OKLAHOMA
Health Care Authority

Drug Utilization Review Board

OHCA Webinar
Wednesday,
October 14, 2020
4:00pm

OHCA Webinar

Register for the meeting using the following website address:
https://odot.webex.com/odot/onstage/g.php?MTID=e973874cb6c1bfb2c6618a3c5c2d8712a

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

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Michyla Adams, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – October 14, 2020

DATE: September 28, 2020

NOTE: In response to COVID-19, the October 2020 meeting will be held via OHCA webinar at 4:00pm. Please register for the meeting using the following website address:
https://odot.webex.com/odot/onstage/g.php?MTID=e973874cb6c1bfb2c6618a3c5c2d8712a

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

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/Fall 2020 Pipeline Update – Appendix B

Action Item – Vote to Prior Authorize Adakveo® (Crizanlizumab-tmca), Oxbryta® (Voxelotor), and Reblozyl® (Luspatercept-aamt) – Appendix C

Action Item – Vote to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/Trastuzumab/Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib) – Appendix D

Action Item – Vote to Prior Authorize Rubraca® (Rucaparib) – Appendix E

Annual Review of Ovarian Cancer Medications and 30-Day Notice to Prior Authorize Zejula® (Niraparib) – Appendix F

Annual Review of Spinal Muscular Atrophy (SMA) Medications and 30-Day Notice to Prior Authorize Evrysdi™ (Risdiplam) – Appendix G

Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/ Ivacaftor and Ivacaftor) – Appendix H

Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet – Appendix I

30-Day Notice to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) – Appendix J

Annual Review of Signifor® LAR (Pasireotide) and 30-Day Notice to Prior Authorize Mycapssa® (Octreotide) – Appendix K

Annual Review of Lambert-Eaton Myasthenic Syndrome (LEMS) Medications [Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine)] – Appendix L

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – October 14, 2020 @ 4:00pm

OHCA Webinar
Register for the meeting here:
https://odot.webex.com/odot/onstage/g.php?MTID=e973874cb6c1bfb2c6618a3c5c2d8712a

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Wilcox

Telephone Conference Participants

DUR Board Members:

Dr. Stephen Anderson –	participating via Webex Teleconference
Dr. Jennifer de los Angeles –	participating via Webex Teleconference
Ms. Jennifer Boyett –	participating via Webex Teleconference
Dr. Markita Broyles –	participating via Webex Teleconference
Dr. Theresa Garton –	participating via Webex Teleconference
Dr. Megan Hanner –	participating via Webex Teleconference
Dr. Lynn Mitchell –	participating via Webex Teleconference
Dr. John Muchmore –	participating via Webex Teleconference
Dr. Lee Muñoz –	participating via Webex Teleconference
Dr. James Osborne –	participating via Webex Teleconference

Public Access to Meeting via Webex:

Register at:
https://odot.webex.com/odot/onstage/g.php?MTID=e973874cb6c1bfb2c6618a3c5c2d8712a

Or join by phone:

Dial: +1-415-655-0002

Event number: 133 077 4146
Event password: OHCA

Public Comment for Meeting:

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing by visiting www.okhca.org/DUR and completing the Speaker Registration Form. Completed Speaker Registration forms should be submitted to *DURPublicComment@okhca.org*. Forms must be received after the DUR Board agenda has been posted and no later than 24 hours before the meeting.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. September 9, 2020 DUR Minutes – Vote
B. September 9, 2020 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/Fall 2020 Pipeline Update – See Appendix B

A. Pharmacy Helpdesk Activity for September 2020
B. Medication Coverage Activity for September 2020
C. Fall 2020 Pipeline Update

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

5. Action Item – Vote to Prior Authorize Adakveo® (Crizanlizumab-tmca), Oxbryta® (Voxelotor), and Reblozyl® (Luspatercept-aamt) – See Appendix C

A. Introduction
B. New U.S. Food and Drug Administration (FDA) Approval(s)
C. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/Trastuzumab/Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib) – See Appendix D

A. New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
B. Product Summaries
C. Recommendations

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

7. Action Item – Vote to Prior Authorize Rubraca® (Rucaparib) – See Appendix E

A. New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
B. Rubraca® (Rucaparib) Product Summary
C. Recommendations

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

8. Annual Review of Ovarian Cancer Medications and 30-Day Notice to Prior Authorize Zejula® (Niraparib) – See Appendix F

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Ovarian Cancer Medications
D. Prior Authorization of Ovarian Cancer Medications
E. Market News and Updates
F. Zejula® (Niraparib) Product Summary
G. Recommendations
H. Utilization Details of Ovarian Cancer Medications

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

9. Annual Review of Spinal Muscular Atrophy (SMA) Medications and 30-Day Notice to Prior Authorize Evrysdi™ (Risdiplam) – See Appendix G

A. Current Prior Authorization Criteria
B. Utilization of SMA Medications
C. Prior Authorization of SMA Medications

D. Market News and Updates
E. Evrysdi™ (Risdiplam) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of SMA Medications

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

10. Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/ Ivacaftor and Ivacaftor) – See Appendix H

A. Current Prior Authorization Criteria
B. Utilization of CFTR Modulators
C. Prior Authorization of CFTR Modulators
D. Market News and Updates
E. Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of CFTR Modulators

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

11. Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet – See Appendix I

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

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

12. 30-Day Notice to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) – See Appendix J

A. Introduction
B. Product Comparison
C. College of Pharmacy Recommendations
D. Utilization Details of Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

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

13. Annual Review of Signifor® LAR (Pasireotide) and 30-Day Notice to Prior Authorize Mycapssa® (Octreotide) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Signifor® LAR (Pasireotide)
D. Prior Authorization of Signifor® LAR (Pasireotide)
E. Market News and Updates
F. Mycapssa® (Octreotide) Product Summary
G. College of Pharmacy Recommendations

Non-Presentation/Questions Only:

14. Annual Review of Lambert-Eaton Myasthenic Syndrome (LEMS) Medications [Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine)] – See Appendix L

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

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

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

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

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

Due to the Veterans' Day holiday, the November DUR meeting will be held on the first Wednesday of the month on November 4, 2020.

A. Targeted Immunomodulator Agents
B. Constipation and Diarrhea Medications
C. Atopic Dermatitis Medications
D. Anticoagulants and Platelet Aggregation Inhibitors

**Future business subject to change.*

17. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF SEPTEMBER 9, 2020

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

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

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

OTHERS PRESENT:	
Sieana Mackiewicz, ODOT	Shane Lambert, OMES
Ronald Cain, Pfizer	Dave Miley, Teva
Burl Beasley, EGID-State of Oklahoma	Brian Maves, Pfizer
Audrey Rattan, Alkermes	Ashley Valentine, Sick Cells
Adam Bloomfield, Sobi	Deron Grothe, Teva
Russell Burkhart, Supporters of SCD Families	Camille Kerr, Regeneron
Evie Knisely, Novartis	John Omick, GBT
Nima Nabavi, Amgen	Doug Pierce, Genentech
Bethany Holderread, Mercer	April Gault, Takeda
Maggie Jalowsky, Sick Cells	Gina Heinen, Novo Nordisk
James Chapman, AbbVie	Rick Dabner, Alnylam
Matthew Bradley, Novartis	Melanie Curlett, Takeda
Doug Wood, ViiV Healthcare	Devin Wilcox
Crystal Henderson, Global Blood Therapeutics	Eardie Curry, Genentech
Marcus McKinley, Supporters of SCD Families	Melissa DuVall, Sobi
John Logan, AbbVie	Nicole Cornett, Immunomedics
Emma Selm, DK Pierce	Rachel Peterson, OHCA
Roxann Dominguez, AbbVie	Kim Bleeker, ODOT
Marc Parker, Sunovion	Shellie Keast, Mercer
Jamie Smutko, Global Blood Therapeutics	David Condrick, Bridgebio
Jason Dickerson, Global Blood Therapeutics	Amber Schrantz, Lilly
Velvet Brown Watts, Supporters SCD Families	

PRESENT FOR PUBLIC COMMENT:	
Kent Ward, M.D.	OUHSC Associate Professor of Pediatrics
Marcus McKinley	Supporters of Families with Sickle Cell Disease, Inc
Russell Burkhart	Supporters of Families with Sickle Cell Disease, Inc
Velvet Brown Watts	Supporters of Families with Sickle Cell Disease, Inc
Jamie Smutko	Global Blood Therapeutics, Inc
Eardie Curry	Genentech

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**
2A: AGENDA ITEM NO. 7 EARDIE CURRY
2B: AGENDA ITEM NO. 9 MARCUS MCKINLEY
2C: AGENDA ITEM NO. 9 RUSSELL BURKHART
2D: AGENDA ITEM NO. 9 VELVET BROWN WATTS
2E: AGENDA ITEM NO. 9 JAMIE SMUTKO
2F: AGENDA ITEM NO. 10 KENT WARD, M.D.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **APPROVAL OF DUR BOARD MEETING MINUTES**
3A: JULY 8, 2020 DUR MINUTES – VOTE
3B: JULY 8, 2020 DUR RECOMMENDATIONS MEMORANDUM
Materials included in agenda packet; presented by Dr. Muchmore
Dr. Garton moved to approve; seconded by Dr. Hanner
ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ACADEMIC DETAILING PROGRAM UPDATE**
4A: PHARMACY HELPDESK ACTIVITY FOR JULY 2020
4B: MEDICATION COVERAGE ACTIVITY FOR JULY 2020
4C: PHARMACY HELPDESK ACTIVITY FOR AUGUST 2020
4D: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2020
4E: ACADEMIC DETAILING PROGRAM UPDATE
Materials included in agenda packet; presented by Dr. Chandler, Dr. Travers
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE TRAMADOL 100MG TABLET**
5A: INTRODUCTION
5B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Dr. Garton moved to approve; seconded by Dr. Mitchell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE KOSELUGO™ (SELUMETINIB), PEMAZYRE™ (PEMIGATINIB), AND QINLOCK™ (RIPRETINIB)**
6A: INTRODUCTION
6B: PRODUCT SUMMARIES
6C: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Anderson moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF BREAST CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ENHERTU® (FAM-TRASTUZUMAB DERUXTECAN-NXKI), PHESGO™ (PERTUZUMAB/TRASTUZUMAB/ HYALURONIDASE-ZZXF), TRODELVY™ (SACITUZUMAB GOVITECAN-HZIY), AND TUKYSA™ (TUCATINIB)**
7A: INTRODUCTION
7B: CURRENT PRIOR AUTHORIZATION CRITERIA
7C: UTILIZATION OF BREAST CANCER MEDICATIONS
7D: PRIOR AUTHORIZATION OF BREAST CANCER MEDICATIONS
7E: MARKET NEWS AND UPDATES

7F: PRODUCT SUMMARIES
7G: RECOMMENDATIONS
7H: UTILIZATION DETAILS OF BREAST CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF PROSTATE CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE RUBRACA® (RUCAPARIB)
8A: INTRODUCTION
8B: CURRENT PRIOR AUTHORIZATION CRITERIA
8C: UTILIZATION OF PROSTATE CANCER MEDICATIONS
8D: PRIOR AUTHORIZATION OF PROSTATE CANCER MEDICATIONS
8E: MARKET NEWS AND UPDATES
8F: RUBRACA® (RUCAPARIB) PRODUCT SUMMARY
8G: RECOMMENDATIONS
8H: UTILIZATION DETAILS OF PROSTATE CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF SICKLE CELL DISEASE (SCD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ADAKVEO® (CRIZANLIZUMAB-TMCA), OXBRYTA® (VOXELOTOR), AND REBLOZYL® (LUSPATERCEPT-AAMT)
9A: CURRENT PRIOR AUTHORIZATION CRITERIA
9B: UTILIZATION OF SCD MEDICATIONS
9C: PRIOR AUTHORIZATION OF SCD MEDICATIONS
9D: MARKET NEWS AND UPDATES
9E: PRODUCT SUMMARIES
9F: COLLEGE OF PHARMACY RECOMMENDATIONS
9G: UTILIZATION DETAILS OF SCD MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF SYNAGIS® (PALIVIZUMAB)
10C: PRIOR AUTHORIZATION OF SYNAGIS® (PALIVIZUMAB)
10D: SEASON COMPARISON
10E: MARKET NEWS AND UPDATES
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF GIVLAARI® (GIVOSIRAN) AND SCENESSE® (AFAMELANOTIDE)
11A: INTRODUCTION
11B: CURRENT PRIOR AUTHORIZATION CRITERIA
11C: UTILIZATION OF GIVLAARI® (GIVOSIRAN) AND SCENESSE® (AFAMELANOTIDE)
11D: PRIOR AUTHORIZATION OF GIVLAARI® (GIVOSIRAN) AND SCENESSE® (AFAMELANOTIDE)
11E: MARKET NEWS AND UPDATES

11F: COLLEGE OF PHARMACY RECOMMENDATIONS
11G: UTILIZATION DETAILS OF GIVLAARI® (GIVOSIRAN) AND SCENESSE® (AFAMELANOTIDE)
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
13A: CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) MODULATORS
13B: HEPATITIS C MEDICATIONS
13C: SPINAL MUSCULAR ATROPHY (SMA) MEDICATIONS
13D: OVARIAN CANCER MEDICATIONS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ADJOURNMENT
The meeting was adjourned at 5:32pm.

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

Memorandum

Date: September 10, 2020

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

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

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

Recommendation 1: Academic Detailing Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Tramadol 100mg Tablet

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of tramadol 100mg tablets into the Short-Acting Special Prior Authorization (PA) category of the Opioid Analgesics Product Based Prior Authorization (PBPA) Tier chart based on cost with the following criteria (changes noted in red in the following Tier chart and approval criteria; only the criteria and Tier chart with changes are listed):

- A patient-specific, clinically significant reason why the member cannot use 2 tramadol 50mg tablets to achieve a 100mg dose must be provided
- An age restriction will apply for members younger than 12 years of age; authorization will require patient-specific, clinically significant information supporting the use of tramadol despite the medication being contraindicated for the member's age

Opioid Analgesics Special Prior Authorization (PA) Approval Criteria:

1. Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, and Subsys® are approved for oncology-related diagnoses only.
2. Unique Strengths of Hydrocodone/Acetaminophen (APAP) Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use generic Norco® (hydrocodone/APAP 5/325mg, 7.5/325mg, or 10/325mg) must be provided.
3. ConZip® [Tramadol Extended-Release (ER) Capsule] Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use the ER tablet formulation must be provided. Tier structure rules apply.
4. Xartemis® XR (Oxycodone/APAP ER Tablet) Approval Criteria:
    a. An acute pain condition requiring around-the-clock opioid treatment; and
    b. A patient-specific, clinically significant reason must be provided for all of the following:
        i. Why the member cannot use any other opioid medication for treatment of acute pain; and
        ii. Why the member requires a long-acting medication for an acute pain condition; and
        iii. Why the member cannot use Oxycontin® (oxycodone ER) and over-the-counter (OTC) APAP individual products in place of this combination product; and
    c. A quantity limit of 4 tablets per day will apply with a maximum approval duration of 10 days; and
    d. The member must not exceed 3,250mg of APAP per day from all sources; and
    e. Tier structure rules still apply.
5. Levorphanol Tablet Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use alternative treatment options for pain (e.g., non-opioid analgesics, lower-tiered opioid analgesics) must be provided.
6. Tramadol 100mg Tablet Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use 2 tramadol 50mg tablets to achieve a 100mg dose must be provided; and
    b. An age restriction will apply for members younger than 12 years of age. For members younger than 12 years of age, the provider must submit patient-specific, clinically significant information supporting the use of tramadol despite the medication being contraindicated for the member's age.

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Short-Acting			
APAP/butalbital/ caff/codeine cap (Fioricet® with Codeine)	oxymorphone IR tab (Opana®)	benzhydrocodone/ APAP tab (Apadaz®)	levorphanol tab
ASA/butalbital/caff/ codeine cap (Fiorinal® with Codeine)	tapentadol IR tab (Nucynta®)	dihydrocodeine/ APAP/caff cap (Trezix®)	**tramadol 100mg tab**
codeine tab		hydrocodone/ APAP oral soln (Zamicet®, Liquicet®)	
codeine/APAP (Tylenol® with Codeine)		hydrocodone/ APAP tab (Xodol®)	
dihydrocodone/ ASA/caff cap (Synalgos-DC®)		oxycodone/APAP tab (Primlev™, Xolox®)	
hydrocodone/ APAP tab (Norco®)		oxycodone tab (Oxaydo®)	
hydrocodone/IBU tab (Vicoprofen®, Ibudone®, Reprexain™)		oxycodone tab (Oxecta®)	
hydromorphone tab (Dilaudid®)		oxycodone tab (RoxyBond™)	
morphine IR tab (MSIR®)			
oxycodone/APAP tab (Percocet®)			***Oncology Only:***
oxycodone/ASA tab (Percodan®)			fentanyl buccal film (Onsolis®)
oxycodone/IBU tab (Combunox™)			fentanyl buccal tab (Fentora®)
oxycodone IR cap (Oxy IR®)			fentanyl nasal spray (Lazanda®)
oxycodone IR tab (Roxicodone®)			fentanyl SL spray (Subsys®)
tramadol/APAP tab (Ultracet®)			fentanyl SL tab (Abstral®)
tramadol tab (Ultram®)			fentanyl transmucosal lozenge (Actiq®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
PA = prior authorization; IR = immediate-release; cap = capsule; tab = tablet; soln = solution; SL = sublingual; APAP = acetaminophen; ASA = aspirin; caff = caffeine; IBU = ibuprofen

Recommendation 3: Vote to Prior Authorize Koselugo™ (Selumetinib), Pemazyre™ (Pemigatinib), and Qinlock™ (Ripretinib)

MOTION CARRIED by unanimous approval.

- The prior authorization of Koselugo™ (selumetinib), Pemazyre™ (pemigatinib), and Qinlock™ (ripretinib) with the following criteria listed in red:
- Based on discussion by the Drug Utilization Review (DUR) Board at the July DUR Board meeting, the approval criteria for Koselugo™ has been updated to remove the age restriction due to the rarity of the disease

Koselugo™ (Selumetinib) Approval Criteria [Neurofibromatosis Type 1 (NF1) Diagnosis]:

1. Member meets all of the following:
   a. ~~Pediatric~~ members 2 years of age and older; and
   b. Diagnosis of NF1 with symptomatic, inoperable plexiform neurofibromas.

Pemazyre™ (Pemigatinib) Approval Criteria [Cholangiocarcinoma Diagnosis]:

1. Diagnosis of unresectable locally advanced or metastatic cholangiocarcinoma; and
2. Must have failed 1 or more prior therapies; and
3. Disease is positive for a fibroblast growth factor receptor 2 (FGFR2) fusion or other FGFR rearrangement.

Qinlock™ (Ripretinib) Approval Criteria [Gastrointestinal Stromal Tumor (GIST) Diagnosis]:

1. Diagnosis of advanced GIST; and
2. Previously received ≥3 kinase inhibitors, including imatinib; and
3. Used as a single-agent.

Recommendation 4: Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/ Trastuzumab/Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Rubraca® (Rucaparib)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Sickle Cell Disease (SCD) Medications and 30-Day Notice to Prior Authorize Adakveo® (Crizanlizumab-tmca), Oxbryta® (Voxelotor), and Reblozyl® (Luspatercept-aamt)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Synagis® (Palivizumab)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Givlaari® (Givosiran) and Scenesse® (Afamelanotide)

NO ACTION REQUIRED.

Recommendation 9: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 10: Future Business

NO ACTION REQUIRED.

cure SMA

Make today a breakthrough.

August 12, 2020

Melody Anthony
Medicaid Director
State of Oklahoma, Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

RE: Evrysdi (risdiplam) for Medicaid Beneficiaries with Spinal Muscular Atrophy

Dear Director Anthony,

On behalf of the largest organization dedicated to finding treatments and a cure for Spinal Muscular Atrophy (SMA), **we are writing to respectfully request that you provide coverage and access to Evrysdi (risdiplam) for Medicaid beneficiaries as indicated by the drug's label.** The U.S. Food and Drug Administration (FDA) approved Evrysdi for the treatment of SMA on August 7, 2020. The treatment was approved for daily oral/enteral route of administration in all individuals with SMA who are two month of age and older. We urge you to ensure that this drug is covered without restriction for all people with SMA over two months old.

SMA is a progressive neurodegenerative disease that impacts 1 in 11,000 births in the US among all races, ethnicities and genders. An estimated 1 in 50 Americans are genetic carriers. SMA robs people of physical strength by affecting the motor nerve cells in the spinal cord, impeding their ability to walk, swallow, and in the most severe cases, the ability to breathe. The disease is an autosomal recessive genetic disease caused by a mutation in the survival motor neuron gene 1 (SMN1).

As an oral treatment for SMA, the burden of administration is decreased, giving more patients potential access to SMA treatment. Covering this treatment without restrictions will allow individuals with SMA to experience a higher quality of life and greater longevity – leading to better outcomes. At the current time approximately 60% of all US patients are not yet treated. There are ongoing urgent unmet needs in our community, especially for our older patients, which this treatment will meet.

Historically, individuals with SMA have required aggressive medical care to survive, especially as the disease progressed and weakness increased with further loss of function. Because of the complexities of the disease, patients traditionally have needed a multi-disciplinary team of healthcare professionals to provide them with care and support. Without treatment, patients with SMA type 1 require permanent ventilation and feeding tubes, and costly, intensive, around the clock care. Those with type 2 and 3 may also require some of these interventions. All of these services place a tremendous financial burden on both families and insurers.

Evrysdi modifies splicing of the backup gene SMN2 to produce more functional full length SMN protein, a protein that is deficient in SMA and is necessary for motor neuron function and survival. Evrysdi is designed to increase and sustain SMN protein levels both throughout the central nervous system and in the peripheral tissues of the body. Evrysdi is a liquid oral treatment that is given daily at home.

Clinical trials have demonstrated Evrysdi's effectiveness. In the FIREFISH trial Part 1, a pivotal global study evaluating Evrysdi safety and efficacy in infants aged 2-7 months with symptomatic SMA type 1, the study showed that 41% of infants (7/17) sat without support for 5 seconds by month 12, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). No infants achieved this milestone in the natural history of SMA type 1.[1] In addition, after 12 months of treatment with Evrysdi, 90% (19/21) of patients were alive without permanent ventilation. After a minimum of 23 months of treatment with Evrysdi, 81% (17/21) of patients were alive without permanent ventilation and reached an age of 28 months or older compared to average age of 13.5 months for death or permanent ventilation in a natural history study.[1] In this cohort, 88% (15/17) of infants were able to feed by mouth and swallow; 13/17 fed exclusively by mouth. In a natural history study, all infants over 12 months of age with SMA type 1 required feeding support.[1] Motor milestone assessment with the Hammersmith Infant Neurological Exam Module 2 (HINE-2) showed 77% (13/17) of infants had more milestones improve versus decline.

In the FIREFISH trial Part 2, a pivotal global study evaluating Evrysdi in infants aged 2-7 months old with symptomatic SMA type 1, the study met its primary endpoint with 29% of infants (12/41; $p<0.0001$) sitting without support for 5 seconds by month 12, as assessed by the BSID-III. No infants achieve this milestone in the natural history of SMA type 1. In addition, 44% (18/41) of infants were able to hold their head upright, 32% (13/41) were able to roll to the side and 5% (2/41) were able to stand with support, as measured by the HINE-2. Approximately 90% (37/41) had a Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) score increase of at least 4 points, with 56% (23/41) achieving a score above 40; the median increase was 20 points. Without treatment, infants with SMA type 1 show a decrease in CHOP-INTEND scores over time. Almost half of the infants (49%) treated with Evrysdi did not require hospitalization up to month 12 compared to up to 7.6 hospitalizations per year for untreated patients with SMA type 1.[2] In addition, 93% were alive at month 12 compared to average age of 13.5 months for death or permanent ventilation in a natural history study.[1] Of the surviving infants, swallowing was maintained in 95% (36/38) and the ability to feed by mouth was maintained in 89% (34/38) compared to natural history.[1]

SUNFISH, a two-part, double-blind, placebo-controlled pivotal study in patients aged 2-25 years with SMA type 2 or type 3. Part 1 (n=51), determined the dose for the confirmatory Part 2 study. Part 2 (n=180) evaluated motor function using total score of Motor Function Measure 32 (MFM-32) at 12 months of treatment in non-ambulatory patients with type 2 or type 3. MFM-32 is a validated scale used to evaluate fine and gross motor function in people with neurological disorders including SMA. The study met its primary endpoint and showed that the MFM-32 change from placebo was significant in people treated with Evrysdi (1.55 point mean difference; p=0.0156). The Revised Upper Limb Module (RULM), a key secondary endpoint, also showed improvement (1.59 point difference; p=0.0028) compared to placebo. As anticipated, exploratory subgroup analyses showed that the strongest responses in MFM-32 versus placebo were observed in the youngest age group (2-5 years) with 78.1% vs. 52.9% achieving ≥3 point increase. Importantly, disease stabilization was observed in the 18-25 years age group (57.1% vs. 37.5%, with stabilization defined as a ≥0 point increase), which is the goal of treatment for those with more established disease.

The exploratory efficacy analysis of SUNFISH study Part 1 assessed motor function, using the MFM-32 scale. In a weighted analysis comparing the data with a robust natural history comparator cohort, MFM-32 change from placebo at month 24 was greater in patients receiving Evrysdi (3.99 point difference [95% CI: 2.34, 5.65] p<0.0001). Even small changes in motor function can result in meaningful

differences in daily living. Results also showed that treatment with Evrysdi led to a median two-fold increase in blood SMN protein levels after four weeks, which was sustained for at least 24 months. This is consistent with previously reported results through 12 months of treatment. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons, which transmit movement signals from the central nervous system to the muscles.

JEWELFISH is an open-label study, assessing safety and pharmacodynamic data in people with SMA aged 6 months-60 years who have previously received other SMA-directed treatments and who currently are receiving Evrysdi . Among the patients who completed 12 months of treatment with Evrysdi, a median two-fold increase in SMN protein versus baseline was observed (n=18), consistent with treatment naïve patients. An early assessment of safety showed a consistent safety profile compared to treatment-naïve patients. No patients had drug related adverse events that led to Evrysdi withdrawal.

As individuals with SMA are life-long patients and regular consumers of significant health care resources, treatment with Evrysdi will very likely reduce their need for other health care services, such as inpatient and outpatient visits, emergency care, physical therapy, occupational therapy, and other related care and services. Participants in the clinical trials have already shown less need for costly, invasive interventions and services. In addition, the caregiver burden is dramatically reduced as patients gain or maintain independence.

Therefore, we ask that this life-changing treatment be covered with no restrictions for Medicaid beneficiaries for whom it has been approved. Decisions about care should be made by patients, their families and their expert clinical care providers, based on what works best for that individual, not on financial or insurance concerns. We believe that no one impacted by SMA should be denied access to a potentially life-saving therapy, intervention or expert care provider. To that end, we are eager to work with you to ensure that the forthcoming coverage and reimbursement policies associated with Evrysdi adequately address the needs of the eligible SMA community.

For more information, please contact Maynard Friesz, Vice President for Policy and Advocacy at Cure SMA at maynard.friesz@curesma.org or 202.871.8004.

Sincerely,

Kenneth Hobby
President

Jill Jarecki, PhD
Chief Scientific Officer

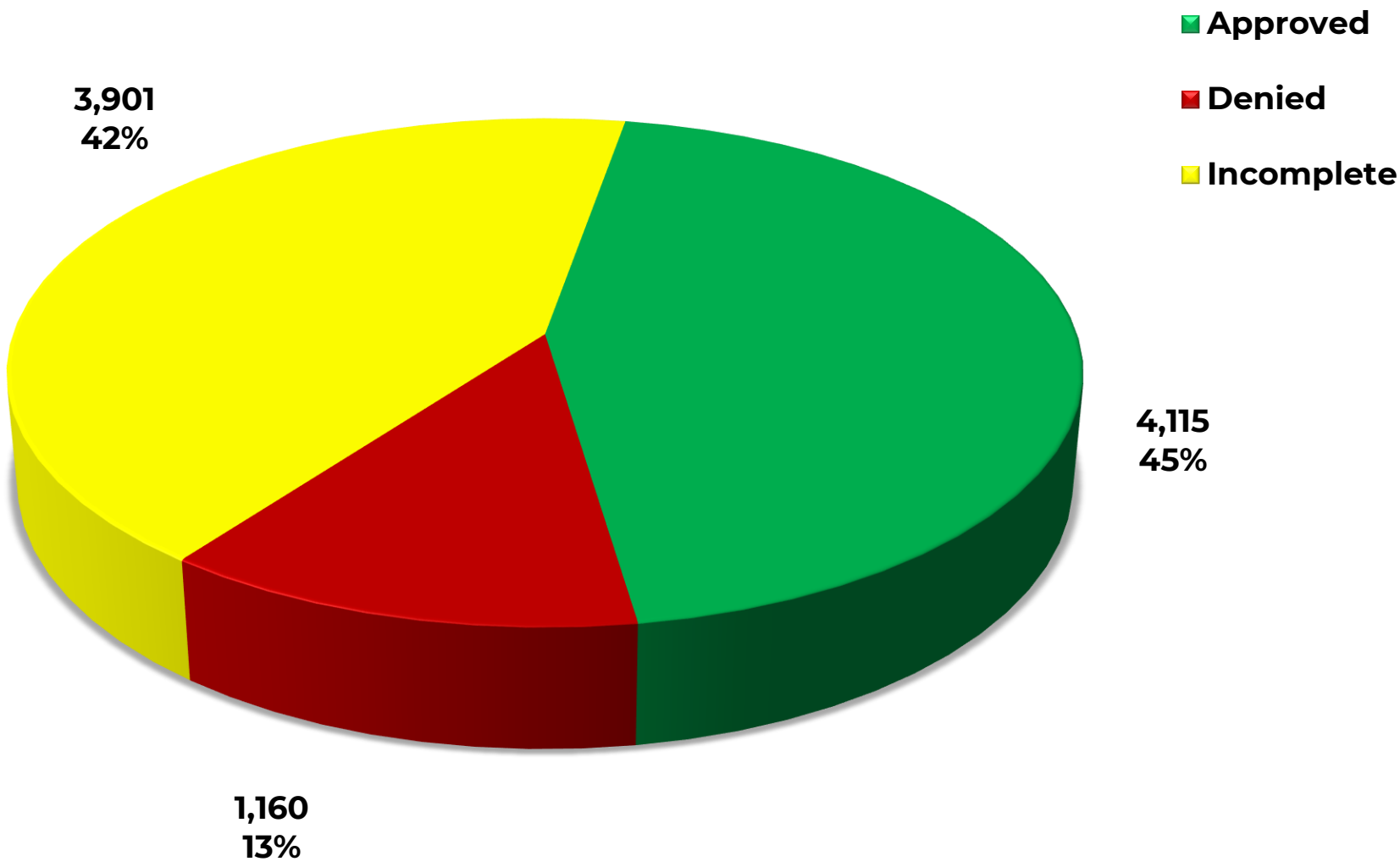
Mary Schroth, M.D.
Chief Medical Officer

References:

1. Finkel, RS, McDermott, MP, Kaufmann, P, et al. Observational study of spinal muscular atrophy type I and implications for clinical trials. *Neurology.* 2014;83(9):810-817.
2. Chatwin, M, Bush, A, Simonds, AK. Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I. *Arch Dis Child.* 2011;96(5):426-432.

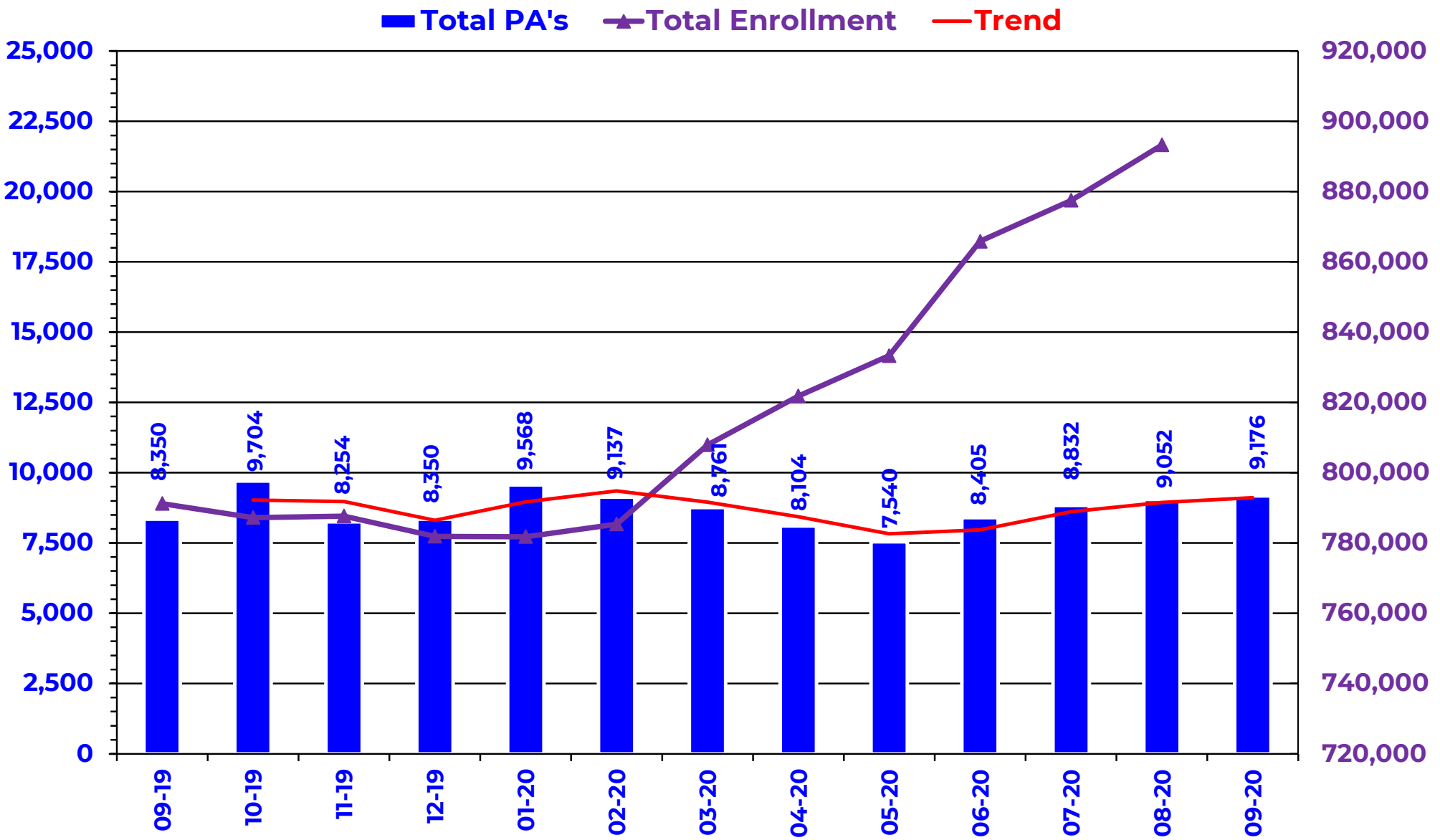
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER 2020



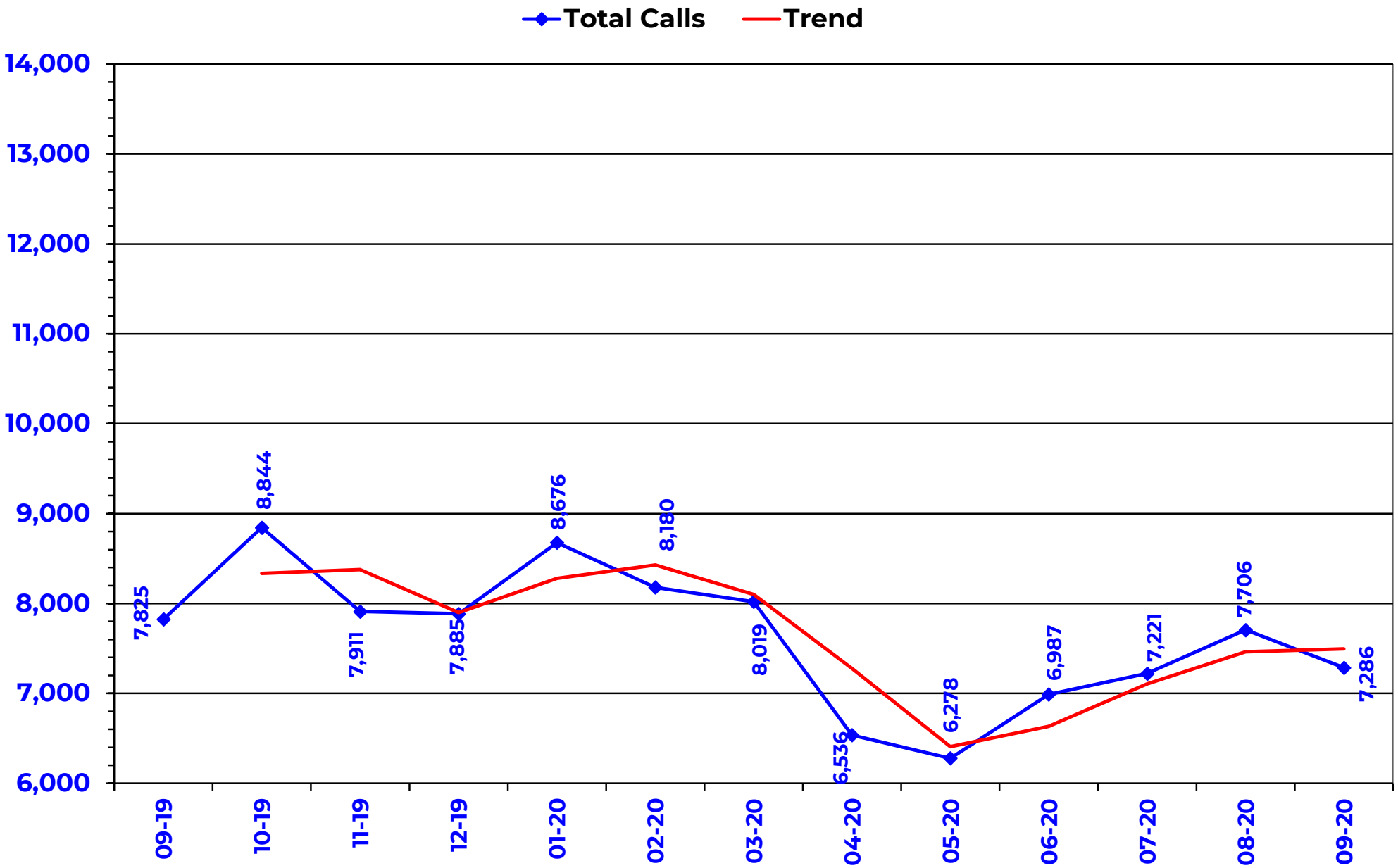
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2019 – SEPTEMBER 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: SEPTEMBER 2019 – SEPTEMBER 2020



Prior Authorization Activity

9/1/2020 Through 9/30/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	91	14	12	65	334
Analgesic - NonNarcotic	15	1	3	11	363
Analgesic, Narcotic	258	82	30	146	154
Angiotensin Receptor Antagonist	11	3	2	6	266
Antiasthma	55	16	8	31	245
Antibiotic	30	13	3	14	276
Anticonvulsant	186	82	8	96	319
Antidepressant	208	52	28	128	323
Antidiabetic	339	93	50	196	355
Antigout	14	7	1	6	323
Antihemophilic Factor	15	12	0	3	262
Antihistamine	37	8	8	21	256
Antimigraine	238	29	93	116	264
Antineoplastic	100	59	10	31	174
Antiulcers	75	11	11	53	134
Anxiolytic	36	1	6	29	360
Atypical Antipsychotics	320	126	39	155	342
Biologics	186	96	13	77	285
Bladder Control	50	8	18	24	358
Blood Thinners	360	201	24	135	343
Botox	48	33	8	7	296
Buprenorphine Medications	60	12	4	44	47
Calcium Channel Blockers	11	4	3	4	141
Cardiovascular	83	33	12	38	319
Chronic Obstructive Pulmonary	189	45	47	97	347
Constipation/Diarrhea Medications	202	35	61	106	216
Contraceptive	21	6	7	8	313
Dermatological	377	110	93	174	153
Diabetic Supplies	749	380	71	298	207
Endocrine & Metabolic Drugs	103	66	9	28	160
Erythropoietin Stimulating Agents	21	13	0	8	113
Fish Oils	17	2	6	9	359
Gastrointestinal Agents	143	29	30	84	203
Genitourinary Agents	21	12	2	7	79
Glaucoma	11	5	0	6	183
Growth Hormones	134	88	7	39	144
Hematopoietic Agents	16	4	3	9	268
Hepatitis C	116	67	12	37	9
Insomnia	59	7	11	41	228
Insulin	171	64	24	83	333
Miscellaneous Antibiotics	15	1	3	11	21
Multiple Sclerosis	71	35	3	33	247
Muscle Relaxant	51	6	14	31	191
Nasal Allergy	69	10	20	39	116

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Neurological Agents	96	28	15	53	203
Neuromuscular Agents	20	9	3	8	296
Ocular Allergy	17	2	5	10	85
Ophthalmic Anti-infectives	13	4	0	9	15
Osteoporosis	16	4	5	7	310
Other*	291	73	43	175	269
Otic Antibiotic	23	2	4	17	8
Pediculicide	16	0	1	15	0
Respiratory Agents	35	24	1	10	244
Statins	24	4	6	14	154
Stimulant	921	429	93	399	345
Testosterone	77	30	19	28	323
Topical Antifungal	29	5	7	17	28
Topical Corticosteroids	69	0	40	29	0
Vitamin	97	28	32	37	164
Pharmacotherapy	67	62	0	5	249
Emergency PAs	0	0	0	0	
Total	**7,227**	**2,685**	**1,098**	**3,444**	
Overrides					
Brand	46	37	1	8	322
Compound	16	12	0	4	70
Diabetic Supplies	12	11	0	1	135
Dosage Change	352	326	1	25	14
High Dose	5	5	0	0	358
Ingredient Duplication	3	2	0	1	16
Lost/Broken Rx	89	84	3	2	21
MAT Override	306	215	4	87	63
NDC vs Age	272	166	19	87	260
NDC vs Sex	10	6	2	2	68
Nursing Home Issue	50	48	1	1	10
Opioid MME Limit	96	38	3	55	146
Opioid Quantity	35	27	2	6	156
Other*	53	45	1	7	14
Quantity vs. Days Supply	551	365	24	162	249
STBS/STBSM	23	20	1	2	92
Stolen	5	4	0	1	20
Third Brand Request	25	19	0	6	32
Overrides Total	**1,949**	**1,430**	**62**	**457**	
Total Regular PAs + Overrides	**9,176**	**4,115**	**1,160**	**3,901**	

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

Denial Reasons	
Unable to verify required trials.	3,170
Does not meet established criteria.	1,190
Lack required information to process request.	694
Other PA Activity	
Duplicate Requests	858
Letters	16,538
No Process	11
Changes to existing PAs	619
Helpdesk Initiated Prior Authorizations	787
PAs Missing Information	30

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

Fall 2020 Pipeline Update

Oklahoma Health Care Authority
October 2020

Introduction

The following report is a pipeline review compiled by the University of Oklahoma College of Pharmacy: Pharmacy Management Consultants. 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.

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

Anticipated Indication(s): Treatment of attention deficit hyperactivity disorder (ADHD)

Clinical Trial(s): Viloxazine (SPN 812) is a non-stimulant, serotonin norepinephrine modulating agent in development for the treatment of ADHD. Viloxazine was evaluated in 4 double-blind, placebo-controlled Phase 3 trials in children and adolescents, ranging in age from 6 to 17 years old. Pediatric patients between the ages of 6 and 11 years were included in the P301 and P303 trials, while adolescent patients 12 to 17 years of age were followed in the P302 and P304 trials. Across all 4 trials, a total of 902 patients received extended-release (ER) viloxazine in dosages of 100mg, 200mg, 400mg, or 600mg. The 600mg dose was only utilized in patients 12 to 17 years of age. The primary endpoint in each study was the change in baseline ADHD-Rating Scale-V (ADHD RS-5) total score in viloxazine versus placebo. Findings showed viloxazine, with the exception of the 600mg dose, was effective in reducing the ADHD RS-5 total score, with specific improvements in the subscales of hyperactivity/impulsivity and inattention. The P301 trial results showed statistically significant improvements in ADHD RS-5 total scores in both the 100mg and 200mg doses after 1 week of treatment (P=0.0004 and P=0.0244, respectively), which was maintained through the end of the trial. Similarly, the P304 trial reported statistically significant improvements in ADHD RS-5 total score with viloxazine 400mg (P=0.0082). Viloxazine 400mg demonstrated improvements on the hyperactivity/impulsivity and inattention subscales, compared with placebo (P=0.0484

and P=0.0042, respectively). Both the 200mg and 400mg doses also met the Clinical Global Impression-Improvement (CGI-I) scale secondary endpoint when compared to placebo (P=0.0042 and P=0.0003, respectively).

Place in Therapy: ADHD impacts roughly 7% to 8% of children, making it the most common neurodevelopment disorder of childhood. Boys are twice as likely as girls to be diagnosed with ADHD. There are primarily 3 types of ADHD, with symptoms consisting of inattention and hyperactivity, which can often interfere with development, behavior, and academic achievement. In the United States, 2/3 of children diagnosed with ADHD are taking medication. After age 6, many children receive medications to help manage ADHD symptoms. Medication therapy decisions for ADHD treatment are largely driven by severity of disease, comorbid conditions, and response. The most frequently prescribed treatments for ADHD are stimulants such as amphetamine and methylphenidate, which can be associated with potential abuse, weight loss, and delayed growth. If stimulant therapy is contraindicated, not recommended, or is unsuccessful, adjuvant therapies such as atomoxetine, guanfacine ER, clonidine ER, and potentially viloxazine (depending on FDA approval) can be utilized. Patients with comorbid conditions, such as anxiety or depression, or who have failed stimulant therapy may be potential candidates for treatment with viloxazine. Viloxazine would also offer another non-controlled treatment option.

Projected FDA Decision: November 8, 2020

SoonerCare Impact: During fiscal year 2020, there was a total of 39,488 members who had a paid pharmacy claim for an ADHD medication. This accounted for 330,284 claims totaling $47,685,174.52 in drug spending with an average cost of $144.38 per claim. These costs do not reflect rebated prices or net costs.

Berotralstat[5,6,7,8,9]

Anticipated Indication(s): Prevention of hereditary angioedema (HAE) attacks

Clinical Trial(s): Berotralstat (BCX7353) is a prophylactic agent in development for the prevention of HAE attacks in adults and adolescents older than 12 years of age. The Phase 3 randomized, double-blind, placebo-controlled APeX-2 trial evaluated daily use of 2 doses (110mg and 150mg) of oral berotralstat in 121 patients with type I or type II HAE. Patients were randomized 1:1:1 to placebo, berotralstat 110mg, or berotralstat 150mg with the primary efficacy endpoint being the rate of investigator confirmed HAE attacks over 24 weeks of the study drug administration. The 110mg dose reduced the HAE attack rate by 30% versus placebo (P=0.024) while the 150mg dose reduced the HAE attack rate by 44% compared to placebo

(P<0.001). Additionally, 50% of patients on the 150mg dose had >70% reduction in HAE attack rate compared to baseline versus 15% of the placebo patients (P=0.002). The 150mg dose showed a reduction in the HAE attack rate by 66% versus placebo in patients with a baseline attack rate of <2 attacks per month (P=0.009). If the baseline monthly attack rate was >2, a 40% reduction in attack rate versus placebo (P=0.05) was observed. Both the 110mg and 150mg dose levels were generally safe and well-tolerated. The most common drug-related adverse event reported in ≥5% of patients were nausea, dyspepsia, and diarrhea. These gastrointestinal side effects were often self-limited and brief in duration. The APeX-2 trial was for 24 weeks at which point the placebo patients were stratified 1:1 to the 110mg and 150mg doses of berotralstat for a total of 48 weeks. The APeX-2 trial and the long-term open-label APeX-S trial confirmed that berotralstat is generally well-tolerated and patients experienced sustained reductions in HAE attack frequency and improved quality of life. Overall, the APeX data suggests that berotralstat use is associated with fewer HAE attacks, reduced severity of attacks, and use of less on-demand medication when compared to placebo.

Place in Therapy: HAE is a rare disease affecting 1 person in 10,000 to 50,000 in the United States. The disease is characterized by unpredictable, potentially fatal recurrent swelling, or angioedema, most commonly affecting the extremities, face, abdomen, and larynx. The angioedema attacks are caused by a dysregulation in the bradykinin-forming pathway. Uncontrolled plasma kallikrein activity leads to overproduction of bradykinin, which results in vasodilation, vascular leakage, and consequent swelling. Management consists of acute treatment of attacks, short-term prophylaxis during precipitating conditions, and long-term prophylaxis for frequent attacks. Current products FDA approved to manage HAE employ a variety of mechanisms of action. Products that increase levels of C1 esterase inhibitor (C1-INH) include danazol or replacement with plasma-derived C1-INH (Berinert®, Cinryze®, Haegarda®) and recombinant C1-INH (Ruconest®). Ecallantide (Kalbitor®) and lanadelumab-flyo (Takhzyro®) are kallikrein inhibitors and icatibant (Firazyr®) is a bradykinin receptor antagonist. Treatment options for acute attacks include Berinert® [administered intravenously (IV)], Ruconest® (IV), Firazyr® [adminstereted subcutaneously (sub-Q)], and Kalibitor® (IV). Danazol (oral) administered 3 times daily, Cinryze® (IV) and Haegarda® (sub-Q) administered every 3 to 4 days, and Takhzyro® (sub-Q) administered every 2 or 4 weeks are used for routine prophylaxis of HAE attacks. Berotralstat is a once-daily oral medication that is a highly selective inhibitor of plasma kallikrein. It is the first product used in the treatment or prevention of HAE that is available as an oral formulation, which is the primary advantage. Additional comparative trials amongst commercially available products are warranted.

Projected FDA Decision: December 3, 2020

SoonerCare Impact: During fiscal year 2020, there were 2 SoonerCare paid pharmacy claims for HAE medications. They were for 2 unique members with a total cost of $78,925.51, equaling $39,462.76 per claim. There were no medical claims in fiscal year 2020 for HAE medications.

Roxadustat[5,6,10,11,12,13]

Anticipated Indication(s): Treatment of anemia of chronic kidney disease (CKD), including dialysis and non-dialysis dependent patients

Clinical Trial(s): The Phase 3, randomized, open-label DOLOMITES trial evaluated the efficacy and safety of roxadustat compared to darbepoetin alfa for the treatment of anemia in non-dialysis dependent adult patients with stage 3-5 CKD. The trial, which enrolled a total of 616 adult patients, showed roxadustat was non-inferior to darbepoetin alfa in correction and maintenance of hemoglobin (Hb) levels. Results showed non-inferiority of roxadustat in the correction of Hb levels during the first 24 weeks of treatment [89.5% vs. 78.0%; 95% confidence interval (CI): 5.66%, 17.36%]. Secondary endpoints tested non-inferiority and superiority. Superiority of roxadustat to darbepoetin alfa was demonstrated with a decrease in low-density lipoprotein (LDL) cholesterol (P<0.01) and in time to first IV iron use (P=0.004). The non-inferiority was shown for mean arterial pressure and time to occurrence of hypertension (HTN). The overall safety profile between roxadustat and darbepoetin alfa was comparable. Pooled cardiovascular safety analyses showed roxadustat did not increase the risk of major adverse cardiovascular events [MACE (all-cause mortality, stroke, and myocardial infarction)], MACE+ (MACE, unstable angina requiring hospitalization, and congestive heart failure requiring hospitalization), and all-cause mortality in non-dialysis dependent patients compared to placebo and dialysis-dependent patients compared to darbepoetin alfa. The overall incidence of treatment-emergent adverse events was comparable between roxadustat and darbepoetin alfa (91.6% and 92.5%, respectively).

The HIMALAYAS trial was an open-label, active-controlled, global Phase 3 trial that included 1,043 incident dialysis patients that were randomized 1:1 to receive roxadustat or epoetin alfa for up to 4.4 years. The United States primary efficacy endpoint was a mean change in Hb levels from baseline to the average over 28-52 weeks. This endpoint was met as the Hb in roxadustat-treated patients increased from 8.4g/dL to 11g/dL versus 8.4g/dL to 10.8g/dL in epoetin alfa-treated patients. Thus, roxadustat was shown to be non-inferior to epoetin alfa, followed by demonstration of superiority (P=0.0005). In addition, patients treated with roxadustat required lower

average monthly IV iron use than those treated with epoetin alfa (P=0.00028). The most common adverse events were HTN, diarrhea, and muscle spasms.

Place in Therapy: It is estimated that there are currently 37 million individuals in the United States with CKD. Anemia is common among these patients and is associated with additional complications such as arrhythmias, heart failure, and hospitalizations leading to a decreased quality of life. Anemia of CKD is treated with iron, vitamin B12, and folic acid supplementation, as well as with erythropoietin stimulating agents [ESAs; epoetin alfa (Epoetin®, Procrit®), darbepoetin alfa (Aranesp®)] and blood transfusions. Roxadustat is a first-in-class oral inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase (PH). Roxadustat increases Hb levels by activating the body's natural protective response to reduce oxygen levels in the blood, which is different from ESAs.

Projected FDA Decision: December 23, 2020

SoonerCare Impact: During fiscal year 2020, there were 22 members that had paid pharmacy claims for ESAs. This accounted for 252 claims totaling $69,902.02 in drug spending with an average cost per claim of $277.39. Additionally, there were 48 members that had paid medical claims for ESAs during fiscal year 2020. This accounted for 229 claims totaling $107,747.97 in drug spending with an average cost per claim of $470.52.

Pipeline Table[5,6]

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
Tramadol	Avenue Therapeutics	Pain	IV	NDA	10-2020
Trastuzumab/ pertuzumab	Roche	Breast Cancer	SC	BLA	10-2020
Zolmitriptan	Zosano	Acute Migraines	TOP	NDA	10-2020
Eflapegrastim	Spectrum/Hanmi	Neutropenia	SC	BLA	10-2020
REGN-EB3	Regeneron	Ebola	IV	BLA; Orphan	10-2020
Loteprednol etabonate	Kala Pharmaceuticals	Dry Eyes	OP	NDA	11-2020
Olanzapine/ samidorphan	Alkermes	Schizophrenia/ Bipolar Disorder	PO	NDA	11-2020
Viloxazine hydrochloride (SPN-812)	Supernus Pharmaceuticals	ADHD	PO	NDA	11-2020
Lisocabtagene maraleucel	Bristol-Myers Squibb/Celgene	DLBCL	IV	BLA; Orphan	11-2020

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
Lonafarnib	Eiger Biopharmaceuticals	HGPS or Progeria and Progeroid Laminopathies	PO	NDA; Orphan	11-2020
Treprostinil	Liquidia Technologies	PAH	INH	NDA	11-2020
Idecabtagene vicluecel	Bristol-Myers Squibb/Bluebird Bio	Multiple Myeloma	IV	BLA; Orphan	11-2020
Setmelanotide	Rhythm Pharmaceuticals	Rare Genetic Disorders of Obesity	SC	NDA; Orphan	11-2020
Naxitamab	Y-mAbs Therapeutics	Neuroblastoma	IV	BLA; Orphan	11-2020
Nifurtimox	Bayer	Chagas Disease	PO	NDA; Orphan	11-2020
Margetuximab	MacroGenics	Breast Cancer	IV	BLA	12-2020
Pralsetinib	Blueprint Medicines	NSCLC	PO	NDA; Orphan	12-2020
Berotralstat	BioCryst	HAE	PO	NDA; Orphan	12-2020
Lumasiran	Alnylam	Hyperoxaluria	IN	NDA; Orphan	12-2020
Roxadustat	Fibrogen/ AstraZeneca	Anemia	PO	NDA	12-2020
Vibegron	Urovant Sciences	Overactive Bladder	PO	NDA	12-2020
Ansofaxine	Luye Pharma	MDD	PO	NDA	12-2020
Tirbanibulin	Athenex	Actinic Keratosis	TOP	NDA	12-2020
Inclisiran	The Medicines Company/Novartis	Hyperlipidemia	SC	NDA; Orphan	12-2020
Tanezumab	Pfizer/Eli Lilly	Osteoarthritis	SC	BLA	12-2020
Omburtamab	Y-mAbs Therapeutics	Brain Cancer	--	Orphan	4Q-2020
Umbralisib	TG Therapeutics	Marginal Zone Lymphoma/ Follicular Lymphoma	PO	Fst trk; Brk thru; Orphan	4Q-2020
Sutimlimab	Sanofi	Cold Agglutinin Disease	IV	BLA	4Q-2020
Narsoplimab	Omeros	HSCT-Associated Thrombotic Micro-angiopathy	IV/SC	Orphan	Late-2020
Buprenorphine	Camurus/ Braeburn	OUD/Pain	SC	Tentative approval	Late-2020

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
Fosdenopterin	BridgeBio Pharma/Origin Biosciences	Molybdenum Cofactor Deficiency	IV	Orphan	Late-2020
Dostarlimab	GlaxoSmithKline	Endometrial Cancer	IV	BLA	01-2021
D-threo-methylphenidate controlled-release	KemPharm	ADHD	PO	NDA	03-2021
Ponesimod	Johnson & Johnson	MS	PO	NDA	03-2021
Dasiglucagon	Zealand Pharma	DM	SC	NDA; Orphan	03-2021
Tivozanib	AVEO Oncology	Renal Cell Cancer	PO	NDA	03-2021
AGIL-AADC (gene therapy)	PTC Therapeutics	Aromatic L-Amino Acid Decarboxylase Deficiency	Intra-cerebral	Orphan	1Q-2021
Leronlimab	CytoDyn	HIV; GVHD	SC	Orphan	1Q-2021
Estetrol/drospirenone	Mayne Pharma/Mithra Pharmaceuticals	Pregnancy Prevention	PO	NDA	04-2021
Melphalan-flufenamide	Oncopeptides AB	Multiple Myeloma	IV	Orphan	2Q-2021
Veliparib	AbbVie	Ovarian Cancer; Breast Cancer	PO	Orphan	2Q-2021
Arimoclomol	Orphazyme	Niemann-Pick Disease	PO	Orphan	1H-2021
Paclitaxel	Oasmia	Ovarian Cancer	IV	Orphan	1H-2021
Casimersen	Sarepta	DMD	IV	Orphan	1H-2021
Ropeginterferon alfa-2b	PharmaEssentia/ AOP Orphan	Polycythemia Vera	SC	Orphan	1H-2021
Budesonide	Calliditas/Kyowa Hakko Kirin	Nephropathy	PO	Orphan	1H-2021

NDA = New Drug Application; BLA = Biologic License Application; Fst trk = fast track; Brk thru = breakthrough; Admin = administration; SC = subcutaneous; PO = oral; TOP = topical; IV = intravenous; IN = intranasal; INH = inhaled; OP = opthalmic; 1Q = 1st quarter; 2Q = 2nd quarter; 4Q = 4th quarter; 1H = 1st half; HIV = human immunodeficiency virus; ADHD = attention-deficit hyperactivity disorder; DLBCL = diffuse large B-cell lymphoma; HGPS = Hutchinson-Gilford Progeria Syndrome; PAH = pulmonary hypertension; HAE = hereditary angioedema; NSCLC = non-small cell lung cancer; MDD = major depressive disorder; HSCT = hematopoietic stem cell transplantation; OUD = opioid-use disorder; MS = multiple sclerosis; DM = diabetes mellitus; GVHD = graft-versus-host disease; DMD = Duchenne musculary dystrophy
*Most biosimilars and oncology medications are excluded from the table. Medications known to have received a Complete Response Letter (CRL) from the FDA that have not resubmitted were also excluded.

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Appendix C

Vote to Prior Authorize Adakveo® (Crizanlizumab-tmca), Oxbryta® (Voxelotor), and Reblozyl® (Luspatercept-aamt)

Oklahoma Health Care Authority
October 2020

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

- **Sickle cell disease (SCD)** is an inherited blood disorder in which the red blood cells (RBCs) are abnormally shaped in a crescent or "sickle" shape, which restricts the flow in blood vessels and limits oxygen delivery to the body's tissues, leading to severe pain and organ damage. It is also characterized by severe chronic inflammation that results in vaso-occlusive crises (VOCs) where patients experience episodes of extreme pain and organ damage. According to the Centers for Disease Control and Prevention (CDC), SCD affects approximately 100,000 Americans. The disease occurs most often in African-Americans, where 1 out of every 365 babies born have the disease.
- **Beta thalassemia**, also known as Cooley's anemia, is an inherited blood disorder that reduces the production of hemoglobin (Hb). In patients with beta thalassemia, low levels of Hb lead to a lack of oxygen in many parts of the body and lead to anemia, which can cause pale skin, weakness, fatigue, and more serious complications. Supportive treatment for patients with beta thalassemia often consists of lifelong regimens of chronic blood transfusions for survival and treatment for iron overload due to the transfusions. Patients with beta thalassemia are also at an increased risk of developing abnormal blood clots.
- **Myelodysplastic syndromes (MDS)** are a group of closely related blood cancers characterized by ineffective production of healthy RBCs, white blood cells, and platelets, which can lead to anemia and frequent or severe infections. People with MDS who develop anemia often require regular blood transfusions to increase the number of healthy RBCs in circulation. Frequent transfusions are associated with an increased risk of iron overload, transfusion reactions, and infections.

New U.S. Food and Drug Administration (FDA) Approval(s)[6,7,8,9,10,11,12,13,14,15]

- **Adakveo® (crizanlizumab-tmca)** was FDA approved in November 2019 to reduce the frequency of VOCs in adults and in pediatric patients 16 years of age and older with SCD. Crizanlizumab is a first-in-class monoclonal antibody that binds to P-selectin, a cell adhesion protein that plays a central role in the multicellular interactions that can lead to

vaso-occlusion in SCD. Adakveo® is supplied as an injection solution in a 100mg/10mL single-dose vial (SDV) and is given via intravenous (IV) infusion by a health care professional as 5mg/kg based on actual body weight over a period of 30 minutes at week 0, week 2, and every 4 weeks thereafter. The efficacy of crizanlizumab was established in SUSTAIN, a 52-week randomized, placebo-controlled, double-blind study in 198 patients with SCD. Patients with any genotype of SCD and a history of 2 to 10 VOCs in the previous 12 months were eligible for the study. Patients who received crizanlizumab 5mg/kg had a lower median annual rate of VOCs vs. patients who received placebo (1.63 vs. 2.98; P=0.010). A total of 36% of patients treated with crizanlizumab 5mg/kg did not experience a VOC vs. 17% of placebo-treated patients during the study period. The median time to first VOC from randomization was 4.1 months in the crizanlizumab 5mg/kg arm vs. 1.4 months in the placebo arm. Reduction of sickle cell-related pain crises was demonstrated in patients on the 5mg/kg dose irrespective of hydroxyurea use or genotype. The efficacy of crizanlizumab beyond 52 weeks has not been studied. The estimated annual cost of Adakveo® based on a 5mg/kg/dose for a 60kg patient, dosed at week 0, week 2, and every 4 weeks thereafter (14 doses in the first year), is $98,998.20.

- **Oxbryta® (voxelotor)** was granted accelerated approval by the FDA in November 2019 for the treatment of SCD in adults and in pediatric patients 12 years of age and older. Voxelotor is an oral, once-daily therapy for patients with SCD and is an HbS polymerization inhibitor that works by increasing Hb's affinity for oxygen. Oxbryta® is supplied as a 500mg oral tablet and the recommended regimen is 1,500mg [(3) 500mg tablets] orally once daily with or without food. The efficacy of voxelotor was established in the HOPE study, a randomized, double-blind, placebo-controlled study in 274 patients with SCD. Patients between 12 and 65 years of age were included in the study if they had confirmed SCD (HbSS, HbSC, HbS/β+-thalassemia, and other genotypic variants of SCD), had 1 to 10 VOC(s) within 12 months prior to enrollment, and baseline Hb ≥5.5 to ≤10.5g/dL. Efficacy was based on Hb response rate defined as a Hb increase of >1.0g/dL from baseline to week 24 in patients treated with voxelotor 1,500mg vs. placebo. The response rate for voxelotor 1,500mg was 51.1% (46/90) vs. 6.5% (6/92) in the placebo group (P<0.001). The annualized adjusted incidence rate of vaso-occlusive events (the number of crises per person-year) was measured as a secondary endpoint and was 2.77 in the voxelotor 1,500mg group and 3.19 in the placebo group. There was no statistically significant difference in the annualized rate of vaso-occlusive events found between either dose of voxelotor and placebo. Oxbryta® was approved by the FDA through an accelerated approval process based on increase in Hb, and post-marketing studies to evaluate additional

evidence of clinical benefit are required by the FDA. A post-approval confirmatory efficacy study, HOPE-KIDS-2, is also ongoing in pediatric patients 2 to 15 years of age with SCD and is measuring the mean change in transcranial doppler (TCD) flow velocity to evaluate reduction in stroke risk as the primary endpoint. The annual cost of Oxbryta® based on the recommended dose of 1,500mg once daily is $124,999.20.

- **Reblozyl® (luspatercept-aamt)** is an erythroid maturation agent supplied as a lyophilized powder for reconstitution in 2 strengths: 25mg and 75mg SDVs. Luspatercept should be reconstituted and administered by a health care professional. Prior to each dose of luspatercept, the patient's Hb and transfusion record should be assessed and reviewed. The recommended starting dose of luspatercept is 1mg/kg once every 3 weeks by subcutaneous (sub-Q) injection. The luspatercept dose should be titrated based on response according to the Reblozyl® *Prescribing Information*. The dose should not be increased more frequently than every 6 weeks and should be discontinued if the patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level or if unacceptable toxicity occurs at any time. Luspatercept is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. The annual cost of Reblozyl® based on the starting dose of 1mg/kg every 3 weeks for a 75kg patient is $175,500.01.
    - **Beta Thalassemia:** In November 2019, the FDA approved Reblozyl® (luspatercept-aamt) for the treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions. Specific to the dose titration for beta thalassemia, if a patient does not achieve a reduction in RBC transfusion burden after 2 consecutive doses (6 weeks) at the 1mg/kg starting dose, the luspatercept dose may be increased to 1.25mg/kg. The dose should not be increased beyond the maximum dose of 1.25mg/kg. The efficacy of luspatercept was established in the BELIEVE study, a randomized, double-blind, placebo-controlled study in 336 patients with beta thalassemia requiring RBC transfusions (6 to 24 RBC units per 24 weeks) with no transfusion-free period >35 days. The BELIEVE study excluded patients with a diagnosis of HbS/β-thalassemia or isolated alpha (α)-thalassemia (e.g., HbH) or who had major organ damage (liver disease, heart disease, lung disease, or renal insufficiency). Patients with recent deep vein thrombosis (DVT), stroke, or recent use of erythropoiesis stimulating agent (ESA), immunosuppressant, or hydroxyurea therapy were also excluded. The primary endpoint was the proportion of patients achieving RBC transfusion burden reduction (≥33% reduction from baseline) with a reduction of at least 2 RBC units from week 13 to

week 24. In the luspatercept arm, 21.4% of patients met the primary endpoint during weeks 13 to 24 vs. 4.5% in the placebo arm [risk difference: 17.0; 95% confidence interval (CI): 10.4, 23.6; P<0.0001].

- **MDS:** In April 2020, the FDA approved Reblozyl® for a second indication, for the treatment of anemia failing an ESA and requiring ≥2 RBC units over 8 weeks in adult patients with very low-to-intermediate risk MDS with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T). Specific to the dose titration for MDS, if the patient is not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1mg/kg starting dose, the luspatercept dose may be increased to 1.33mg/kg. If the patient is still not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1.33mg/kg dose level, the luspatercept dose may be increased to 1.75mg/kg. The dose should not be increased more frequently than every 6 weeks (2 doses) or beyond the maximum dose of 1.75mg/kg. The efficacy of luspatercept for MDS was established in the MEDALIST study, a randomized, double-blind, placebo-controlled study in 229 patients with International Prognostic Scoring System-Revised (IPSS-R) of very low, low, or intermediate-risk MDS-RS and who require RBC transfusions (≥2 RBC units over 8 weeks). For eligibility, patients were required to have had an inadequate response to prior treatment with an ESA, be intolerant of ESAs, or were ESA naïve and unlikely to respond due to endogenous serum erythropoietin >200U/L. The study excluded patients with deletion 5q (del 5q), white blood cell count >13Gi/L, neutrophils <0.5Gi/L, platelets <50Gi/L, or with prior use of a disease modifying agent for treatment of MDS. The primary endpoint was the proportion of patients who were RBC transfusion independent, defined as the absence of any RBC transfusion during any consecutive 8-week period occurring entirely within weeks 1 through 24, which was met in 37.9% and 13.2% of patients receiving luspatercept and placebo, respectively (common risk difference: 24.6; 95% CI: 14.5, 34.6; P<0.0001). Patients with a decrease in transfusion requirement or increase in Hb could continue on the blinded study drug thereafter until unacceptable toxicity, loss of efficacy, or disease progression. The absence of RBC transfusion during any consecutive 12-week period occurring during weeks 1 to 24 or during weeks 1 to 48 did not meet statistical significance.

Recommendations

The College of Pharmacy recommends the prior authorization of Adakveo® (crizanlizumab-tmca), Oxbryta® (voxelotor), and Reblozyl® (luspatercept-aamt) with the following criteria:

Adakveo® (Crizanlizumab-tmca) Approval Criteria:

1. An FDA approved indication to reduce the frequency of vaso-occlusive crises (VOCs) in adult members and in pediatric members 16 years of age and older with sickle cell disease (SCD); and
2. Member must have a history of VOCs; and
3. Adakveo® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
4. Prescriber must verify Adakveo® will be administered by a trained health care provider. The prior authorization request must indicate how Adakveo® will be administered; and
    a. Adakveo® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Adakveo® must be shipped via cold chain supply to the member's home and administered by a home health provider, and the member or member's caregiver must be trained on the proper storage of Adakveo®; and
5. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
6. Approval quantities will be dependent on the member's weight and will include loading doses at week 0 and 2, then subsequent doses every 4 weeks in accordance with package labeling; and
7. Initial approvals will be for the duration of 3 months. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Oxbryta® (Voxelotor) Approval Criteria:

1. An FDA approved indication for the treatment of sickle cell disease (SCD) in members 12 years of age and older; and
2. Member must have a history of vaso-occlusive crises (VOCs); and
3. Member must have baseline hemoglobin ≥5.5 to ≤10.5g/dL; and
4. Oxbryta® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. The member must not be taking concomitant strong CYP3A4 inhibitors (e.g., fluconazole, ketoconazole) or the prescriber must verify the dose

of Oxbryta® will be reduced during concomitant use according to package labeling; and
6. Prescriber must verify that the dose of Oxbryta® will be reduced in accordance with package labeling for members with severe hepatic impairment; and
7. The member must not be taking concomitant strong or moderate CYP3A4 inducers (e.g., rifampin) or the prescriber must verify the dose of Oxbryta® will be adjusted during concomitant use according to package labeling; and
8. A quantity limit of 3 tablets per day will apply; and
9. Initial approvals will be for the duration of 6 months. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Reblozyl® (Luspatercept-aamt) Approval Criteria [Beta Thalassemia Diagnosis]:

1. An FDA approved indication for the treatment of adult members with beta thalassemia who require regular red blood cell (RBC) transfusions; and
2. Member must require regular RBC transfusions (no transfusion-free period >35 days during the prior 6 month period); and
3. Reblozyl® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of beta thalassemia (or an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating beta thalassemia); and
4. The prescriber must verify the member's hemoglobin will be monitored prior to each Reblozyl® administration; and
5. Prescriber must verify Reblozyl® will be administered by a trained health care provider; and
6. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
7. Approval quantities will be dependent on member weight and every 3 week dosing in accordance with package labeling; and
8. Initial approvals will be for the duration of 4 months. Further approvals will not be granted if the member does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose of 1.25mg/kg (allows for initial dosing of 6 weeks at 1mg/kg). Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

Reblozyl® (Luspatercept-aamt) Approval Criteria [Myelodysplastic Syndromes (MDS) Diagnosis]:

1. An FDA approved indication for the treatment of adult members with very low-to-intermediate risk MDS with ring sideroblasts (MDS-RS) or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) with anemia failing an erythropoiesis stimulating agent (ESA) and requiring ≥2 red blood cell (RBC) units over 8 weeks; and
2. Member must have had an inadequate response to prior treatment with an ESA, be intolerant of ESAs, or have a serum erythropoietin level >200U/L; and
3. Member must not have been previously treated with a disease modifying agent for the treatment of MDS; and
4. Prescriber must verify the member does not have deletion 5q (del 5q); and
5. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber and in accordance with package labeling; and
6. Reblozyl® must be prescribed by, or in consultation with, a hematologist, oncologist, or a specialist with expertise in treatment of MDS (or an advanced care practitioner with a supervising physician who is a hematologist, oncologist, or specialist with expertise in treating MDS); and
7. The prescriber must verify the member's hemoglobin will be monitored prior to each Reblozyl® administration; and
8. Prescriber must verify Reblozyl® will be administered by a trained health care provider; and
9. A recent (within the last 3 months) weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
10. Approval quantities will be dependent on member weight and every 3 week dosing in accordance with package labeling; and
11. Initial approvals will be for the duration of 6 months. Further approvals will not be granted if the member does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose of 1.75mg/kg or if unacceptable toxicity occurs at any time. Subsequent approvals will be for 1 year if the prescriber documents the member is responding well to treatment.

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Appendix D

Vote to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/ Trastuzumab/Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib)

Oklahoma Health Care Authority
October 2020

New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)[1,2,3,4]

- **May 2019:** The FDA approved Herzuma® (trastuzumab-pkrb), a biosimilar to Herceptin® (trastuzumab), in combination with cisplatin and capecitabine or 5-fluorouracil for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease, and for adjuvant treatment of HER2-positive and node positive or node negative [estrogen receptor (ER)/progesterone receptor (PR) negative or with 1 high risk feature] breast cancer as a single-agent following multi-modality anthracycline based therapy. With these approvals, Herzuma® now has all of the same indications as Herceptin®.
- **December 2019:** A poster session presented at the San Antonio Breast Cancer Symposium provided information to support the use of pertuzumab and trastuzumab in combination with paclitaxel for HER2-positive metastatic breast cancer (MBC). Most clinical studies investigating the efficacy and safety of pertuzumab and trastuzumab used docetaxel as the taxane. A retrospective cohort study, using the nationwide Flatiron Health Electronic Health Record (EHR)-derived de-identified database, was conducted and the findings determined that paclitaxel used with pertuzumab and trastuzumab is highly active and well tolerated and may be an effective alternative to docetaxel-based combination therapy. These findings are consistent with a Phase 3b study (PERUSE) that was designed to assess the safety and efficacy of investigator-selected taxane with pertuzumab and trastuzumab in HER2-positive MBC. Preliminary findings suggested that paclitaxel appeared to be a valid alternative to docetaxel, offering similar progression-free survival and overall response rate with a predictable safety profile.
- **December 2019:** The FDA granted accelerated approval to Enhertu® (fam-trastuzumab deruxtecan-nxki) for the treatment of patients with

unresectable or HER2-positive MBC who have received ≥2 prior anti-HER2-based regimens in the metastatic setting.

- **December 2019:** The FDA approved Lynparza® (olaparib) for the maintenance treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*) metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.
- **February 2020:** The FDA approved Nerlynx® (neratinib) in combination with capecitabine for the treatment of adult patients with advanced or HER2-positive MBC who have received ≥2 prior anti-HER2-based regimens in the metastatic setting.
- **April 2020:** The FDA approved Tukysa™ (tucatinib) in combination with trastuzumab and capecitabine, for the treatment of adult patients with advanced unresectable or HER2-positive MBC, including patients with brain metastases, who have received ≥1 prior anti-HER2-based regimen(s) in the metastatic setting.
- **April 2020:** The FDA approved Trodelvy™ (sacituzumab govitecan-hziy) for the treatment of adult patients with triple-negative MBC who received ≥2 prior therapies for metastatic disease.
- **May 2020:** The FDA approved an expanded indication for Lynparza® (olaparib) to include its use in combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either a deleterious or suspected deleterious BRCA mutation and/or genomic instability.
- **May 2020:** The FDA approved Tecentriq® (atezolizumab) for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high programmed death ligand-1 (PD-L1) expression [PD-L1 stained ≥50% of tumor cells (TC ≥50%) or PD-L1 stained tumor-infiltrating immune cells (IC) covering ≥10% of the tumor area (IC≥10%)], with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
- **May 2020⁺:** The FDA approved Lynparza® (olaparib) for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone.
- **May 2020:** The FDA approved Tecentriq® (atezolizumab) in combination with bevacizumab for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

- **June 2020:** The FDA approved Phesgo™, a new fixed-dose combination of pertuzumab, trastuzumab, and hyaluronidase–zzxf, for the treatment of HER2-positive breast cancer.

[+] The recommendations for Lynparza® for the indication of mCRPC will be provided in the Prostate Cancer Medications vote report [Vote to Prior Authorize Rubraca® (Rucaparib)], which is also being presented at the October 2020 Drug Utilization Review (DUR) Board meeting.

Product Summaries[5,6,7,8]

Enhertu® (Fam-Trastuzumab Deruxtecan-nxki):

- **Therapeutic Class:** HER2-directed antibody and topoisomerase inhibitor conjugate
- **Indication(s):** Treatment of adult patients with unresectable or HER2-positive MBC who have received ≥2 prior anti-HER2-based regimens in the metastatic setting
- **How Supplied:** 100mg lyophilized powder for reconstitution in single-dose vials (SDVs)
- **Dose:** 5.4mg/kg given as an intravenous (IV) infusion once every 3 weeks (21-day cycle)
- **Cost:** Wholesale Acquisition Cost (WAC) of $2,295.97 per vial; cost will vary due to weight-based dosing

Phesgo™ (Pertuzumab/Trastuzumab/Hyaluronidase-zzxf):

- **Therapeutic Class:** Combination of HER2/neu receptor antagonists (pertuzumab and trastuzumab) and an endoglycosidase (hyaluronidase)
- **Indication(s):**
  - In combination with chemotherapy:
    - Neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer
    - Adjuvant treatment of patients with HER2-positive early stage breast cancer at high risk of recurrence
  - In combination with docetaxel:
    - Treatment of HER2-positive MBC in patients who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease
- **How Supplied:**
  - 1,200mg pertuzumab/600mg trastuzumab/30,000 units hyaluronidase/15mL (80mg/40mg/2,000 units/mL) solution in SDVs
  - 600mg pertuzumab/600mg trastuzumab/20,000 units hyaluronidase/10mL (60mg/60mg/2,000 units/mL) solution in SDVs
- **Dose:** Phesgo™ has different dosage and administration instructions than IV pertuzumab and trastuzumab products:

- Initial dose: 1,200mg/600mg/30,000 units administered subcutaneously (sub-Q)
- Maintenance dose: After the initial dose, 600mg/600mg/20,000 units administered sub-Q every 3 weeks
    - Neoadjuvant: Every 3 weeks with chemotherapy by IV infusion preoperatively for 3 to 6 cycles
    - Adjuvant: Every 3 weeks with chemotherapy by IV infusion postoperatively for a total of 1 year (up to 18 cycles)
    - MBC: Every 3 weeks with docetaxel by IV infusion every 3 weeks until disease progression or unmanageable toxicity

- **Cost:** WAC of $12,706.95 per 1,200mg/600mg/30,000 units/15mL vial; WAC of $8,471.00 per 600mg/600mg/20,000 units/10mL vial; cost will vary based on indication

Trodelvy™ (Sacituzumab Govitecan-hziy):

- **Therapeutic Class:** Trophoblast cell-surface antigen-2 (TROP-2)-directed antibody and topoisomerase inhibitor conjugate
- **Indication(s):** Treatment of adult patients with triple-negative MBC who have received ≥2 prior therapies for metastatic disease
- **How Supplied:** 180mg lyophilized powder for reconstitution in SDVs
- **Dose:** 10mg/kg once weekly via IV infusion on days 1 and 8 of continuous 21-day treatment cycles
- **Cost:** WAC of $2,012.50 per vial; cost will vary due to weight-based dosing

Tukysa™ (Tucatinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Use in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or HER2-positive MBC, including patients with brain metastases
- **How Supplied:** 50mg and 150mg oral tablets
- **Dose:** 300mg [(2) 150mg tablets] taken orally twice daily; 50mg strength available for dose reductions/modifications
- **Cost:** WAC of $76.67 per 50mg tablet and $154.17 per 150mg tablet, resulting in a cost per 30 days of $18,500.40 based on the recommended dosing of 300mg [(2) 150mg tablets] twice daily

Recommendations

- The prior authorization of Enhertu® (fam-trastuzumab deruxtecan-nxki), Phesgo™ (pertuzumab/trastuzumab/hyaluronidase-zzxf), Trodelvy™ (sacituzumab govitecan-hziy), and Tukysa™ (tucatinib) with the following criteria listed in red:

Enhertu® (Fam-Trastuzumab Deruxtecan-nxki) Approval Criteria [Breast Cancer Diagnosis]:

1. Adult members with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
2. Member has received ≥2 prior anti-HER2-based regimens in the metastatic setting.

Phesgo™ (Pertuzumab/Trastuzumab/Hyaluronidase-zzxf) Approval Criteria [Breast Cancer Diagnosis]:

1. Human epidermal growth factor receptor 2 (HER2)-positive disease; and
2. Used in 1 of the following settings:
   a. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer; or
   b. Adjuvant treatment of members with early stage breast cancer; or
   c. In combination with docetaxel for members with metastatic disease.

Trodelvy™ (Sacituzumab Govitecan-hziy) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of triple-negative breast cancer; and
2. Metastatic disease; and
3. Member must have received ≥2 therapies for metastatic disease.

Tukysa™ (Tucatinib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced unresectable or metastatic breast cancer; and
2. Used in combination with trastuzumab and capecitabine; and
3. Disease is human epidermal growth factor receptor 2 (HER2)-positive; and
4. Following progression of ≥1 prior anti-HER2 regimen(s) in the metastatic setting.

- Update the current Herzuma® (trastuzumab-pkrb), Lynparza® (olaparib), Nerlynx® (neratinib), Perjeta® (pertuzumab), and Tecentriq® (atezolizumab) prior authorization criteria based on new FDA approved indications (changes noted in red in the following approval criteria; only criteria with changes are listed):

Herzuma® (Trastuzumab-pkrb), 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 growth factor receptor 2 (HER2)-positive metastatic gastric or gastroesophageal junction adenocarcinoma; and

2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab) must be provided.

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

1. Diagnosis of metastatic breast cancer; and
2. Member must have shown progression on previous chemotherapy in any setting; and
~~3. Human epidermal growth factor receptor 2 (HER2) negative; and~~
4. Positive test for a germline BRCA-mutation (*gBRCAm*); and
5. Members with hormone receptor (HR) positive disease must have failed prior endocrine therapy or are not considered to be a candidate for endocrine therapy.

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

1. Diagnosis of metastatic pancreatic adenocarcinoma with known germline BRCA1/BRCA2 mutation; and
2. Maintenance therapy as a single-agent; and
3. In members who have not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

Lynparza® (Olaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), advanced disease; and
    b. Previous treatment with ≥~~3~~ 2 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 Disease:**
    a. ~~Member~~ Disease must be in a complete or partial response to ~~first-line platinum-based~~ primary chemotherapy; and
        i. Used as a single-agent in members with a diagnosis of deleterious or suspected deleterious *gBRCAm* or somatic BRCA-mutated (*sBRCAm*), advanced ovarian cancer; or
        ii. Used in combination with bevacizumab following a primary therapy regimen that included bevacizumab; 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.

Nerlynx® (Neratinib) Approval Criteria [Recurrent or Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic breast cancer; and

2. Member must have human epidermal growth factor receptor 2 (HER2)-positive breast cancer; and
3. Used in combination with capecitabine; or
4. Used in combination with capecitabine or paclitaxel if brain metastases are present.

Tecentriq® (Atezolizumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Diagnosis of metastatic disease; and
2. Used in combination with bevacizumab; and
3. Member has not received prior systemic therapy.

Tecentriq® (Atezolizumab) Approval Criteria [Melanoma Diagnosis]:

1. Unresectable or metastatic disease; and
2. BRAF V600 mutation-positive; and
3. In combination with cobimetinib and vemurafenib.

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

1. **Diagnosis of Non-Squamous Non-Small Cell Lung Cancer (NSCLC):**
    a. First-line therapy for metastatic disease; and
    b. The member does not have epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF, MET exon 14 skipping, or RET mutations; and
    c. Used in combination with bevacizumab, paclitaxel, and carboplatin (maximum of 6 cycles) or in combination with paclitaxel (protein bound) and carboplatin; and
    d. Atezolizumab and bevacizumab may be continued after the above combination in members without disease progression (applies to the bevacizumab/paclitaxel/carboplatin regimen); or
2. **Diagnosis of NSCLC:**
    a. For first-line therapy for metastatic disease:
        i. Used as a single-agent; and
        ii. The member does not have EGFR, ALK, ROS1, BRAF, MET exon 14 skipping, or RET mutations; and
        iii. High programmed death ligand-1 (PD-L1) expression determined by 1 of the following:
            1. PD-L1 stained ≥50% of tumor cells (TC≥50%); or
            2. PD-L1 stained tumor-infiltrating immune cells (IC) covering ≥10% of the tumor area (IC≥10%); or
    b. For subsequent therapy for metastatic disease:
        i. Used as a single-agent only.

Perjeta® (Pertuzumab) Approval Criteria [Breast Cancer Diagnosis]:

1. Human epidermal growth factor receptor 2 (HER2)-positive; and

2. Used in 1 of the following settings:
    a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
        i. Used in combination with trastuzumab and docetaxel; or
    b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):
        i. Used in combination with trastuzumab and docetaxel or paclitaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel or paclitaxel); or
    c. Adjuvant systemic therapy for members with node positive, HER2-positive tumors or members with high-risk node negative tumors [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or younger than 35 years of age]:
        i. Used in combination with trastuzumab and paclitaxel following doxorubicin/cyclophosphamide (AC); or
        ii. Used in combination with trastuzumab and docetaxel following AC; or
        iii. Used in combination with docetaxel/carboplatin/trastuzumab (TCH).

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Appendix E

Vote to Prior Authorize Rubraca® (Rucaparib)

Oklahoma Health Care Authority
October 2020

New U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)[1]

- **December 2019:** The FDA approved Xtandi® (enzalutamide) for the treatment of patients with metastatic, castration-sensitive prostate cancer (mCSPC). Xtandi® was previously approved by the FDA for the treatment of patients with castration-resistant prostate cancer (CRPC).
- **May 2020[+]:** The FDA approved Lynparza® (olaparib) for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic CRPC (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone.
- **May 2020:** The FDA granted accelerated approval to Rubraca® (rucaparib) for the treatment of patients with deleterious BRCA mutation (germline and/or somatic)-mCRPC who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy.

[+] Other new indications for Lynparza® (olaparib) and the accompanying recommendations are included in the Breast Cancer Medications vote report [Vote to Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/Trastuzumab/ Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib)], which is also being presented at the October 2020 Drug Utilization Review (DUR) Board meeting.

Rubraca® (Rucaparib) Product Summary[2]

Rubraca® (Rucaparib):

- **Therapeutic Class:** Poly [adenosine diphosphate (ADP)-ribose] polymerase (PARP) inhibitor
- **Indication(s):**
  - Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
  - Treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with ≥2 chemotherapies

    - Treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated mCRPC who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy
- **How Supplied:** 200mg, 250mg, and 300mg oral tablets
- **Dose:** 600mg orally twice daily
    - For treatment of mCRPC, patients should also receive concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or should have undergone a bilateral orchiectomy
- **Cost:** The Wholesale Acquisition Cost (WAC) is $139.18 per tablet, regardless of strength, resulting in a monthly cost of $16,701.60 at the recommended dosing of 600mg [(2) 300mg tablets] twice daily

Recommendations

- The prior authorization of Rubraca® (rucaparib) with the following criteria listed in red:

Rubraca® (Rucaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of recurrent or refractory disease; and
    b. Previous treatment with ≥2 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
    c. Disease is associated with a deleterious or suspected deleterious BRCA mutation; and
    d. Used as a single-agent; or
2. **Maintenance Treatment of Advanced Disease:**
    a. Diagnosis of advanced or recurrent disease; and
    b. Disease must be in a complete or partial response to platinum-based chemotherapy; and
    c. Used as a single-agent.

Rubraca® (Rucaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Member must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
    a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in BRCA1 or BRCA2.

- Update the current Lynparza® (olaparib) and Xtandi® (enzalutamide) prior authorization criteria based on new FDA approved indications

(changes noted in red in the following approval criteria; only criteria with changes are listed):

Lynparza® (Olaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Members must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
    a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in a homologous recombination gene.

Xtandi® (Enzalutamide) Approval Criteria [Castration-Sensitive Prostate Cancer (CSPC) Diagnosis]:

1. Diagnosis of metastatic CSPC.

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[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 09/15/2020. Last accessed 09/15/2020.

[2] Rubraca® Prescribing Information. Clovis Oncology, Inc. Available online at: https://clovisoncology.com/pdfs/RubracaUSPI.pdf. Last revised 05/2020. Last accessed 09/15/2020.

Appendix F

Fiscal Year 2020 Annual Review of Ovarian Cancer Medications and 30-Day Notice to Prior Authorize Zejula® (Niraparib)

Oklahoma Health Care Authority
October 2020

Introduction[1,2]

According to the National Cancer Institute, in 2020, there will be an estimated 21,750 new cases of ovarian cancer, with an estimated 13,940 deaths attributed to the disease.[1] Ovarian malignancies consist of multiple histopathologic forms. The most common of these is epithelial ovarian cancer which accounts for ~90% of all ovarian neoplasms. The remaining 10% of ovarian cancer cases are comprised of germ cell, sex-cord stromal, carcinosarcomas, clear-cell, mucinous, and serous tumors. To date, there are no effective large-scale population-based screening options to detect early ovarian cancers. Most ovarian neoplasms are diagnosed in later stages making the disease more difficult to cure. Current 5-year overall survival is about 46.5% with only 40% of women ever obtaining cure. There are several different types of treatments available for patients with ovarian cancer, including surgery, radiation, hormone therapy, monoclonal antibodies, targeted therapy, and immunotherapy. However, traditional chemotherapy, especially platinum and taxane oncolytics, remain the backbone of both adjuvant and metastatic treatment regimens. Anti-angiogenesis agents such as bevacizumab also play a large role in the treatment of these cancers. Newer targeted agents, including poly [adenosine diphosphate (ADP)-ribose] polymerase (PARP) inhibitors, and immunotherapy have recently become therapeutic options in upfront, relapsed/refractory, and maintenance settings.[2]

Use of evidence-based expert consensus guidelines is imperative in the treatment of cancers. The National Comprehensive Cancer Network (NCCN) Compendium contains authoritative, scientifically derived information designed to support decision making about the appropriate use of drugs and biologics in patients with cancer. These evidence-based guidelines should be used for optimal outcomes of cancer patients.[2]

Current Prior Authorization Criteria

The following prior authorization criteria are current pending a vote by the Drug Utilization Review (DUR) Board at the October 2020 DUR Board meeting; please refer to the Breast Cancer Medications vote report [Vote to

Prior Authorize Enhertu® (Fam-Trastuzumab Deruxtecan-nxki), Phesgo™ (Pertuzumab/Trastuzumab/ Hyaluronidase-zzxf), Trodelvy™ (Sacituzumab Govitecan-hziy), and Tukysa™ (Tucatinib)] and the Prostate Cancer Medications vote report [Vote to Prior Authorize Rubraca® (Rucaparib)] in the October 2020 DUR packet for additional information.

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

1. Diagnosis of metastatic breast cancer; and
2. Member must have shown progression on previous chemotherapy in any setting; and
3. Positive test for a germline BRCA-mutation (*gBRCAm*); and
4. Members with hormone receptor (HR) positive disease must have failed prior endocrine therapy or are not considered to be a candidate for endocrine therapy.

Lynparza® (Olaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), advanced disease; and
    b. Previous treatment with ≥2 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 Disease:**
    a. Disease must be in a complete or partial response to primary chemotherapy; and
        i. Used as a single-agent in members with a diagnosis of deleterious or suspected deleterious *gBRCAm* or somatic BRCA-mutated (*sBRCAm*), advanced ovarian cancer; or
        ii. Used in combination with bevacizumab following a primary therapy regimen that included bevacizumab; or
    b. Complete or partial response to second-line or greater platinum-based chemotherapy (no mutation required); and
    c. A quantity limit based on FDA approved dosing will apply.

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

1. Diagnosis of metastatic pancreatic adenocarcinoma with known germline BRCA1/BRCA2 mutation; and
2. Maintenance therapy as a single-agent; and
3. In members who have not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

Lynparza® (Olaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Members must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
    a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in a homologous recombination gene.

Rubraca® (Rucaparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of recurrent or refractory disease; and
    b. Previous treatment with ≥2 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
    c. Disease is associated with a deleterious or suspected deleterious BRCA mutation; and
    d. Used as a single-agent; or
2. **Maintenance Treatment of Advanced Disease:**
    a. Diagnosis of advanced or recurrent disease; and
    b. Disease must be in a complete or partial response to platinum-based chemotherapy; and
    c. Used as a single-agent.

Rubraca® (Rucaparib) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. Diagnosis of metastatic CRPC; and
2. Member must have failed previous first-line therapy; and
3. Used as a single-agent except for the following:
    a. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy; and
4. Disease must be positive for a mutation in BRCA1 or BRCA2.

Utilization of Ovarian Cancer Medications: Fiscal Year 2020

The following utilization data includes medications indicated for ovarian cancer; the data does not differentiate between ovarian cancer diagnoses and other diagnoses, for which use may be appropriate.

Fiscal Year Comparison

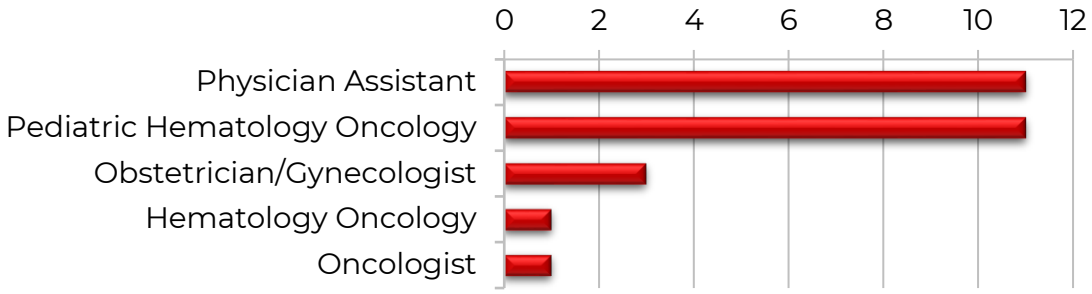
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	10	53	$450,093.52	$8,492.33	$283.08	2,670	1,590
2020	7	27	$216,334.15	$8,012.38	$267.08	1,230	810
% Change	**-30.00%**	**-49.10%**	**-51.90%**	**-5.70%**	**-5.70%**	**-53.90%**	**-49.10%**
Change	**-3**	**-26**	**-$233,759.37**	**-$479.95**	**-$16.00**	**-1,440**	**-780**

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

Demographics of Members Utilizing Ovarian Cancer Medications

- Due to the small number of members utilizing ovarian cancer medications during fiscal year 2020, detailed demographic information could not be provided.

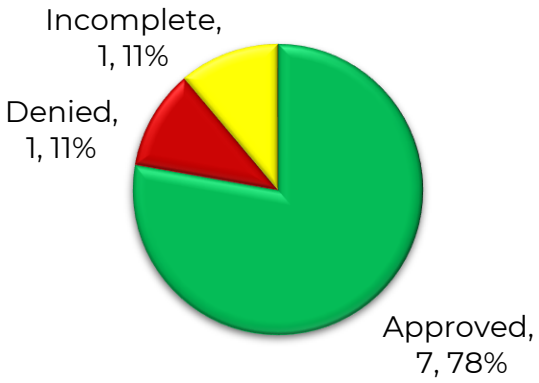
Top Prescriber Specialties of Ovarian Cancer Medications By Number of Claims



Prior Authorization of Ovarian Cancer Medications

There were 9 prior authorization requests submitted for ovarian cancer medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[2,3,4]

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

- **December 2019:** The FDA approved Lynparza® (olaparib) for the maintenance treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*) metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.
- **April 2020:** The FDA approved Zejula® (niraparib) for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy. In 2019, niraparib received FDA approval for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer treated with ≥3 prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status. Positive HRD status is defined by either a deleterious or suspected deleterious BRCA mutation or genomic instability and disease progression after response to >6 months of platinum-based chemotherapy. Niraparib was originally FDA approved in 2017 for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in a complete or partial response to platinum-based chemotherapy.
- **May 2020:** The FDA approved an expanded indication for Lynparza® (olaparib) to include its use in combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer in a complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with HRD positive status.
- **May 2020:** The FDA approved Lynparza® (olaparib) for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone.
- **May 2020:** The FDA granted accelerated approval to Rubraca® (rucaparib) for the treatment of patients with deleterious BRCA mutation (germline and/or somatic)-mCRPC who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy.

Guideline Update(s):

- The largest changes in the NCCN Ovarian Cancer Guidelines are focused on post-remission therapy (i.e., maintenance) including the role of PARP inhibitors and bevacizumab. The evidence for using post-

remission therapy is greatest in patients with advanced ovarian cancers. Data is limited for patients with stage II disease.[2]

- Another change in the guidelines involves the inclusion of several oral targeted therapies for the treatment of recurrent ovarian cancer. Entrectinib and larotrectinib have been added as options for neurotrophic receptor tyrosine kinase (*NTRK*) gene-fusion positive tumors, and trametinib is now an option for patients with low-grade serous carcinomas.

Zejula® (Niraparib) Product Summary[5]

Zejula® (Niraparib):

- **Therapeutic Class:** PARP inhibitor
- **Indication(s):**
  - Maintenance treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients in a complete or partial response to first-line platinum-based chemotherapy
  - Maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients in a complete or partial response to platinum-based chemotherapy
  - Treatment advanced ovarian, fallopian tube, or primary peritoneal cancer in patients who have been treated with ≥3 prior chemotherapy regimens and whose cancer is associated with HRD positive status
- **How Supplied:** 100mg capsules
- **Dose:**
  - First-line Maintenance Treatment of Advanced Ovarian Cancer:
    - Patients weighing <77kg (<170lbs) or a platelet count of <150,000/µL: 200mg orally once daily
    - Patients weighing ≥77kg (≥170lbs) and a platelet count of ≥150,000/µL: 300mg orally once daily
  - Maintenance Treatment of Recurrent Ovarian Cancer:
    - 300mg orally once daily
  - Treatment of Advanced Ovarian Cancer after ≥3 Chemotherapies:
    - 300mg orally once daily
- **Cost:** Wholesale Acquisition Cost (WAC) of $241.96 per 100mg capsule, resulting in a cost per 30 days of $21,776.40 based on the recommended dosing of 300mg [(3) 100mg capsules] once daily

Recommendations

- The prior authorization of Zejula® (niraparib) with the following criteria listed in red:

Zejula® (Niraparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Single-Agent Treatment of Advanced Recurrent/Refractory Disease:**
    a. Diagnosis of recurrent or refractory disease; and
    b. Previous treatment with ≥3 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
    c. Diagnosis is associated with homologous recombination deficiency (HRD) positive status defined by either:
        i. A deleterious or suspected deleterious BRCA mutation; or
        ii. Genomic instability and progression >6 months after response to last platinum-based chemotherapy; and
    d. Used as a single-agent; or
2. **Treatment of Advanced Recurrent/Refractory Disease in Combination with Bevacizumab:**
    a. Used in combination with bevacizumab for platinum-sensitive persistent disease or recurrence; and
    b. Meets 1 of the following:
        i. As immediate treatment for serially rising CA-125 in members who previously received chemotherapy, or
        ii. Evidence of radiographic and/or clinical relapse in members with previous complete remission and relapse ≥6 months after completing prior chemotherapy; or
3. **Maintenance Treatment of Advanced Disease:**
    a. Diagnosis of advanced or recurrent disease; and
    b. Disease must be in a complete or partial response to platinum chemotherapy; and
    c. Used as a single-agent.

- Update the current Mekinist® (trametinib) prior authorization criteria based on NCCN Compendium approval (changes noted in red in the following approval criteria; only criteria with changes are listed):

Mekinist® (Trametinib) Approval Criteria [Serous Ovarian Cancer Diagnosis]:

1. Diagnosis of persistent disease or recurrent low-grade serous carcinoma; and
2. Meets 1 of the following:
    a. Immediate treatment for serially rising CA-125 in members who previously received chemotherapy; or
    b. Progression on primary, maintenance, or recurrence therapy; or
    c. Stable or persistent disease (if not on maintenance therapy); or
    d. Complete remission and relapse <6 months after completing chemotherapy; or

e. Radiographic and/or clinical relapse in members with previous complete remission and relapse ≥6 months after completing prior chemotherapy.

Utilization Details of Ovarian Cancer Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	17	3	$97,568.47	5.67	$5,739.32
MEKINIST TAB 2MG	7	3	$82,437.15	2.33	$11,776.74
SUBTOTAL	**24**	**6**	**$180,005.62**	**4**	**$7,500.23**
NIRAPARIB PRODUCTS					
ZEJULA CAP 100MG	3	1	$36,328.53	3	$12,109.51
SUBTOTAL	**3**	**1**	**$36,328.53**	**3**	**$12,109.51**
TOTAL	**27**	**7***	**$216,334.15**	**3.86**	**$8,012.38**

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

[1] National Institutes of Health (NIH). Surveillance, Epidemiology, and End Results (SEER) Program Populations. Cancer Stat Facts: Ovarian Cancer. *National Cancer Institute, DCCPS, Surveillance Research Program*. Available online at: https://seer.cancer.gov/statfacts/html/ovary.html. Last Accessed 09/01/2020.
[2] National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Ovarian Cancer Version 1.2020. *National Comprehensive Cancer Network*. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Issued 03/11/2020. Last accessed 09/01/2020.
[3] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 09/15/2020. Last accessed 09/15/2020.
[4] FDA. Drugs@FDA: FDA-Approved Drugs. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Last accessed 09/15/2020.
[5] Zejula® Prescribing Information. GlaxoSmithKline. Available online at: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Zejula/pdf/ZEJULA-PI-PIL.PDF. Last revised 04/2020. Last accessed 09/15/2020.

Appendix G

Fiscal Year 2020 Annual Review of Spinal Muscular Atrophy (SMA) Medications and 30-Day Notice to Prior Authorize Evrysdi™ (Risdiplam)

Oklahoma Health Care Authority
October 2020

Current Prior Authorization 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 ≥16 hours of respiratory assistance per day continuously for >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 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 must be conducted 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 pretreatment 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).
    a. Only (1) 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

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 ≥16 hours of respiratory assistance per day continuously for >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 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 Zolgensma® *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 Spinraza® (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.

Utilization of SMA Medications: Fiscal Year 2020

Fiscal Year Comparison

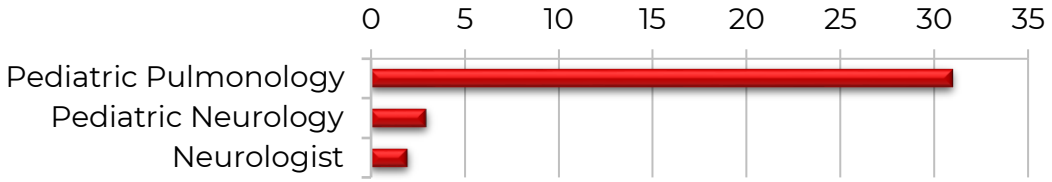
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	15	33	$3,769,588.47	$114,229.95	$1,262.42	180	2,986
2020	17	36	$12,299,577.75	$341,654.94	$3,858.09	169	3,188
% Change	**13.30%**	**9.10%**	**226.28%**	**199.09%**	**205.61%**	**-6.10%**	**6.80%**
Change	**2**	**3**	**$8,529,989.28**	**$227,424.99**	**$2,595.67**	**-11**	**202**

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

Demographics of Members Utilizing SMA Medications

- Due to the small number of members utilizing SMA medications, detailed demographic information could not be provided; however, all paid claims were for pediatric members.

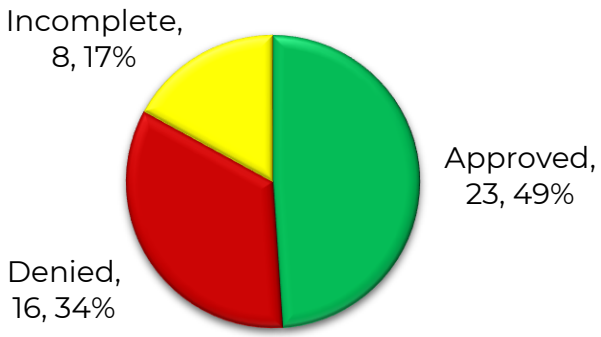
Top Prescriber Specialties of SMA Medications By Number of Claims



Prior Authorization of SMA Medications

There were 47 prior authorization requests submitted for SMA medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

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

- **August 2020:** The FDA approved Evrysdi™ (risdiplam) to treat patients 2 months of age and older with SMA. Evrysdi™ is the first oral drug approved to treat SMA. The FDA granted this application Fast Track, Priority Review, and Orphan Drug designations and awarded a Rare Pediatric Disease Priority Review Voucher.

News:

- **March 2020:** In an observational study in Germany, an analysis of real-world data from 10 academic clinical sites showed nusinersen was associated with improvements in Hammersmith Functional Motor Scale Expanded (HFMSE) scores in adult patients. In the study, 124 patients 16 to 64 years of age with confirmed SMA received nusinersen for ≥6 months. Of this group, 92 patients were assessed at 10 months, and 57 were assessed at 14 months. The primary outcome was the change in HFMSE score versus baseline, assessed at months 6, 10, and 14. Compared with baseline, mean improvements in HFMSE scores among patients taking nusinersen were 1.73 points [95% confidence interval (CI) 1.05-2.41; P<0.0001] at 6 months, 2.58 points (95% CI 1.76-3.39; P<0.0001) at 10 months, and 3.12 points (95% CI 2.06-4.19; P<0.0001) at 14 months.
- **July 2020:** Biogen announced plans to initiate a Phase 4 clinical study to evaluate its SMA treatment Spinraza® (nusinersen) in infants and children who were previously treated with Zolgensma® (onasemnogene abeparvovec-xioi). The study will examine whether nusinersen's production of the survival motor neuron (SMN) protein, which supports sitting, walking, and basic life functions, can benefit patients previously treated with onasemnogene abeparvovec-xioi. Biogen plans to begin enrolling patients in the first quarter of 2021 and will enroll up to 60 children up to 3 years of age who have potential for additional clinical improvement after treatment with onasemnogene abeparvovec-xioi.
- **July 2020:** A report published in the journal *Neurology* suggests nusinersen offers only modest, if any, benefit in improving motor function for adult patients with SMA. In the observed group, nusinersen was associated with significant risks and adverse events. Neuromuscular clinic charts of 22 adult patients with Type 2 or Type 3 SMA were reviewed between 2017 and 2019. The median age was 36 years (range 20–71), and most patients could not walk unassisted. There were 10 patients who had significant respiratory impairment necessitating ventilation and 2 patients had a tracheostomy. Additionally, 17 patients had severe scoliosis. Of the 22 patients observed, only 10 were treated with nusinersen for 6 to 24 months.

Bone laminectomies were required for intrathecal (IT) access for 3 patients and 1 patient developed bowel and bladder incontinence following the procedure. Although 5 patients in the treatment group reported subjective improvements, there was no significant motor gain or improved stability during the median 1-year follow-up, as measured by the percentage of change in Medical Research Council score (%MRC) of upper and lower limb strength (MRC evaluates gross motor strength at the shoulders, elbows, wrists, hips, knees, and feet). Moreover, treated patients experienced serious side effects, including post–lumbar puncture headache, bacterial meningitis, and proteinuria. Most patients in the untreated group had stable %MRC, although 3 showed a slight decline. Due to lack of improvement, recurrent pneumonia, or proteinuria, 3 patients stopped treatment after 12 to 24 months. Half of the treated patients reported modest improvement in function, but there were no significant objective changes, which may point to a placebo effect.

Pipeline:

- **AVXS-101:** In March 2020, AveXis announced new data from STRONG, its Phase 1/2 study for AVXS-101, met the primary efficacy endpoint. AVXS-101 is a 1-time, IT administered gene therapy. The 32 patients in this study included SMA Type 2 patients who had 3 copies of the *SMN2* gene and who were able to sit but unable to stand or walk at the time of study entry. Patients were divided into 2 groups based on age at time of treatment: patients 6 months to 1 year of age and patients 2 to 4 years of age. As of the data cut-off, these patients had been treated with 1 of 3 doses: Dose A (6.0×10^{13}vg), Dose B (1.2×10^{14}vg), and Dose C (2.4×10^{14}vg). Those in the 2 to 4 years of age group (N=12) received Dose B and met the primary efficacy endpoint, achieving a mean increase of 6 points from baseline ($P<0.0021$) in HFMSE at 12 months post-dosing compared to a natural history group. This is twice the clinically meaningful threshold established in previous SMA studies. In addition, nearly all patients (92%) in this group achieved a clinically meaningful ≥3-point increase in HFMSE at any post-baseline visit during the study period, demonstrating a consistent response and a difference from the natural history control group ($P<0.0001$). In October 2019, the FDA placed a partial hold on the AVXS-101 IT program following findings from a small, AveXis-initiated pre-clinical study in which animals treated with AVXS-101 IT showed dorsal root ganglia mononuclear cell inflammation, sometimes accompanied by neuronal cell degeneration or loss. AveXis submitted a response to the FDA with further characterization and a commitment to further study these preclinical findings, along with a thorough analysis of clinical safety showing no clinical reports of sensory neuronopathy in 335 patients following

treatment with AVXS-101 [intravenous (IV) and IT administration] as of December 31, 2019. The FDA is expected to respond to the submission sometime this year.

- **BIIB110:** Biogen is currently evaluating BIIB110 for SMA in a Phase 1 study. BIIB110 is a hybrid activin II receptor (ACTIIR) ligand trap that sequesters both myostatin and activins while sparing the related ligand bone morphogen protein 9 (BMP9). Inhibition of the myostatin pathway is a genetically validated target for muscle enhancement. This targeted mechanism of action may result in greater muscle mass, function, and improved safety compared to other myostatin inhibition approaches.
- **Branaplam:** In December 2019, Novartis announced the decision to suspend development of branaplam, its rival to Roche's risdiplam. Both risdiplam and branaplam are ribonucleic acid (RNA)-splicing drugs that are designed to switch on the *SMN2* gene, compensating for the loss of the *SMN1* gene in SMA. Branaplam had reached the Phase 2 testing stage in SMA. Novartis plans to continue developing branaplam for other disease indications.
- **Reldesemtiv:** In 2017, the FDA granted reldesemtiv Orphan Drug designation and in July 2019, the European Medical Agency (EMA) did the same. Reldesemtiv is a fast skeletal muscle troponin activator designed to improve muscle contraction by slowing calcium release from regulatory proteins (troponins) in skeletal muscle fibers. It is currently being studied as a potential add-on therapy for patients with SMA and as a treatment for amyotrophic lateral sclerosis (ALS). Results from a Phase 2 clinical study of reldesemtiv in patients with SMA showed that reldesemtiv met its primary objective to determine potential pharmacodynamic (PD) effects after multiple oral doses in patients with SMA, and secondary objectives to evaluate the safety, tolerability, and pharmacokinetics (PK) of reldesemtiv. The study enrolled 70 patients 12 years of age and older who were given 150mg or 450mg twice daily or placebo. Dose-dependent increases in Six Minute Walk Distance (6MWD) in ambulatory patients was noted at both post-baseline time points, week 4 and week 8. The study also showed increases vs. placebo in Maximal Expiratory Pressure (MEP) in both treatment groups. Adverse events were similar between groups receiving reldesemtiv and placebo.
- **SRK-015:** In November 2019, Scholar Rock announced preliminary PK/PD results from TOPAZ, the Phase 2 proof-of-concept study of SRK-015 for the treatment of patients with SMA. The planned preliminary PK/PD analysis, which included data from 29 patients with SMA, showed dose-proportional drug exposure and demonstrated target engagement, as evidenced by dose-dependent increases of up to 100-fold in the serum levels of latent myostatin following SRK-015 treatment

(2mg/kg and 20mg/kg doses). SRK-015 is a highly selective inhibitor of the precursor, or latent form, of myostatin and was specifically designed to avoid interactions with related targets such as activins, GDF-11, or BMPs, to potentially improve the therapeutic profile compared to traditional non-selective inhibitors. TOPAZ is an ongoing study evaluating the safety and efficacy of SRK-015 dosed IV every 4 weeks (Q4W) over a 12-month treatment period. The study is anticipated to enroll approximately 55 patients with Type 2 or Type 3 SMA in the United States and Europe across 3 distinct cohorts. Patients in cohorts 1 and 2 are being treated with SRK-015 dosed 20mg/kg Q4W, and patients in cohort 3 are randomized to either 20mg/kg or 2mg/kg Q4W. The primary objectives of the cohorts are to assess safety and clinically meaningful motor functional outcomes, using assessments such as the Revised Hammersmith Scale (RHS) and HFMSE.

Evrysdi™ (Risdiplam) Product Summary[12]

Indication(s): Evrysdi™ (risdiplam) is a survival of motor neuron 2 (SMN2) splicing modifier indicated for the treatment of SMA in patients 2 months of age and older.

Dosing:

- Evrysdi™ is supplied as a powder for oral solution available in an amber glass bottle and packaged with a bottle adapter, (2) 6mL reusable oral syringes, and (2) 12mL reusable oral syringes.
- Prior to dispensing to the patient, the powder must be constituted to the oral solution by a pharmacist following the *Instructions for Constitution* available in the *Prescribing Information*.
- Evrysdi™ constituted oral solution should be stored refrigerated at 2°C to 8°C (36°F to 46°F). Evrysdi™ can be stored for 64 days refrigerated once in solution form; any unused portion should be discarded 64 days after constitution.
- Prior to administration of the first dose, it is recommended a health care provider discuss with the patient or caregiver how to prepare the prescribed daily dose using the reusable oral syringe provided.
- The recommended dose of risdiplam is 0.2mg/kg to 5mg (depending on the patient's age and weight) taken orally once daily after a meal.
- Evrysdi™ must be taken immediately after it is drawn up into the oral syringe. If the dose is not taken within 5 minutes, it should be discarded from the oral syringe, and a new dose should be prepared.
- Evrysdi™ cannot be mixed with formula or milk.
- It is recommended patients drink water after taking Evrysdi™ to ensure the drug has been completely swallowed.

- If the patient is unable to swallow and has a nasogastric or gastrostomy tube, Evrysdi™ can be administered via the tube. The tube should be flushed with water after delivering the medication.

Mechanism of Action: Risdiplam is a SMN2 splicing modifier designed to treat patients with SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using in vitro assays and studies in transgenic animal models of SMA, risdiplam was shown to increase exon 7 inclusion in SMN2 messenger RNA (mRNA) transcripts leading to production of full-length SMN protein in the brain.

Contraindications: None.

Safety:

- **Effect of Risdiplam on Substrates of Multidrug and Toxin Extrusion (MATE) Protein Transporters:** Risdiplam may increase plasma concentrations of drugs eliminated via MATE1 or MATE2-K, such as metformin. It is recommended to avoid coadministration of risdiplam with MATE substrates. If coadministration cannot be avoided, monitoring for drug-related toxicities and consideration of dosage reduction of the coadministered drug if needed is recommended.
- **Pregnancy:** There are no adequate data on the developmental risk associated with the use of risdiplam in pregnant women. In animal studies, administration of risdiplam during pregnancy or throughout pregnancy and lactation resulted in adverse effects on development (embryofetal mortality, malformations, decreased fetal body weights, and reproductive impairment in offspring) at or above clinically relevant drug exposures.
- **Lactation:** There are no data on the presence of risdiplam in human milk, the effects on the breastfed infant, or the effects on milk production. Risdiplam was excreted in the milk of lactating rats following oral administration of risdiplam.
- **Females and Males of Reproductive Potential:** Studies of risdiplam in juvenile and adult rats and in monkeys demonstrated adverse effects on the reproductive organs, including germ cells, in males at clinically-relevant plasma exposures.
    - Pregnancy testing is recommended for females of reproductive potential prior to initiating risdiplam.
    - Risdiplam may cause embryofetal harm when administered to a pregnant woman. It is recommended that female patients of reproductive potential use effective contraception during treatment with risdiplam and for at least 1 month after the last dose.
    - Male fertility may be compromised by treatment with risdiplam. Male patients of reproductive potential should be counseled on the

potential effects on fertility. Male patients may consider sperm preservation prior to treatment.

- **Pediatric Use:** The safety and effectiveness in pediatric patients younger than 2 months of age have not been established.
- **Hepatic Impairment:** The safety and efficacy of risdiplam in patients with hepatic impairment have not been studied. Because risdiplam is predominantly metabolized in the liver, hepatic impairment may potentially increase the exposures to risdiplam. It is recommended to avoid use of risdiplam in patients with impaired hepatic function.

Adverse Reactions:

- The most common adverse reactions (reported in ≥10% of patients treated with risdiplam and at an incidence > placebo) in Study 2 Part 2 (patients with SMA Type 2 or 3, later onset SMA) were fever, diarrhea, and rash.
- The most frequent adverse reactions reported in infantile-onset SMA (SMA Type 1) patients treated with risdiplam in Study 1 were similar to those observed in later-onset SMA patients in Study 2. Additionally, the following adverse reactions were reported in ≥10% of patients: upper respiratory tract infection, pneumonia, constipation, and vomiting.

Efficacy:

- **Study 1 (FIREFISH):** FIREFISH was an open-label, 2-part study to investigate the efficacy, safety, PK, and PD of risdiplam in patients with Type 1 SMA (symptom onset between 28 days and 3 months of age). Part 1 of Study 1 (N=21) provided efficacy and safety data. Additional safety information is provided by Part 2 of Study 1. Patients in Part 1 were enrolled in 1 of 2 dosage cohorts. Effectiveness was established based on the ability to sit without support for ≥5 seconds [as measured by Item 22 of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III) gross motor scale] and on survival without permanent ventilation. Permanent ventilation was defined as requiring a tracheostomy or >21 consecutive days of either non-invasive ventilation (≥16 hours per day) or intubation, in the absence of an acute reversible event. The median age of onset of clinical signs and symptoms of Type 1 SMA in patients enrolled in Part 1 of Study 1 was 2 months (range: 0.9 to 3). The median age at enrollment was 6.7 months (range: 3.3 to 6.9), and the median time between onset of symptoms and first dose was 4 months (range: 2 to 5.8). All patients had genetic confirmation of homozygous deletion or compound heterozygosity predictive of loss of function of the *SMN1* gene and had 2 *SMN2* gene copies. In Study 1 Part 1, the median duration of risdiplam treatment was 14.8 months (range: 0.6 to 26), and 19 patients were treated for a minimum duration of 12 months. Of the patients who were treated with

the recommended dosage of risdiplam 0.2mg/kg/day, 41% (7/17) were able to sit independently for ≥5 seconds after 12 months of treatment. These results indicate a clinically meaningful deviation from the natural history of untreated infantile-onset SMA. After 12 months of treatment with risdiplam, 90% (19/21) of patients were alive without permanent ventilation (and reached 15 months of age or older). After a minimum of 23 months of treatment with risdiplam, 81% (17/21) of all patients were alive without permanent ventilation and reached an age of 28 months or older (median 32 months; range 28 to 45 months). As described in the natural history of untreated infantile-onset SMA, patients would not be expected to attain the ability to sit independently, and ≤25% of these patients would be expected to survive without permanent ventilation beyond 14 months of age.

- **Study 2 (SUNFISH):** SUNFISH was a 2-part, multicenter study to investigate the efficacy, safety, PK, and PD of risdiplam in patients diagnosed with SMA Type 2 or Type 3. Study 2 Part 1 was a dose-finding and exploratory study in 51 patients (14% ambulatory). Part 2 was a randomized, double-blind, placebo-controlled study. The primary endpoint in Study 2 Part 2 was the change from baseline to month 12 in the Motor Function Measure 32 (MFM32) score. A key secondary endpoint was the proportion of patients with a ≥3-point change from baseline to month 12 in the MFM32 total score. The MFM32 measures motor function abilities that relate to daily functions. The total MFM32 score is expressed as a percentage (range: 0 to 100) of the maximum possible score, with higher scores indicating greater motor function. Another key secondary endpoint was the Revised Upper Limb Module (RULM). The RULM is a tool used to assess motor performance of the upper limbs in SMA patients. It tests proximal and distal motor functions of the arm. The total score ranges from 0 (none of the activities can be performed) to 37 (all the activities are achieved fully without any compensatory maneuvers). Study 2 Part 2 enrolled 180 non-ambulatory patients with Type 2 (71%) or Type 3 (29%) SMA. Patients were randomized 2:1 to receive risdiplam at the recommended dosage or placebo. Randomization was stratified by age group (2 to 5, 6 to 11, 12 to 17, or 18 to 25 years of age). The median age of patients at the start of treatment was 9 years (range 2 to 25), and the median time between onset of initial SMA symptoms and first treatment was 102.6 months (range 1 to 275). The primary analysis on the change from baseline in MFM32 total score at month 12 showed a clinically meaningful and statistically significant difference between patients treated with risdiplam and placebo (P=0.0156).

Cost Comparison:

Product	Cost Per Unit	Cost For First Year	Cost Per Year For Maintenance
Evrysdi™ (risdiplam) 0.75mg/mL oral solution	**$139.63**	**$335,112.00***	**$335,112.00***
Spinraza® (nusinersen) 12mg/5mL intrathecal solution	$25,500.00	$892,500.00⁺	$382,500.00⁺

Unit = milliliter (mL)
*For Evrysdi™, cost for first year and cost per year for maintenance is based on the maximum recommended dose of 5mg per day or 240mL per 36 day supply.
⁺For Spinraza®, cost for first year is based on the recommended dosing of 4 loading doses followed by 12mg every 4 months; cost per year for maintenance dosing is based on 12mg every 4 months.
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 Evrysdi™ (risdiplam) with the following criteria:

Evrysdi™ (Risdiplam) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in members 2 months of age and older; 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 ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Evrysdi™ must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Prescriber must agree to monitor member's liver function prior to initiating Evrysdi™ and periodically while receiving Evrysdi™ treatment; and
6. Pharmacy must confirm Evrysdi™ will be constituted to an oral solution by a pharmacist prior to dispensing and must confirm Evrysdi™ will be shipped via cold chain supply to adhere to the storage and handling requirements in the Evrysdi™ *Prescribing Information*; and
7. Prescriber must confirm the member or caregiver has been counseled on the proper storage of Evrysdi™ and has been instructed on how to prepare the prescribed daily dose of Evrysdi™ prior to administration of the first dose; and

8. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
9. Female members of reproductive potential must be willing to use effective contraception during treatment with Evrysdi™ and for at least 1 month after the last dose; and
10. Prescriber must verify male members of reproductive potential have been counseled on the potential effects on fertility and the potential compromised male fertility is acceptable; and
11. Member will not be approved for concomitant treatment with Spinraza® (nusinersen); and
12. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
13. A baseline assessment must be provided using a functionally appropriate exam [e.g., Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale Expanded (HFMSE), Hammersmith Infant Neurological Exam (HINE), Upper Limb Module (ULM) Test]; and
14. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is compliant with Evrysdi™ and 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; and
15. Member's recent weight must be provided to ensure accurate dosing in accordance with Evrysdi™ *Prescribing Information*; and
16. A quantity limit of 240mL per 36 days will apply.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Spinraza® (nusinersen) and Zolgensma® (onasemnogene abeparvovec-xioi) 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 ≥16 hours of respiratory assistance per day continuously for >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 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. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam); and
7. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing must be conducted at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
8. 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
9. 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
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 clinically-significant improvement or maintenance of function from pretreatment 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
11. Approval quantity will be based on Spinraza® *Prescribing Information* and FDA approved dosing regimen(s).
    a. Only (1) 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

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 ≥16 hours of respiratory assistance per day continuously for

>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 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 Zolgensma® *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 Evrysdi™ (risdiplam) or Spinraza® (nusinersen) following Zolgensma® infusion (current authorizations for risdiplam or 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.

Utilization Details of SMA Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
NUSINERSEN PRODUCTS					
SPINRAZA INJ 12MG/5ML	32	14	$3,799,532.65	2.29	$118,735.40
SUBTOTAL	**32**	**14**	**$3,799,532.65**	**2.29**	**$118,735.40**
ONASEMNOGENE ABEPARVOVEC-XIOI PRODUCTS					
ZOLGENSMA INJ 2x5.5ML/2x8.3ML KIT	1	1	$2,125,011.41	1	$2,125,011.41
ZOLGENSMA INJ 6x8.3ML KIT	1	1	$2,125,010.87	1	$2,125,010.87
ZOLGENSMA INJ 2x5.5ML/4x8.3ML KIT	1	1	$2,125,011.41	1	$2,125,011.41
ZOLGENSMA INJ 1x5.5ML/2x8.3ML KIT	1	1	$2,125,011.41	1	$2,125,011.41
SUBTOTAL	**4**	**4**	**$8,500,045.10**	**1**	**$2,125,011.28**
TOTAL	**36**	**17***	**$12,299,577.75**	**2.12**	**$341,654.94**

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

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[3] WCG™ FDA News. Biogen to Test Spinal Muscular Atrophy Drug Spinraza® after Treatment with Zolgensma®. Available online at: https://www.fdanews.com/articles/198155-biogen-to-test-spinal-muscular-atrophy-drug-spinraza-after-treatment-with-zolgensma?utm_campaign=Drug%20Daily%20Bulletin&utm_medium=email&_hsmi=91774194&_hsenc=p2ANqtz--8eoIT9_babD-1O56cxlDbdFCVDWRs-3__ZeFquKanCf0XJ_7naTY9PS0ZVHEQy4_rOz_iGmCsE9dcwM8SwRR3GfZRKsDP0nvLT3LFRd6xahcKD1Q&utm_content=91774194&utm_source=hs_email. Issued 07/22/2020. Last accessed 09/17/2020.
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[9] Taylor P. Novartis Pulls Rival to Roche's Risdiplam in SMA, Says Market Limited. *Pharmaphorum*. Available online at: https://pharmaphorum.com/news/novartis-pulls-rival-to-roches-risdiplam-in-sma-says-market-limited/. Issued 12/06/2019. Last accessed 09/17/2020.
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Appendix H

Fiscal Year 2020 Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor)

Oklahoma Health Care Authority
October 2020

Current Prior Authorization Criteria

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 of age or older; and
4. A quantity limit of 2 tablets or granule packets per day or 56 tablets or granule packets per 28 days will apply; and
5. An age restriction of 6 months 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 granule 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's instructions for use; and
3. Member must be 6 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®.

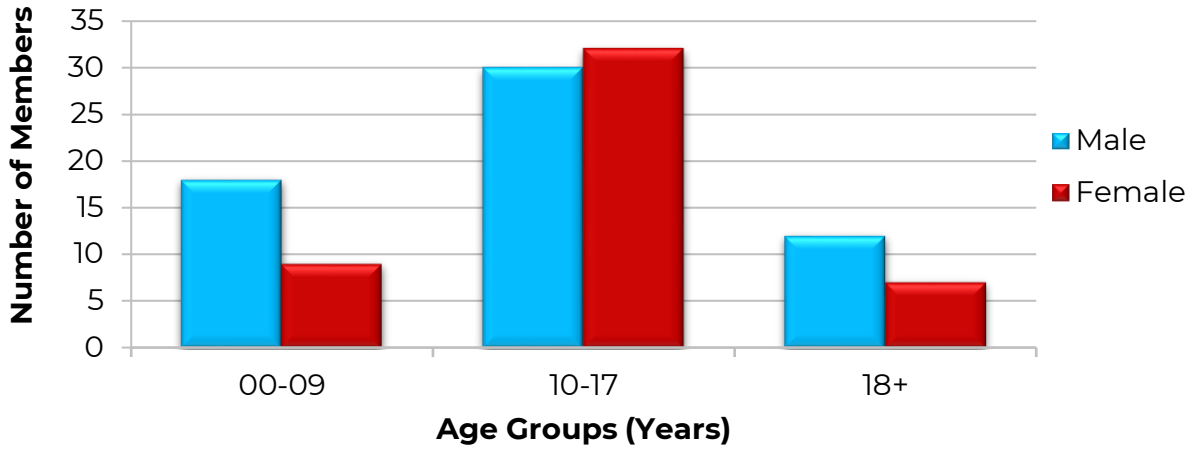
Utilization of CFTR Modulators: Fiscal Year 2020

Comparison of Fiscal Years

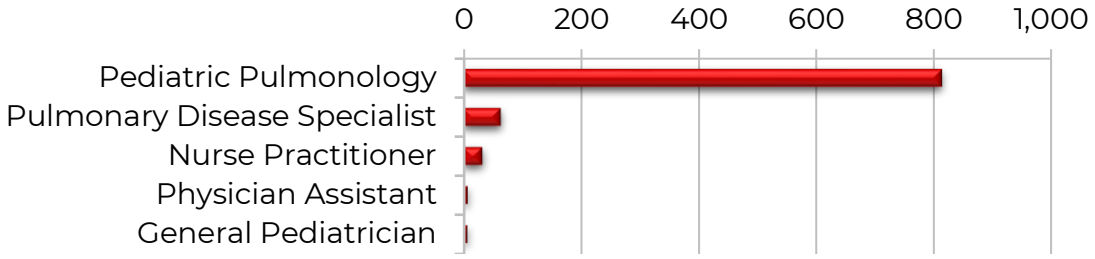
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	77	696	$14,646,144.00	$21,043.31	$751.55	49,952	19,488
2020	108	926	$20,670,236.40	$22,322.07	$797.22	65,100	25,928
% Change	**40.30%**	**33.00%**	**41.10%**	**6.10%**	**6.10%**	**30.30%**	**33.00%**
Change	**31**	**230**	**$6,024,092.40**	**$1,278.76**	**$45.67**	**15,148**	**6,440**

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

Demographics of Members Utilizing CFTR Modulators



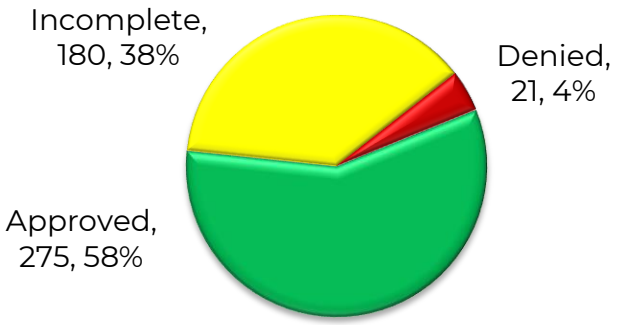
Top Prescriber Specialties of CFTR Modulators by Number of Claims



Prior Authorization of CFTR Modulators

There were 476 prior authorization requests submitted for CFTR modulators during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Kalydeco® (ivacaftor tablets): August 2029
- Orkambi® (lumacaftor/ivacaftor tablets and granules): December 2030
- Kalydeco® (ivacaftor granules): February 2033
- Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor tablets): July 2033
- Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets): April 2035

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

- **October 2019:** The FDA approved the first triple combination therapy, Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor tablets), for patients 12 years of age and older with cystic fibrosis (CF) who have at least 1 *F508del* mutation in the *CFTR* gene, which is estimated to represent 90% of the CF population. CF is a rare, progressive, life-threatening disease caused by a defective protein that results from mutations in the *CFTR* gene causing the formation of thick mucus that builds up in the lungs, digestive tract, and other parts of the body. This

leads to severe respiratory and digestive problems as well as other complications such as infections and diabetes. The FDA granted Trikafta® Orphan Drug, Priority Review, Fast Track, and Breakthrough Therapy designations.

- **September 2020:** The FDA approved an age expansion for Kalydeco® (ivacaftor) to include patients with CF as young as 4 months of age who have 1 mutation in the *CFTR* gene that is responsive to ivacaftor. Kalydeco® was previously approved in the United States and Europe for the treatment of CF in patients 6 months of age and older. The FDA approval is based on data from a 24-week Phase 3 open-label safety cohort (ARRIVAL) consisting of 6 children with CF ages 4 months to younger than 6 months who have 1 of 10 mutations in the *CFTR* gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D* or *R117H*). This cohort demonstrated a safety profile similar to that observed in older children and adults.

Pipeline:

- **MRT5005:** Translate Bio announced in September 2020 that enrollment and dosing in its Phase 1/2 clinical trial for MRT5005 in CF has resumed, with multiple clinical sites being open for enrollment. In March 2020, enrollment and dosing in the clinical trial was put on hold in response to the COVID-19 pandemic. MRT5005 is the first clinical-stage messenger ribonucleic acid (mRNA) product candidate designed to address the underlying cause of CF by delivering mRNA encoding fully functional CFTR protein to the lung epithelial cells through nebulization. MRT5005 is being developed to treat all patients with CF, regardless of the underlying genetic mutation, including those with limited or no CFTR protein. The randomized, double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005 is designed to enroll at least 40 adult patients with CF who have 2 Class I and/or Class II mutations. The primary endpoint of the trial will be the safety and tolerability of single and multiple escalating doses of MRT5005 administered by nebulization. Percent predicted forced expiratory volume in 1 second (ppFEV$_1$), which is a well-defined and accepted endpoint measuring lung function, will also be measured at pre-defined time points throughout the trial. The Phase 1/2 clinical trial of MRT5005 for the treatment of CF is being conducted in collaboration with the CF Foundation Therapeutics Development Network and the Emily's Entourage Patient Registry. The FDA has granted MRT5005 Orphan Drug, Fast Track, and Rare Pediatric Disease designations.
- **Lenabasum:** In June 2020, Corbus Pharmaceuticals announced that the last patient completed their final visit in the company's Phase 2b JBT101-CF-002 trial of lenabasum for the treatment of CF. Topline results from the trial are on track to readout in the third quarter of 2020.

Lenabasum is a novel, oral, synthetic, investigational compound that selectively binds as an agonist to the cannabinoid receptor type 2 (CB2). CB2 is preferentially expressed on activated immune cells and on fibroblasts, muscle cells, and endothelial cells. In both animal and human trials conducted to date, lenabasum has induced the production of pro-resolving lipid mediators that activate endogenous pathways, which resolve inflammation and speed bacterial clearance without immunosuppression. Data from animal models and human clinical trials suggest that lenabasum can reduce expression of genes and proteins involved in inflammation and fibrosis. Lenabasum is being developed to resolve chronic inflammation in patients with CF, systemic sclerosis, dermatomyositis, and systemic lupus erythematosus (SLE). The Phase 2b JBT101-CF-002 trial is a multinational, 426-patient trial evaluating the efficacy and safety of lenabasum in CF. It is a double-blind, randomized, placebo-controlled trial, with patients receiving lenabasum 5mg twice daily, lenabasum 20mg twice daily, or placebo twice daily for 28 weeks, with 4 weeks safety follow-up off active treatment. The primary efficacy endpoint is the event rate of pulmonary exacerbation. Secondary efficacy outcomes include other measures of pulmonary exacerbation, change in $ppFEV_1$, and change in CF Questionnaire-Revised respiratory domain score. The Phase 2b CF trial is funded in part by a development award for up to $25 million from the CF Foundation. Lenabasum has been granted Orphan Drug and Fast Track designations for the treatment of CF by the FDA and Orphan Drug designation for the treatment of CF from the European Medicines Agency (EMA).

- **LUNAR-CF:** In August 2019, it was reported that the CF Foundation 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 patients 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.
- **Posenacaftor (PTI-801)/Dirocaftor (PTI-808)/Nesolicaftor (PTI-428):** Posenacaftor, dirocaftor, and nesolicaftor are investigational CFTR modulators being studied in multiple Phase 2 trials conducted to test the safety and effectiveness of these drugs both alone and in

combination with each other. Posenacaftor is a corrector, a type of modulator designed to fix the defective CFTR protein so that it can move to the proper place on the cell surface. Dirocaftor is a potentiator; once the CFTR protein reaches the cell surface, potentiators help facilitate the opening of the chloride channel to allow chloride and sodium to move in and out of the cell. Nesolicaftor is a new type of modulator called an amplifier. Amplifiers increase the amount of CFTR protein in the cell. This makes more CFTR protein available for other therapies, such as correctors and potentiators, to work on. In February 2020, Proteostasis Therapeutics announced the publication of nonclinical data on the mechanism of action of nesolicaftor. The article, entitled "Amplifiers Co-Translationally Enhance CFTR Biosynthesis via PCBP1-Mediated Regulation of CFTR mRNA," was published online in the *Journal of Cystic Fibrosis* on February 14, 2020.

- **Deutivacaftor (VX-561):** Deutivacaftor (VX-561) is deuterated ivacaftor under investigation as a once daily potentiator designed to keep CFTR proteins at the cell surface open longer to improve the flow of sodium and water across the cell membrane, which helps hydrate and clear mucus from the airways. Deutivacaftor is being studied in a Phase 2 trial to evaluate the efficacy and safety of use in patients 18 years of age and older with CF. The active comparator in the trial is ivacaftor 150mg, and the primary outcome is the absolute change in ppFEV$_1$ from baseline to 12 weeks.
- **VX-121/Tezacaftor/Deutivacaftor (VX-561):** VX-121/tezacaftor/deutivacaftor (VX-561) are being investigated in a Phase 2 trial to evaluate the safety and efficacy in patients 18 years of age and older with CF. VX-121 and tezacaftor are designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the CFTR protein.
- **Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor):** In September 2020, Vertex Pharmaceuticals announced the company has completed a global Phase 3 trial of Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) in children 6 through 11 years of age with CF who have either 2 copies of the *F508del* mutation or 1 copy of the *F508del* mutation and 1 minimal function mutation. Based on the results of this trial, Vertex plans to submit a supplemental New Drug Application (sNDA) to the FDA in the fourth quarter of 2020, with additional global regulatory submissions to follow.
- **Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor), Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor) and Kalydeco® (Ivacaftor):** In September 2020, Vertex Pharmaceuticals announced the FDA accepted 3 sNDAs for Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor), Symdeko® (tezacaftor/ivacaftor and ivacaftor), and Kalydeco® (ivacaftor). These regulatory submissions are intended to expand the

labels to include additional rare *CFTR* mutations, allowing patients with CF not previously eligible for these medicines an opportunity to benefit from treatment that targets the underlying cause of their disease. In addition, these regulatory submissions may also allow certain patients with CF who are currently eligible for Kalydeco® to become eligible for Symdeko® or Trikafta® and certain patients currently eligible for Symdeko® may become eligible for Trikafta®. The FDA has assigned a Prescription Drug User Fee Act (PDUFA) target action date of December 30, 2020. The regulatory submissions are based on data from an *in vitro* cell assay showing that these rare *CFTR* mutations respond to 1 or more of these CFTR modulator regimens. Data generated from this model, along with Phase 3 clinical data, have already led to the inclusion of nearly 30 additional ultra-rare and rare mutations in the United States for Kalydeco® and Symdeko®, including the first ever FDA approval based on *in vitro* data for a Kalydeco® label expansion in patients with residual function *CFTR* mutations.

- **Orkambi® (Lumacaftor/Ivacaftor):** Vertex Pharmaceuticals is currently conducting a Phase 3, 2-part, open-label trial for Orkambi® (lumacaftor/ivacaftor) to evaluate the safety and pharmacokinetics in patients ages 1 year to younger than 2 years of age who have CF and are homozygous for the *F508del* mutation.
- **Kalydeco® (Ivacaftor):** Vertex Pharmaceuticals is currently conducting a Phase 3, 2-arm, open-label trial for Kalydeco® (ivacaftor) to evaluate the safety and pharmacodynamics of long-term ivacaftor treatment in patients with CF who have an approved ivacaftor-responsive mutation ages 0 to younger than 24 months at treatment initiation. The estimated study completion date is June 2021.

Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Product Summary[15,16]

Indication(s): Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is a combination of ivacaftor (a CFTR potentiator), tezacaftor, and elexacaftor indicated for the treatment of CF in patients 12 years of age and older who have at least 1 *F508del* mutation in the *CFTR* gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least 1 *F508del* mutation.

Dosing:

- Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is supplied as a fixed-dose combination tablet containing elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg and co-packaged with an ivacaftor 150mg tablet.
- The recommended regimen for Trikafta® is 2 tablets containing elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg in the morning and 1 ivacaftor 150mg tablet in the evening.

- The morning and evening doses should be taken approximately 12 hours apart with fat-containing food.
- Trikafta® should not be used in patients with severe hepatic impairment. Trikafta® is not recommended in patients with moderate hepatic impairment unless the benefit exceeds the risk. The dose of Trikafta® should be reduced if used in patients with moderate hepatic impairment. Liver function tests should be closely monitored.
- The dose of Trikafta® should be reduced when co-administered with drugs that are moderate CYP3A inhibitors (e.g., fluconazole, erythromycin) or strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, clarithromycin).
- Consuming food or drinks containing grapefruit during Trikafta® treatment should be avoided.

Mechanism of Action: Elexacaftor and tezacaftor bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of *F508del-CFTR* to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface. The combined effect of elexacaftor, tezacaftor, and ivacaftor is an increased quantity and function of *F508del-CFTR* at the cell surface, resulting in increased CFTR activity as measured by CFTR-mediated chloride transport.

Contraindication(s): None.

Safety:

- **Elevated Liver Function Tests [LFTs: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), or Bilirubin)]:** Elevated transaminases and elevated bilirubin have been observed in patients with CF treated with Trikafta®. Assessments of LFTs are recommended for all patients prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter. For patients with a history of hepatobiliary disease or LFT elevations, more frequent monitoring should be considered. In the event of significant elevations in LFTs, [e.g., ALT or AST >5x the upper limit of normal (ULN) or ALT or AST >3x ULN with bilirubin >2x ULN], dosing should be interrupted and laboratory tests closely followed until the abnormalities resolve. Following the resolution of LFT elevations, the benefits and risks of resuming treatment should be taken into consideration.
- **Use with CYP3A Inducers:** Concomitant use with strong CYP3A inducers (e.g., rifampin, St. John's wort) significantly decreases ivacaftor exposure and is expected to decrease elexacaftor and tezacaftor exposure, which may reduce the efficacy of Trikafta®. Therefore, co-

administration of strong CYP3A inducers with Trikafta® is not recommended.

- **Cataracts:** Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ivacaftor-containing regimens. Baseline and follow-up examinations are recommended in pediatric patients initiating Trikafta® treatment.

Adverse Reactions: The most common adverse drug reactions to Trikafta® (occurring in ≥5% of patients and at a frequency higher than placebo by ≥1%) were headache, upper respiratory tract infection, abdominal pain, diarrhea, rash, increased ALT, nasal congestion, increased blood creatine phosphokinase, increased AST, rhinorrhea, rhinitis, influenza, sinusitis, and increased blood bilirubin.

Efficacy: The efficacy of Trikafta® was established in 2 randomized, double-blind trials in patients with CF 12 years of age and older. Study 1 was a 24-week, placebo-controlled trial in 403 patients who had an *F508del* mutation on 1 allele and a mutation on the second allele that results in either no CFTR protein or a CFTR protein that is not responsive to ivacaftor and tezacaftor/ivacaftor. Study 2 was a 4-week, active-controlled trial in 107 patients who were homozygous for the *F508del* mutation. In Study 2, patients were randomized to receive Trikafta® or Symdeko® (tezacaftor/ivacaftor and ivacaftor). The primary efficacy endpoint was the mean absolute change in $ppFEV_1$.

- In Study 1, the treatment difference between Trikafta® and placebo for the mean absolute change from baseline in $ppFEV_1$ at week 4 was 13.8 percentage points [95% confidence interval (CI): 12.1, 15.4; P<0.0001]. The treatment difference was sustained through week 24. The number of pulmonary exacerbation events (event rate per year calculated based on 48 weeks per year) from baseline through week 24 was 0.37 and 0.98 for Trikafta® and placebo, respectively (P<0.0001).
- In Study 2, treatment with Trikafta® vs. Symdeko® resulted in a statistically significant improvement in $ppFEV_1$ of 10 percentage points (95% CI: 7.4, 12.6; P<0.0001).

Cost Comparison:

Medication	Cost Per Unit	Cost Per 28 Days	Cost Per Year
Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) 100mg/50mg/75mg and 150mg⁺	**$284.48**	**$23,896.32**	**$286,755.84**
Symdeko® (tezacaftor/ivacaftor and ivacaftor) 100mg/150mg and 150mg*	$400.00	$22,400.00	$268,800.00

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = tablet
⁺Trikafta® dose based on 2 tablets (containing elexacaftor 100mg/tezacaftor 50mg/ivacaftor 75mg) in the morning and 1 tablet (containing ivacaftor 150mg) in the evening.
*Symdeko® dose based on 1 tablet (containing tezacaftor 100mg/ivacaftor 150mg) in the morning and 1 tablet (containing ivacaftor 150mg) in the evening.

Recommendations

The College of Pharmacy recommends the prior authorization of Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) and recommends updating the age restriction of Kalydeco® (ivacaftor) based on the FDA-approved age expansion with the following criteria (changes and new criteria shown in red):

Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene; 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's instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® 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 Trikafta® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify that the member does not have severe hepatic impairment; and

9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and
10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
11. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
12. 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 than with a previous CFTR therapy must be provided for members who switched from Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor).

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 4 ~~6~~ months of age or older; and
4. A quantity limit of 2 tablets or granule packets per day or 56 tablets or granule packets per 28 days will apply; and
5. An age restriction of 6 months 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.

Utilization Details of CFTR Modulators: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
IVACAFTOR PRODUCTS						
KALYDECO TAB 150MG	91	11	$2,151,869.25	$844.53	$23,646.91	10.41%
KALYDECO PAK 50MG	12	2	$286,889.94	$853.84	$23,907.50	1.39%
SUBTOTAL	**103**	**13**	**$2,438,759.19**	**$845.62**	**$23,677.27**	**11.80%**
TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS						
SYMDEKO TAB 100-150MG	241	46	$5,225,346.30	$774.35	$21,681.93	25.28%
SYMDEKO TAB 50-75MG	46	9	$1,030,923.78	$800.41	$22,411.39	4.99%
SUBTOTAL	**287**	**55**	**$6,256,270.08**	**$778.53**	**$21,798.85**	**30.27%**
LUMACAFTOR/IVACAFTOR COMBINATION PRODUCTS						
ORKAMBI GRA 150-188MG	83	11	$1,737,231.24	$747.52	$20,930.50	8.40%
ORKAMBI TAB 100-125MG	26	12	$502,988.25	$690.92	$19,345.70	2.43%
ORKAMBI GRA 100-125MG	15	4	$313,959.60	$747.52	$20,930.64	1.52%
ORKAMBI TAB 200-125MG	9	1	$188,374.14	$747.52	$20,930.46	0.91%
SUBTOTAL	**133**	**28**	**$2,742,553.23**	**$736.45**	**$20,620.70**	**13.26%**
ELEXACAFTOR/TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS						
TRIKAFTA TAB 100-50-75/150MG	403	67	$9,232,653.90	$818.21	$22,909.21	44.67%
SUBTOTAL	**403**	**67**	**$9,232,653.90**	**$818.21**	**$22,909.21**	**44.67%**
TOTAL	**926**	**108***	**$20,670,236.40**	**$797.22**	**$22,322.07**	**100%**

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

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Appendix I

Fiscal Year 2020 Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet

Oklahoma Health Care Authority
October 2020

Introduction

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, Mavyret® (glecaprevir/pibrentasvir) and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) were reviewed in December 2017, and Harvoni® (ledipasvir/sofosbuvir) oral pellets and Sovaldi® (sofosbuvir) oral pellets were reviewed in October 2019.

In February 2017, the DUR Board voted to remove the minimum METAVIR equivalent 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. The total HCV drug spending per fiscal year (July 1st to June 30th) since the DAAs were recommended to be prior authorized is shown in the following table.

Fiscal Year	Total HCV Drug Spending
Fiscal Year 2015	$21,863,385.60
Fiscal Year 2016	$32,105,818.63
Fiscal Year 2017	$26,475,372.50
Fiscal Year 2018	$36,248,488.07
Fiscal Year 2019	$24,798,344.80
Fiscal Year 2020	$19,716,822.77

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 from F2 to F1 on 07/01/2017 and to F0 on 01/01/2018.

Current Prior Authorization Criteria

Epclusa® (sofosbuvir/velpatasvir) and Mavyret® (glecaprevir/pibrentasvir) are the preferred DAAs for SoonerCare based on supplemental rebate agreements. Use of an alternative DAA for the treatment of HCV including Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) 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:

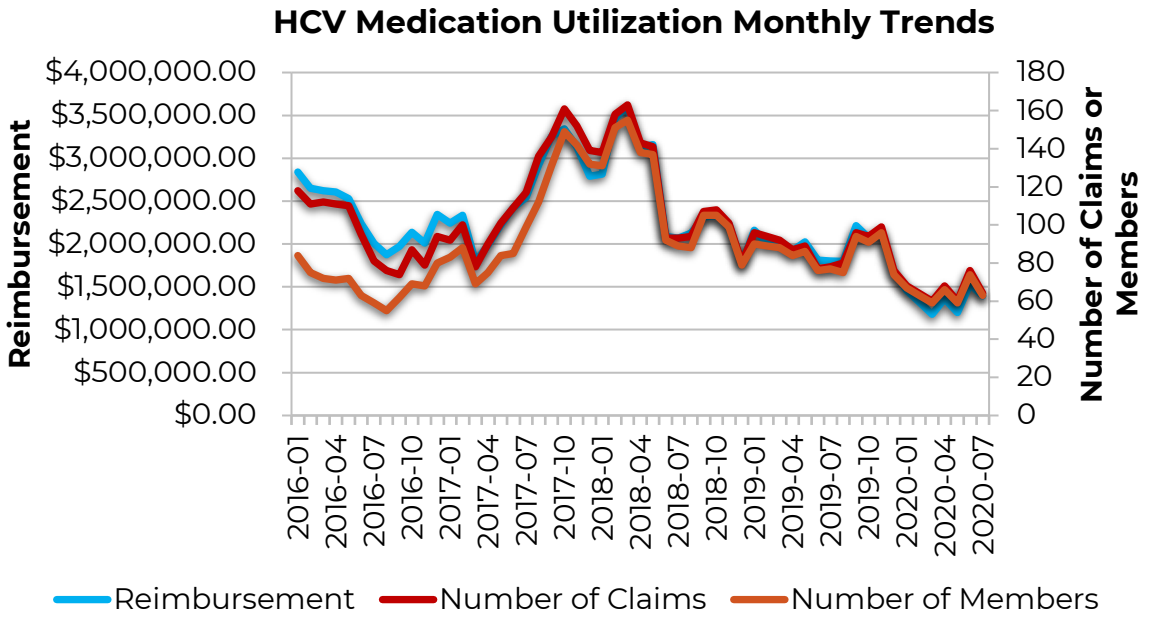
1. FDA approved age appropriate to the requested medication; and
2. An FDA approved diagnosis of chronic hepatitis C (CHC) and an FDA-indicated genotype (GT) appropriate to the requested medication; and
3. Requested hepatitis C medication must be prescribed by a gastroenterologist, infectious disease 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. 2 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 (<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 negative 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

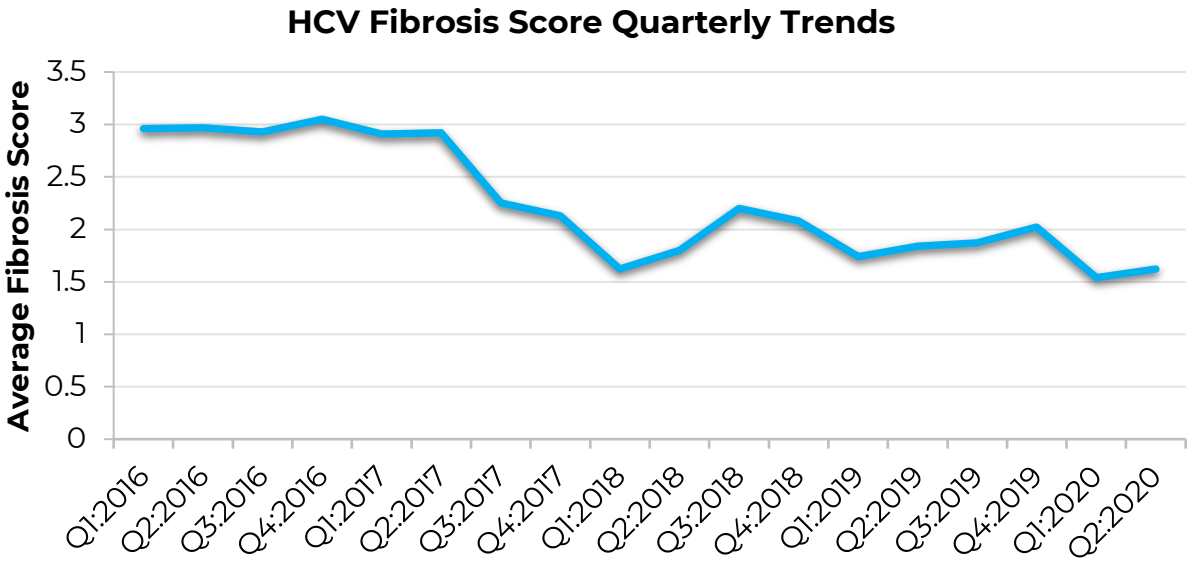
19. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 16 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Trends of Hepatitis C Medication Utilization: 2016 to 2020

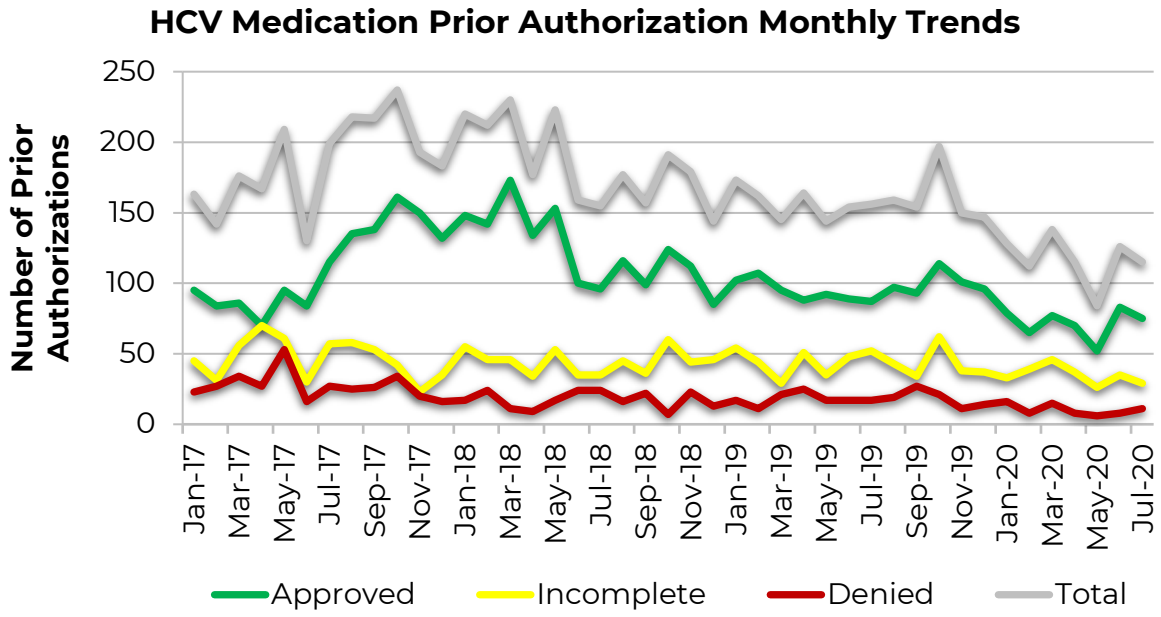
The following is a line graph representing the monthly trend in reimbursement, number of claims, and number of members utilizing HCV medications since January 2016. A steep increase can be seen following the minimum METAVIR fibrosis score change of F2 to F1 (July 1, 2017), and again following the change to F0 (January 1, 2018). Recently, in 2020, the 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 45.3% from quarter (1) 2016 (Q1:2016) to quarter (2) 2020 (Q2:2020).



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 1st and 2nd quarter of 2020 show trends in total requests and approvals declining. 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*	2,256 Members
Genotype	**Genotype 1:** 67.3% **Genotype 2:** 16.7% **Genotype 3:** 15.0% **Genotype 4:** 0.4% **Genotype 6:** 0.1% **Multiple Genotypes:** 0.5%
Fibrosis Score	**Average:** 2.32 **F0:** 11.7% **F1:** 15.8% **F2:** 28.3% **F3:** 16.7% **F4:** 27.5%
Pre-Treatment Viral Load (HCV RNA)	**Average:** 3,722,704 IU/mL
Prior Treatment Experience	**Treatment-Experienced Members:** 9.3% **Treatment-Naïve Members:** 90.7%
Treatment Length	**Average:** 11.2 weeks **8 weeks:** 33.5% **12 weeks:** 61.6% **16 weeks:** 1.2% **24 weeks:** 3.7%
Compliance[¥]	**Before PA:** 18.8% of members noncompliant **After PA:** 3.1% of members noncompliant
SVR Cure Rate/Cost Per Cure	94.6% Cure Rate[+] Estimated cost per cure in the SoonerCare population is $102,963.83 to $230,006.10. Range due to partial response rate.

*Table includes data collected from 08/06/2014 to 08/31/2020
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%).
Costs do not reflect rebated prices or net costs.

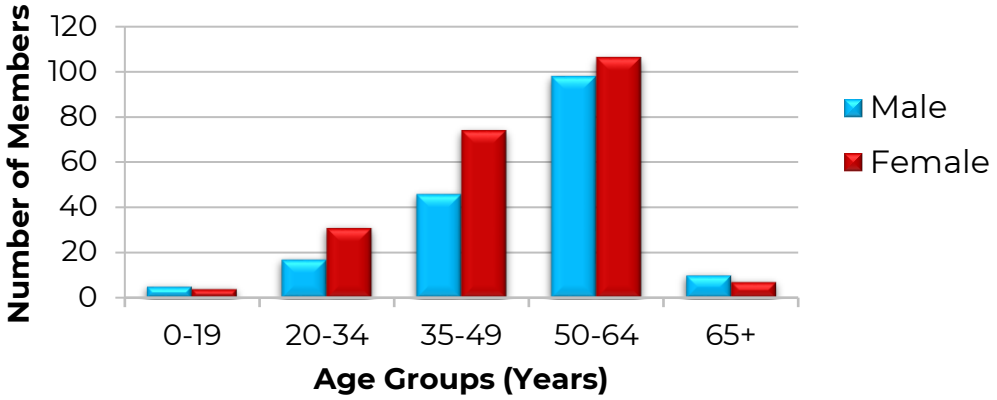
Utilization of Hepatitis C Medications: Fiscal Year 2020

Comparison of Fiscal Years

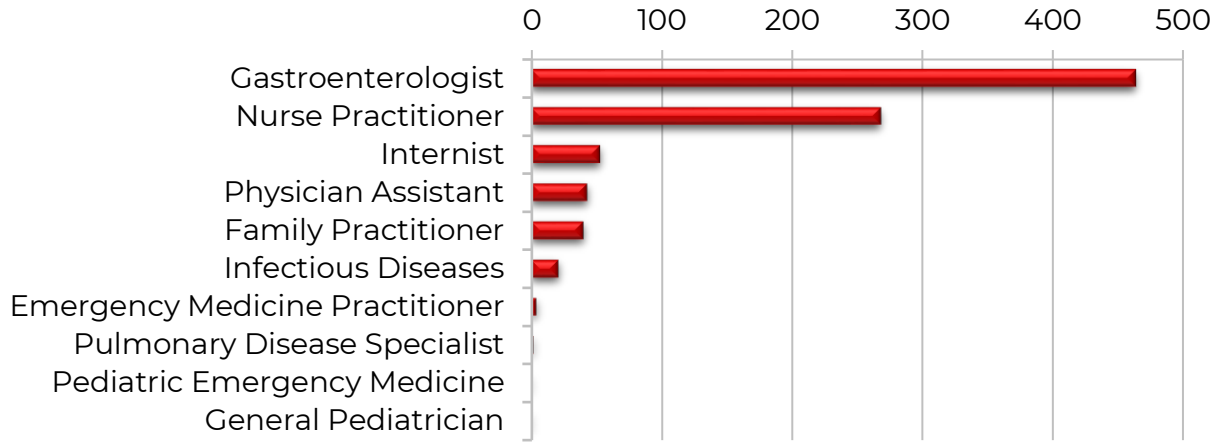
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	470	1,103	$24,798,344.80	$22,482.63	$799.59	45,204	31,014
2020	398	897	$19,716,822.77	$21,980.85	$786.69	38,085	25,063
% Change	**-15.30%**	**-18.70%**	**-20.50%**	**-2.20%**	**-1.60%**	**-15.70%**	**-19.20%**
Change	**-72**	**-206**	**-$5,081,522.03**	**-$501.78**	**-$12.90**	**-7,119**	**-5,951**

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

Demographics of Members Utilizing Hepatitis C Medications



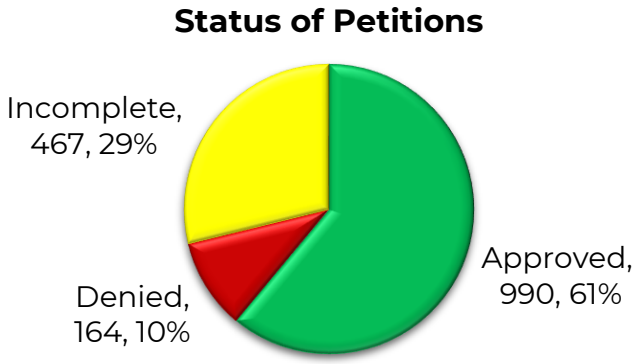
Top Prescriber Specialties of Hepatitis C Medications by Number of Claims



Prior Authorization of Hepatitis C Medications

There were 1,621 prior authorization requests submitted for 470 unique members for hepatitis C medications during fiscal year 2020. 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 2020.



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

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

New U.S. FDA Approval(s) and Label Update(s):

- **Epclusa® (Sofosbuvir/Velpatasvir) Label Update:** In November 2019, the FDA approved Epclusa® for the treatment of chronic HCV infection in patients with severe renal impairment including patients with end stage renal disease (ESRD) on dialysis.
- **Harvoni® (Ledipasvir/Sofosbuvir) Label Update:** In November 2019, the FDA approved Harvoni® for the treatment of chronic HCV infection in patients with severe renal impairment including patients with ESRD on dialysis.
- **Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Label Update:** In November 2019, the FDA approved Vosevi® for the treatment of chronic HCV infection in patients with severe renal impairment including patients with ESRD on dialysis.
- **Zepatier® (Elbasvir/Grazoprevir) Label Update:** In December 2019, the FDA added a contraindication for use of Zepatier® in patients with moderate or severe hepatic impairment or those with any history of prior hepatic decompensation due to the risk of hepatic decompensation.
- **Epclusa® (Sofosbuvir/Velpatasvir) in Pediatric Patients:** In March 2020, the FDA approved Epclusa® for the treatment of chronic HCV in pediatric patients 6 years of age and older or weighing at least 17kg with GT-1, -2, -3, -4, -5, or -6. Epclusa® was previously approved in adult patients for the same indications. Along with the expanded indication, the FDA also approved a new 200mg sofosbuvir/50mg velpatasvir

strength oral tablet. Previously, Epclusa® was only available as a 400mg sofosbuvir/100mg velpatasvir oral tablet. The recommended dose for patients weighing 17 to <30kg is 200mg/50mg daily. The recommended dose for patients weighing ≥30kg is 400mg/100mg daily. Launch plans for the 200mg/50mg tablet strength are pending.

- **Harvoni® (Ledipasvir/Sofosbuvir) Label Update:** In March 2020, the FDA approved a label update for Harvoni® to include the addition of Instructions for Use (IFU) for the oral pellets.
- **Epclusa® (Sofosbuvir/Velpatasvir) Label Update:** In July 2020, the FDA approved Epclusa® for the treatment of chronic HCV infection in treatment-naïve and treatment-experienced liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh A).

Guideline Update(s):

- **August 2020:** The AASLD/ISDA released simplified HCV treatment recommendations for treatment-naïve adults without cirrhosis and with compensated cirrhosis. Recommended regimens for treatment-naïve adults without cirrhosis include Mavyret® (glecaprevir/pibrentasvir) for 8 weeks or Epclusa® (sofosbuvir/velpatasvir) for 12 weeks. Recommended regimens for treatment-naïve adults with compensated cirrhosis include Mavyret® (glecaprevir/pibrentasvir) for 8 weeks for GT-1, -2, -3, -4, -5, or -6 or Epclusa® (sofosbuvir/velpatasvir) for 12 weeks for GT-1, -2, -4, -5, or -6. The current SoonerCare preferred DAAs are in line with this update from the AASLD/ISDA.

News:

- **July 2020:** A post-hoc analysis from 8 pooled trials involving over 2,300 patients revealed that 8 weeks of Mavyret® (glecaprevir/pibrentasvir) was efficacious and well tolerated in treatment-naïve patients with all HCV genotype infections, with or without cirrhosis.

Regimen Comparison[7,9,10]

The following table shows the current AASLD/IDSA simplified 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 for all DAA medications; 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. The sustained virologic response 12 weeks after therapy completion (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.

		SVR**						
Regimen	**Total Cost**	**GT-1a**	**GT-1b**	**GT-2**	**GT-3**	**GT-4**	**GT-5**	**GT-6**
Treatment-Naïve Adults without Cirrhosis								
GLEC/PIB 8 wks	$25,769.52	99%Ω	99%Ω	98%Ω	95%Ω	93%Ω	95%Ω	100%Ω
SOF/VEL 12 wks	$23,999.64	98%	99%	100%	95%	100%	97%	100%
Treatment-Naïve Adults with Compensated Cirrhosis								
GLEC/PIB 8 wks	$25,769.52	98%Ω	98%Ω	100%Ω	95%Ω	100%Ω	100%Ω	100%Ω
SOF/VEL 12 wks	$23,999.64	98%	99%	100%	93%	100%	97%	100%

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
ΩMay include some treatment-experienced patients.
GT = genotype; GLEC = glecaprevir; PIB = pibrentasvir; SOF = sofosbuvir; VEL = velpatasvir; wks = weeks

Recommendations

The College of Pharmacy recommends the prior authorization of Epclusa® (sofosbuvir/velpatasvir) 200mg/50mg tablets with criteria similar to the higher strength Epclusa® 400/100mg tablets. Additionally, the College of Pharmacy recommends updating the Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) prior authorization criteria based on new FDA label updates. The following criteria will apply (changes and additions noted in red):

Epclusa® (Sofosbuvir/Velpatasvir 400/100mg and 200/50mg Tablets) Approval Criteria:

1. Member must be ~~18~~ 6 years of age or older or weighing at least 17kg; 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. Requests for the generic formulation will require a patient-specific, clinically significant reason why the member cannot use the brand formulation; and***
4. Epclusa® 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. 2 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, -2, -3, -4, -5, -6:**
        i. Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A): Epclusa® for 12 weeks; or
        ii. Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C): Epclusa® + weight based ribavirin for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. 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
11. 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
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
14. Female members must not be pregnant and must have a negative 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 ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine equivalent, amiodarone,

omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses >10mg; and
16. If member is using antacids they must agree to separate antacid and Epclusa® administration by 4 hours; 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 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. Members 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 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance. ****The brand formulation of Epclusa® 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.*

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

1. Member must be 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 why 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. 2 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; or
        ii. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA >6 million IU/mL: Harvoni® for 12 weeks; or
        iii. Treatment-experienced without cirrhosis: Harvoni® for 12 weeks; or
        iv. Treatment-experienced with compensated cirrhosis:
            1. Harvoni® with weight-based ribavirin for 12 weeks; or
            2. Harvoni® for 24 weeks; or
        v. Treatment-naïve or treatment-experienced with decompensated cirrhosis: Harvoni® with weight-based ribavirin for 12 weeks; or
    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; or
    c. **GT-4, GT-5, or GT-6:**
        i. Treatment-naïve or treatment-experienced with or without compensated cirrhosis: Harvoni® for 12 weeks; or
    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 negative 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 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.*

Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) Approval Criteria:

1. Member must be 18 years of age or older; 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. Vosevi® 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 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 (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. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
6. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **Adult patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) GT-1, -2, -3, -4, -5, -6:**
        i. **GT-1, -2, -3, -4, -5, -6 patients who were previously treated with an HCV regimen containing an NS5A inhibitor** (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir): Vosevi® for 12 weeks; or
        ii. **GT-1a or -3 patients who were previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor:** Vosevi® for 12 weeks; or
    b. New regimens will apply as approved by the FDA; 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. 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 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. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
15. Female members must not be pregnant and must have a negative 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 ribavirin users); and
16. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine twice daily equivalent, omeprazole doses >20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses >40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and
17. If member is using antacids they must agree to separate antacid and Vosevi® administration by 4 hours; 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. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members 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 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Utilization Details of Hepatitis C Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	% COST	COST/ CLAIM
SOFOSBUVIR/VELPATASVIR PRODUCTS						
EPCLUSA TAB 400-100MG	554	226	$13,468,978.15	2.45	68.31%	$24,312.23
SUBTOTAL	**554**	**226**	**$13,468,978.15**	**2.45**	**68.31%**	**$24,312.33**
GLECAPREVIR/PIBRENTASVIR PRODUCTS						
MAVYRET TAB 100-40MG	221	120	$2,844,804.57	1.84	14.43%	$12,872.42
SUBTOTAL	**221**	**120**	**$2,844,804.57**	**1.84**	**14.43%**	**$12,872.42**
SOFOSBUVIR/LEDIPASVIR PRODUCTS						
HARVONI TAB 90-400MG	82	41	$2,583,650.09	2	13.10%	$31,507.93
HARVONI TAB 45-200MG	15	5	$472,671.15	3	2.40%	$31,511.41
SUBTOTAL	**97**	**46**	**$3,056,321.24**	**2.11**	**15.50%**	**$31,508.47**
SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR PRODUCTS						
VOSEVI TAB 400-100-100MG	13	5	$324,098.71	2.6	1.64%	$24,930.67
SUBTOTAL	**13**	**5**	**$324,098.71**	**2.6**	**1.64%**	**$24,930.67**
RIBAVIRIN PRODUCTS						
RIBAVIRIN CAP 200MG	5	3	$495.92	1.67	0.00%	$99.18
RIBAVIRIN TAB 200MG	4	2	$250.49	2	0.00%	$62.62
SUBTOTAL	**9**	**5**	**$746.41**	**1.8**	**0.00%**	**$82.93**
ELBASVIR/GRAZOPREVIR PRODUCTS						
ZEPATIER TAB 50-100MG	3	1	$21,873.69	3	0.11%	$7,291.23
SUBTOTAL	**3**	**1**	**$21,873.69**	**3**	**0.11%**	**$7,291.23**
TOTAL	**897**	**398***	**$19,716,822.77**	**2.25**	**100%**	**$21,980.85**

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

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[10] Epclusa® Prescribing Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf. Last revised 07/2020. Last accessed 09/18/2020.

Appendix J

30-Day Notice to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

Oklahoma Health Care Authority
October 2020

Introduction[1,2,3]

Cystinosis is a condition that affects approximately 1 in 100,000 to 200,000 newborns worldwide and is characterized by accumulation of the amino acid cystine within the cells. Cystinosis is inherited in an autosomal recessive manner and is caused by mutations in the *CTNS* gene. Mutations in the *CTNS* gene lead to a deficiency of a transporter protein called cystinosin, which normally moves cystine out of the lysosomes. When cystinosin is defective or missing, cystine accumulates and forms crystals in the lysosomes. Excess cystine damages cells in the kidneys and the eyes and may also affect other organs.

There are 3 distinct types of cystinosis (listed in order of decreasing severity): nephropathic cystinosis, intermediate cystinosis, and non-nephropathic or ocular cystinosis. Nephropathic cystinosis begins in infancy and causes poor growth and a particular type of kidney damage (renal Fanconi syndrome). Untreated children typically will experience kidney failure by age 10. By around the age of 2 years, cystine crystals may be present in the cornea. The buildup of these crystals in the cornea causes eye pain and photophobia. Other signs and symptoms that may occur in untreated patients include muscle deterioration, blindness, inability to swallow, diabetes, thyroid and nervous system problems, and male infertility. The signs and symptoms of intermediate cystinosis are the same as nephropathic cystinosis, but occur at a later age, usually in adolescence.

Patients with non-nephropathic or ocular cystinosis typically experience eye pain and photophobia due to cystine crystals in the cornea, but usually do not develop kidney malfunction or other signs and symptoms of cystinosis. In October 2012, the U.S. Food and Drug Administration (FDA) approved Cystaran™ (cysteamine 0.44% ophthalmic solution) for the treatment of corneal cystine crystal accumulation in patients with cystinosis. Cysteamine lowers the cystine content of cells by converting cystine to cysteine and cysteine-cysteamine mixed disulfides, thus reducing corneal cystine crystal accumulation. In August 2020, the FDA approved Cystadrops® (cysteamine 0.37% ophthalmic solution) for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

Product Comparison[4,5]

	Cystaran™ (cysteamine 0.44%)	Cystadrops® (cysteamine 0.37%)
FDA Approval	2012	2020
Indication(s)	Treatment of corneal cystine crystal accumulation in patients with cystinosis	
Dosage Form	Ophthalmic solution containing 6.5mg/mL of cysteamine hydrochloride equivalent to 4.4mg/mL of cysteamine (0.44%)	Ophthalmic solution containing 3.8mg/mL of cysteamine (0.37%)
Dosing	1 drop in each eye every waking hour	1 drop in each eye 4 times daily during waking hours
How Supplied	15mL bottle	5mL bottle
Storage	Before use, store in the freezer (-13°F to 5°F); thaw for approximately 24 hours before use. Store thawed bottle at 36°F to 77°F for up to 1 week; discard bottle after 1 week of use.	Before use, store in the refrigerator (36°F to 46°F). After opening, store at room temperature (68°F to 77°F); discard bottle 7 days after opening.
Wholesale Acquisition Cost (WAC)	$108.04 per mL ($1,620.60 per bottle)	$350.00 per mL ($1,750.00 per bottle)

Costs do not reflect rebated prices or net costs. Cystaran™ was first FDA approved in 2012 and has a significant federal rebate.

Recommendations

The College of Pharmacy recommends the prior authorization of Cystadrops® (cysteamine 0.37% ophthalmic solution) and Cystaran™ (cysteamine 0.44% ophthalmic solution) with the following criteria:

Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication for the treatment of corneal cystine crystal accumulation in patients with cystinosis; and
2. The requested medication must be prescribed by, or in consultation with, an ophthalmologist; and
3. Prescriber must verify that the member has been counseled on the proper storage of the requested medication; and
4. For Cystadrops®, a patient-specific, clinically significant reason (beyond convenience) why the member cannot use Cystaran™ must be provided; and
5. A quantity limit of 4 bottles per month will apply.

Utilization Details of Cystaran™ (Cysteamine 0.44% Ophthalmic Solution): Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CYSTEAMINE PRODUCTS						
CYSTARAN SOL 0.44%	2	1	$7,729.15	$3,864.58	2	100%
TOTAL	**2**	**1***	**$7,729.15**	**$3,864.58**	**2**	**100%**

SOL = solution
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Cystaran™ was first FDA approved in 2012 and has a significant federal rebate.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

[1] National Institutes of Health (NIH) Genetics Home Reference. Cystinosis. Available online at: https://ghr.nlm.nih.gov/condition/cystinosis#. Last accessed 09/28/2020.
[2] National Organization for Rare Disorders. Cystinosis. Available online at: https://rarediseases.org/rare-diseases/cystinosis/#:~:text=Ocular%20symptoms%20of%20cystinosis%20can%20be%20treated%20with,suffering%20from%20pain%20due%20to%20repeated%20corneal%20erosions. Last accessed 09/28/2020.
[3] Park B. Cystadrops® Approved to Treat Corneal Crystal Deposits in Cystinosis. *MPR*. Available online at: https://www.empr.com/home/news/cystadrops-cysteamine-solution-fda-approved-crystal-deposits-cystinosis/#:~:text=The%20Food%20and%20Drug%20Administration%20%28FDA%29%20has%20approved,cystine%20crystals%20throughout%20the%20body%2C%20including%20the%20eyes. Issued 08/27/2020. Last accessed 09/28/2020.
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Appendix K

Fiscal Year 2020 Annual Review of Signifor® LAR (Pasireotide) and 30-Day Notice to Prior Authorize Mycapssa® (Octreotide)

Oklahoma Health Care Authority
October 2020

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

Acromegaly is a rare, but serious condition caused by persistent hypersecretion of growth hormone (GH). Excess GH causes the liver to secrete insulin-like growth factor-1 (IGF-1), which is the cause of many of the clinical manifestations of acromegaly. Acromegaly is most commonly seen in adults with a mean age of 40 to 45 years. Excess GH in children prior to the closure of the epiphyseal growth plates results in pituitary gigantism and not acromegaly. Some clinical manifestations of acromegaly include overgrowth of the skin, connective tissues, cartilage, bone, and viscera, excessive sweating, jaw overgrowth, joint pain, and cardiomyopathy.

The estimated prevalence of acromegaly in Europe is 30 to 70 cases per 1 million people. The most common cause of acromegaly is a somatotroph (GH-secreting) adenoma of the anterior pituitary, which accounts for nearly 1/3 of patients with acromegaly. Other causes include a specific gene mutation and various neuroendocrine tumors. The goals of acromegaly treatment are to normalize IGF-1 and GH levels, reverse the effects of the tumor, and minimize risk of long-term mortality.

Acromegaly treatment guidelines recommend transsphenoidal surgery as the primary therapy in most patients. Medication therapy is recommended in patients who have persistent disease after surgery or for patients in which surgical intervention is not an option. There are 3 medication classes used as adjuvant treatment in patients with acromegaly: dopamine agonists (DAs), somatostatin analogs (SSAs) or somatostatin receptor ligands (SRLs), and GH receptor antagonists. In patients with significant disease, there are 3 SSAs/SRLs used to treat acromegaly, all of which are available in long-acting release (LAR) formulations: octreotide, lanreotide, and pasireotide. Currently the guidelines do not recommend 1 SSA/SRL over the others. Pegvisomant is also recommended for significant disease. Pegvisomant is a GH receptor antagonist given as a daily subcutaneous (sub-Q) injection, but due to adverse effects and the risk of increasing tumor size, pegvisomant is reserved for patients who have an inadequate response or intolerability to SSAs/SRLs. In patients with only modest elevations of IGF-1 and mild signs of GH excess, a trial of a DA, usually cabergoline, is the initial adjuvant therapy.

Cushing's disease is caused by a pituitary gland tumor that over secretes adrenocorticotropic hormone (ACTH) causing hypercortisolemia that results in the manifestation of Cushing's syndrome. Nearly 80% of cases of Cushing's syndrome are caused by Cushing's disease (caused by an ACTH-secreting pituitary adenoma). The estimated prevalence of Cushing's syndrome is 40 cases per 1 million people. Cushing's disease is most commonly seen in adults in the 3rd and 4th decade of life, and it is more prevalent in women than men.

Diagnosing Cushing's disease can be difficult because the symptoms can be non-specific. Clinical characteristics of Cushing's syndrome include obesity, buffalo-hump, rounded face, osteoporosis, protein wasting, hirsutism, menstrual irregularities, and mild-to-severe psychiatric disturbances. A diagnostic cortisol level in conjunction with clinical characteristics can confirm Cushing's syndrome. There are several lab tests that can then be used in conjunction with the presence of a pituitary tumor to confirm the diagnosis of Cushing's disease.

Guidelines recommend transsphenoidal surgery as first-line therapy for Cushing's disease. For patients who are not cured by surgery or who are not candidates for surgery, medical treatments can decrease the synthesis and secretion of cortisol. Steroidogenesis inhibitors (e.g., mitotane, ketoconazole, metyrapone, etomidate) work through different mechanisms to reduce cortisol. Mifepristone, a glucocorticoid receptor antagonist, can be used to control the clinical symptoms of Cushing's disease. ACTH-lowering agents, including DAs and pasireotide, can also decrease the levels of cortisol in patients. Radiation therapy is another option for patients with Cushing's disease. In addition, on March 6, 2020, Isturisa® (osilodrostat), a cortisol synthesis inhibitor, received U.S. Food and Drug Administration (FDA) approval for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. The goal of therapy is to keep patients from being in a chronic hypercortisol state, which can increase morbidity and mortality due to cardiovascular factors leading to heart defects.

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 release (LAR) somatostatin analogs (SSAs) are not appropriate for the member; and
3. Pasireotide LAR must be prescribed by, 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 2020

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

Prior Authorization of Signifor® LAR (Pasireotide)

There were no prior authorization requests submitted for Signifor® LAR (pasireotide) during fiscal year 2020.

Market News and Updates[7,8,9,10]

Anticipated Patent Expiration(s):

- Signifor® LAR (pasireotide): May 2028
- Mycapssa® (octreotide): February 2036

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

- **June 2020:** The FDA approved Mycapssa® [octreotide delayed-release (DR) capsules] for the long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. Mycapssa® is the first and only oral SSA approved by the FDA.

Pipeline:

- **Seliciclib:** Seliciclib is an oral drug candidate being studied to treat Cushing's disease as well as other disease states. It is a cell cycle inhibitor that aims to target the tumor in the pituitary gland by blocking cyclin-dependent kinase 2 (CDK2) and cyclin E, which work to regulate cell growth. By inhibiting CDK2 and cyclin E, seliciclib may be able to shrink the pituitary tumor. Sixteen clinical trials have been conducted with seliciclib for various indications, but it is currently being

evaluated in a Phase 2 trial to evaluate if the drug can safely normalize urinary free cortisol levels by reducing pituitary corticotroph tumor ACTH production.

- **Levoketoconazole:** The ongoing Phase 3 trial, LOGICS, is designed to assess safety, efficacy, and tolerability of levoketoconazole in patients with endogenous Cushing's syndrome. Patients were randomized to either levoketoconazole, up to a dose of 1,200mg, or placebo for a maximum of 9.5 weeks. A previous trial, SONICS, achieved its primary outcome, with 31% of patients treated with 600mg of levoketoconazole twice daily achieving normalization of urinary free cortisol levels after a 6-month maintenance phase.
- **Veldoreotide:** Veldoreotide is being developed by Strongbridge Biopharma for the treatment of acromegaly. Veldoreotide is an SSA and demonstrates an ability similar to octreotide to suppress GH, but has reduced propensity to inhibit postprandial insulin in short-term Phase 1 and 2 trials in healthy volunteers. Veldoreotide has been granted Orphan Drug designation by the FDA and the European Medicines Agency (EMA).

Mycapssa® (Octreotide) Product Summary[11,12,13]

Indication(s): Mycapssa® (octreotide) is an oral SSA indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

Dosing:

- Mycapssa® is supplied as 20mg DR capsules.
- Mycapssa® should be initiated at a dosage of 40mg daily, administered as 20mg orally twice daily.
- The dosage should be titrated in increments of 20mg based on IGF-1 levels and the patient's signs and symptoms.
- The maximum recommended dosage of Mycapssa® is 80mg daily.
- Mycapssa® should be taken orally with a glass of water on an empty stomach at least 1 hour before a meal or at least 2 hours after a meal.

Mechanism of Action: Octreotide is an SSA, but is a more potent inhibitor of GH, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone (LH) response to gonadotropin-releasing hormone (GnRH), decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide.

Contraindication(s):

- Hypersensitivity to octreotide or any of the components of Mycapssa®.

Safety:

- **Cholelithiasis and Complications of Cholelithiasis:** Mycapssa® may inhibit gallbladder contractility and decrease bile secretion, which may lead to gallbladder abnormalities or sludge. Gallbladder-related adverse reactions have been reported in clinical trials in patients receiving Mycapssa®. There have been post marketing reports of cholelithiasis in patients taking SSAs, including cholecystitis, cholangitis, and pancreatitis and requiring cholecystectomy. It is recommended patients be monitored periodically and if complications of cholelithiasis are suspected, Mycapssa® should be discontinued and the patient should be treated appropriately.
- **Hyperglycemia and Hypoglycemia:** Mycapssa® alters the balance between the counter-regulatory hormones, insulin, glucagon, and GH, which may result in hypoglycemia, hyperglycemia, or diabetes mellitus. In clinical trials with Mycapssa®, the following adverse reactions were reported: increased blood glucose (7%), hypoglycemia (4%), and diabetes mellitus (1%). Blood glucose levels should be monitored when Mycapssa® treatment is initiated or when the dose is adjusted, and antidiabetic treatment should be adjusted accordingly.
- **Thyroid Function Abnormalities:** Mycapssa® suppresses the secretion of thyroid-stimulating hormone (TSH), which may result in hypothyroidism. In clinical trials with Mycapssa®, the following adverse reactions were reported: hypothyroidism (1%), increased TSH (1%), and decreased free T4 (1%). It is recommended to assess thyroid function periodically during treatment.
- **Cardiac Function Abnormalities:** Cardiac conduction abnormalities and other electrocardiogram (ECG) changes have occurred during treatment with octreotide. In clinical trials with Mycapssa®, the following adverse reactions were reported: bradycardia (2%), conduction abnormalities (1%), and arrhythmias/tachycardia (2%). These ECG changes may occur in patients with acromegaly. Dose adjustments of concomitantly used drugs that have bradycardia effects (i.e., beta blockers) may be necessary.

Adverse Reactions: In clinical trials, the most common adverse reactions (incidence ≥5%) following administration of Mycapssa® were nausea, diarrhea, elevated blood glucose, vomiting, abdominal discomfort, dyspepsia, sinusitis, and osteoarthritis.

Efficacy: The efficacy of Mycapssa® was established in 2 trials. The first trial was a Phase 3, multicenter, open-label, dose-titration, baseline-controlled trial in 155 patients with acromegaly. Patients who had received an injectable SRL for ≥3 months, with complete or partial control [IGF-1 <1.3x the upper limit of normal (ULN) for age and 2-hour integrated GH <2.5ng/ml], were switched to

40mg/day oral octreotide capsules and the dose was escalated to 60mg/day and then up to 80mg/day to control IGF-1. The treatment period lasted ≥13 months and was comprised of a dose escalation period (2-5 months) followed by a fixed-dose period (8-11 months). The fixed-dose period included the time periods up to the completion of the core and extension treatment phases (at 7 and 13 months, respectively). Oral octreotide was administered in the morning and evening with dosages beginning at 20mg twice daily. The primary efficacy endpoint was defined as the proportion of responders at the end of the core treatment, with an exact 95% confidence interval (CI) in the modified intent-to-treat (mITT) population, and response was defined as IGF-1 <1.3x ULN for age and integrated GH <2.5ng/mL. Overall, 65% of all enrolled patients were responders up to 7 months (mITT population, CI: 58.4-74.2) and 62% were responders up to 13 months (CI: 54.9-71.7), as compared to 88.7% at the baseline visit while on injectable SRLs. The effect was durable as 85% of patients initially controlled on oral octreotide maintained this response up to 13 months. While controlled on oral octreotide, GH levels were reduced compared to baseline, and acromegaly-related symptoms improved. The most commonly reported adverse events were gastrointestinal, neurologic, and musculoskeletal in nature, including nausea, diarrhea, headache, dizziness, arthralgia, and back pain.

The second trial, the CHIASMA OPTIMAL trial, was a randomized, double-blind, placebo-controlled, 9-month Phase 3 trial of octreotide capsules. The trial enrolled 56 adults with acromegaly whose disease was controlled with injectable SSAs (octreotide or lanreotide). The percentage of patients with previous pituitary surgery was 88%. Patients were randomized 1:1 to either octreotide capsules or placebo. Patients were dose titrated from 40mg per day (20mg in the morning and 20 mg in the evening) to up to a maximum of 80mg per day. The primary endpoint was the proportion of patients who maintained their biochemical response at the end of the 9-month period which was measured using the average of the last 2 IGF-1 levels ≤1.0x ULN (assessed at weeks 34 and 36). A total of 58% of patients treated with Mycapssa® versus 19% of patients treated with placebo maintained their chemical response. Roughly 25% of patients treated with Mycapssa® discontinued Mycapssa® and began treatment with other SSAs at some point during the 9-month study.

Cost Comparison:

Medication	Cost Per Unit	Cost Per 28 Days	Cost Per Year
Mycapssa® (octreotide) 20mg capsule	**$92.00**	**$5,152.00**	**$66,976.00**
Sandostatin® LAR depot (octreotide) 20mg vial	$3,535.49	$3,535.49	$45,961.37
Signifor® LAR (pasireotide) 40mg vial	$13,058.40	$13,058.40	$169,759.20

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = capsule or vial; LAR = long-acting release

Recommendations

The College of Pharmacy recommends the prior authorization of Mycapssa® (octreotide) with the following criteria:

Mycapssa® (Octreotide) Approval Criteria:

1. An FDA approved indication for long-term maintenance treatment in members with acromegaly who have responded to and tolerated treatment with octreotide or lanreotide; and
2. Member has elevated insulin-like growth factor-1 (IGF-1) levels for age and/or gender; and
3. Member has a documented trial with injectable octreotide or lanreotide, and the prescriber must verify that the member responded to and tolerated treatment with octreotide or lanreotide; and
4. A patient-specific, clinically significant reason why the member cannot continue treatment with injectable octreotide or lanreotide must be provided; and
5. Mycapssa® must be prescribed by, or in consultation with, an endocrinologist; and
6. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and
7. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member's IGF-1 level has decreased or normalized since initiating treatment; and
8. A quantity limit of 120 capsules per 30 days will apply.

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Appendix L

Fiscal Year 2020 Annual Review of Lambert-Eaton Myasthenic Syndrome (LEMS) Medications [Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine)]

Oklahoma Health Care Authority
October 2020

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

Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disorder characterized by the gradual onset of muscle weakness, typically initially affecting the proximal arm and leg muscles. This may be followed by progression of muscle weakness to the shoulders, feet, hands, eyes, and speech and swallowing muscles. Autonomic symptoms such as dry mouth, dry eyes, constipation, impotence, and decreased sweating are also sometimes seen. LEMS is caused by autoantibodies which attack and damage P/Q-type voltage-gated calcium channels (VGCC) located on presynaptic motor neurons at the neuromuscular junction. In healthy individuals, the VGCC are responsible for allowing an influx of calcium ions into the motor neuron which subsequently triggers the release of the neurotransmitter acetylcholine. When the VGCC are damaged in LEMS, the amount of acetylcholine released from the motor neurons is reduced, resulting in diminished muscle strength.

LEMS can be categorized as either paraneoplastic (associated with a concurrent cancer diagnosis) or non-paraneoplastic (not associated with a cancer diagnosis). Approximately 50-60% of patients with LEMS have the paraneoplastic variety, which is most commonly associated with small cell lung cancer (SCLC). An estimated 3% of SCLC patients will develop LEMS, with the symptoms of LEMS often becoming apparent before SCLC is diagnosed. Paraneoplastic LEMS is thought to occur because the same types of VGCC are expressed on SCLC tumor cells. In paraneoplastic LEMS, the immune system mistakes the body's own VGCC on motor neurons for VGCC located on cancer cells. The diagnosis of LEMS is made through a combination of clinical features, laboratory identification of specific VGCC antibodies, and characteristic electrodiagnostic findings.

The incidence of LEMS is approximately 0.5 per 1 million population. The worldwide prevalence is estimated to be 3-4 per 1 million population. In the United States, there are approximately 400 known cases of LEMS. The median age of onset is 60 years for paraneoplastic LEMS and occurs most commonly in men with a history of cigarette smoking. Non-paraneoplastic LEMS occurs more commonly in women and in a wider age range, with 2

peaks in age of onset seen at age 35 years and age 60 years. Pediatric LEMS does occur, but is extremely uncommon, with only 11 pediatric cases having been reported in the literature according to the National Organization for Rare Disorders.

There is currently no cure for LEMS. The goal of treatment consists primarily of symptomatic relief following the treatment of any underlying malignancy, if present. The first-line option for the treatment of both subtypes of LEMS is 3,4-diaminopyridine, also known as amifampridine, a voltage-gated potassium channel blocker. In refractory cases, additional therapies to enhance the activity of acetylcholine or suppress the activity of the immune system are sometimes utilized. Therapies such as pyridostigmine, guanidine, corticosteroids, intravenous immune globulin (IVIg), plasmapheresis, and rituximab are occasionally used for this purpose. In November 2018, the U.S. Food and Drug Administration (FDA) approved Firdapse® (amifampridine) for the treatment of adults with LEMS. In May 2019, the FDA approved Ruzurgi® (amifampridine) for the treatment of LEMS in pediatric patients 6 years of age to younger than 17 years of age. Both formulations of amifampridine are contraindicated in patients with a history of seizures and should be used with caution in patients taking other medications which can lower the seizure threshold. Both formulations are available as 10mg functionally-scored tablets which can be taken without regard to food. Additionally, Ruzurgi® can be prepared as a 1mg/mL suspension for patients who require a dosage in <5mg increments, have difficulty swallowing tablets, or require feeding tubes.

Cost Comparison:

Medication	Cost Per Tablet	Cost Per 30 Days*
Firdapse® (amifampridine) 10mg tablet	$179.80	$43,152.00
Ruzurgi® (amifampridine) 10mg tablet	$80.00	$24,000.00

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.
*Costs per 30 days based on the maximum daily dose of 80mg/day for Firdapse® and 100mg/day for Ruzurgi®.

Current Prior Authorization Criteria

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

1. An FDA approved diagnosis of Lambert-Eaton myasthenic syndrome (LEMS); and
2. LEMS diagnosis must be confirmed by 1 of the following:
    a. A high titer anti-P/Q-type voltage-gated calcium channel (VGCC) antibody assay; or

b. A confirmatory electrodiagnostic study [e.g., repetitive nerve stimulation (RNS), needle electromyography (EMG), single-fiber electromyography (SFEMG)]; and

3. The requested medication must be prescribed by, or in consultation with, a neurologist or oncologist; and
4. Member must not have a history of seizures or be taking medications that lower the seizure threshold (e.g., bupropion, tramadol, amphetamines, theophylline); and
5. For Firdapse®, a patient-specific, clinically significant reason why the member cannot use Ruzurgi® must be provided; and
6. For Firdapse®, a quantity limit of 240 tablets per 30 days will apply. For Ruzurgi®, a quantity limit of 300 tablets per 30 days will apply; and
7. Initial approvals will be for 6 months. Continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with the requested medication.

Utilization of LEMS Medications: Fiscal Year 2020

Fiscal Year 2020 Utilization

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2020	1	1	$0.00+	$0.00+	$0.00+	120	30

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
Please note: There was no SoonerCare utilization of LEMS medications during fiscal year 2019 (07/01/2018 to 06/30/2019).
+ The 1 paid claim in fiscal year 2020 was for a member for whom SoonerCare was not the primary payer; therefore, the reimbursed amount is not a true reflection of the cost of the medication for SoonerCare.

Demographics of Members Utilizing LEMS Medications

- There was 1 unique member utilizing Firdapse® (amifampridine) during fiscal year 2020. However, due to the limited number of members utilizing LEMS medications, detailed demographic information could not be provided.
- There was no SoonerCare utilization of Ruzurgi® (amifampridine) during fiscal year 2020.

Top Prescriber Specialties of LEMS Medications by Number of Claims

- There was 1 paid claim for Firdapse® (amifampridine) during fiscal year 2020, which was prescribed by an internal medicine specialist in consultation with a neurologist.

Prior Authorization of LEMS Medications

There was 1 prior authorization request submitted and approved for 1 unique member for Firdapse® (amifampridine) during fiscal year 2020. There were no prior authorization requests submitted for Ruzurgi® (amifampridine) during fiscal year 2020.

Market News and Updates[8,9,10,11,12,13,14]

Anticipated Patent Expiration(s):

- There are no unexpired patents for Firdapse® (amifampridine) or Ruzurgi® (amifampridine).

Anticipated Exclusivity Expiration(s):

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

News:

- **June 2019:** Catalyst Pharmaceuticals filed a lawsuit against the FDA in June 2019 regarding the approval of Ruzurgi®. Prior to the approval of Ruzurgi®, Catalyst's Firdapse® had been granted 7 years of exclusivity in adult patients. However, Catalyst believes their exclusivity period is being violated by information regarding efficacy in adult patients contained in the label for Ruzurgi®, and this information constitutes illegal off-label marketing of Ruzurgi® which has only been FDA approved for use in pediatric patients. In July 2020, a magistrate judge considering the lawsuit recommended siding with the FDA and Jacobus Pharmaceuticals to deny Catalyst's motion for summary judgement. Despite this recommendation, Catalyst announced they plan to continue defending their exclusivity period in adult patients with LEMS.

Pipeline:

- **Amifampridine:** Catalyst Pharmaceuticals, the manufacturer of Firdapse®, is currently investigating the use of amifampridine in other disease states. Patients are currently being enrolled into a Phase 3 study evaluating amifampridine for the treatment of a specific subcategory of myasthenia gravis known as muscle-specific receptor tyrosine kinase (MuSK)-positive myasthenia gravis (MuSK-MG). In addition, Catalyst is initiating a clinical development plan to evaluate the use of amifampridine for the treatment of spinal muscular atrophy (SMA).
- **GV-58:** GV-58 is a selective P/Q- and N-type VGCC agonist which was identified as a potential LEMS treatment strategy in a preclinical study in mice. Whereas amifampridine indirectly increases the amount of acetylcholine released by blocking potassium channels, GV-58 works

directly on the VGCC which are damaged in LEMS. GV-58 increases the amount of time the VGCC remain open, resulting in increased calcium influx and more acetylcholine released from motor neurons. GV-58 was studied in a novel LEMS passive-transfer mouse model in which mice were given daily intraperitoneal injections of human LEMS patient antibodies for up to 30 days to generate the LEMS phenotype in the mice.

Recommendations

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

Utilization Details of LEMS Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
AMIFAMPRIDINE PRODUCTS						
FIRDAPSE TAB 10MG	1	1	$0.00	$0.00	1	100%
TOTAL	**1**	**1***	**$0.00⁺**	**$0.00⁺**	**1**	**100%**

TAB = tablet
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020
⁺The 1 paid claim in fiscal year 2020 was for a member for whom SoonerCare was not the primary payer; therefore, the reimbursed amount is not a true reflection of the cost of the medication for SoonerCare.

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Appendix M

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 25, 2020

FDA Approves First Drug to Treat Group of Rare Blood Disorders in Nearly 14 Years

The FDA approved Nucala (mepolizumab) for adults and children 12 years of age and older with hypereosinophilic syndrome (HES) for ≥6 months without another identifiable non-blood related cause of the disease. The new indication for Nucala is the first approval for HES patients in nearly 14 years. The FDA granted Nucala Fast Track, Priority Review, and Orphan Drug designations for this indication.

Nucala was evaluated in a randomized, double-blind, multicenter, placebo-controlled study in 108 patients with HES. In the study, patients were randomly assigned to receive Nucala or placebo by injection every 4 weeks. The study compared the proportion of patients who experienced a HES flare during the 32-week treatment period. An HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils on ≥2 occasions. The study compared the proportions of patients with ≥1 flare over a 32-week treatment period, as well as the time to the first flare. Fewer patients in the Nucala treatment group (28%) had HES flares compared to patients in the placebo group (56%), with a 50% relative reduction. In addition, the time to the first HES flare was later, on average, for patients treated with Nucala vs. placebo.

The most common side effects of Nucala in patients with HES included upper respiratory tract infection and extremity pain.

Nucala is also FDA approved for patients 6 years of age and older with severe asthma with an eosinophilic phenotype and for adult patients with eosinophilic granulomatosis with polyangiitis.

FDA NEWS RELEASE

For Immediate Release: September 24, 2020

FDA Takes Actions to Help Lower U.S. Prescription Drug Prices

The United States Department of Health and Human Services (DHS) and the FDA took actions to help provide safe, effective, and more affordable drugs to American patients as part of the Safe Importation Action Plan, fulfilling the aspect of the July Executive Order on drug pricing to complete the rulemaking allowing states to import certain prescription drugs from Canada.

The final rule implements a provision of federal law that allows FDA-authorized programs to import certain prescription drugs from Canada under specific conditions that ensure the importation poses no additional risk to the public's health and safety while achieving a significant reduction in the cost of covered products to the American consumer. The final guidance for industry describes procedures drug manufacturers can follow to facilitate importation of prescription drugs, including biological products, that are FDA-approved, manufactured abroad, authorized for sale in any foreign country, and originally intended for sale in that foreign country.

The rule allows states (including the District of Columbia and territories), Indian tribes, and pharmacists and wholesalers (in certain future circumstances), to submit

importation program proposals to the FDA for review and authorization. An importation program can be co-sponsored by a state, Indian tribe, pharmacist, or wholesaler. Referred to as Section 804 Importation Programs, these programs will be managed by the respective sponsor and any co-sponsors and authorized by the FDA to facilitate the importation of certain prescription drugs that are approved in Canada and, with appropriate labeling, meet the conditions of an FDA-approved drug application. Eligible prescription drugs would have to be relabeled with the required United States labeling and undergo testing for authenticity, degradation, and to ensure that the drugs meet established specifications and standards. These programs will also have to demonstrate significant cost reductions of the covered products to the American consumer.

The final guidance issued today describes procedures for a drug manufacturer to obtain a National Drug Code (NDC) for certain FDA-approved prescription drugs, including biological products and combination products, that were originally manufactured and intended for sale in that foreign country. The use of an additional NDC for these products may allow greater flexibility for drug companies to offer these products at a lower price than what their current distribution contracts require. Prescription drugs, including biological products, imported under the pathway described in the final guidance could be available to patients in a variety of settings, including hospitals, health care providers' offices, or licensed pharmacies, and would include the FDA-approved labeling (including *Prescribing Information*).

FDA NEWS RELEASE

For Immediate Release: September 23, 2020

FDA Requiring Labeling Changes for Benzodiazepines

The FDA announced in a Drug Safety Communication that it is requiring an update to the *Boxed Warning*, the agency's most prominent safety warning, and requiring class-wide labeling changes for benzodiazepines to include the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions to help improve their safe use.

In 2019, an estimated 92 million benzodiazepine prescriptions were dispensed from United States outpatient pharmacies, with alprazolam (38%) being the most common followed by clonazepam (24%) and lorazepam (20%). In 2018, an estimated 50% of patients dispensed oral benzodiazepines received them for 2 months or longer. Most benzodiazepines are recommended for use for periods of weeks or months.

In addition to requiring an update to the *Boxed Warning*, the FDA is requiring other changes to the *Warnings and Precautions*, *Drug Abuse and Dependence,* and *Patient Counseling Information* sections of the *Prescribing Information* for all benzodiazepine products. The agency is also requiring revisions to the existing patient *Medication Guides* for these medicines to help educate patients and caregivers about these risks.

This action is part of the FDA's ongoing effort to promote the public health by minimizing risks associated with inappropriate use of controlled substances while enabling appropriate access to these products for medical use.

FDA NEWS RELEASE

For Immediate Release: September 10, 2020

FDA Warns Website Operators Illegally Selling Opioids to Consumers

The FDA has issued warning letters to 17 website operators for illegally selling unapproved and misbranded opioids online in violation of the Federal Food, Drug, and

Cosmetic Act. Misbranded opioids include those offered for sale without a prescription, as well as opioids that lack adequate directions for use.

The opioids offered for sale include products such as tramadol and oxycodone. These prescription drugs have significant risks of addiction, abuse, and misuse, which can lead to overdose and death. These drugs should only be used under the supervision of a licensed health care provider. These warning letters are a continuation of the FDA's commitment to take action against the illegal sale of opioids over the internet.

Prescription drugs purchased from illegal online pharmacies, including opioids, may put patients' health at risk because the products, while being marketed as authentic, may be counterfeit, contaminated, expired, or otherwise unsafe. Additionally, several of these websites offer opioids online without a prescription, posing significant risks to consumers. Illegal online pharmacies can also pose other risks to consumers, including credit card fraud, identity theft, and computer viruses.

FDA NEWS RELEASE

For Immediate Release: September 1, 2020

FDA Provides Guidance to Industry for Detecting and Preventing Nitrosamines in Drugs

Since the discovery of impurities called nitrosamines in some types of drugs >2 years ago, the FDA has undertaken a thorough investigation in an effort to protect patients. The FDA has been working, in collaboration with regulatory counterparts around the world, to find and remove drugs with unacceptable nitrosamine impurities from the United States' drug supply. The FDA is also taking proactive efforts to help ensure that in the future, drugs can be free from unsafe levels of these impurities from the start of production.

In a continued effort to be transparent and provide guidance to manufacturers on how to detect and prevent unacceptable levels of nitrosamine impurities, the FDA published the Control of Nitrosamine Impurities in Human Drugs as guidance for immediate implementation. This guidance recommends steps, including a comprehensive risk assessment strategy and other actions, that manufacturers can take to reduce or prevent the presence of nitrosamine impurities in their drugs.

The source of these impurities can be related to the drug's manufacturing process, the materials used in manufacturing, the drugs' chemical structure, or even the conditions in which drugs are stored or packaged. Under FDA's oversight, manufacturers are responsible for mitigating these impurities.

The most common nitrosamine impurity is N-nitrosodimethylamine (NDMA). The FDA and the international scientific community do not expect NDMA to cause harm when ingested at low levels; however, given that genotoxic substances such as NDMA may increase the risk of cancer if people are exposed to them above certain levels and over long periods of time, manufacturers have recalled drugs with NDMA levels higher than the FDA's recommended acceptable intake levels. Patients taking medications with potential nitrosamine impurities should not stop taking their medications and should talk with their health care professional about concerns and other treatment options.

FDA NEWS RELEASE

For Immediate Release: August 28, 2020

COVID-19 Update: FDA Broadens Emergency Use Authorization for Veklury (Remdesivir) to Include All Hospitalized Patients for Treatment of COVID-19

The FDA broadened the scope of the existing emergency use authorization (EUA) for the drug Veklury (remdesivir) to include treatment of all hospitalized adult and pediatric patients with suspected or laboratory-confirmed COVID-19, irrespective of their severity of disease.

In May 2020, the FDA issued an EUA that authorized Veklury for the treatment of hospitalized adult and pediatric patients with severe COVID-19. As noted in the initial issuance of the EUA, the emergency use of Veklury was limited to those patients with severe disease, which was defined as patients with low blood oxygen levels or needing oxygen therapy or more intensive breathing support such as a mechanical ventilator.

Based on the FDA's ongoing review of the EUA, including its review of the totality of scientific information now available, it has been determined that it is reasonable to believe Veklury may be effective for the treatment of suspected or laboratory-confirmed COVID-19 in all hospitalized adult and pediatric patients. The FDA's review has also concluded that the known and potential benefits of Veklury outweigh the known and potential risks for these uses.

One randomized, double-blind, placebo-controlled clinical study (ACTT-1), conducted by the National Institute of Allergy and Infectious Diseases, evaluated how long it took for patients to recover from COVID-19 within 29 days of being treated. The study looked at 1,062 hospitalized subjects with mild, moderate, and severe COVID-19 who received Veklury (N=541) or placebo (N=521), plus standard of care. Recovery was defined as either being discharged from the hospital or being hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care. The median time to recovery from COVID-19 was 10 days for the Veklury group compared to 15 days for the placebo group, a statistically significant difference. Overall, the odds of clinical improvement at day 15 were also statistically significantly higher in the Veklury group when compared to the placebo group. In hospitalized patients with mild-to-moderate disease, the results for time to recovery as well as the odds of improvement at day 15 numerically favored the Veklury group and were consistent with the overall study results.

A separate randomized, open-label multi-center clinical study (Study GS-US-540-5774) of hospitalized adult patients with moderate COVID-19 compared treatment with Veklury for 5 days (N=191) and treatment with Veklury for 10 days (N=193) with standard of care (N=200). Researchers evaluated the clinical status of patients on day 11. Overall, the odds of a patient's COVID-19 symptoms improving were statistically significantly higher in the 5-day Veklury group at day 11 when compared to those receiving only standard of care. The odds of improvement with the 10-day treatment group when compared to those receiving only standard of care were numerically favorable, but not statistically significantly different. At day 28, mortality was ≤2% in all treatment groups. Limitations of this trial included the open-label design.

FDA NEWS RELEASE

For Immediate Release: August 31, 2020

FDA Approves First-of-its-Kind Automated Insulin Delivery and Monitoring System for Use in Young Pediatric Patients

The FDA approved the MiniMed 770G System for children 2 to 6 years of age with type 1 diabetes. MiniMed 770G System is a hybrid closed-loop diabetes management

device that is intended to automatically monitor blood glucose and provide appropriate basal insulin doses with little or no input from the patients or their caregivers. The 770G System is a first-of-a-kind device approved for patients 2 to 6 years of age. It is the first legally marketed device that can automatically adjust insulin delivery based on continuous glucose monitor values for this patient population.

The MiniMed 770G System, a bluetooth-enabled version of the previously approved MiniMed 670G System, works by measuring glucose levels in the body every 5 minutes and automatically adjusting insulin delivery by either administering or withholding insulin. The system includes a sensor that attaches to the body to measure glucose levels under the skin; an insulin pump strapped to the body; and an infusion patch connected to the pump with a catheter that delivers insulin. While the device automatically adjusts insulin levels, patients need to manually request insulin doses to counter carbohydrate consumption at mealtime.

The FDA evaluated data from a clinical study that included 46 children 2 to 6 years of age with type 1 diabetes. Study patients wore the device for approximately 3 months to evaluate the performance of the device during both the at-home periods, as well as a hotel period, to stress the system with sustained daily exercise. That study found no serious adverse events and that the device is safe for use.

Risks associated with use of the system may include hypoglycemia, hyperglycemia, as well as skin irritation or redness around the device's infusion patch. As part of this approval, the FDA is requiring the device manufacturer to conduct a post-market study to evaluate device performance in real-world settings in children 2 to 6 years of age.

FDA NEWS RELEASE

For Immediate Release: August 17, 2020

FDA Approves Treatment for Rare Disease Affecting Optic Nerves, Spinal Cord

The FDA approved Enspryng (satralizumab-mwge) for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults who are anti-aquaporin-4 (AQP4) antibody-positive. This is the third approved treatment for NMOSD. The FDA granted Enspryng Fast Track and Orphan Drug designations.

NMOSD is a rare autoimmune disease of the central nervous system that mainly affects the optic nerves and spinal cord. In patients with NMOSD, the body's immune system mistakenly attacks healthy cells and proteins in the body, most often those in the optic nerves and spinal cord. Individuals with NMOSD typically have attacks of optic neuritis, which causes eye pain and vision loss. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. Estimates vary, but NMOSD is thought to impact approximately 4,000 to 8,000 Americans.

The effectiveness and safety of Enspryng for the treatment of NMOSD were demonstrated in (2) 96-week clinical studies. The first study included 95 adult patients; 64 of these patients were anti-AQP4 positive. During this study, treatment with Enspryng reduced the number of NMOSD relapses by 74% in patients who were anti-AQP4 positive compared to treatment with a placebo. The second study included 76 adult patients; 52 of these patients were anti-AQP4 positive. During the second study, treatment with Enspryng reduced the number of relapses in patients who were anti-AQP4 positive by 78% compared to treatment with a placebo. There was no evidence of a benefit in patients who were anti-AQP4 antibody negative in either trial.

The *Prescribing Information* for Enspryng includes a warning for increased risk of infection, including serious and potentially fatal infections (such as potential reactivation

of hepatitis B and tuberculosis). Other warnings and precautions for Enspryng include elevated liver enzymes, decreased neutrophil counts, and hypersensitivity reactions. The most common side effects observed were the common cold, headache, upper respiratory tract infection, inflammation of the lining of the stomach, rash, joint pain, extremity pain, fatigue, and nausea.

Current Drug Shortages Index (as of September 28, 2020):

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

Amifostine Injection	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
AVYCAZ® (ceftazidime and avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Azithromycin Tablets	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Chlorothiazide (Diuril) Oral Suspension	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***

Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Doxycycline Hyclate Injection	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Floxuridine for Injection, USP	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydralazine Hydrochloride Injection, USP	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***

Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sertraline Hydrochloride Oral Solution, USP	***Currently in Shortage***
Sertraline Hydrochloride Tablets	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Timolol Maleate Ophthalmic Solution	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Tobramycin Lyophilized Powder for Injection	***Currently in Shortage***
Triamcinolone Acetonide (Triesence) Injection, Suspension	***Currently in Shortage***

Trifluridine Ophthalmic Solution	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***