) to quarter (2) 2019 (Q2:2019).



Prior authorization requests as well as approvals increased following the fibrosis score transitions. For comparison, total requests increased by 35.0% when comparing January 2017 to January 2018. Additionally, the percentage of approved prior authorizations per month increased from 58.3% to 67.3% for January 2017 and January 2018, respectively. Recent trends in the 2nd quarter of 2019 show trends in total requests and approvals are similar to June 2017. Incomplete prior authorizations are typically a result of incomplete prior authorization submissions or failure to complete the prior authorization form. Denials are rare and most commonly a result of the member being dual eligible in which their primary prescription drug plan would reimburse for the medication. Approvals are granted for 28 days of therapy each time to monitor adherence, so members will have a prior authorization request for each refill of therapy.



Hepatitis C Summary Statistics for Treated Members

Parameter	Details
Number of Unduplicated Treated Members*	1,915 Members
Genotype	**Genotype 1:** 67.7% **Genotype 2:** 16.7% **Genotype 3:** 14.5% **Genotype 4:** 0.5% **Multiple Genotypes:** 0.6%
Fibrosis Score	**Average:** 2.42 **F0:** 9.8% **F1:** 14.4% **F2:** 29.2% **F3:** 17.0% **F4:** 29.5% **Decompensated:** 0.1%
Pre-Treatment Viral Load (HCV RNA)	**Average:** 3,540,961 IU/mL
Prior Treatment Experience	**Treatment-Experienced Members:** 10.2% **Treatment-Naïve Members:** 89.8%
Treatment Length	**Average:** 11.3 weeks **8 weeks:** 32.5% **12 weeks:** 62.0% **16 weeks:** 1.3% **24 weeks:** 4.2%
Compliance¥	**Before PA:** 18.8% of members noncompliant **After PA:** 2.9% of members noncompliant
SVR Cure Rate/Cost Per Cure	94.4% Cure Rate+ Estimated cost per cure in the SoonerCare population is $88,796.90 to $175,476.62. Range due to partial SVR response rate.

*Table includes data collected from 07/01/2014 to 09/01/2019

HCV RNA = hepatitis C virus ribonucleic acid; PA = prior authorization; SVR = sustained virologic response at least 12 weeks after therapy completion

¥Compliance before prior authorization was defined as an appropriate regimen length of 12 or 24 weeks.

+The cure rate is based only on members for whom SoonerCare was able to obtain SVR responses (SVR response rate: 50.6%). Costs do not reflect rebated prices or net costs.

Utilization of Hepatitis C Medications: Fiscal Year 2019

Comparison of Fiscal Years

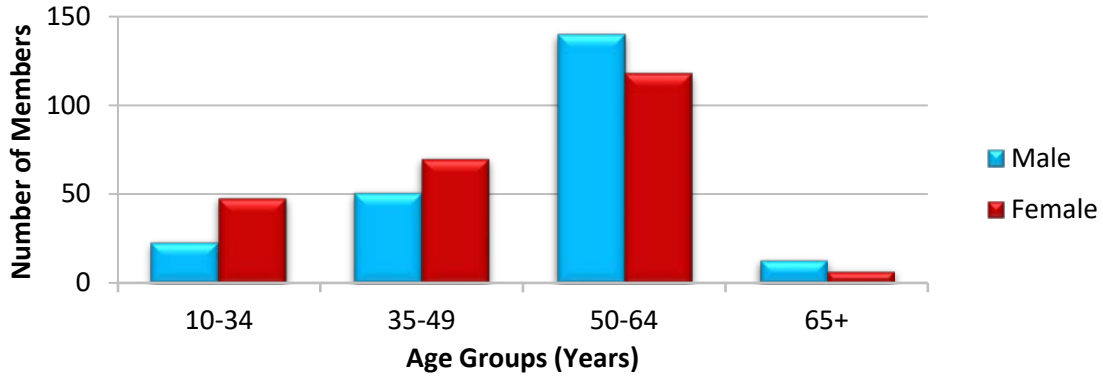
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	683	1,687	$36,248,488.07	$21,486.95	$767.65	77,199	47,220
2019	470	1,103	$24,798,344.80	$22,482.63	$799.59	45,204	31,014
% Change	**-31.20%**	**-34.60%**	**-31.60%**	**4.60%**	**4.20%**	**-41.40%**	**-34.30%**
Change	**-213**	**-584**	**-$11,450,143.27**	**$995.68**	**$31.94**	**-31,995**	**-16,206**

*Total number of unduplicated members.

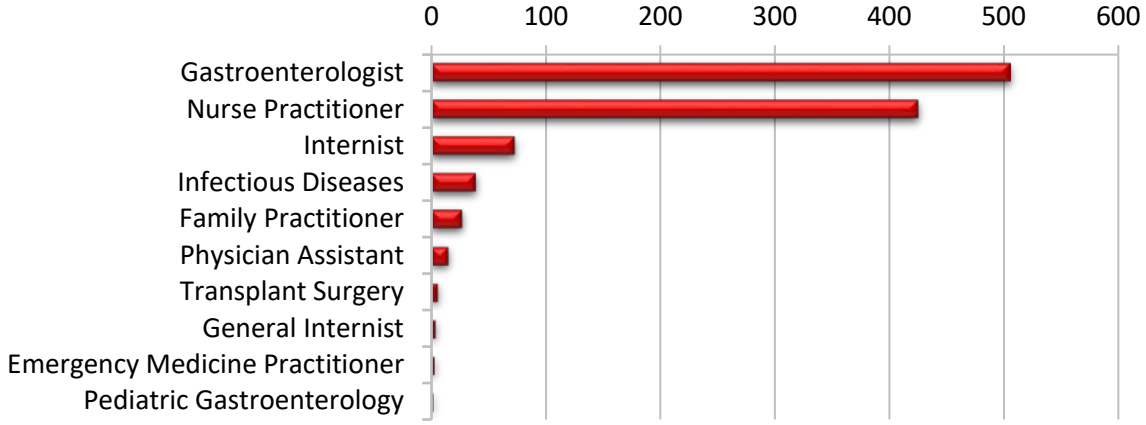
Costs do not reflect rebated prices or net costs.

Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

Demographics of Members Utilizing Hepatitis C Medications



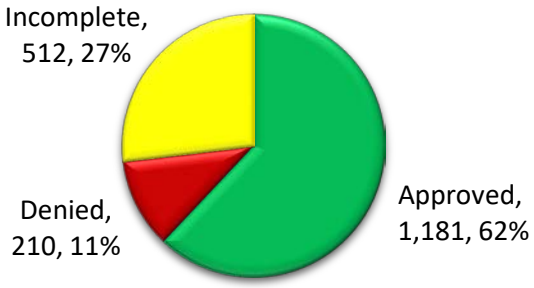
Top Prescriber Specialties of Hepatitis C Medications by Number of Claims



Prior Authorization of Hepatitis C Medications

There were 1,903 prior authorization requests submitted for 586 unique members for hepatitis C medications during fiscal year 2019. Approvals are granted for 28 days of therapy each time, so members will have a prior authorization request for each refill of therapy. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



Market News and Updates[3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24]

Anticipated Patent Expiration(s):

- Zepatier® (elbasvir/grazoprevir): May 2031

- Epclusa® (sofosbuvir/velpatasvir): January 2034
- Vosevi® (sofosbuvir/velpatasvir/voxilaprevir): July 2034
- Mavyret™ (glecaprevir/pibrentasvir): June 2035

Discontinuation(s):

- **Olysio® (simeprevir):** In December 2017, Janssen announced the discontinuation of Olysio®. The discontinuation was voluntary and was not related to product quality, safety, or efficacy. Olysio® was no longer available effective May 25, 2018.
- **Technivie™ (ombitasvir/paritaprevir/ritonavir) and Viekira XR™ (ombitasvir/ paritaprevir/ritonavir/dasabuvir ER):** In May 2018, AbbVie, Inc. announced the discontinuation of Technivie™ and Viekira XR™. The discontinuations were voluntary and were not related to product quality, safety, or efficacy. Both products were available until January 1, 2019.
- **Daklinza™ (daclatasvir):** In January 2019, the FDA announced the discontinuation of Bristol Myers Squibb's Daklinza™ 30mg and 60mg tablets following the announcement of the discontinuation of the 90mg tablets in December 2018. Bristol Myers Squibb has indicated distribution of the 30mg and 60mg tablets ceased in June 2019. The discontinuation was voluntary and was not related to product quality, safety, or efficacy.

FDA Approval(s) and Label Update(s):

- **Mavyret™ (glecaprevir/pibrentasvir) Label Update:** In August 2018, the FDA approved updates to the Mavyret™ product labeling to include new data from the M14-730 HCV/HIV-1 co-infection study, and from the M13-596 liver and renal transplant study. Label updates included a revision to the *Dosage and Administration* section to state that Mavyret™ is recommended for 12 weeks in liver or kidney transplant recipients with HCV, and a 16-week treatment duration is recommended for genotype (GT) 1 HCV-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A protease inhibitor or in GT 3-infected patients who are pegylated interferon/ribavirin/sofosbuvir treatment-experienced.
- **Mavyret™ (glecaprevir/pibrentasvir) in Pediatric Patients:** In April 2019, the FDA approved Mavyret™ for the treatment of all 6 GTs of HCV in children 12 to 17 years of age. Mavyret™ was previously approved for the treatment of HCV in adults in 2017.
- **Harvoni® (ledipasvir/sofosbuvir) in Pediatric Patients:** In August 2019, the FDA approved Harvoni® for the treatment of chronic HCV in pediatric patients 3 years of age and older with GT 1, 4, 5, or 6. Harvoni® was previously approved in patients 12 years and older for the same indications. Along with the expanded indication, the FDA also approved a new oral pellet formulation of Harvoni® in 2 strengths: 33.75mg ledipasvir/150mg sofosbuvir or 45mg ledipasvir/200mg sofosbuvir as well as a new tablet strength: 45mg ledipasvir/200mg sofosbuvir. Previously, Harvoni® was only available as a 90mg ledipasvir/400mg sofosbuvir oral tablet. The recommended dose for patients weighing at least 35kg is 90mg/400mg per day. The recommended dose for patients weighing 17kg to <35kg is 45mg/200mg per day, and the recommended dose for patients weighing <17kg is 33.75/150mg per day. Launch plans for the oral pellets and new oral tablet strength are pending.

- **Sovaldi® (sofosbuvir) in Pediatric Patients:** In August 2019, the FDA approved Sovaldi® for the treatment of chronic HCV in pediatric patients 3 years of age and older with GT 2 or 3. Sovaldi® was previously approved in patients 12 years and older for the same indications. Along with the expanded indication, the FDA also approved a new oral pellet formulation of Sovaldi® in 2 strengths: 150mg or 200mg as well as a new tablet strength: 200mg. Previously, Sovaldi® was only available as a 400mg oral tablet. The recommended dose for patients weighing at least 35kg is 400mg per day. The recommended dose for patients weighing 17kg to <35kg is 200mg per day, and the recommended dose for patients weighing <17kg is 150mg per day. Launch plans for the oral pellets and new oral tablet strength are pending.
- **Mavyret™ (glecaprevir/pibrentasvir) in Pediatric Patients:** In September 2019, the FDA approved Mavyret™ to be used as an 8-week treatment course for the treatment of HCV in patients with compensated cirrhosis who are treatment naïve. Previously the 8-week treatment course was only approved for treatment-naïve patients without cirrhosis; HCV-infected patients with compensated cirrhosis previously required treatment for 12 weeks. The approval applies to all 6 GTs of HCV.

Safety Update(s):

- **Serious Liver Injury:** In August 2019, the FDA issued a Drug Safety Communication regarding the risk of rare cases of worsening liver function or liver failure in patients with moderate-to-severe liver impairment who used Mavyret™ (glecaprevir/ pibrentasvir), Zepatier® (elbasvir/grazoprevir), or Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) to treat chronic HCV. All of these medicines contain an HCV protease inhibitor and are not indicated for use in patients with moderate-to-severe liver impairment. The FDA indicated that in many of the reported cases, liver failure occurred in patients who had signs and symptoms of moderate-to-severe liver impairment (Child-Pugh B or C) or other serious liver problems and should not have been treated with these medicines. In most cases, liver failure or decompensation typically occurred within the first 4 weeks of starting treatment and symptoms resolved or new onset worsening of liver function improved after stopping the medication.

Guideline Update(s):

- **September 2019:** The Kidney Disease: Improving Global Outcomes (KDIGO) 2018 clinical practice guideline for the prevention, diagnosis, evaluation, and treatment of HCV infection in chronic kidney disease (CKD) patients was published in the *Annals of Internal Medicine*. The guideline comprised 66 recommendations related to HCV in adult CKD patients. Key recommendations include: screening all patients for HCV infection upon initiation of dialysis or kidney transplant; evaluating all CKD and kidney transplant patients for antiviral therapy; timing of HCV treatment in relation to kidney transplantation (before vs. after) should be based on individual and environmental factors; patients receiving a kidney from an HCV-positive donor can be treated for HCV after transplant; and HCV-positive kidney donors who do not have cirrhosis should undergo HCV treatment before donation.

News:

- **September 2018:** Gilead Sciences, Inc. announced plans to launch authorized generic versions of Epclusa® (sofosbuvir/velpatasvir) and Harvoni® (ledipasvir/sofosbuvir) through a subsidiary, Asegua Therapeutics, LLC. The authorized generics launched at a list price of $24,000 for the most common course of therapy and became available in January 2019. Gilead also announced they are pursuing other innovative financing models including a potential subscription model.
- **October 2018:** Merck, the manufacturer of Zepatier® (elbasvir/grazoprevir), reduced the list price of Zepatier® by 60%. The Wholesale Acquisition Cost (WAC) declined from $650.00 per tablet to $260.00 per tablet.
- **November 2018:** An 8-week regimen of Mayvret™ (glecaprevir/pibrentasvir) resulted in 100% rate of SVR 12 weeks after treatment in treatment-naïve patients with chronic HCV GT 1,2,4,5 and 6 and compensated cirrhosis. Currently 12 weeks of Mavyret™ is indicated for HCV-infected patients with compensated cirrhosis, while 8 weeks of Mavyret™ is indicated for patients without cirrhosis.
- **January 2019:** The Centers for Disease Control and Prevention (CDC) estimated Oklahoma ranks second in the United States for prevalence of HCV (1.82 per 100 population). The Oklahoma State Health Department indicated that a major contributing factor to the high occurrence of HCV in Oklahoma is injection drug use. Among people 18 to 29 years of age, HCV increased by 400%, and admission for opioid injection increased by 622%. Those 30 to 39 years of age saw an increase of HCV by 325%, and admission for opioid injection increased by 83%.
- **January 2019:** Alcohol-associated liver disease (ALD) has replaced HCV as the number 1 reason for liver transplants in the United States according to research published in the *Journal of the American Medical Association* (*JAMA*). Researchers proposed that the shift may be due to increased availability of HCV treatment and ease of treating the disease with DAA agents.
- **February 2019:** A study published in the journal *Health Affairs* found that the introduction of abuse-deterrent OxyContin® (oxycodone ER) may have contributed to an increase in HCV infections because some drug abusers switched from the prescription opioid to injectable heroin. Investigators found that states with above-average rates of OxyContin® misuse prior to the reformulation saw HCV infections increase 3 times as fast as in other states, suggesting that efforts to deter misuse of opioids may have unintended consequences.
- **June 2019:** Louisiana Medicaid and Corrections announced a deal with Asegua Therapeutics, a subsidiary of Gilead Sciences, which would allow the state to provide HCV treatment under a novel approach referred to as the "Netflix Model". Under the "Netflix Model" the state will receive an unrestricted supply of generic Epclusa® (sofosbuvir/velpatasvir) while capping the state's expenditures. The state expects that in the early years of the deal, the state is likely to get more of the drug than it pays for. In later years, Louisiana may pay for more than it uses. The deal allows the state to potentially eradicate the disease in a short time while maintaining a stable budget by spreading the cost over several years.
- **July 2019:** Results from a study of 800 patients published in the journal *Gastroenterology* found that DAA drugs for HCV reduced deaths from cirrhosis and liver

cancer by 46%. In addition, the authors found no evidence that DAAs increase the risk of liver cancer recurrence, as was previously feared. The authors of the study indicated that previous studies compounded the misunderstandings of DAA therapy by not accounting for timing of therapy relative to liver cancer diagnosis, not including a comparison group, and not properly considering clinical differences among patients.

- **September 2019:** The United States Preventative Services Task Force (USPSTF) issued a draft recommendation statement and a draft evidence review recommending screening all adults 18 to 79 years of age for HCV infection ("B" Recommendation). Previously USPSTF recommended HCV screening only in patients at high-risk for infection and 1-time screening in adults born between 1945 and 1965.

Pipeline:

- **Hepatitis C Vaccine:** Results of a Phase 1/2 study of an HCV vaccine candidate in patients at high-risk of HCV infection due to use of injected drugs are expected in mid-2019. The vaccine candidate was previously found to elicit an appropriate T-cell-mediated immunity in healthy volunteers. The vaccine is composed of a replication-defective chimpanzee adenovirus (ChAd) vector encoding nonstructural (NS) proteins NS3, NS4, and NS5. Testing confirmed that ChAd3-NS was well tolerated and highly immunogenic, and responses were sustained for at least 1 year after boosting with a heterologous adenoviral vector. Investigators have indicated that the genetic diversity, including 7 GTs and 80 subtypes, of the virus has contributed to challenges in development. The genetic diversity of HCV exceeds that of human immunodeficiency virus-1 (HIV).
- **Ruzasvir/Uprifosbuvir:** Combination ruzasvir 60mg and uprifosbuvir 450mg resulted in varying efficacy by HCV GT in HCV-infected patients. Study results published in the *Journal of Viral Hepatology* in February 2019 included participants with HCV GT 1 through 6 (N=160). Participants received ruzasvir 60mg plus uprifosbuvir 450mg orally once daily for 12 weeks. The primary endpoint was SVR 12 weeks after the end of treatment. After follow-up, the rates of SVR at 12 weeks were 96% for HCV GT1a infection, 100% for GT1b, 97% for GT2, 77% for GT3, 90% for GT4, and 67% for GT6. A total of 11 serious adverse events were reported by 5 participants, but none were considered drug related.

Regimen Comparison[25,26,27,28,29]

The following table shows the current AASLD/IDSA guidance recommended regimens of DAA medications for the treatment of chronic HCV infection in treatment-naïve patients with or without compensated cirrhosis. The table is not all-inclusive and excludes regimens considered "alternative" in the guidance as opposed to "recommended"; regimens are ordered as they are recommended in the guidance. Specific regimens are used in particular patient populations depending on comorbidities, pre-treatment viral load, prior HCV treatment experience, fibrosis stage, cirrhosis status, and baseline viral polymorphisms. SVR rates found in clinical studies should not be compared across studies, but can be used as a measure of clinical efficacy for each regimen. SVR rates were obtained from studies cited in the AASLD/IDSA treatment guidance or from an individual product's package labeling. SVR rates may vary across studies even when used in similar patient populations. Some SVR percentages in the following table

may contain treatment-experienced patients or combined cirrhotic and non-cirrhotic patients if the study did not differentiate. Overall SVR percentages for genotypic subtypes may be reported together if the study did not differentiate.

Genotype	Host Factors	Treatment Regimen	Total Cost	SVR**
Genotype 1a	Treatment-naïve, Non-cirrhotic	**EBR/GZR** 12 wks	$21,840.00	92%+
		GLEC/PIB 8 wks	$25,695.60	99% (1a & 1b)Ω
		LED/SOF 8 or 12 wks	$23,999.92-$35,999.88	93% or 96%
		VEL/SOF 12 wks	$23,999.64	98%¥
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$21,840.00	92%+
		GLEC/PIB 12 wks	$38,543.40	99% (1a & 1b)Ω
		LED/SOF 12 wks	$35,999.88	94% (1a & 1b)
		VEL/SOF 12 wks	$23,999.64	98%¥
Genotype 1b	Treatment-naïve, Non-cirrhotic	**EBR/GZR** 12 wks	$21,840.00	98%¥
		GLEC/PIB 8 wks	$25,695.60	99% (1a & 1b)Ω
		LED/SOF 8 or 12 wks	$23,999.92-$35,999.88	98%
		VEL/SOF 12 wks	$23,999.64	99%¥
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$21,840.00	98%
		GLEC/PIB 12 wks	$38,543.40	99% (1a & 1b)Ω
		LED/SOF 12 wks	$35,999.88	94% (1a & 1b)
		VEL/SOF 12 wks	$23,999.64	99%¥
Genotype 2	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$25,695.60	98%Ω
		VEL/SOF 12 wks	$23,999.64	99%-100%¥
	Treatment-naïve, Cirrhotic	**VEL/SOF** 12 wks	$23,999.64	99%-100%¥
		GLEC/PIB 12 wks	$38,543.40	100%Ω
Genotype 3	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$25,695.60	94.9%
		VEL/SOF 12 wks	$23,999.64	98%
	Treatment-naïve, Cirrhotic	**GLEC/PIB** 12 wks	$38,543.40	98%
		VEL/SOF 12 wks	$23,999.64	93%
Genotype 4	Treatment-naïve, Non-cirrhotic	**GLEC/PIB** 8 wks	$25,695.60	93%Ω
		VEL/SOF 12 wks	$23,999.64	100%¥
		EBR/GZR 12 wks	$21,840.00	97%
		LED/SOF 12 wks	$35,999.88	93%-100%
	Treatment-naïve, Cirrhotic	**VEL/SOF** 12 wks	$23,999.64	100%¥
		GLEC/PIB 12 wks	$38,543.40	100%Ω
		EBR/GZR 12 wks	$21,840.00	97%
		LED/SOF 12 wks	$35,999.88	93%-100%
Genotype 5 or 6	Treatment-naïve, Cirrhotic & Non-cirrhotic	**GLEC/PIB** 8 wks (non) 12 wks (cirrhotic)	$25,695.60-$38,543.40	GT5: 100%, GT6: 100%Ω GT5: 100%, GT6: 100%Ω
		VEL/SOF 12 wks	$23,999.64	GT5: 97%, GT6: 100%
		LED/SOF 12 wks	$35,999.88	GT5: 93%, GT6: 96%

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.

**SVR = Sustained virologic response 12 weeks after therapy completion in clinical studies

+Lower % accounts for those with baseline resistance associated variants (RAVs); lower % shown is for 12 weeks without ribavirin.

ΩMay include some treatment-experienced patients.

¥Percentage includes cirrhotic & non-cirrhotic patients.

SOF = sofosbuvir; LED = ledipasvir; GT = genotype; EBR = elbasvir; GZR = grazoprevir; VEL = velpatasvir; GLEC = glecaprevir; PIB = pibrentasvir; wks = weeks

Recommendations

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 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 weight-based ribavirin for 12 weeks; or
            2. Harvoni® for 24 weeks
        v. Treatment-naïve or treatment-experienced with decompensated cirrhosis: Harvoni® with weight-based 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 weight-based 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. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
15. 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
16. 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
17. 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
18. 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
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. 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

21. 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 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 weight-based ribavirin and peginterferon alfa for 12 weeks
    b. **GT-2:**
        i. Treatment-naïve, non-cirrhotic: Sovaldi® with weight-based ribavirin for 12 weeks
        ii. Treatment-naïve, cirrhotic: Sovaldi® with weight-based ribavirin for 12 or 16 weeks
        iii. Treatment-experienced, non-cirrhotic or cirrhotic:
            1. Sovaldi® with weight-based ribavirin for 12 or 16 weeks; or

2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks

c. **GT-3:**
   i. Treatment-naïve or experienced, non-cirrhotic and cirrhotic:
      1. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks; or
      2. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)

d. **GT-4:**
   i. Treatment-naïve or experienced, non-cirrhotic and cirrhotic:
      1. Sovaldi® with weight-based 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.
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 genotype-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 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. Liver or Kidney Transplant Recipients: 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 genotype 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.

Utilization Details of Hepatitis C Medications: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	% COST	COST/ CLAIM
SOFOSBUVIR/VELPATASVIR PRODUCTS						
EPCLUSA TAB 400-100MG	479	188	$11,657,679.93	2.55	47.01%	$24,337.54

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	% COST	COST/ CLAIM
SUBTOTAL	**479**	**188**	**$11,657,679.93**	**2.55**	**47.01%**	**$24,337.54**
SOFOSBUVIR/LEDIPASVIR PRODUCTS						
HARVONI TAB 90-400MG	275	133	$8,505,742.36	2.07	34.30%	$30,929.97
SUBTOTAL	**275**	**133**	**$8,505,742.36**	**2.07**	**34.30%**	**$30,929.97**
GLECAPREVIR/PIBRENTASVIR PRODUCTS						
MAVYRET TAB 100-40MG	221	110	$2,851,695.49	2.01	11.50%	$12,903.60
SUBTOTAL	**221**	**110**	**$2,851,695.49**	**2.01**	**11.50%**	**$12,903.60**
ELBASVIR/GRAZOPREVIR PRODUCTS						
ZEPATIER TAB 50-100MG	79	33	$1,099,909.19	2.39	4.44%	$13,922.90
SUBTOTAL	**79**	**33**	**$1,099,909.19**	**2.39**	**4.44%**	**$13,922.90**
SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR PRODUCTS						
VOSEVI TAB 400-100-100MG	27	9	$673,060.11	3	2.71%	$24,928.15
SUBTOTAL	**27**	**9**	**$673,060.11**	**3**	**2.71%**	**$24,928.15**
RIBAVIRIN PRODUCTS						
RIBAVIRIN TAB 200MG	14	7	$1,426.75	2	0.01%	$101.91
RIBAVIRIN CAP 200MG	6	2	$637.31	3	0.00%	$106.22
SUBTOTAL	**20**	**9**	**$2,064.06**	**2.22**	**0.01%**	**$103.20**
INTERFERON PRODUCTS						
PEGASYS INJ 180 MCG/0.5ML	2	1	$8,193.66	2	0.03%	$4,096.83
SUBTOTAL	**2**	**1**	**$8,193.66**	**2**	**0.03%**	**$4,096.83**
TOTAL	**1,103**	**470***	**$24,798,344.80**	**2.35**	**100%**	**$22,482.63**

*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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[1] Gilead Sciences, Inc. U.S. Food and Drug Administration Approves Gilead's Sovaldi™ (Sofosbuvir) for the Treatment of Chronic Hepatitis C. *Business Wire*. Available online at: http://www.gilead.com/news/press-releases/2013/12/us-food-and-drug-administration-approves-gileads-sovaldi-sofosbuvir-for-the-treatment-of-chronic-hepatitis-c. Issued 12/06/2013. Last accessed 09/23/2019.

[2] Janssen Therapeutics. Olysio™ (simeprevir) Receives FDA Approval for Combination Treatment of Chronic Hepatitis C. Available online at: https://www.jnj.com/media-center/press-releases/olysio-simeprevir-receives-fda-approval-for-combination-treatment-of-chronic-hepatitis-c. Issued 11/22/2013. Last accessed 09/23/2019.

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Appendix N

Fiscal Year 2019 Annual Review of Signifor® LAR (Pasireotide)

Oklahoma Health Care Authority
October 2019

Current Prior Authorization Criteria

Signifor® LAR (Pasireotide) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Members with acromegaly who have had an inadequate response to surgery or for whom surgery is not an option; or
    b. Members with Cushing's disease from a pituitary tumor for whom pituitary surgery is not an option or has not been curative; and
2. For a diagnosis of acromegaly, the member must have a documented trial with octreotide long-acting or lanreotide depot with an inadequate response or have a patient-specific, clinically significant reason why the other long-acting somatostatin analogs (SSAs) are not appropriate for the member; and
3. Pasireotide LAR must be prescribed by an endocrinologist or in consultation with an endocrinologist; and
4. Pasireotide LAR must be administered by a health care professional; and
5. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and
6. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored when starting treatment and periodically thereafter; and
7. Authorizations will be for the duration of 12 months; and
8. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Utilization of Signifor® LAR (Pasireotide): Fiscal Year 2019

There were no SoonerCare paid claims for Signifor® LAR (pasireotide) during fiscal year 2019 (fiscal year 2019 = 07/01/2018 to 06/30/2019).

Prior Authorization of Signifor® LAR (Pasireotide)

There were no prior authorization requests submitted for Signifor® LAR (pasireotide) during fiscal year 2019.

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

Anticipated Patent Expiration(s):

- Pasireotide (Signifor® LAR): May 2028

Pipeline:

- **Mycapssa® (Octreotide) Capsule:** In July 2019, Chiasma, Inc. announced positive results from the company's pivotal Phase 3 CHIASMA OPTIMAL clinical study evaluating its octreotide oral capsule product candidate (Mycapssa®) for the maintenance treatment of adults with acromegaly. A total of 58% of the patients receiving octreotide capsules maintained their insulin-like growth factor 1 (IGF-1) response compared to 19% of the patients receiving placebo (P=0.008). Chiasma plans to submit a New Drug Application (NDA) to the FDA by the end of 2019; if FDA approved, Mycapssa® would be the first oral somatostatin analogue (SSA) available for the treatment of acromegaly.
- **Osilodrostat:** In March 2019, data from the Phase 3, multicenter, double-blind randomized withdrawal study (LINC-3) of osilodrostat in 137 patients with Cushing's disease were presented at ENDO 2019: The Endocrine Society Annual Meeting. Results of the trial demonstrated osilodrostat to be a highly effective treatment for Cushing's disease, with good tolerability. Compared to placebo, osilodrostat maintained mean urinary free cortisol (mUFC) less than the upper limit of normal after randomized withdrawal and normalized mUFC in two-thirds of enrolled patients after 48 weeks, with few patients discontinuing treatment due to adverse events.
- **Veldoreotide:** Veldoreotide is being developed by Strongbridge Biopharma for the treatment of acromegaly. Veldoreotide is a SSA, which demonstrates an ability similar to octreotide to suppress growth hormone, but has reduced propensity to inhibit postprandial insulin in short-term Phase 1 and 2 studies in healthy volunteers. It has been granted Orphan Drug designation by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

Recommendations

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

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Appendix O

Industry News and Updates

Oklahoma Health Care Authority
October 2019

Introduction

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

News and Updates[1,2,3]

News:

- **Angiotensin II Receptor Blocker (ARB) Impurities:** The Center for Drug Evaluation and Research (CDER) Director Janet Woodcock stated that the U.S. Food and Drug Administration (FDA) believes the risks posed to patients by nitrosomine impurities found in some blood pressure medications are "likely much lower" than initially thought. The FDA initially predicted that if 8,000 individuals took the highest valsartan dose (320mg) contaminated with n-nitrosodimethylamine (NDMA) from recalled batches every day for 4 years, there "may be 1 additional case of cancer over the lifetimes" of those individuals. However, according to Woodcock, "in reality, the vast majority of patients exposed…received much smaller amounts of the impurity than this worst-case scenario, and since not all ARBs are affected, it's very likely that a patient taking an ARB for 4 years would not have always received 1 of the affected products".
- **Ranitidine:** The FDA announced in September 2019 that some medicines containing ranitidine have been found to have low levels of NDMA and the agency is evaluating whether this poses a risk to patients. Woodcock stated the FDA is working with industry partners and international regulators to identify the source of this impurity in ranitidine and would provide an update as more information becomes available. As of the date of the announcement, the FDA is not calling for individuals to stop taking ranitidine but they advise patients who are taking prescription ranitidine and who wish to discontinue use of the drug to talk to their health care professional about other treatment options.
- **Immunotherapy:** According to a new study published in the journal *Nature*, chimeric antigen receptor T-cell (CAR-T) treatment can cure certain kinds of heart failure (HF) in mice. CAR-T is a type of immunotherapy that relies on engineered white blood cells that seek out and destroy malignant cells in the body and has proved life-changing for some patients with blood cancers. The technology was used to target scar tissue that stiffens the heart and prevents it from fully relaxing between beats in patients with HF. The scientists learned that mice and other animals have fibroblast activation protein (FAP) on scar tissue cells, so they engineered CAR-T cells to seek out the protein. The treatment worked to clear out scar tissue in mouse hearts, and it did not seem to damage other tissues. The investigators of the study now plan to repeat the experiment in dogs. Dr. Richard Lee, professor of stem cell and regenerative biology at Harvard who

was not involved in the study, agreed that the study is innovative and at least a proof of principle. However, some medical experts questioned if it would be feasible to use the therapy to treat HF patients, at least in the near future, due to the cost and the side effects.

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Appendix P

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: September 6th, 2019

FDA approves first treatment for patients with rare type of lung disease

The FDA approved Ofev® (nintedanib) capsules to slow the rate of decline in pulmonary function in adults with interstitial lung disease associated with systemic sclerosis or scleroderma, called SSc-ILD. It is the first FDA-approved treatment for this rare lung condition.

Scleroderma is a rare disease that causes tissue throughout the body, including the lungs and other organs, to thicken and scar. Interstitial lung disease or ILD is a condition affecting the interstitium, which is part of the lung's structure, and is 1 of the most common disease manifestations of sclerderma. SSc-ILD is a progressive lung disease in which lung function declines over time, and it can be debilitating and life-threatening. ILD is the leading cause of death among people with scleroderma, typically resulting from a loss of pulmonary function that occurs when the lungs cannot supply enough oxygen to the heart. Approximately 100,000 individuals in the United States have scleroderma, and approximately half of scleroderma patients have SSc-ILD.

The effectiveness of Ofev® to treat SSc-ILD was studied in a randomized, double-blind, placebo-controlled trial of 576 patients ages 20 to 79 years with the disease. Patients received treatment for 52 weeks, with some patients treated up to 100 weeks. The primary test for efficacy measured the forced vital capacity, or FVC, which is a measure of lung function, defined as the amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible. Those who took Ofev® had less lung function decline compared to those on placebo.

The overall safety profile observed in the Ofev® treatment group was consistent with the known safety profile of the therapy. The most frequent serious adverse event reported in patients treated with Ofev® was pneumonia (2.8% Ofev® vs. 0.3% placebo). Adverse reactions leading to permanent dose reductions were reported in 34% of Ofev®-treated patients compared to 4% of placebo-treated patients. Diarrhea was the most frequent adverse reaction that led to permanent dose reduction in patients treated with Ofev®.

The prescribing information for Ofev® includes warnings for patients with moderate or severe hepatic impairment, those with elevated liver enzymes and drug-induced liver injury and patients with gastrointestinal disorders. Ofev® may also cause embryo-fetal toxicity that can result in fetal harm, arterial thromboembolic events (blood clots), bleeding, and gastrointestinal perforation. P-gp and CYP3A4 inhibitors may increase nintedanib exposure, and patients taking these inhibitors should be closely monitored for tolerability of Ofev®. Common side effects noted with Ofev® include diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, weight loss, and hypertension.

Ofev® was originally approved in 2014 for adult patients with idiopathic pulmonary fibrosis (IPF), which is another interstitial lung condition.

Ofev® received Priority Review designation, under which the FDA's goal is to take action on an application within 6 months where the agency determines that the drug, if approved, would significantly improve the safety or effectiveness of treating, diagnosing, or preventing a serious condition. Ofev® 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 Ofev® to treat SSc-ILD to Boehringer Ingelheim Pharmaceuticals, Inc.

FDA NEWS RELEASE

For Immediate Release: September 20th, 2019

FDA approves first oral GLP-1 treatment for type 2 diabetes

The FDA approved Rybelsus® (semaglutide) oral tablets to improve control of blood sugar in adult patients with type 2 diabetes (T2DM), along with diet and exercise. Rybelsus® is the first glucagon-like peptide (GLP-1) receptor protein treatment approved for use in the United States that does not need to be injected. GLP-1 drugs are non-insulin treatments for people with T2DM.

T2DM is the most common form of diabetes, occurring when the pancreas cannot make enough insulin to keep blood sugar at normal levels. GLP-1, which is a normal body hormone, is often found in insufficient levels in T2DM patients. Like GLP-1, Rybelsus® slows digestion, prevents the liver from making too much sugar, and helps the pancreas produce more insulin when needed.

The efficacy and safety of Rybelsus® in reducing blood sugar in patients with T2DM were studied in several clinical trials, 2 of which were placebo-controlled and several of which were compared to other GLP-1 injection treatments. Rybelsus® was studied as a stand-alone therapy and in combination with other diabetes treatments, including metformin, sulfonylureas (insulin secretagogues), sodium-glucose co-transporter-2 (SGLT-2) inhibitors, insulins, and thiazolidinediones, all in patients with T2DM.

In the placebo-controlled studies, Rybelsus® as a stand-alone therapy resulted in a significant reduction in blood sugar (hemoglobin A1c) compared with placebo, as determined through HbA1c tests, which measure average levels of blood sugar over time. After 26 weeks, 69% of those taking 7mg once daily and 77% of those taking 14mg once daily of Rybelsus® decreased their HbA1c to lower than 7%, compared with 31% of patients on placebo.

The prescribing information for Rybelsus® includes a *Boxed Warning* to advise health care professionals and patients about the potential increased risk of thyroid c-cell tumors, and that Rybelsus® is not recommended as the first choice of medicine for treating diabetes. Patients who have ever had medullary thyroid carcinoma (MTC) or who have a family member who has ever had MTC are advised not to use Rybelsus®. Additionally, patients who have ever had an endocrine system condition called multiple endocrine neoplasia syndrome type 2 (MEN 2) are advised not to use Rybelsus®. Rybelsus® is not for use in patients with type 1 diabetes and people with diabetic ketoacidosis.

Rybelsus also has warnings about pancreatitis (inflammation of the pancreas), diabetic retinopathy (damage to the eye's retina), hypoglycemia (low blood sugar), acute kidney injury, and hypersensitivity reactions. It is not known whether Rybelsus® can be used by patients who have had pancreatitis. The risk of hypoglycemia increased when Rybelsus® was used in combination with sulfonylureas or insulin.

Rybelsus® should be taken at least 30 minutes before the first food, beverage, or other oral medication of the day, with no more than 4 ounces of plain water. Rybelsus® slows digestion, so patients should discuss other medications they are taking with their health care provider before starting Rybelsus®. The most common side effects are nausea, diarrhea, vomiting, decreased appetite, indigestion, and constipation.

The approval of Rybelsus® was granted to Novo Nordisk.

FDA NEWS RELEASE

For Immediate Release: September 24th, 2019

FDA approves first live, non-replicating vaccine to prevent smallpox and monkeypox

The FDA announced the approval of Jynneos® Smallpox and Monkeypox Vaccine, Live, Non-Replicating, for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection. This is the only currently FDA-approved vaccine for the prevention of monkeypox disease.

Jynneos® will be available for those determined to be at high risk of either smallpox or monkeypox infection. This vaccine is also part of the Strategic National Stockpile (SNS), the nation's largest supply of potentially life-saving pharmaceuticals and medical supplies for use in a public health emergency that is severe enough to cause local supplies to be depleted. The availability of this vaccine in the SNS will help ensure that the vaccine is accessible in the U.S. if needed.

Smallpox, which is caused by the variola virus, emerged in human populations thousands of years ago and is a highly contagious and often fatal infectious disease. A person infected with smallpox typically develops a rash characterized by raised pocks on the face and body. The smallpox virus is spread through saliva and droplets from the respiratory tract or by direct or indirect contact with the virus as it is shed from skin lesions. The virus can also be spread through other body fluids and contaminated clothing or bed linen. If a person is infected with smallpox and they are in close contact with others, the virus can spread quickly.

Monkeypox, which does not occur naturally in the United States, is a rare disease caused by infection with monkeypox virus, which causes symptoms similar to, but milder than, smallpox. Monkeypox begins with fever, headache, muscle aches, and exhaustion and can be fatal, even though it is typically milder than smallpox. It is transmitted to people from various wild animals, such as rodents and primates. In 2003, the U.S. experienced an outbreak of monkeypox, which was the first time human monkeypox was reported outside of Africa.

Jynneos® does not contain the viruses that cause smallpox or monkeypox. It is made from a vaccinia virus, a virus that is closely related to, but less harmful than, variola or monkeypox viruses and can protect against both of these diseases. Jynneos® contains a modified form of the vaccinia virus called Modified Vaccinia Ankara, which does not cause disease in humans and is non-replicating, meaning it cannot reproduce in human cells.

The effectiveness of Jynneos® for the prevention of smallpox was determined in a clinical study comparing the immune responses in study participants who received either Jynneos® or ACAM2000, an FDA-approved

vaccine for the prevention of smallpox. The study included approximately 400 healthy adults, 18 through 42 years of age who had never been vaccinated for smallpox, in which half of the study participants received 2 doses of Jynneos® administered 28 days apart, and half received 1 dose of ACAM2000. The group vaccinated with Jynneos® had an immune response that was not inferior to immune responses to ACAM2000. Vaccine effectiveness for the prevention of smallpox was also inferred from supportive animal studies that showed prior vaccination with Jynneos® protected non-human primates who were exposed to viruses related to the smallpox virus.

The effectiveness of Jynneos® for the prevention of monkeypox disease is inferred from the antibody responses in the smallpox clinical study participants and from studies in non-human primates that showed protection of animals vaccinated with Jynneos® who were exposed to the monkeypox virus.

The safety of Jynneos® was assessed in more than 7,800 individuals who received at least 1 dose of the vaccine. The most commonly reported side effects were pain, redness, swelling, itching, firmness at the injection site, muscle pain, headache, and fatigue. No safety concerns that would require a Medication Guide have been identified for Jynneos®. Jynneos® is administered in 2 doses given 4 weeks apart.

The FDA granted the approval of Jynneos® to Bavarian Nordic A/S. The FDA granted the application Priority Review and with this approval, the FDA issued a material threat medical countermeasure (MCM) priority review voucher to Bavarian Nordic A/S. The Federal Food, Drug, and Cosmetic Act, as amended by the 21st Century Cures (Cures) Act, authorizes the FDA to award priority review vouchers to sponsors of approved material threat MCM product applications that meet certain criteria.

FDA NEWS RELEASE

For Immediate Release: September 26th, 2019

FDA approves treatment for adults and children with all genotypes of hepatitis C and compensated cirrhosis that shortens duration of treatment to 8 weeks

The FDA expanded the approval of Mavyret™ (glecaprevir and pibrentasvir) tablets for an 8-week duration for the treatment of adults and children ages 12 years and older or weighing at least 99 pounds who have chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection and compensated cirrhosis and have not been previously treated for HCV (treatment-naïve). Mavyret™ is now the first 8-week treatment approved for all treatment-naïve adult and certain pediatric patients with HCV genotypes 1 through 6 both without cirrhosis and with compensated cirrhosis. Standard treatment length for patients with compensated cirrhosis was previously 12 weeks or more.

HCV is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. According to the U.S. Centers for Disease Control and Prevention, an estimated 2.7 to 3.9 million people in the U.S. have chronic HCV, and children born to HCV-positive mothers are at risk for HCV infection. Researchers estimate there are 23,000 to 46,000 children in the United States with HCV infection.

The efficacy and safety of Mavyret™ was established in clinical trials, which cumulatively evaluated more than 2,500 people with HCV genotype 1, 2, 3, 4, 5, or 6 infection who received Mavyret for 8, 12, or 16 weeks duration.The trials included patients with HIV-co-infection, kidney or liver transplant recipients, and patients with advanced kidney disease, including those requiring hemodialysis.

The efficacy of HCV treatment regimens are measured by the proportion of people in clinical trials achieving virologic cure. Virologic cure is the lack of detectable HCV in the blood at certain time points after completion of HCV therapy, known as sustained virologic response (SVR). SVR at 12 weeks post-treatment (SVR 12) is the standard measure of virologic cure. SVR 12 rates for Mavyret™ have ranged from 91 to 100% across clinical trials.The most common adverse reactions in patients taking Mavyret™ are headache and fatigue. Mavyret™ is contraindicated in patients with moderate or severe liver impairment (Child-Pugh B or C) or in those with any history of liver decompensation. It is also contraindicated in patients taking the drugs atazanavir and rifampin.

The FDA granted the approval of Mavyret to AbbVie, Inc.

FDA NEWS RELEASE

For Immediate Release: September 27th, 2019

FDA approves first treatment for children with rare diseases that cause inflammation of small blood vessels

The FDA approved Rituxan® (rituximab) injection to treat granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in children 2 years of age and older in combination with glucocorticoids (steroid hormones). It is the first approved treatment for children with these rare vasculitis diseases, in which a patient's

small blood vessels become inflamed, reducing the amount of blood that can flow through them. This can cause serious problems and damage to organs, most notably the lungs and the kidneys. It also can impact the sinuses and skin.
The safety profile in pediatric patients with GPA, formerly known as Wegener's granulomatosis, and MPA was consistent in type, nature and severity with the known safety profile of Rituxan® in adult patients with autoimmune diseases, including GPA and MPA. The pediatric clinical trial consisted of 25 patients ages 6 to 17 years with active GPA and MPA who were treated with Rituxan® or non-U.S.-licensed rituximab in an international multicenter, open-label, single-arm, uncontrolled study. All patients were given methylprednisolone prior to starting treatment.
During the clinical trial, after a 6-month remission induction phase where patients were treated only with Rituxan® or non-U.S.-licensed rituximab and glucocorticoids, patients who had not achieved remission – or who had progressive disease or an uncontrolled flare-up – could receive additional treatment, including other therapies, at the discretion of the investigator. In total, 14 of the patients were in remission at the 6-month mark. After 18 months, all 25 patients were in remission. Additional pharmacokinetic (exposure) and safety information supported the use of Rituxan® in patients 2 years to 5 years of age with GPA/MPA. The most common side effects in the pediatric study were infections, infusion-related reactions and nausea. Hypogammaglobulinemia (reduced serum immunoglobulin levels) has also been observed in pediatric GPA and MPA patients treated with the study products.
The most common side effects of Rituxan® are infections, infusion-related reactions, abnormally low level of lymphocytes in the blood (lymphopenia), and anemia. Health care professionals are advised to monitor patients for tumor lysis syndrome (a treatment complication where tumor cells are killed off at the same time and released into the bloodstream), cardiac adverse reactions, damage to kidneys (renal toxicity), and bowel obstruction and perforation (small hole formation).
The doctor and patient information for Rituxan® contains a *Boxed Warning* to draw attention to increased risks of the following: fatal infusion reactions; potentially fatal severe skin and mouth reactions; hepatitis B virus reactivation that may cause serious liver problems, including liver failure and death; and progressive multifocal leukoencephalopathy, a rare, serious brain infection that can result in severe disability or death. This product must be dispensed with a patient Medication Guide that provides important information about the drug’s uses and risks.
Rituxan® was approved to treat adult patients with GPA and MPA in 2011. It is also approved to treat 4 additional diseases, first gaining approval to treat Non-Hodgkin's lymphoma in 1997.
Rituxan® received priority review designation, under which the FDA’s goal is to take action on an application within 6 months where the agency determines that the drug, if approved, would significantly improve the safety or effectiveness of treating, diagnosing, or preventing a serious condition. Rituxan® 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 Rituxan® to Genentech.

Safety Announcements

FDA informs patients, providers and manufacturers about potential cybersecurity vulnerabilities for connected medical devices and health care networks that use certain communication software

[10/01/2019] The FDA is informing patients, health care professionals, IT staff in health care facilities, and manufacturers of a set of cybersecurity vulnerabilities, referred to as “URGENT/11,” that—if exploited by a remote attacker—may introduce risks for medical devices and hospital networks. URGENT/11 affects several operating systems that may then impact certain medical devices connected to a communications network, such as wi-fi and public or home Internet, as well as other connected equipment such as routers, connected phones, and other critical infrastructure equipment. These cybersecurity vulnerabilities may allow a remote user to take control of a medical device and change its function, cause denial of service, or cause information leaks or logical flaws, which may prevent a device from functioning properly or at all.
To date, the FDA has not received any adverse event reports associated with these vulnerabilities. The public was first informed of these vulnerabilities in a July 2019 advisory sent by the Department of Homeland Security. The FDA is providing additional information regarding the source of these vulnerabilities and recommendations for reducing or avoiding risks the vulnerabilities may pose to certain medical devices.
The URGENT/11 vulnerabilities exist in a third-party software, called IPnet, that computers use to communicate with each other over a network. This software is part of several operating systems and may be

incorporated into other software applications, equipment and systems. The software may be used in a wide range of medical and industrial devices. Though the IPnet software may no longer be supported by the original software vendor, some manufacturers have a license that allows them to continue to use it without support. Therefore, the software may be incorporated into a variety of medical and industrial devices that are still in use today.

Security researchers, manufacturers and the FDA are aware that the following operating systems are affected, but the vulnerability may not be included in all versions of these operating systems:

- VxWorks (by Wind River)
- Operating System Embedded (OSE) (by ENEA)
- INTEGRITY (by GreenHills)
- ThreadX (by Microsoft)
- ITRON (by TRON)
- ZebOS (by IP Infusion)

The agency is asking manufacturers to work with health care providers to determine which medical devices, either in their health care facility or used by their patients, could be affected by URGENT/11 and develop risk mitigation plans. Patients should talk to their health care providers to determine if their medical device could be affected and to seek help right away if they notice the functionality of their device has changed.

The FDA takes reports of vulnerabilities in medical devices very seriously and this safety communication includes recommendations to manufacturers for continued monitoring, reporting, and remediation of medical device cybersecurity vulnerabilities. The FDA is recommending that manufacturers conduct a risk assessment, as described in the FDA's cybersecurity postmarket guidance, to evaluate the impact of these vulnerabilities on medical devices they manufacture and develop risk mitigation plans. Medical device manufacturers should work with operating system vendors to identify available patches and other recommended mitigation methods, work with health care providers to determine any medical devices that could potentially be affected, and discuss ways to reduce associated risks.

Some medical device manufacturers are already actively assessing which devices may be affected by URGENT/11 and are identifying risk and remediation actions. In addition, several manufacturers have already proactively notified customers of affected products, which include medical devices such as an imaging system, an infusion pump, and an anesthesia machine. The FDA expects that additional medical devices with 1 or more of the cybersecurity vulnerabilities will be identified.

The FDA will continue its work with manufacturers and health care delivery organizations—as well as security researchers and other government agencies—to help develop and implement solutions to address cybersecurity issues throughout a device's total product lifecycle. The FDA will continue to assess new information concerning the URGENT/11 vulnerabilities and will keep the public informed if significant new information becomes available.

Current Drug Shortages Index (as of Oct 2nd, 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***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***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***
Difluprednate (Durezol) Ophthalmic Emulsion	***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 Sol	***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***
Haloperidol 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 Sol-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***
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 Ext-Release Oral Susp	***Currently in Shortage***
Metoclopramide Injection, USP	***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***
Nelarabine (Arranon) Injection	***Currently in Shortage***
Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***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***
Prednisolone Acetate 1% Ophthalmic Suspension	***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 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
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***
Valsartan Tablets	***Currently in Shortage***
Vinblastine Sulfate Injection	***Currently in Shortage***