Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
September 11, 2019
4:00pm

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

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

DATE: August 29, 2019

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

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

Call to Order

Public Comment Forum – Appendix A

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

Action Item – Nomination of Drug Utilization Review (DUR) Board Officers

Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – Appendix C

Action Item – Vote to Prior Authorize Zolgensma® (Onasemnogene Abeparvovec-xioi) – Appendix D

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

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

Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Nubeqa™ (Darolutamide) – Appendix G

Action Item – Annual Review of Crysvita® (Burosumab-twza) – Appendix H

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

30-Day Notice to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam) – Appendix J

Annual Review of Synagis® (Palivizumab) – Appendix K

Annual Review of Sickle Cell Disease (SCD) Medications – Appendix L

Industry News and Updates – Appendix M

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

Future Business

Adjournment

Oklahoma Health Care Authority

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

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum – See Appendix A

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

Items to be presented by Dr. Muchmore, Chairman:

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

A. July 10, 2019 DUR Minutes – Vote
B. July 10, 2019 DUR Recommendations Memorandum
C. Correspondence

Items to be presented by Dr. Muchmore, Chairman:

4. Action Item – Nomination of Drug Utilization Review (DUR) Board Officers

A. Nominations of DUR Board Chair and Vice Chair – Vote

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

5. Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – See Appendix C

A. Pharmacy Helpdesk Activity for July 2019
B. Medication Coverage Activity for July 2019
C. Pharmacy Helpdesk Activity for August 2019
D. Medication Coverage Activity for August 2019
E. Chronic Medication Adherence Program Update

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

6. Action Item – Vote to Prior Authorize Zolgensma® (Onasemnogene Abeparvovec-xioi) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item –Vote to Prior Authorize Bryhali™ (Halobetasol Propionate 0.01% Lotion), Duobrii™ (Halobetasol Propionate/Tazarotene 0.01%/0.045% Lotion), and Lexette™ (Halobetasol Propionate 0.05% Foam) and to Update the Topical Corticosteroids Product Based Prior Authorization Tier Chart and Criteria – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp) – See Appendix F

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Breast Cancer Medications
D. Prior Authorization of Breast Cancer Medications
E. Market News and Updates
F. Product Summaries
G. Recommendations
H. Utilization Details of Breast Cancer Medications

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

9. Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Nubeqa™ (Darolutamide) – See Appendix G

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Prostate Cancer Medications
D. Prior Authorization of Prostate Cancer Medications
E. Market News and Updates
F. Nubeqa™ (Darolutamide) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Prostate Cancer Medications

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

10. Action Item – Annual Review of Crysvita® (Burosumab-twza) – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Crysvita® (Burosumab-twza)
D. Prior Authorization of Crysvita® (Burosumab-twza)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

11. Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Welchol® (Colesevelam Chewable Bar) and Ezallor™ Sprinkle (Rosuvastatin Capsule) – See Appendix I

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

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

12. 30-Day Notice to Prior Authorize Sorilux® (Calcipotriene 0.005% Foam) – See Appendix J

A. Introduction
B. Sorilux® (Calcipotriene 0.005% Foam) Product Summary
C. College of Pharmacy Recommendations

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

13. Annual Review of Synagis® (Palivizumab) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Synagis® (Palivizumab)
C. Prior Authorization of Synagis® (Palivizumab)
D. Season Comparison
E. Market News and Updates
F. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

14. Annual Review of Sickle Cell Disease (SCD) Medications – See Appendix L

A. Current Prior Authorization Criteria

B. Utilization of SCD Medications
C. Prior Authorization of SCD Medications
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of SCD Medications

Non-Presentation; Questions Only:

15. Industry News and Updates – See Appendix M

A. Introduction
B. News and Updates

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

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

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

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

A. Turalio™ (Pexidartinib)
B. Hepatitis C Medications
C. Acute Lymphoblastic Leukemia and Chronic Myeloid Leukemia Medications
D. Cystic Fibrosis Medications
E. Signifor® LAR (Pasireotide)
F. Amyloidosis Medications
G. Various Antibiotics

**Future business subject to change.*

18. Adjournment

Appendix A

Changes to Public Comment Procedure

Oklahoma Health Care Authority
September 2019

Public Comment Procedure

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

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

Appendix B

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JULY 10, 2019

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Thomas Ha, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator		x
Shellie Keast, Ph.D.; Assistant Professor	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist		x
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Michael Nguyen, Pharm.D.		x
Laura Tidmore, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Visiting Pharmacy Student(s): Justin Wilson, Ashley Elms		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Deputy State Medicaid Director	x	
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Sr. Director of Pharmacy	x	
Kelli Brodersen, Marketing Coordinator	x	
Susan Eads, J.D.; Director of Litigation	x	
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director		x
Thomas Nunn, D.O.; Medical Director	x	
Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director; CEO		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Bob Atkins, Biogen	Andrea Stratton, Avexis	Erica Brumleve, GSK
Karen Ward, Avexis	Tara McKinley, Otsuka	Sumar Bieda, Abbott
Rhonda Clark, Indivior	Trebla Grant, Kite	Randy Huetsch, Kite
Marc Parker, Sunovion	Denise Roberts, Shatterproof	Jim Chapman, AbbVie
Shelley Thompson, Alkermes	Gwendolyn Caldwell, PhRMA	Cris Valladares, Celgene
Jennifer Norman, Integris	Ken Clemons	Tami Sova, Biogen
Doug Wood, ViiV	Scott Tremaine, Sarepta	Valerie Ng, Indivior
GeriLynn Utter, Orexo	Clinton Migdat, Orexo	Aaron Shan, BI
Mark Pahl, Pahl Pharmaceutical	Pauline Whelan, Orexo	Brian Maves, Pfizer
Robert Katz, OUHSC		

PRESENT FOR PUBLIC COMMENT:	
Robert Katz	OUHSC
Jennifer Norman	Integris Children's
Tami Sova	Biogen
Karen Ward	Avexis
Denise Roberts	Shatterproof
Gerilynn Utter	Orexo
Mark Pahl	Pahl Pharmaceutical

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA ITEM NO. 9 DENISE ROBERTS
2B: AGENDA ITEM NO. 9 GERILYNN UTTER
2C: AGENDA ITEM NO. 9 MARK PAHL
2D: AGENDA ITEM NO. 11 DR. ROBERT KATZ
2E: AGENDA ITEM NO. 11 DR. JENNIFER NORMAN
2F: AGENDA ITEM NO. 11 TAMI SOVA
2G: AGENDA ITEM NO. 11 KAREN WARD

ACTION: NONE REQUIRED

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

3A: JUNE 12, 2019 DUR MINUTES – VOTE
3B: JUNE 12, 2019 DUR RECOMMENDATIONS MEMORANDUM

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/SOONERPSYCH PROGRAM UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR JUNE 2019
4B: PHARMACY HELPDESK ACTIVITY FOR JUNE 2019
4C: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Abbott, Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE JORNAY PM™ [METHYLPHENIDATE EXTENDED-RELEASE (ER) CAPSULE], EVEKEO ODT™ [AMPHETAMINE ORALLY DISINTEGRATING TABLET (ODT)], ADHANSIA XR™ (METHYLPHENIDATE ER CAPSULE), AND SUNOSI™ (SOLRIAMFETOL TABLET)

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Dr. Munoz moved to approve; seconded by Dr. Huddleston

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE BALVERSA™ (ERDAFITINIB)

6A: INTRODUCTION

6B: RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ANNOVERA™ (SEGESTERONE ACETATE/ETHINYL ESTRADIOL VAGINAL SYSTEM), BIJUVA™ (ESTRADIOL/PROGESTERONE CAPSULE), CEQUA™ (CYCLOSPORINE 0.09% OPHTHALMIC SOLUTION), CORLANOR® (IVABRADINE ORAL SOLUTION), CROTAN™ (CROTAMITON 10% LOTION), GLOPERBA® (COLCHICINE ORAL SOLUTION), GLYCATE® (GLYCOPYRROLATE TABLET), KHAPZORY™ (LEVOLEUCOVORIN INJECTION), QMIIZ™ ODT [MELOXICAM ORALLY DISINTEGRATING TABLET (ODT)], SECONAL SODIUM™ (SECOBARBITAL SODIUM CAPSULE), TAPERDEX™ (DEXAMETHASONE TABLET), TIGLUTIK™ (RILUZOLE ORAL SUSPENSION), TOBRADEX® ST (TOBRAMYCIN/DEXAMETHASONE 0.3%/0.05% OPHTHALMIC SUSPENSION), TOLSURA™ (ITRACONAZOLE CAPSULE), AND YUTIQ™ (FLUOCINOLONE ACETONIDE INTRAVITREAL IMPLANT)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE ABILIFY MYCITE® (ARIPIPRAZOLE TABLET WITH SENSOR), ARISTADA INITIO® [ARIPIPRAZOLE LAUROXIL EXTENDED-RELEASE (ER) INJECTABLE SUSPENSION], AND PERSERIS™ [RISPERIDONE ER SUBCUTANEOUS (SUB-Q) INJECTABLE SUSPENSION]

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE CASSIPA® (BUPRENORPHINE/NALOXONE) AND LEVORPHANOL

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF BOTULINUM TOXINS

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF BOTULINUM TOXINS

10C: PRIOR AUTHORIZATION OF BOTULINUM TOXINS

10D: MARKET NEWS AND UPDATES

10E: COLLEGE OF PHARMACY RECOMMENDATIONS

10F: UTILIZATION DETAILS OF BOTULINUM TOXINS
Materials included in agenda packet; presented by Dr. Adams
Dr. Huddleston moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF SPINAL MUSCULAR ATROPHY MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZOLGENSMA® (ONASEMNOGENE ABEPARVOVEC-XIOI)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF SPINRAZA® (NUSINERSEN)
11C: PRIOR AUTHORIZATION OF SPINRAZA® (NUSINERSEN)
11D: MARKET NEWS AND UPDATES
11E: ZOLGENSMA® (ONASEMNOGENE ABEPARVOVEC-XIOI) PRODUCT SUMMARY
11F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF TOPICAL CORTICOSTEROIDS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BRYHALI™ (HALOBETASOL PROPIONATE 0.01% LOTION), DUOBRII™ (HALOBETASOL PROPIONATE/TAZAROTENE 0.01%/0.045% LOTION), AND LEXETTE™ (HALOBETASOL PROPIONATE 0.05% FOAM)
12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF TOPICAL CORTICOSTEROIDS
12C: PRIOR AUTHORIZATION OF TOPICAL CORTICOSTEROIDS
12D: MARKET NEWS AND UPDATES
12E: COLLEGE OF PHARMACY RECOMMENDATIONS
12F: UTILIZATION DETAILS OF TOPICAL CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Nawaz, Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF QBREXZA™ (GLYCOPYRRONIUM)
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF QBREXZA™ (GLYCOPYRRONIUM)
13C: PRIOR AUTHORIZATION OF QBREXZA™ (GLYCOPYRRONIUM)
13D: MARKET NEWS AND UPDATES
13E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: INDUSTRY NEWS AND UPDATES
14A: INTRODUCTION
14B: NEWS AND UPDATES
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
16A: SYNAGIS® (PALIVIZUMAB)
16B: SICKLE CELL MEDICATIONS
16C: BREAST CANCER MEDICATIONS
16D: PROSTATE CANCER MEDICATIONS
16E: ANTIHYPERLIPIDEMICS

16F: CRYSVITA® (BUROSUMAB-TWZA)

**Future business subject to change.*

Materials included in agenda packet; Non-presentation; Questions only

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT

The meeting was adjourned at 5:38pm.

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

Memorandum

Date: July 11, 2019

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

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

From: Melissa Abbott, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of July 10, 2019

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Jornay PM™ [Methylphenidate Extended-Release (ER) Capsule], Evekeo ODT™ [Amphetamine Orally Disintegrating Tablet (ODT)], Adhansia XR™ (Methylphenidate ER Capsule), and Sunosi™ (Solriamfetol Tablet)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the ADHD and Narcolepsy Medications Product Based Prior Authorization (PBPA) category:

1. The placement of Jornay PM™ (methylphenidate ER capsule) and Adhansia XR™ (methylphenidate ER capsule) into Tier-3. Current Tier-3 criteria will apply.

2. The placement of Evekeo ODT™ (amphetamine ODT) into the Special Prior Authorization (PA) Tier. Current Special PA criteria will apply.
3. Updating the current Special PA approval criteria for Methylin® chewable tablets and solution to prefer the brand formulation of Methylin® solution based on net costs.
4. The prior authorization of Sunosi™ (solriamfetol) in the Narcolepsy Medications category. Criteria similar to the current approval criteria for Xyrem® (sodium oxybate) will apply.

Proposed changes are shown in red in the following ADHD Medications Tier Chart and ADHD Medications and Narcolepsy Medications approval criteria:

ADHD Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Adzenys ER™ (amphetamine ER susp) Adzenys XR-ODT® (amphetamine ER-ODT) Cotempla XR-ODT™ (methylphenidate ER ODT) Daytrana® (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) Dyanavel® XR (amphetamine ER susp) Evekeo® (amphetamine) **Evekeo ODT™ (amphetamine ODT)** Methylin® (methylphenidate soln & chew tabs) Mydayis® (amphetamine/ dextroamphetamine ER) ProCentra® (dextroamphetamine) Zenzedi® (dextroamphetamine)
Short-Acting			
Adderall® (amphetamine/ dextroamphetamine)			
Long-Acting			
Vyvanse® (lisdexamfetamine caps and chew tabs)+	Adderall XR® (amphetamine/ dextroamphetamine ER)		
Methylphenidate			
Short-Acting			
Focalin® (dexmethylphenidate) Methylin® (methylphenidate) Ritalin® (methylphenidate)			
Long-Acting			
Aptensio XR® (methylphenidate ER) Focalin XR® brand name only (dexmethylphenidate ER) Metadate CD® (methylphenidate ER) QuilliChew ER® (methylphenidate ER chew tabs) Ritalin LA® (methylphenidate ER)	dexmethylphenidate ER (generic Focalin XR®) Quillivant XR® (methylphenidate ER susp)	**Adhansia XR™ (methylphenidate ER)** Concerta® (methylphenidate ER) **Jornay PM™ (methylphenidate ER)** Metadate ER® (methylphenidate ER) Methylin ER® (methylphenidate ER) methylphenidate ER 72mg Ritalin SR® (methylphenidate ER)	

ADHD Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Non-Stimulants			
Intuniv® (guanfacine ER) Strattera® (atomoxetine)		Kapvay® (clonidine ER)[Δ]	

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Placement of products shown in blue is based on net cost after rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.
[+]Unique criteria applies for the diagnosis of binge eating disorder (BED).
[Δ]Unique criteria applies in addition to tier trial requirements.
ADHD = attention deficit hyperactivity disorder; PA= prior authorization; ER = extended-release; SR = sustained-release; caps = capsules; ODT = orally disintegrating tablet; chew tabs = chewable tablets; soln = solution; susp = suspension

ADHD Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least 1 long-acting Tier-1 stimulant that resulted in an inadequate response:
   a. Trials should have been within the last 180 days; and
   b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician; and
3. For Quillivant XR®, an age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least 1 long-acting Tier-1 stimulant that resulted in an inadequate response; and
3. A previously failed trial with at least 1 long-acting Tier-2 stimulant that resulted in an inadequate response:
   a. Trials should have been within the last 365 days; and
   b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why the member cannot use the available long-acting lower tiered formulations.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
   a. An FDA approved diagnosis; and

b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, a long-acting Tier-2 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets must be provided.

ADHD Medications Special Prior Authorization (PA) Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra®, and Zenzedi® Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications must be provided.
2. Adzenys XR-ODT®, Adzenys ER™, Cotempla XR-ODT™, Daytrana®, Dyanavel® XR, and Evekeo ODT™ Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of stimulant medications that can be used for members who cannot swallow capsules or tablets must be provided; and
   c. An age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
3. Methylin® Chewable Tablets and Solution Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use methylphenidate immediate-release tablets must be provided; and
   c. Use of Methylin® chewable tablets or generic Methylin® solution will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Methylin® solution (brand name Methylin® solution is the preferred product); and
   d. An age restriction of 10 years and younger will apply. Members older than 10 years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
4. Mydayis® Approval Criteria:
   a. A covered diagnosis; and
   b. Member must be 13 years of age or older; and
   c. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications must be provided.

ADHD Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum dose are not covered.
2. Prior authorization is required for all tiers for members older than 20 years of age and for members younger than 5 years of age. All prior authorization requests for members younger than 5 years of age must be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria [Binge Eating Disorder (BED) Diagnosis]:
   a. An FDA approved diagnosis of moderate-to-severe BED; and

b. Member must be 18 years of age or older; and
c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
d. Authorizations will not be granted for the purpose of weight loss without the diagnosis of BED or for the diagnosis of obesity alone. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
e. A quantity limit of 30 capsules or chewable tablets per 30 days will apply; and
f. Initial approvals will be for the duration of 3 months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

Narcolepsy Medications Approval Criteria:

1. An FDA approved diagnosis; and
2. Use of Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
    a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; and
3. Use of Provigil® (modafinil) requires a previously failed trial (within the last 180 days) with Nuvigil® and a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
4. Use of Sunosi™ (solriamfetol) or Xyrem® (sodium oxybate) requires previously failed trials (within the last 180 days) with Tier-1 and Tier-2 stimulants from different chemical categories, Provigil®, and Nuvigil®, unless contraindicated, that did not yield adequate results; and
5. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea; and
6. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

Recommendation 3: Vote to Prior Authorize Balversa™ (Erdafitinib)

MOTION CARRIED by unanimous approval.

Balversa™ (Erdafitinib) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Tumor positive for *FGFR2* or *FGFR3* genetic mutation; and
3. Use in second-line or greater treatments including:
    a. Following at least 1 line of platinum-containing chemotherapy; and
    b. Within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Recommendation 4: Vote to Prior Authorize Annovera™ (Segesterone Acetate/Ethinyl Estradiol Vaginal System), Bijuva™ (Estradiol/Progesterone Capsule), Cequa™ (Cyclosporine 0.09% Ophthalmic Solution), Corlanor® (Ivabradine Oral Solution), Crotan™ (Crotamiton 10% Lotion), Gloperba®

(Colchicine Oral Solution), Glycate® (Glycopyrrolate Tablet), Khapzory™ (Levoleucovorin Injection), Qmiiz™ ODT [Meloxicam Orally Disintegrating Tablet (ODT)], Seconal Sodium™ (Secobarbital Sodium Capsule), TaperDex™ (Dexamethasone Tablet), Tiglutik™ (Riluzole Oral Suspension), TobraDex® ST (Tobramycin/Dexamethasone 0.3%/0.05% Ophthalmic Suspension), Tolsura™ (Itraconazole Capsule), and Yutiq™ (Fluocinolone Acetonide Intravitreal Implant)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Annovera™ (segesterone acetate/ethinyl estradiol vaginal system), Bijuva™ (estradiol/progesterone capsule), and Cequa™ (cyclosporine 0.09% ophthalmic solution) with the following criteria:

Annovera™ (Segesterone Acetate/Ethinyl Estradiol Vaginal System) Approval Criteria:

1. An FDA approved indication to prevent pregnancy in women; and
2. A patient-specific, clinically significant reason why the member cannot use NuvaRing® (etonogestrel/ethinyl estradiol vaginal ring) or all other available formulations of estrogen/progestin contraception must be provided; and
3. A quantity limit of 1 vaginal system per year will apply.

Bijuva™ (Estradiol/Progesterone Capsule) Approval Criteria:

1. An FDA approved indication for the treatment of moderate-to-severe vasomotor symptoms due to menopause in women with an intact uterus; and
2. A patient-specific, clinically significant reason why the member cannot use all other available estrogen/progestin products indicated for vasomotor symptoms of menopause must be provided; and
3. A quantity limit of 30 capsules (1 pack) per 30 days will apply.

Cequa™ (Cyclosporine 0.09% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication to increase tear production in patients with keratoconjunctivitis sicca (dry eye); and
2. A patient-specific, clinically significant reason why the member cannot use Restasis® (cyclosporine 0.05% ophthalmic emulsion), which is available without a prior authorization, must be provided; and
3. A quantity limit of 60 single-use vials (1 box) per 30 days will apply.

The College of Pharmacy also recommends the prior authorization of Corlanor® (ivabradine oral solution) and to update the current Corlanor® (ivabradine tablet) approval criteria to be consistent with package labeling (proposed changes shown in red).

Corlanor® (Ivabradine Tablet and Oral Solution) Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. To reduce the risk of hospitalization for worsening heart failure (HF) in adult patients with stable, symptomatic chronic HF with reduced left ventricular ejection fraction; or
    b. For the treatment of stable, symptomatic HF due to dilated cardiomyopathy (DCM) in patients 6 months of age and older; and

2. For a diagnosis of worsening HF in adults:
    a. The prescriber must verify that the member has left ventricular ejection fraction ≤35%; and
    b. The prescriber must verify that the member is in sinus rhythm with a resting heart rate ≥70 beats per minute; and
    c. The member must be on maximal/maximally tolerated doses of beta-blockers or have a contraindication to beta-blockers; and
3. For a diagnosis of DCM in patients 6 months of age or older:
    a. The prescriber must verify that the member has left ventricular ejection fraction ≤45%; and
    b. The prescriber must verify that the member is in sinus rhythm with a resting heart rate (HR) as follows:
        i. Age 6 to 12 months, HR ≥105 beats per minute (bpm); or
        ii. Age 1 to 3 years, HR ≥95 bpm; or
        iii. Age 3 to 5 years, HR ≥75 bpm; or
        iv. Age 5 to 18 years, HR ≥70 bpm; and
    c. The prescriber must verify that dose titration will be followed according to package labeling; and
    d. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
4. Authorization of Corlanor® solution for members >40kg requires a patient-specific, clinically significant reason why Corlanor® tablets cannot be used; and
5. For Corlanor® tablets, a quantity limit of 60 tablets per 30 days will apply; and
6. For Corlanor® solution, a quantity limit of 112 ampules (4 boxes) per 28 days will apply.

The College of Pharmacy also recommends the addition of Crotan™ (crotamiton 10% lotion) to the current Eurax® (crotamiton lotion/cream) criteria and the addition of Gloperba® (colchicine oral solution) to the current Colcrys® (colchicine tablet) and Mitigare® (colchicine capsule) criteria (proposed changes shown in red).

Eurax® (Crotamiton 10% Lotion/Cream) and Crotan™ (Crotamiton 10% Lotion) Approval Criteria:

1. An FDA approved diagnosis of scabies or pruritic skin; and
2. Member must be 18 years of age or older; and
3. For a diagnosis of scabies, member must have used permethrin 5% cream in the past 7 to 14 days with inadequate results; and
4. For a diagnosis of pruritic skin, a patient-specific, clinically significant reason why the member cannot use other available topical treatments used for pruritic skin must be provided; and
5. For authorization of Crotan™, a patient-specific, clinically significant reason why the member cannot use Eurax® must be provided; and
6. A quantity limit of 1 tube or bottle per 30 days will apply.

Colcrys® (Colchicine Tablet), ~~and~~ Mitigare® (Colchicine Capsule), and Gloperba® (Colchicine Oral Solution) Approval Criteria:

1. A quantity of 6 tablets/capsules for a 3-day supply is available without prior authorization for treatment of acute gouty attacks; and
2. Failure of allopurinol after 6 months of treatment defined by persistent gouty attacks with serum urate levels greater than 6.0mg/dL; and
3. A patient-specific, clinically significant reason why colchicine/probenecid would not be a viable option for the member must be provided; and
4. For authorization of Gloperba®, a patient-specific, clinically significant reason why the member cannot use colchicine tablets or capsules must be provided; and
5. A quantity limit of 60 tablets/capsules per 30 days or 300mL per 30 days will apply for gout; and
6. Members with the diagnosis of Familial Mediterranean Fever verified by genetic testing will be approved for up to 2.4mg per day.

Additionally, the College of Pharmacy recommends the prior authorization of Glycate® (glycopyrrolate tablet) and Khapzory™ (levoleucovorin injection) with the following criteria:

Glycate® (Glycopyrrolate Tablet) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of peptic ulcer disease (PUD) in patients 12 years of age and older; and
2. A patient-specific, clinically significant reason why the member cannot use glycopyrrolate 1mg and 2mg tablets, which are available without a prior authorization, must be provided.

Khapzory™ (Levoleucovorin Injection) Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Rescue after high-dose methotrexate (MTX) therapy in patients with osteosarcoma; or
    b. Diminishing the toxicity associated with overdosage of folic acid antagonists or impaired MTX elimination; or
    c. Treatment of patients with metastatic colorectal cancer in combination with fluorouracil; and
2. A patient-specific, clinically significant reason why the member cannot use generic leucovorin injection or generic levoleucovorin calcium injection must be provided.

The College of Pharmacy recommends the placement of Qmiiz™ ODT (meloxicam ODT) into the Special Prior Authorization (PA) Tier of the Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Product Based Prior Authorization (PBPA) category. Current Special PA Criteria will apply. The proposed change is shown in red in the following NSAIDs Tier Chart.

NSAIDs Special Prior Authorization (PA) Approval Criteria:

1. A unique indication for which a Tier-1 or Tier-2 medication is not appropriate; or
2. Previous use of at least 2 Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically-significant reason why a special formulation is needed over a Tier-1 product.

4. Additionally, use of Tivorbex® will require a patient-specific, clinically significant reason why the member cannot use all other available generic indomethacin products.
5. Additionally, use of Celebrex® (celecoxib) 400mg capsules will require a diagnosis of Familial Adenomatous Polyposis (FAP) and a patient-specific, clinically significant reason why the member cannot use 2 celecoxib 200mg capsules to achieve a 400mg dose.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)*		
Tier-1	**Tier-2**	**Special PA**
celecoxib (Celebrex®) 50mg, 100mg, & 200mg caps	diclofenac potassium (Cataflam®)	celecoxib (Celebrex®) 400mg caps
diclofenac epolamine (Flector® patch)	diclofenac sodium/ misoprostol (Arthrotec®)	diclofenac (Zorvolex®)
diclofenac ER (Voltaren® XR)	diclofenac sodium (Voltaren®) 25mg tabs	diclofenac potassium (Cambia®) powder pack
diclofenac sodium (Voltaren®) 50mg & 75mg tabs	etodolac (Lodine®) 200mg & 300mg caps	diclofenac potassium (Zipsor®) caps
diclofenac sodium 1% (Voltaren® Gel)	etodolac ER (Lodine® XL)	diclofenac sodium (Dyloject™)
etodolac (Lodine®) 400mg & 500mg tabs	naproxen sodium (Anaprox®) 275mg & 550mg tabs	diclofenac sodium (Pennsaid®) topical drops
flurbiprofen (Ansaid®)	oxaprozin (Daypro®)	fenoprofen (Nalfon®)
ibuprofen (Motrin®)	piroxicam (Feldene®)	ibuprofen/famotidine (Duexis®)
ketoprofen (Orudis®)	tolmetin (Tolectin®)	indomethacin (Indocin®) susp & ER caps
meloxicam (Mobic®)		indomethacin (Tivorbex®)
nabumetone (Relafen®)		ketoprofen ER (Oruvail®)
naproxen (Naprosyn®)		ketorolac tromethamine (Sprix®) nasal spray
naproxen EC (Naprosyn®)		meclofenamate (Meclomen®)
sulindac (Clinoril®)		mefenamic acid (Ponstel®)
		meloxicam (Vivlodex®) caps
		meloxicam ODT (Qmiiz™ ODT)
		naproxen sodium ER (Naprelan®)
		naproxen/esomeprazole (Vimovo®)

ER = extended-release; EC = enteric coated; caps = capsules; tabs = tablets; susp = suspension; ODT = orally disintegrating tablet; PA = prior authorization
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

The College of Pharmacy recommends the prior authorization of Seconal Sodium™ (secobarbital sodium capsule), TaperDex™ (dexamethasone tablet dose pack), and Tiglutik™ (riluzole suspension) with the following criteria:

Seconal Sodium™ (Secobarbital Sodium Capsule) Approval Criteria:

1. An FDA approved indication for 1 of the following:
   a. The short-term treatment of insomnia; or
   b. A preanesthetic; and
2. A patient-specific, clinically significant reason why the member cannot use other cost-effective therapeutic alternatives must be provided; and

3. For the short-term treatment of insomnia, a quantity limit of 1 capsule per day not to exceed 14 capsules per 30 days will apply.

TaperDex™ (Dexamethasone Tablet Dose Pack) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use dexamethasone 1.5mg individual tablets, which are available without a prior authorization, must be provided.

Tiglutik™ (Riluzole Suspension) Approval Criteria:

1. An FDA approved indication for the treatment of amyotrophic lateral sclerosis (ALS); and
2. A patient-specific, clinically significant reason why the member cannot use riluzole tablets, even when tablets are crushed, must be provided; and
3. A quantity limit of 20mL per day or 600mL per 30 days will apply.

The College of Pharmacy recommends the placement of TobraDex® ST (tobramycin/ dexamethasone 0.3%/0.05% ophthalmic suspension) into Tier-2 of the Ophthalmic Antibiotics/Steroid Combination Products PBPA category. Current Tier-2 criteria will apply. The proposed change is shown in red in the following Ophthalmic Antibiotic/Steroid Combination Products Tier Chart.

Ophthalmic Antibiotic/Steroid Combination Tier-2 Approval Criteria:

1. Prescription written by optometrists/ophthalmologists; or
2. When requested medication is being used for pre/post-operative prophylaxis.

Ophthalmic Antibiotic/Steroid Combination Products*	
Tier-1	**Tier-2**
neomycin/polymyxin B/dexamethasone (Maxitrol®) susp & oint	bacitracin/polymyxin B/neomycin/HC oint
sulfacetamide/prednisolone sol	gentamicin/prednisolone (Pred-G®) susp & oint
tobramycin/dexamethasone (TobraDex®) susp+	neomycin/polymyxin B/HC (Cortisporin®) susp
	sulfacetamide/prednisolone (Blephamide®) susp & oint
	tobramycin/dexamethasone (TobraDex®) oint
	tobramycin/dexamethasone (TobraDex® ST) susp
	tobramycin/loteprednol (Zylet®) susp

oint = ointment; susp = suspension; HC = hydrocortisone; sol = solution
*Tier structure(s) based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NDAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Brand preferred.

Finally, the College of Pharmacy recommends the prior authorization of Tolsura™ (itraconazole capsule) and Yutiq™ (fluocinolone acetonide intravitreal implant) with the following criteria:

Tolsura™ (Itraconazole Capsule) Approval Criteria:

1. An FDA approved indication of 1 of the following fungal infections in immunocompromised and non-immunocompromised adult patients:
   a. Blastomycosis, pulmonary and extrapulmonary; or
   b. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis; or

c. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy; and

2. A patient-specific, clinically significant reason why the member cannot use itraconazole 100mg capsules, which are available without prior authorization, must be provided.

Yutiq™ (Fluocinolone Acetonide Intravitreal Implant) Approval Criteria:

1. An FDA approved diagnosis of chronic, non-infectious uveitis affecting the posterior segment of the eye; and
2. Yutiq™ must be administered by an ophthalmologist; and
3. Prescriber must verify that the member will be monitored for increased intraocular pressure and cataract development; and
4. A patient-specific, clinically significant reason why the member requires Yutiq™ in place of local corticosteroids must be provided; and
5. A quantity limit of 1 implant per eye every 36 months will apply.

Recommendation 5: Vote to Prior Authorize Abilify MyCite® (Aripiprazole Tablet with Sensor), Aristada Initio® [Aripiprazole Lauroxil Extended-Release (ER) Injectable Suspension], and Perseris™ [Risperidone ER Subcutaneous (Sub-Q) Injectable Suspension]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Atypical Antipsychotic Medications Product Based Prior Authorization (PBPA) category:

1. The placement of Aristada Initio® (aripiprazole lauroxil) into Tier-3. Aristada Initio® (aripiprazole lauroxil) is currently in Tier-1 due to supplemental rebate participation. If the manufacturer chooses not to participate in supplemental rebates, Aristada Initio® may be moved up to the higher tier.
2. The placement of Perseris™ (risperidone ER sub-Q injection) into Tier-3. Current Tier-3 criteria will apply.
3. The placement of Abilify MyCite® (aripiprazole tablets with sensor) into Tier-3 with the following criteria:

Abilify MyCite® (Aripiprazole Tablet with Sensor) Approval Criteria:

1. An FDA approved diagnosis; and
2. Member must not have dementia-related psychosis; and
3. A patient-specific, clinically significant reason why the member cannot use all oral or injectable Tier-1 or Tier-2 medications. Tier structure rules continue to apply. Please note, the ability of Abilify MyCite® to improve patient compliance or modify aripiprazole dosage has not been established; and
4. Previous use of aripiprazole tablets and a patient-specific, clinically significant reason why the Tier-1 aripiprazole tablets are no longer appropriate for the member must be provided; and
5. The prescriber agrees to closely monitor patient adherence; and

6. Patients should be capable and willing to use the MyCite® App and follow the *Instructions for Use* and ensure the MyCite® App is compatible with their specific smartphone; and
7. ~~Initial~~ Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and patient compliance greater than 80% with prescribed therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to oral aripiprazole tablets or to any of the oral or injectable Tier-1 or Tier-2 medications must be provided. Tier structure rules continue to apply.

Atypical Antipsychotic Medications*		
Tier-1	**Tier-2**	**Tier-3**
aripiprazole (Abilify®)¥	asenapine (Saphris®)	**aripiprazole tablet with sensor (Abilify MyCite®)~**
aripiprazole IM (Abilify Maintena®)	lurasidone (Latuda®)	brexpiprazole (Rexulti®)
aripiprazole lauroxil IM (Aristada®)		cariprazine (Vraylar®)
aripiprazole lauroxil IM (Aristada Initio®)		clozapine (Fazaclo®)
clozapine (Clozaril®)◊		clozapine oral susp (Versacloz®)
olanzapine (Zyprexa®)		iloperidone (Fanapt®)
paliperidone IM (Invega Sustenna®)		olanzapine/fluoxetine (Symbyax®)^
paliperidone IM (Invega Trinza®)**		paliperidone (Invega®)
quetiapine (Seroquel®)		**risperidone ER sub-Q (Perseris™)**
quetiapine ER (Seroquel XR®)		
risperidone (Risperdal®)		
risperidone IM (Risperdal Consta®)		
ziprasidone (Geodon®)		

ER = extended-release; IM = intramuscular; susp = suspension; sub-Q = subcutaneous
*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Placement of products shown in blue is based on net cost after rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.
◊Clozapine does not count towards a Tier-1 trial.
**Use of Invega Trinza® requires members to have been adequately treated with the 1-month paliperidone ER injection (Invega Sustenna®) for at least 4 months.
¥Aripiprazole (Abilify®) orally disintegrating tablet (ODT) is considered a special formulation and will require a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation.
^In addition to the Tier-3 criteria requirements, approval of olanzapine/fluoxetine (Symbyax®) requires a patient-specific, clinically significant reason why the member cannot use olanzapine and fluoxetine as individual components.
~Unique criteria applies for Abilify MyCite® (aripiprazole tablet with sensor).

Recommendation 6: Vote to Prior Authorize Cassipa® (Buprenorphine/ Naloxone) and Levorphanol

MOTION CARRIED.

The College of Pharmacy, in partnership with the Oklahoma Health Care Authority (OHCA), recommends the implementation of a daily morphine milligram equivalent (MME) limit of 90 to coincide with Centers for Medicare and Medicaid Services (CMS) safety alerts.

1. Prior authorization would be required for members exceeding the 90 MME limit per day. Prior authorizations would require patient-specific, clinically significant reasoning for daily doses of 90 MME or greater. Prescribers must provide reasoning for why tapering to below the MME limit is not appropriate for the member.
2. Requests for members exceeding the 90 MME limit per day can be approved when there is documentation of pain associated with end-of-life care, palliative care, or hospice. Oncology, sickle cell disease, and hemophilia diagnoses would also be excluded from the MME limit.

Furthermore, the College of Pharmacy, in partnership with the OHCA, recommends that select medication assisted treatment (MAT) products no longer require prior authorization. In addition, it is recommended to update the quantity limit for buprenorphine-containing medications used for MAT to 16mg bioequivalent buprenorphine per day (proposed changes noted in red). Each request for greater than 16mg bioequivalent buprenorphine per day will be evaluated on a case-by-case basis.

The College of Pharmacy recommends the following:

1. The placement of levorphanol tartrate into the Special Prior Authorization (PA) Tier of the Opioid Analgesics Product Based Prior Authorization (PBPA) category with the following criteria listed in red.
2. The prior authorization of Cassipa® (buprenorphine/naloxone sublingual films) with the following criteria (proposed changes noted in red).

Levorphanol Tartrate Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use alternative ~~lower-tiered short-acting~~ treatment options for pain (e.g., non-opioid analgesics, lower-tiered opioid analgesics) must be provided.

Suboxone® [Buprenorphine/Naloxone Sublingual (SL) Tablets and Films], Subutex® (Buprenorphine SL Tablets), Zubsolv® (Buprenorphine/Naloxone SL Tablets), Bunavail® (Buprenorphine/Naloxone Buccal Films), and Cassipa® (Buprenorphine/Naloxone SL Films) Approval Criteria:

1. Brand formulation Suboxone® SL films and generic buprenorphine/naloxone SL tablets are the preferred products. Authorization of Bunavail®, Zubsolv®, Cassipa®, and generic Suboxone® SL films requires a patient-specific, clinically significant reason why brand formulation Suboxone® SL films or generic buprenorphine/naloxone SL tablets are not appropriate; and
2. Subutex® (buprenorphine) 2mg and 8mg SL tablets will only be approved if the member is pregnant or has a documented serious allergy or adverse reaction to naloxone; and
3. For Cassipa®, the member must have been titrated to a dose of 16mg buprenorphine using another buprenorphine product prior to approval; and
4. Buprenorphine products FDA approved for a diagnosis of opioid abuse/dependence must be prescribed by a licensed practitioner who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
5. Member must have an FDA approved diagnosis of opioid abuse/dependence; and

6. Concomitant treatment with opioids (including tramadol) will be denied; and
7. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
8. The following limitations will apply:
    a. **Suboxone®** 2mg/0.5mg, 4mg/1mg~~, and 8mg/2mg~~ SL tablets and films: A quantity limit of 90 SL units per 30 days will apply.
    b. **Suboxone®** 8mg/2mg SL tablets and films: A quantity limit of 60 SL units per 30 days will apply.
    c. **Suboxone®** 12mg/3mg SL films: A quantity limit of 30 ~~60~~ SL films per 30 days will apply.
    d. **Subutex®** 2mg ~~and 8mg~~ SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.
    e. **Subutex®** 8mg SL tablets: A quantity limit of 60 SL tablets per 30 days will apply.
    f. **Zubsolv®** 0.7mg/0.18mg, 1.4mg/0.36mg, 2.9mg/0.71mg~~, and 5.7mg/1.4mg~~ SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.
    g. **Zubsolv®** 5.7mg/1.4mg ~~and 8.6mg/2.1mg~~ SL tablets: A quantity limit of 60 SL tablets per 30 days will apply.
    h. **Zubsolv®** 8.6mg/2.1mg and 11.4mg/2.9mg SL tablets: A quantity limit of 30 SL tablets per 30 days will apply.
    i. **Bunavail®** 2.1mg/0.3mg ~~and 4.2mg/0.7mg~~ buccal films: A quantity limit of 90 buccal films per 30 days will apply.
    j. **Bunavail®** 4.2mg/0.7mg buccal films: A quantity limit of 60 buccal films per 30 days will apply.
    k. **Bunavail®** 6.3mg/1mg buccal films: A quantity limit of 30 ~~60~~ buccal films per 30 days will apply.
    l. **Cassipa®** 16mg/4mg SL films: A quantity limit of 30 SL films per 30 days will apply.

High-Dose Buprenorphine Products Approval Criteria:

1. Each request for >16 ~~24~~mg bioequivalent buprenorphine per day will be evaluated on a case-by-case basis; and
2. A taper schedule, dates of an attempted taper with reason for failure, or a patient-specific, clinically significant reason why a taper schedule or attempt is not appropriate for the member should be documented on the prior authorization request; and
3. Opioid urine drug screens should be submitted with high-dose requests that plan to continue high-dose treatment longer than the duration of 1 month; and
    a. Urine drug screens must show the absence of opioid medications other than buprenorphine products for continued approval; or
    b. Prescriber must document a patient-specific reason the member should continue therapy, reason for opioid use, and document a plan for member to discontinue opioid use; and
4. Symptoms associated with withdrawal at lower doses or symptoms requiring high doses should be listed on the prior authorization request; and
5. Each approval will be for the duration of 1 month. If urine drug screen and other documentation are submitted indicating high-dose therapy is necessary, an approval can be granted for the duration of 3 months; and

6. Continued high-dose authorization after the 3-month approval will require a new (recent) urine drug screen.

Recommendation 7: Annual Review of Botulinum Toxins

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the current prior authorization criteria for Botox® (onabotulinumtoxinA) for the prevention of migraine headaches, to be consistent with the current approval criteria for the calcitonin gene-related peptide (CGRP) inhibitors for the prevention of migraine headaches (proposed changes noted in red):

Approval Criteria for Botox® for Prevention of Migraine Headaches *(other botulinum toxins will not be approved for this diagnosis)*:

1. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); and
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
2. Migraine headache exacerbation secondary to other medical conditions or medication therapies have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
3. Member has no contraindications to Botox® injections; and
4. FDA indications are met:
    a. Member is 18 years of age or older; and
    b. Member has documented chronic migraine headaches:
        i. Frequency of 15 or more headache days per month with 8 or more migraine days per month and occurring for more than 3 months; and
        ii. Duration of 4 hours of headache per day or longer; and
5. The member has failed medical migraine preventative therapy including at least 2 agents with different mechanisms of action. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blockers); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
6. Member is not frequently taking medications which are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and

c. Opioids (≥10 days/month for >3 months); and
d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
e. Ergotamine-containing medications (≥10 days/month for >3 months); and
f. Triptans (≥10 days/month for >3 months); and

7. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last 6 months by a neurologist for chronic migraine headaches and Botox® recommended as treatment (not necessarily prescribed or administered by a neurologist); and
9. ~~Members who smoke or use tobacco products will not be approved.~~ Prescriber must verify that other aggravating factors that are contributing to the development of chronic migraine headaches are being treated when applicable (e.g., smoking); and
10. Member will not use the requested medication concurrently with a calcitonin gene-related peptide (CGRP) inhibitor for the prevention of migraine headaches.

Recommendation 8: Annual Review of Spinal Muscular Atrophy Medications and 30-Day Notice to Prior Authorize Zolgensma® (Onasemnogene Abeparvovec-xioi)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Bryhali™ (Halobetasol Propionate 0.01% Lotion), Duobrii™ (Halobetasol Propionate/Tazarotene 0.01%/0.045% Lotion), and Lexette™ (Halobetasol Propionate 0.05% Foam)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Qbrexza™ (Glycopyrronium)

NO ACTION REQUIRED.

Recommendation 11: Industry News and Updates

NO ACTION REQUIRED.

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

NO ACTION REQUIRED.

Recommendation 13: Future Business

NO ACTION REQUIRED.

Director Pasternik-Ikard:

My name is Denise Roberts. I write as an Oklahoma resident and mother of two sons, Matthew and Dillan, who died due to opioid overdoses.

I've been closely following the Drug Utilization Review Board process, and testified in support of the Oklahoma Health Care Authority expanding treatment options available to SoonerCare enrollees struggling with opioid use disorder. You may read my recent column in the *Daily Oklahoman* – "Knock down barriers to addiction treatment."

As you know, the Review Board will next meet on July 10 to issue its formal recommendation to you and the department. As Director, I urge you to make available all FDA-approved medications to treat opioid addiction. During a public health crisis like this, it is critical that we empower physicians and eliminate "prior authorization" and similar barriers to treatment.

I plan to be in attendance once again when the committee meets July 10. It may be too late for my children, but there are thousands of Oklahomans who deserve the best possible chance at recovery.

Thank you for your consideration, and please don't hesitate to contact me if you have any questions.

Sincerely,
Denise Roberts

Oklahoma Society of Addiction Medicine
A Chapter of American Society of Addiction Medicine

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Wednesday, July 3, 2019

Becky Pasternik-Ikard, RN, JD
Chief Executive Officer, Oklahoma Health Care Authority
John Muchmore, MD, PhD
Chair, Drug Utilization Review Board
Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

Re: Support for Increased Access to and Coverage of All Opioid Dependence Treatment Medications

Dear Ms. Pasternik-Ikard, Dr. Muchmore, and Members of the Drug Utilization Review Board,

On behalf of the Oklahoma Society of Addiction Medicine (OKSAM), the medical specialty society representing Oklahoma physicians and other clinicians specializing in the treatment of addiction, OKSAM would like to extend its appreciation to the Drug Utilization Review Board for its ongoing attention to access and coverage of medication-assisted treatment (MAT) for Medicaid beneficiaries suffering from opioid use disorder (OUD). At a time when Oklahoma is experiencing the tragic impacts of the opioid addiction and overdose epidemic, patients and their families deserve a response that eliminates barriers to proven, effective OUD treatment. To that end, OKSAM urges the Board to increase access to treatment by covering all formulations of each type of MAT and rejecting case-by-case review of buprenorphine doses over 16mg per day.

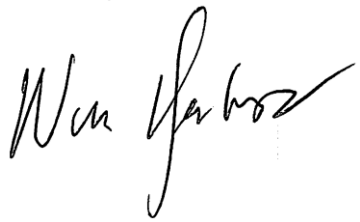
OKSAM is dedicated to increasing access to and improving the quality of addiction treatment for patients in Oklahoma. For patients suffering from OUD, access to timely treatment is of the utmost importance. When a patient presents themselves for treatment, it is vital that the patient be stabilized as quickly as possible through the use of MAT combined with psychosocial and recovery support services, as appropriate. MAT has routinely been shown to decrease by 75% the likelihood that a patient experiences mortality related to addiction. However, when prior authorization and other utilization controls delay a prescription, patients cannot receive treatment as quickly as is medically necessary.[i] In fact, a recent survey of physicians found that 92% of respondents reported care delays due to prior authorization, with 64% reporting a delay of at least one business day.[ii] This lag in treatment can have disastrous consequences for patients with OUD. A delay of just one day is enough time for a patient to relapse, overdose, or suffer a myriad of other experiences that can adversely affect their treatment outcome and even threaten their life, making prior authorization and other utilization review requirements not only a regulatory burden for clinicians but also a source of potential harm for patients. For these reasons, OKSAM strongly recommends that the Board increase access to treatment by eliminating prior authorization and covering all formulations of each type of MAT.

In addition to timely treatment, patients must receive care that is guided by their individual needs and their clinician's professional judgment. Guidelines recommending a limit of 16mg

bioequivalent buprenorphine per day, while useful for general reference, do not consider the medical history or needs of individual patients. Indeed, the Food and Drug Administration Drug approves dosing to a limit of 24mg per day and doses over 16mg may be medically appropriate, particularly for those patients using the most dangerous substances intravenously. Utilization policy requiring a case-by-case review of dosing greater than 16mg bioequivalent buprenorphine per day will lead to disruption and delays for patients receiving medically appropriate care within FDA dosing limits. For this reason, OKSAM respectfully requests that the Board reject a case-by-case review requirement for buprenorphine dosing over 16mg per day. Such a limit is medically inappropriate and will create barriers to treatment at a time when patients most need access to care.

OKSAM shares the state of Oklahoma's goal of increasing access to high-quality, evidence-based, and comprehensive addiction treatment. We strongly urge the Oklahoma Health Care Authority's Drug Utilization Review Board to open access to all formulations of each type of MAT and to reject arbitrary buprenorphine dose limits to ensure patients receive the right care when they need it, thus saving lives. Please do not hesitate to contact Dr. William Yarborough, at [redacted], if OKSAM can be of any service to you. We look forward to working with you.

Sincerely,



William H. Yarborough, MD, FACP, FASAM
President, Oklahoma Society of Addiction Medicine

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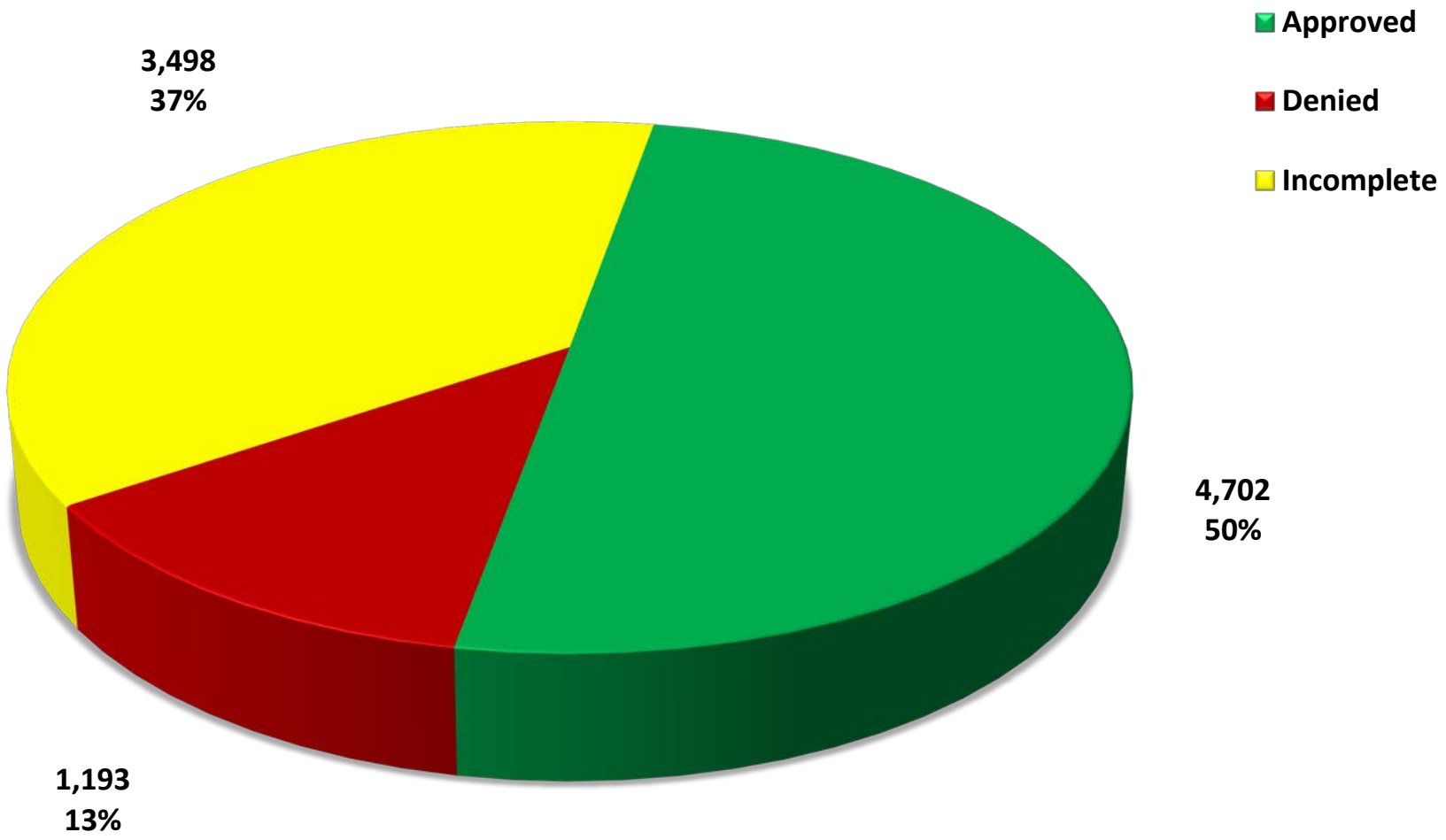
[i] Legal Action Center. (2015). Confronting an Epidemic: The Case for Eliminating Barriers to Medication Assisted Treatment of Heroin and Opioid Addiction. Washington, D.C: Legal Action Center. Available at https://lac.org/resources/substance-use-resources/medication-assisted-treatment-resources/case-for-eliminating-barriers-to-medication-assisted-treatment-of-heroin-and-opioid-addiction/

[ii] The American Medical Association. Survey of 1,000 Physicians to investigate attitudes towards prior authorization. United States, 2017. Available at: https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc/prior-auth-2017.pdf

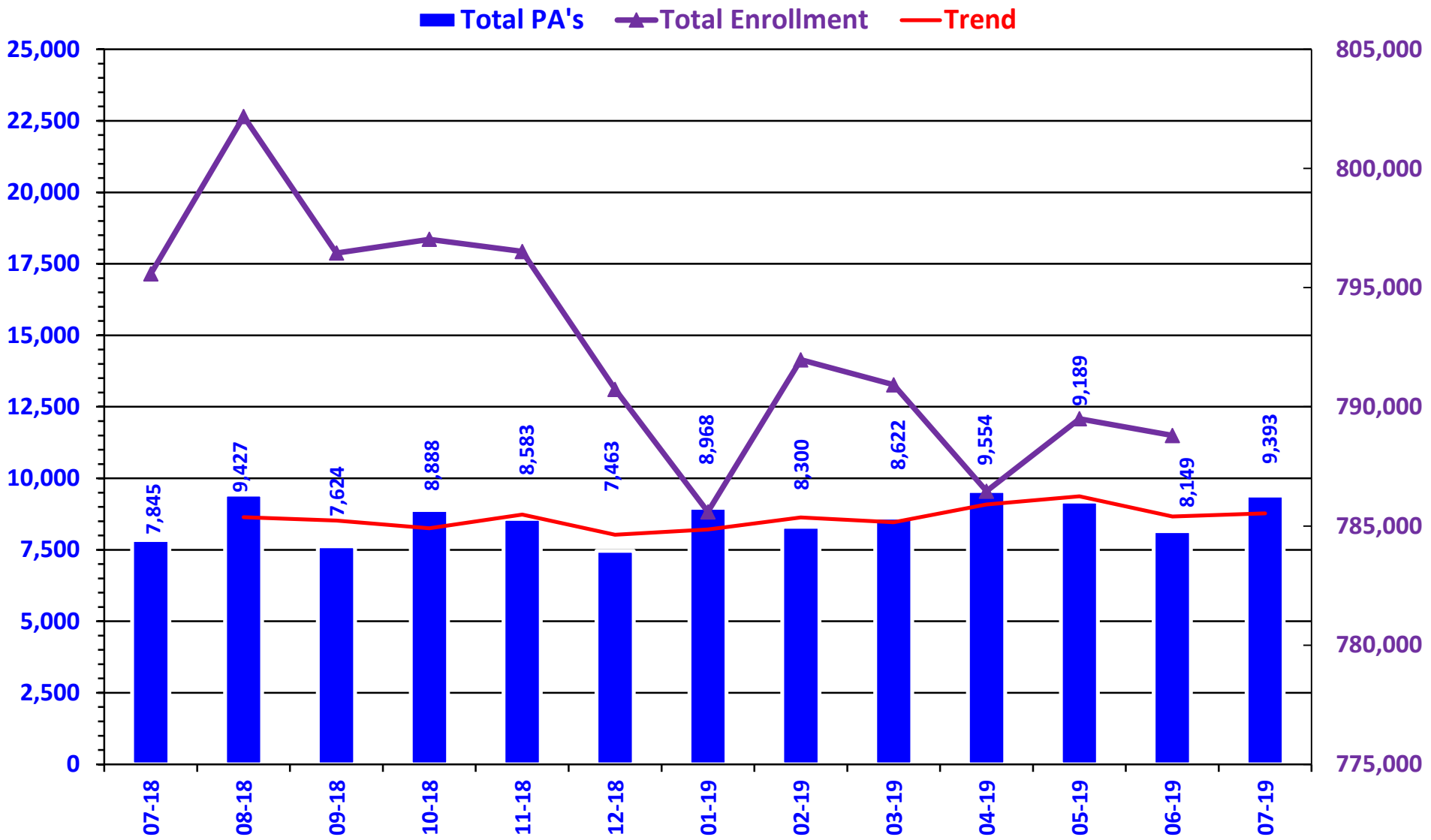
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: JULY 2019



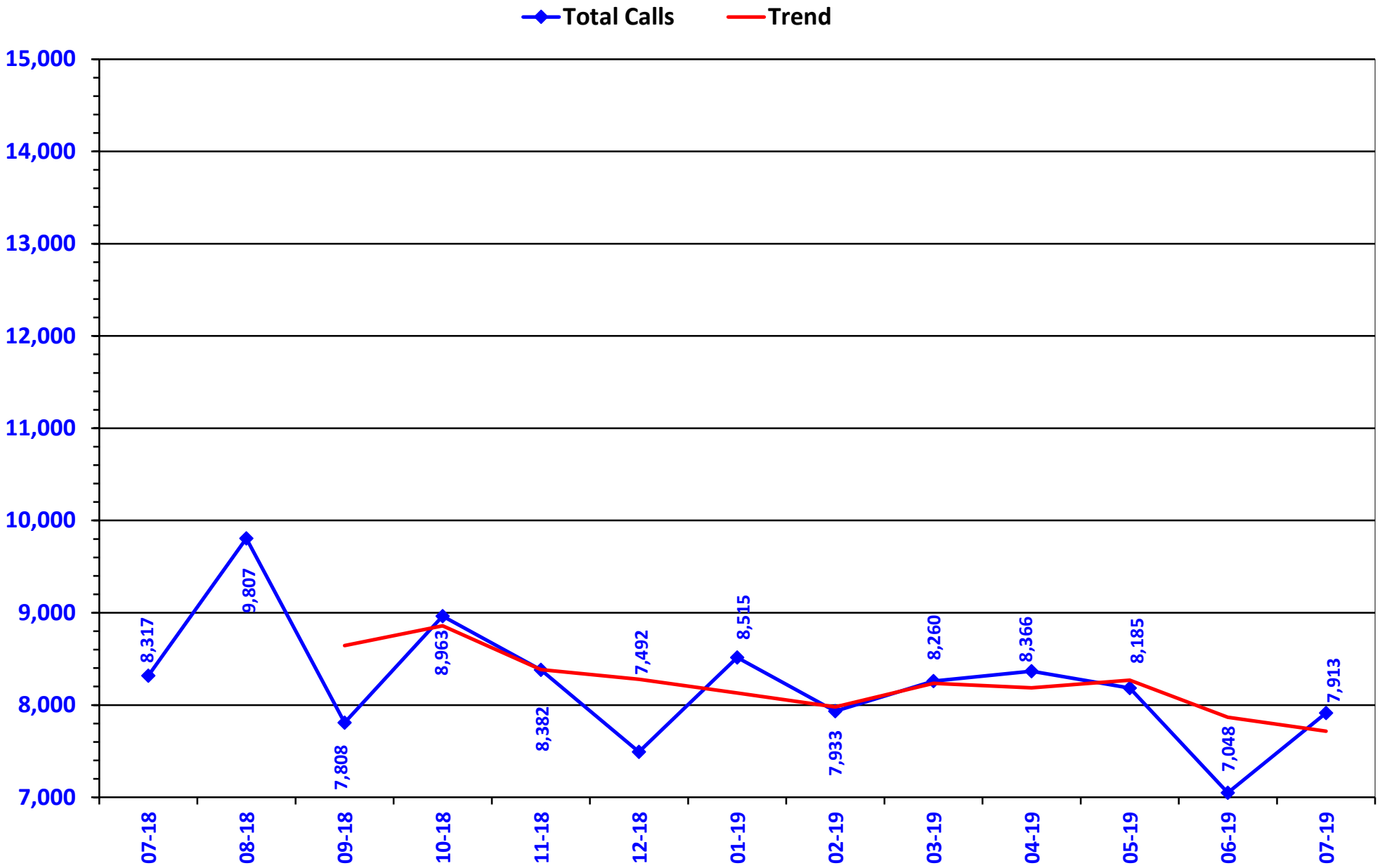
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JULY 2018 – JULY 2019



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JULY 2018 – JULY 2019



Prior Authorization Activity

7/1/2019 Through 7/31/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	65	4	17	44	357
Analgesic - NonNarcotic	19	1	7	11	50
Analgesic - Narcotic	369	173	42	154	168
Angiotensin Receptor Antagonist	12	3	2	7	241
Antiasthma	109	22	28	59	283
Antibiotic	28	16	2	10	262
Anticonvulsant	199	73	22	104	304
Antidepressant	196	45	38	113	339
Antidiabetic	286	91	51	144	347
Antihistamine	17	6	4	7	268
Antimigraine	166	16	46	104	249
Antineoplastic	102	58	15	29	158
Antiparasitic	21	4	5	12	3
Antiulcers	142	51	37	54	92
Anxiolytic	18	3	1	14	168
Atypical Antipsychotics	242	130	15	97	342
Biologics	148	86	13	49	324
Bladder Control	37	8	13	16	314
Blood Thinners	348	207	20	121	332
Botox	71	48	17	6	321
Buprenorphine Medications	622	412	25	185	75
Cardiovascular	61	27	6	28	346
Chronic Obstructive Pulmonary Disease	206	47	43	116	322
Constipation/Diarrhea Medications	137	24	47	66	231
Contraceptive	18	12	0	6	332
Corticosteroid	11	0	3	8	0
Dermatological	369	108	94	167	130
Diabetic Supplies	638	381	32	225	203
Diuretic	12	8	0	4	318
Endocrine & Metabolic Drugs	171	84	19	68	149
Erythropoietin Stimulating Agents	25	15	2	8	93
Fibromyalgia	17	2	1	14	356
Fish Oils	13	0	6	7	0
Gastrointestinal Agents	118	23	32	63	143
Genitourinary Agents	13	2	5	6	186
Growth Hormones	120	87	17	16	159
Hepatitis C	154	86	17	51	8
HFA Rescue Inhalers	55	2	5	48	245
Insomnia	31	1	8	22	176
Insulin	132	43	15	74	338
Miscellaneous Antibiotics	23	1	8	14	7
Multiple Sclerosis	40	20	4	16	224
Muscle Relaxant	54	11	13	30	43
Nasal Allergy	51	5	17	29	176
Neurological Agents	132	53	27	52	242
Nsaids	28	1	5	22	361
Ocular Allergy	48	6	16	26	84
Ophthalmic Anti-infectives	10	3	3	4	14
Osteoporosis	22	11	0	11	291
Other*	329	73	70	186	257

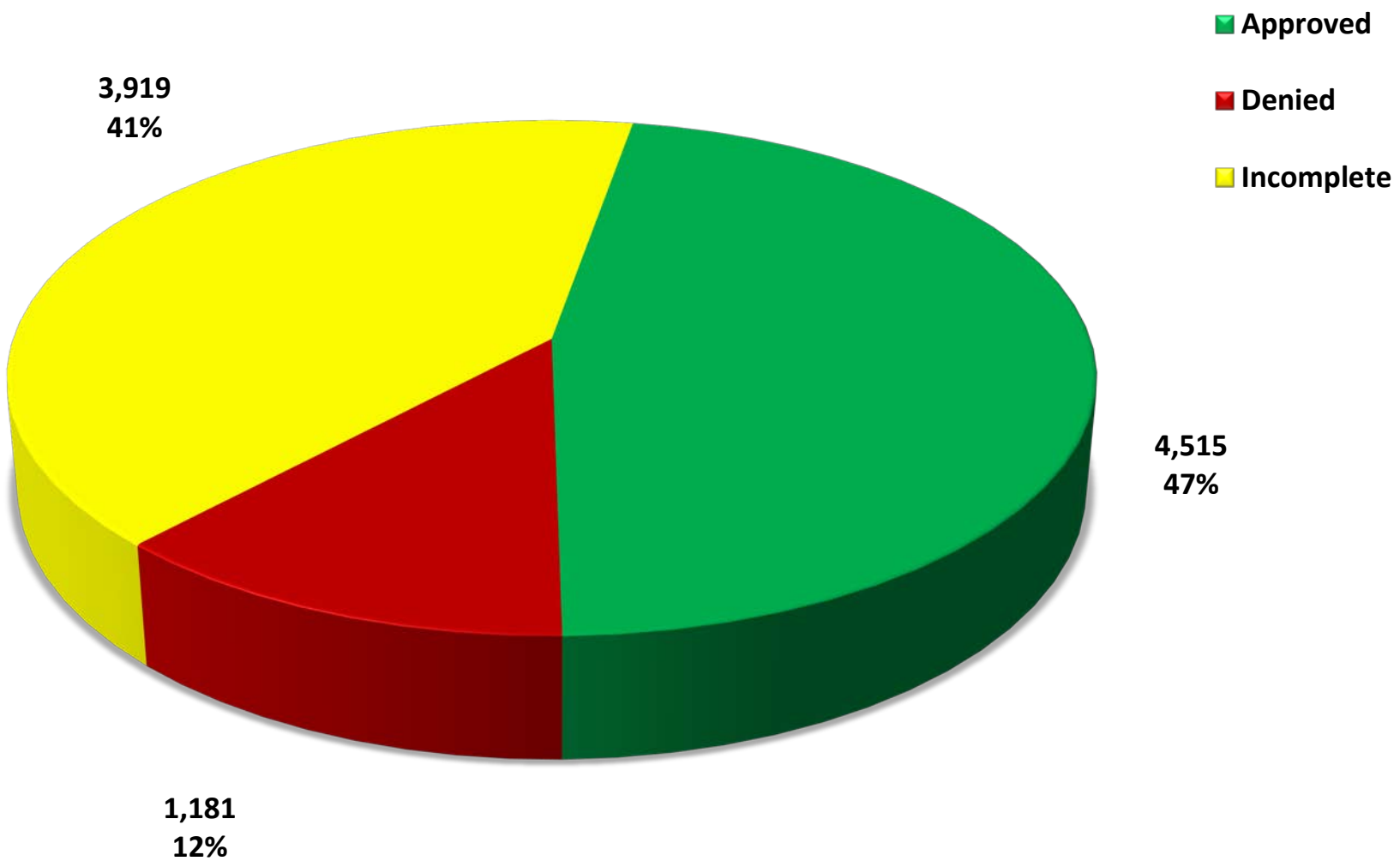
* Includes any therapeutic category with less than 10 prior authorizations for the month.

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Otic Antibiotic	31	3	2	26	6
Pediculicide	30	0	3	27	0
Respiratory Agents	19	14	0	5	274
Statins	13	5	3	5	211
Stimulant	601	317	54	230	341
Testosterone	60	16	19	25	346
Topical Antifungal	31	3	7	21	44
Topical Corticosteroids	70	1	42	27	119
Vitamin	100	20	47	33	206
Pharmacotherapy	102	86	0	16	299
Emergency PAs	0	0	0	0	
Total	**7,312**	**3,058**	**1,112**	**3,142**	
Overrides					
Brand	40	21	4	15	233
Compound	18	15	0	3	36
Cumulative Early Refill	1	1	0	0	180
Diabetic Supplies	12	11	0	1	141
Dosage Change	376	347	2	27	13
High Dose	5	4	0	1	207
Ingredient Duplication	9	7	0	2	14
Lost/Broken Rx	101	95	3	3	14
MAT Override	2	2	0	0	52
NDC vs Age	286	182	36	68	245
Nursing Home Issue	63	60	0	3	18
Opioid MME Limit	110	64	5	41	76
Opioid Quantity	28	20	1	7	150
Other	44	39	4	1	12
Quantity vs. Days Supply	898	712	22	164	206
STBS/STBSM	27	21	1	5	93
Stolen	12	10	1	1	14
Temporary Unlock	2	2	0	0	1
Third Brand Request	47	31	2	14	30
Overrides Total	**2,081**	**1,644**	**81**	**356**	
Total Regular PAs + Overrides	**9,393**	**4,702**	**1,193**	**3,498**	

Denial Reasons	
Unable to verify required trials.	2,862
Does not meet established criteria.	1,218
Lack required information to process request.	607
Other PA Activity	
Duplicate Requests	600
Letters	13,522
No Process	19
Changes to existing PAs	780

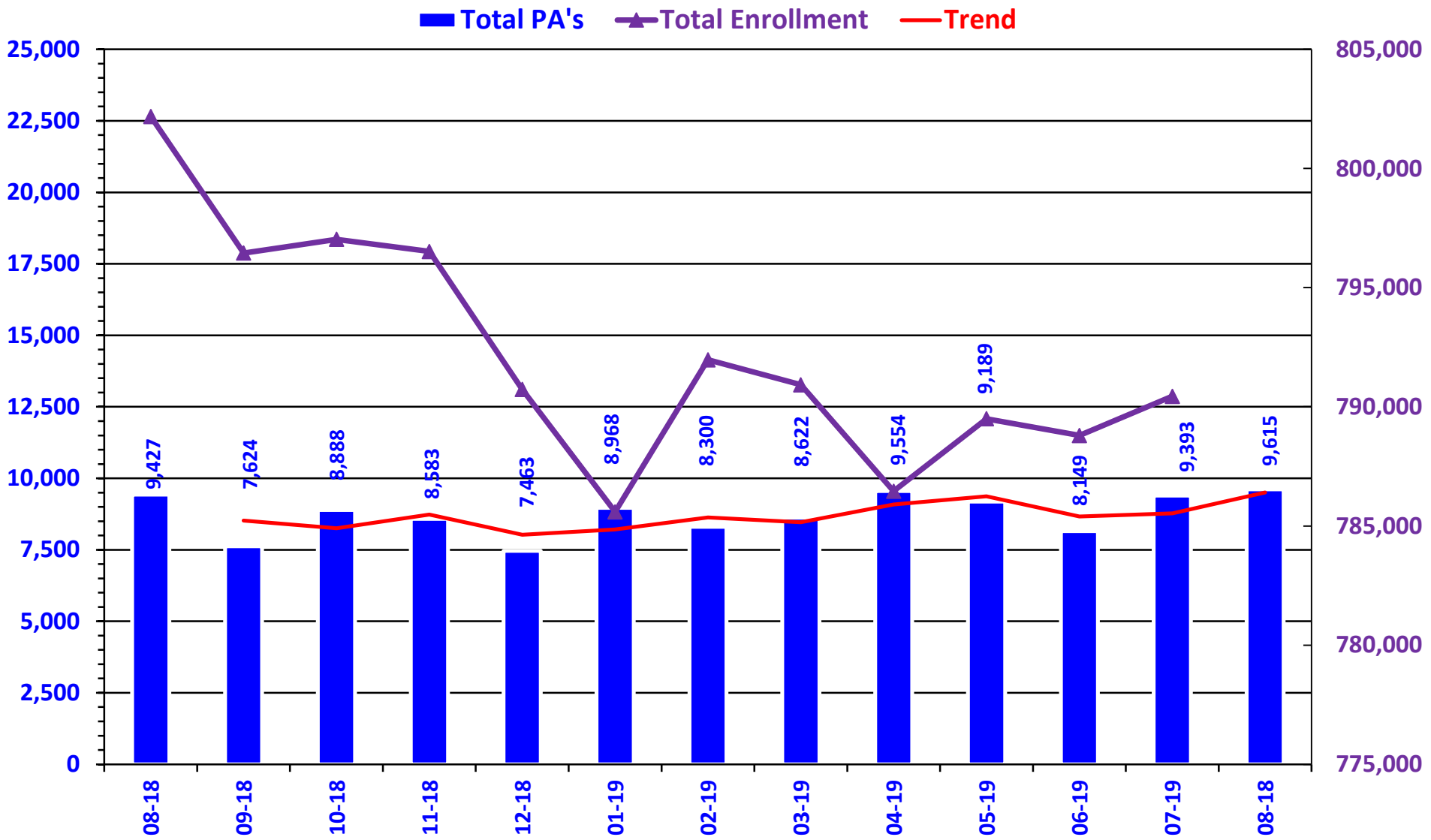
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: AUGUST 2019



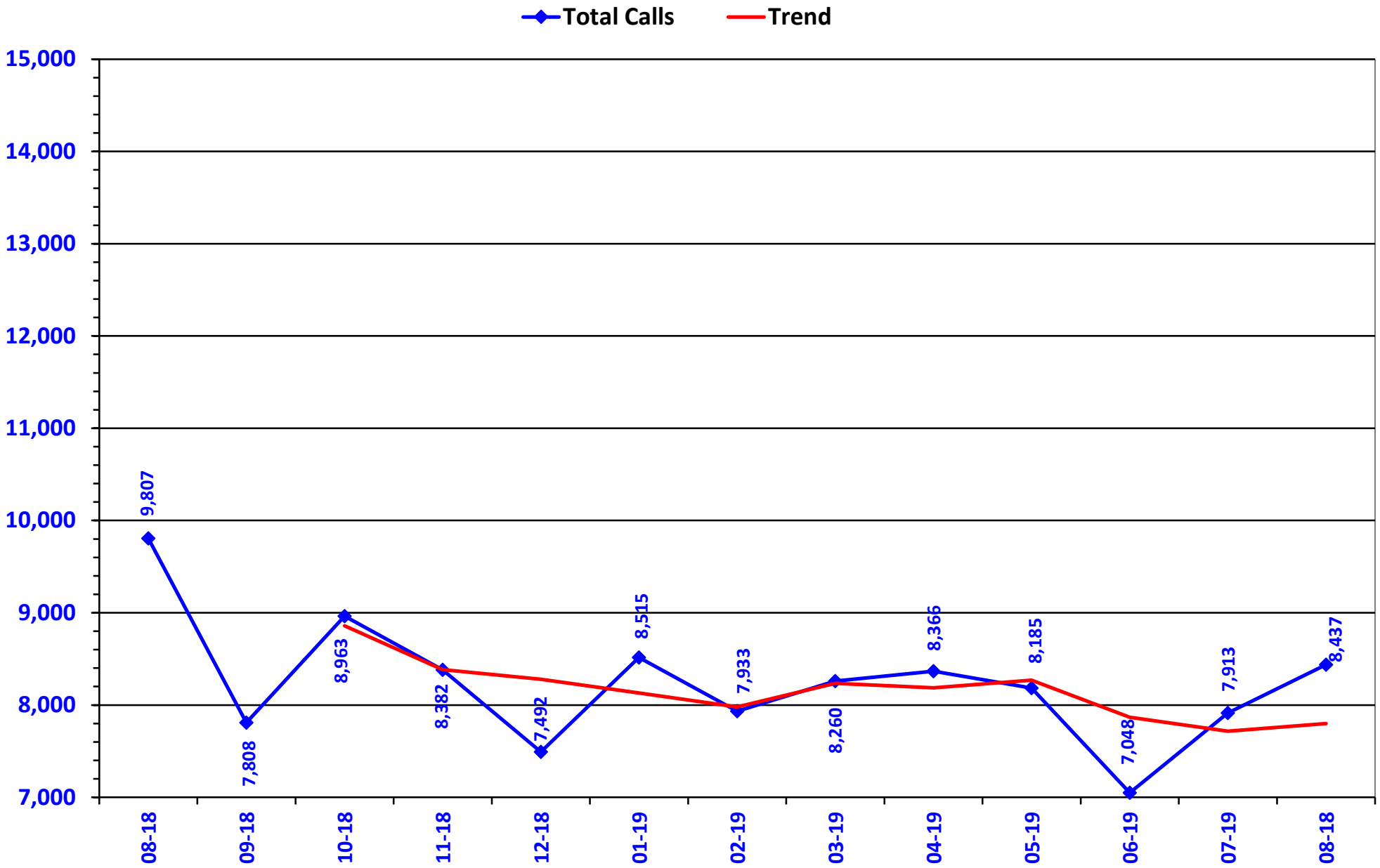
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: AUGUST 2018 – AUGUST 2019



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
AUGUST 2018 – AUGUST 2019



Prior Authorization Activity

8/1/2019 Through 8/31/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	94	5	24	65	359
Analgesic - NonNarcotic	19	1	4	14	31
Analgesic - Narcotic	425	170	37	218	157
Angiotensin Receptor Antagonist	10	2	3	5	359
Antiasthma	108	26	32	50	299
Antibiotic	36	21	4	11	269
Anticonvulsant	198	81	23	94	320
Antidepressant	182	45	33	104	318
Antidiabetic	262	76	52	134	355
Antihemophilic Factor	10	7	0	3	194
Antihistamine	23	2	14	7	224
Antimigraine	182	26	44	112	155
Antineoplastic	114	77	5	32	165
Antiparasitic	19	2	2	15	2
Antiulcers	144	44	47	53	105
Anxiolytic	15	0	3	12	0
Atypical Antipsychotics	231	118	19	94	345
Biologics	169	107	11	51	271
Bladder Control	42	9	9	24	285
Blood Thinners	308	184	10	114	337
Botox	34	26	5	3	357
Buprenorphine Medications	110	18	7	85	73
Calcium Channel Blockers	11	0	5	6	0
Cardiovascular	85	26	13	46	327
Chronic Obstructive Pulmonary Disease	212	42	56	114	337
Constipation/Diarrhea Medications	159	25	50	84	175
Contraceptive	21	16	0	5	319
Corticosteroid	10	1	4	5	53
Dermatological	343	102	83	158	116
Diabetic Supplies	620	355	20	245	202
Diuretic	12	8	0	4	357
Endocrine & Metabolic Drugs	134	77	18	39	152
Erythropoietin Stimulating Agents	20	11	1	8	111
Fibromyalgia	121	6	2	113	304
Fish Oils	10	0	8	2	0
Gastrointestinal Agents	109	30	22	57	195
Glaucoma	13	1	6	6	117
Growth Hormones	116	88	7	21	160
Hepatitis C	156	94	19	43	9
HFA Rescue Inhalers	68	0	7	61	0
Insomnia	43	5	11	27	189
Insulin	154	57	16	81	315
Miscellaneous Antibiotics	15	2	1	12	8
Multiple Sclerosis	53	21	11	21	176
Muscle Relaxant	46	6	17	23	22
Nasal Allergy	67	7	19	41	203
Neurological Agents	100	36	14	50	207
Neuromuscular Agents	12	10	1	1	330
NSAIDs	37	2	10	25	360
Ocular Allergy	27	2	5	20	84

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	15	9	2	4	356
Other*	297	59	63	175	251
Otic Antibiotic	28	6	5	17	10
Pediculicide	46	0	11	35	0
Respiratory Agents	26	13	0	13	198
Statins	17	1	8	8	359
Stimulant	808	383	95	330	346
Testosterone	78	22	19	37	339
Topical Antifungal	35	6	9	20	75
Topical Corticosteroids	65	2	24	39	207
Vitamin	104	18	45	41	141
Pharmacotherapy	143	117	0	26	292
Emergency PAs	0	0	0	0	
Total	**7,171**	**2,713**	**1,095**	**3,363**	
Overrides					
Brand	48	32	3	13	272
Compound	25	20	0	5	131
Cumulative Early Refill	1	1	0	0	180
Diabetic Supplies	13	12	0	1	156
Dosage Change	425	401	2	22	11
High Dose	6	6	0	0	266
Ingredient Duplication	6	4	0	2	9
Lost/Broken Rx	121	112	2	7	16
MAT Override	55	45	0	10	45
NDC vs Age	322	201	30	91	245
Nursing Home Issue	76	75	0	1	13
Opioid MME Limit	331	188	10	133	85
Opioid Quantity	43	35	2	6	147
Other*	46	40	3	3	14
Prescriber Temp Unlock	1	0	0	1	0
Quantity vs. Days Supply	824	563	33	228	191
STBS/STBSM	38	20	1	17	99
Stolen	24	21	0	3	18
Third Brand Request	39	26	0	13	14
Overrides Total	**2,444**	**1,802**	**86**	**556**	
Total Regular PAs + Overrides	**9,615**	**4,515**	**1,181**	**3,919**	

Denial Reasons	
Unable to verify required trials.	3,051
Does not meet established criteria.	1,205
Lack required information to process request.	831
Other PA Activity	
Duplicate Requests	644
Letters	12,668
No Process	6
Changes to existing PAs	872
Helpdesk Initiated Prior Authorizations	704
PAs Missing Information	42

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
September 2019

Prescriber Mailing: Maintenance Diabetes and Cardiovascular Medications

The Chronic Medication Adherence (CMA) educational mailing is processed quarterly and sent to prescribers with members on chronic maintenance medications for diabetes mellitus (DM), blood pressure (BP), or cholesterol. The purpose of the CMA mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Previously, prescribers were selected randomly to receive letters if they met the inclusion criteria for the mailing module. In February 2016, the CMA mailing changed to sending the educational letters to the same consistent prescribers. Included prescribers receive 4 letters per year to better inform them of their SoonerCare patients using maintenance medications and to make their patients' adherence more convenient to track over time including any improvements or changes. In February 2018, the mailing was updated to include both cardiovascular (CV) and DM medications in each mailing rather than alternating with each mailing. Inclusion criteria required the prescriber to have at least 3 SoonerCare patients taking DM, BP, and cholesterol medications. The consistent prescriber list is updated approximately once every 2 years to account for prescribers who move out of state, retire, or no longer contract with SoonerCare. The review period for each mailing is 1 year, and patients are assigned to prescribers if they are the last prescriber of record for a maintenance medication on SoonerCare paid pharmacy claims.

Each mailing includes a prescriber summary report with a "star rating" based on the prescriber's overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is ≥80%. A patient is considered non-adherent if their PDC is <80%. A higher percentage (and corresponding star rating) is better and indicates that more of their patients are adherent to their maintenance medications. Each mailing also includes a list of medication adherence patient resources intended to offer prescribers methods to improve their patients' adherence.

Mailing Summaries

The following table only outlines mailings that have included both CV and DM modules in 1 mailing.

Date Letter Processed	Total Letters Mailed	Total Members Included
February 2018	278	7,190
May 2018	274	7,038

Date Letter Processed	Total Letters Mailed	Total Members Included
August 2018	272	6,900
November 2018	259	6,411
February 2019	256	6,036
May 2019	240	5,557

Star Ratings

The star ratings for the percentage of patients that are adherent to CV or DM medications are based on the 2019 Medicare Star Ratings. However, a rating of 0 stars is exclusive to SoonerCare. The following key is shown to illustrate the star ratings and adherence percentages for each star rating.

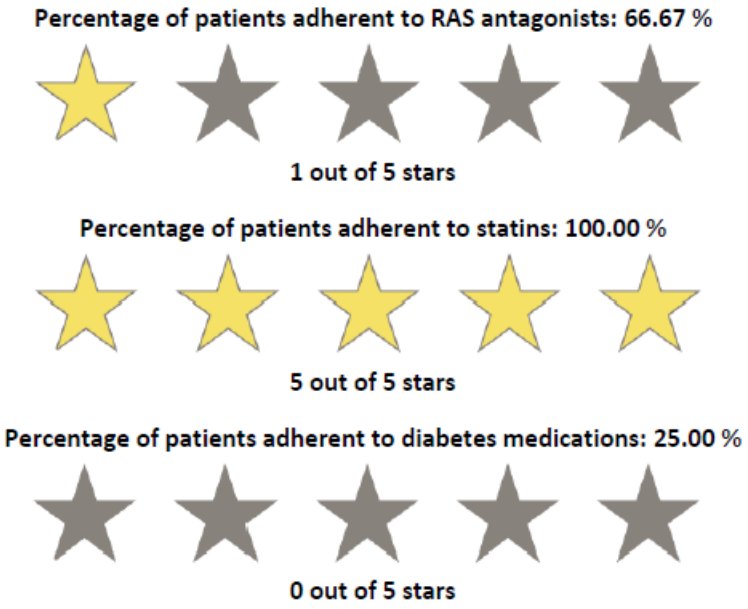
- **CV Star Ratings:** CV star ratings address adherence to maintenance renin angiotensin system (RAS) antagonists [i.e., angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors] and HMG-CoA reductase inhibitors (i.e., statins). Adherence is shown in the Provider Summary Report as a percentage for RAS antagonists and as a percentage for statins, with a corresponding star rating for each category.
- **DM Star Ratings:** DM star ratings address adherence to maintenance medications for DM excluding insulin and Symlin® (pramlintide). Adherence is shown in the Provider Summary Report as a percentage and corresponding star rating for all DM medications (excluding insulin and Symlin®).

Star Ratings	RAS Antagonists	Statins	DM Meds
★★★★★ **5 Stars: Excellent**	≥89%	≥88%	≥88%
★★★★☆ **4 Stars: Above Average**	≥87% to <89%	≥84% to <88%	≥86% to <88%
★★★☆☆ **3 Stars: Average**	≥86% to <87%	≥82% to <84%	≥84% to <86%
★★☆☆☆ **2 Stars: Below Average**	≥84% to <86%	≥80% to <82%	≥82% to <84%
★☆☆☆☆ **1 Star: Poor**	≥60% to <84%	≥60% to <80%	≥60% to <82%
☆☆☆☆☆ **0 Stars: Very Poor**	<60%	<60%	<60%

RAS = renin angiotensin system; DM = diabetes mellitus; meds = medications

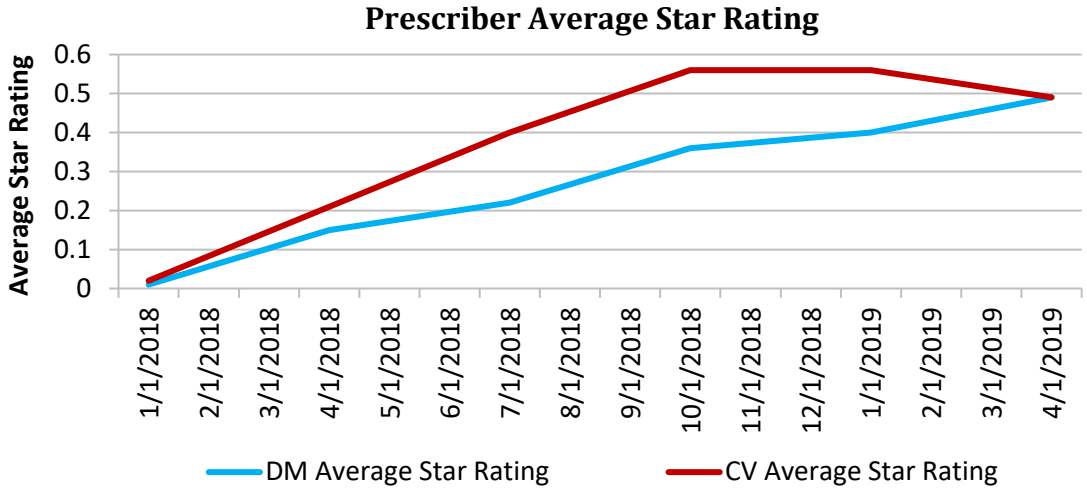
Example Star Rating[1]

Report date: <Report Date>
Provider: <Provider Name>
NPI: <Prescriber NPI>
SoonerCare Provider ID: <Provider ID>

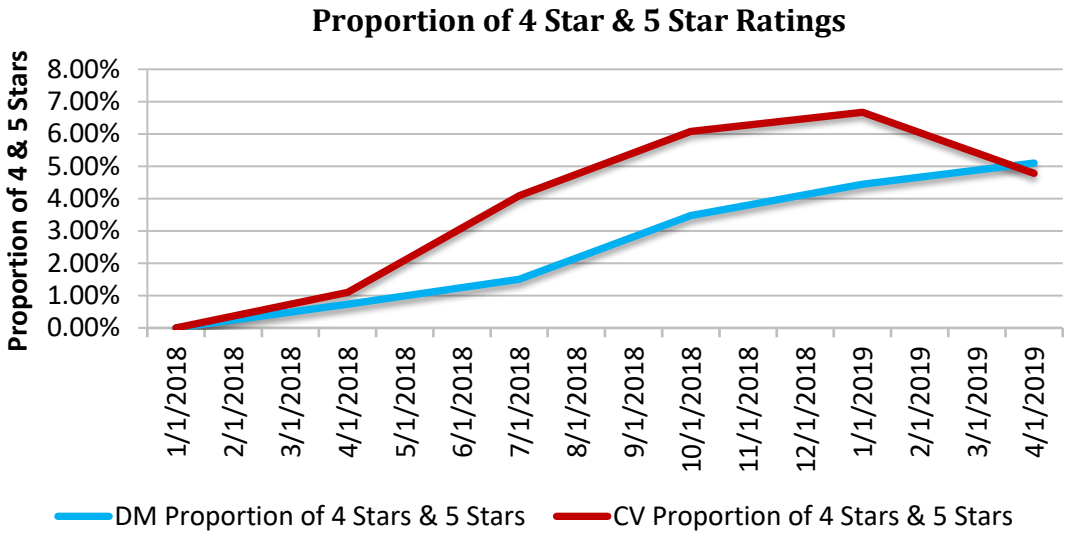


Chronic Medication Adherence Trends

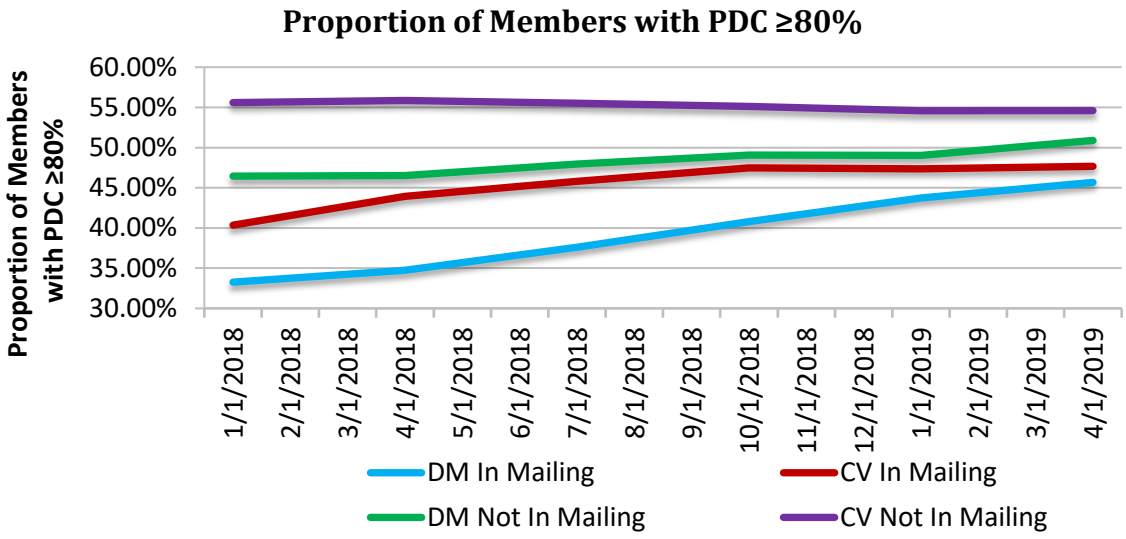
The following line graph shows trends in the average star rating for prescribers included in the mailing since February 2018. This graph is specific to those prescribers included in the mailings and differentiates between DM and CV (i.e., statins and RAS antagonists) modules. It is important to note that the prescriber mailing list was updated in February 2018 to include a larger number of prescribers as well as prescribers who were not previously receiving a mailing. Prescribers selected for initial inclusion in the mailing were those prescribers with a 0 star rating and at least 3 patients in all categories (DM, statins, and RAS antagonists). An overall increase in the average star rating was seen for both mailing modules. Despite favorable increases in the average star ratings, opportunities for further enhancements continue to exist.



The following line graph shows trends in the proportion of prescribers with 4 star and 5 star ratings included in the mailing since February 2018. This graph is specific to those prescribers included in the mailings and differentiates between DM and CV modules. It is important to note that the prescriber mailing list was updated in February 2018 to include a larger number of prescribers as well as prescribers who were not previously receiving a mailing. An overall increase in the proportion of 4 star and 5 star ratings was seen for both mailing modules. Similar to the average star rating, while favorable increases were seen, opportunities for further enhancements continue to exist.



The following line graph shows trends in the proportion of members with a PDC ≥80% for those with prescribers included in the mailing compared to those with prescribers not included in the mailing for both modules since February 2018. Those considered adherent had a PDC of ≥80%. It is important to note that the prescriber mailing list was updated in February 2018 to include a larger number of prescribers as well as prescribers who were not previously receiving a mailing. Please note, the vertical axis starts at 30% in order to reflect small changes.



Unlike prescribers included in the mailings, members included in the mailings are not consistent and may change over time due to medication discontinuations or changing to a prescriber not included in the mailing. Despite member variability, an increase in the proportion of members with a PDC ≥80% was seen for both modules for those prescribers included in the mailing compared to a relatively linear trend for prescribers not included in the mailing. This indicates prescriber mailings may have a positive impact on the proportion of members with PDC ≥80%.

Analysis

There is evidence to show that member PDC improved as a result of the mailings over time. The CV member PDC was on average 3.52% higher in April 2019 as compared to January 2018 [P<0.0001; 95% confidence interval (CI): 2.16% to 4.87% higher] for prescribers included in the mailing. For prescribers not included in the mailing, the CV member PDC was on average 0.051% lower in April 2019 as compared to January 2018 (P=0.91; 95% CI: 0.912% lower to 0.811% higher).

For those prescribers included in the mailing, the DM member PDC was on average 5.88% higher in April 2019 as compared to January 2018 (P<0.0001; 95% CI: 3.72% to 8.04% higher). For prescribers not included in the mailing, the DM member PDC was on average 2.08% higher in April 2019 as compared to January 2018 (P=0.0018; 95% CI: 0.78% to 3.38% higher).

Mailing Status	Medication Class	Average PDC Change	P-Value	Confidence Interval
In Mailing	CV	3.52%	P<0.0001	2.16% to 4.87%
Not In Mailing	CV	-0.051%	P=0.91	-0.912% to 0.811%
In Mailing	DM	5.88%	P<0.0001	3.72% to 8.04%
Not in Mailing	DM	2.08%	P=0.0018	0.78% to 3.38%

CV = cardiovascular; DM = diabetes mellitus; PDC = proportion of days covered

Conclusions

Data specific to prescribers in the mailing shows a statistically significant improvement in member PDC for both DM and CV as well as an overall increase in average star ratings. Trends in prescriber specific measures continue to show improvement, and while favorable increases were seen, opportunities for further enhancements continue to exist. The College of Pharmacy will continue to monitor member adherence with the goal of achieving a member PDC of ≥80% and a 5 star rating of prescriber percentage of adherent members. New interventions will be implemented where appropriate, and results will be reported to the Drug Utilization Review (DUR) Board when available.

[1] Centers for Medicare & Medicaid Services (CMS): Medicare 2019 Part C & D Star Rating Technical Notes. Available online at: https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovgenin/performancedata.html. Last revised 03/21/2019. Last accessed 08/09/2019.

Appendix D

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

Oklahoma Health Care Authority
September 2019

Introduction[1,2,3]

Zolgensma® (onasemnogene abeparvovec-xioi) is an adeno-associated virus (AAV) vector-based gene therapy designed to deliver a fully functional copy of human *survival motor neuron* (*SMN*) gene into the target motor neuron cells. The U.S. Food and Drug Administration (FDA) approved Zolgensma® on May 24, 2019 for the treatment of children younger than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *SMN1* gene. SMA is caused by a bi-allelic mutation in the *SMN1* gene, which results in insufficient SMN protein expression. Zolgensma® is supplied as a customized kit to meet dosing requirements for each patient. Each kit contains 2 to 9 vials of onasemnogene abeparvovec-xioi. The recommended dose of onasemnogene abeparvovec-xioi is 1.1×10^{14} vector genomes per kilogram (vg/kg) of body weight. Onasemnogene abeparvovec-xioi is for single-dose intravenous (IV) infusion only. It is recommended to administer onasemnogene abeparvovec-xioi as an IV infusion over 60 minutes. The most common adverse effects of onasemnogene abeparvovec-xioi in clinical trials were elevated aminotransferases and vomiting. Onasemnogene abeparvovec-xioi has a *Boxed Warning* due to the risk of acute serious liver injury. Patients with pre-existing liver impairment may be at higher risk. It is recommended to assess liver function of all patients prior to infusion and to administer systemic corticosteroids to all patients before and after onasemnogene abeparvovec-xioi infusion. It is recommended to continue to monitor liver function for at least 3 months after infusion.

The efficacy of onasemnogene abeparvovec-xioi in pediatric patients younger than 2 years of age with SMA with bi-allelic mutations in the *SMN1* gene was evaluated in an open-label, single-arm clinical trial (ongoing) and an open-label, single-arm, ascending-dose clinical trial (completed). In these clinical trials, patients experienced onset of clinical symptoms consistent with SMA before 6 months of age. All patients had genetically confirmed bi-allelic *SMN1* gene deletions, 2 copies of the *SMN2* gene, and absence of the c.859G>C modification in exon 7 of *SMN2* gene (which predicts a milder phenotype). All patients had baseline anti-AAV9 antibody titers of ≤1:50, measured by enzyme-linked immunosorbent assay (ELISA). Onasemnogene abeparvovec-xioi was delivered as a single-dose IV infusion in both trials.

Efficacy was established on the basis of survival and achievement of developmental motor milestones, such as sitting without support. Survival was defined as time from birth to either death or permanent ventilation. Permanent ventilation was defined as requiring invasive ventilation (tracheostomy) or respiratory assistance for 16 or more hours per day [including non-invasive ventilator (NIV) support] continuously for 14 or more days in the absence of an acute reversible illness, excluding perioperative ventilation. Efficacy was also supported by

assessments of ventilator use, nutritional support, and scores on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND).

The ongoing clinical trial enrolled 21 patients with infantile-onset SMA. None of the 21 patients required NIV support before treatment with onasemnogene abeparvovec-xioi, and all patients could exclusively feed orally (i.e., no need for non-oral nutrition). The mean CHOP-INTEND score at baseline was 31.0 (range 18 to 47). All patients received 1.1×10^{14} vg/kg of onasemnogene abeparvovec-xioi. The mean age of the 21 patients at the time of treatment was 3.9 months (range 0.5 to 5.9 months). As of the March 2019 data cutoff, 19 patients were alive without permanent ventilation (i.e., event-free survival) and were continuing in the trial, while 1 patient died at 7.8 months of age due to disease progression and 1 patient withdrew from the study at 11.9 months of age. The 19 surviving patients who were continuing in the study ranged in age from 9.4 to 18.5 months. By the data cutoff, 13 of the 19 patients remaining in the study reached 14 months of age without permanent ventilation. Assessment of the other co-primary efficacy endpoint found that 10 of the 21 patients (47.6%) achieved the ability to sit without support for ≥30 seconds between 9.2 and 16.9 months of age (mean age was 12.1 months). Based on the natural history of the disease, patients who met the study entry criteria would not be expected to attain the ability to sit without support, and only approximately 25% of these patients would be expected to survive (i.e., being alive without permanent ventilation) beyond 14 months of age. In addition, 16 of the 19 patients had not required daily NIV use. Comparison of the results of the ongoing clinical trial to available natural history data of patients with infantile-onset SMA provides primary evidence of the effectiveness of onasemnogene abeparvovec-xioi.

The completed clinical trial enrolled 15 patients with infantile-onset SMA: 3 patients in a low-dose cohort and 12 patients in a high-dose cohort. At the time of treatment, the mean age of patients in the low-dose cohort was 6.3 months (range 5.9 to 7.2 months) and 3.4 months (range 0.9 to 7.9 months) in the high-dose cohort. The dosage received by patients in the low-dose cohort was approximately one-third of the dosage received by patients in the high-dose cohort. However, the precise dosages of onasemnogene abeparvovec-xioi received by patients in this completed clinical trial are unclear due to a change in the method of measuring onasemnogene abeparvovec-xioi concentration and due to decreases in the concentration of stored onasemnogene abeparvovec-xioi over time. The retrospectively-estimated dosage range in the high-dose cohort is approximately 1.1×10^{14} to 1.4×10^{14} vg/kg. By 24 months following onasemnogene abeparvovec-xioi infusion, 1 patient in the low-dose cohort met the endpoint of permanent ventilation; all 12 patients in the high-dose cohort were alive without permanent ventilation. None of the patients in the low-dose cohort were able to sit without support or able to stand or walk; in the high-dose cohort, 9 of the 12 patients (75.0%) were able to sit without support for ≥30 seconds, and 2 patients (16.7%) were able to stand and walk without assistance. Comparison of the results of the low-dose cohort to the results of the high-dose cohort shows a dose-response relationship that supports the effectiveness of onasemnogene abeparvovec-xioi.

The safety and effectiveness of repeat administration of onasemnogene abeparvovec-xioi have not been evaluated. The use of onasemnogene abeparvovec-xioi in patients with advanced

SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated.

Cost: The Wholesale Acquisition Cost (WAC) of Zolgensma® (onasemnogene abeparvovec-xioi) is $2,125,000 per 1-time infusion.

Recommendations

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

Zolgensma® (Onasemnogene Abeparvovec-xioi) Approval Criteria:

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

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

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
    a. Type 1; or
    b. Type 2; or

   c. Type 3 with symptoms; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as at least 16 hours of respiratory assistance per day continuously for more than 21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or be an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
6. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
7. Spinraza® must be administered in a health care facility by a specialist experienced in performing lumbar punctures; and
   a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
8. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
   a. Hammersmith Infant Neurological Exam (HINE); or
   b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
   c. Upper Limb Module (ULM) Test; or
   d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
9. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically-significant improvement or maintenance of function from 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 one 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

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[1] U.S. Food and Drug Administration (FDA) News Release: FDA approves innovative gene therapy to treat pediatric patients with spinal muscular atrophy, a rare disease and leading genetic cause of infant mortality. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease. Issued 05/24/2019. Last accessed 08/08/2019.

[2] Zolgensma® Prescribing Information. AveXis, Inc. Available online at: https://www.avexis.com/content/pdf/prescribing_information.pdf. Issued 05/2019. Last accessed 08/08/2019.

[3] Novartis. AveXis Announces Innovative Zolgensma® Gene Therapy Access Programs for US Payers and Families. Available online at: https://www.novartis.com/news/media-releases/avexis-announces-innovative-zolgensma-gene-therapy-access-programs-us-payers-and-families. Issued 05/24/2019. Last accessed 08/08/2019.

Appendix E

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

Oklahoma Health Care Authority
September 2019

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

- **Bryhali™ (Halobetasol Propionate 0.01% Lotion):** In November 2018, the U.S. Food and Drug Administration (FDA) approved Bryhali™ (halobetasol propionate 0.01% lotion) for the topical treatment of plaque psoriasis in adults. Bryhali™ lotion is a potent to super potent, once-daily topical corticosteroid (TCS) that contains 0.01% halobetasol propionate in a vehicle lotion. It is recommended to apply a thin layer of lotion to the affected areas and rub in gently once daily. Treatment beyond 8 weeks is not recommended and the total dosage should not exceed approximately 50g per week. Treatment with Bryhali™ should be discontinued if control is achieved before 8 weeks. Bryhali™ is available in 2 package sizes, 60g and 100g. The Wholesale Acquisition Cost (WAC) of Bryhali™ is $4 per gram, resulting in a cost of $240 to $400 per tube depending on package size. Halobetasol propionate is also available generically as a 0.05% cream and 0.05% ointment and as the brand name formulations Ultravate® 0.05% lotion and Lexette™ 0.05% foam.
- **Duobrii™ (Halobetasol Propionate/Tazarotene 0.01%/0.045% Lotion):** In April 2019, the FDA approved Duobrii™ (halobetasol propionate/tazarotene 0.01%/0.045% lotion) for the topical treatment of plaque psoriasis in adults. Duobrii™ is the first TCS (halobetasol) and retinoid (tazarotene) combination product and is available in a once-daily lotion formulation. It is recommended to apply Duobrii™ as a thin layer once daily to cover the affected areas only. The total dosage should not exceed 50g per week because of the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression. Treatment with Duobrii™ should be discontinued once control is achieved. The long-term safety of Duobrii™ was established in a 1-year, open-label study in patients with plaque psoriasis. Patients used Duobrii™ once daily for 8 weeks and were re-evaluated every 4 weeks for 1 year. Continuous treatment was allowed up to 24 weeks and as needed for up to 52 weeks. Treatment related adverse events >2% were application site reactions such as itching, pain, irritation, and inflamed hair follicles. Duobrii™ is available in a 100g tube and the current WAC is $8.25 per gram or $825 per tube. Halobetasol propionate is available generically as a 0.05% cream and 0.05% ointment and as the brand name formulations Ultravate® 0.05% lotion, Bryhali™ 0.01% lotion, and Lexette™ 0.05% foam. Tazarotene is available as 0.05% and 0.1% topical cream and gel (Tazorac®). Tazarotene cream and gel currently require prior authorization.

- **Lexette™ (Halobetasol Propionate 0.05% Foam):** In May 2018, the FDA approved Lexette™ (halobetasol propionate 0.05% foam), a potent TCS indicated for the treatment of plaque psoriasis in adults. It is recommended to apply Lexette™ as a thin uniform film to the affected skin and rub in gently twice daily for up to 2 weeks. The total dosage should not exceed 50g per week and Lexette™ should be discontinued once control is achieved. Treatment beyond 2 consecutive weeks is not recommended. If no improvement is seen within 2 weeks, the diagnosis should be reassessed. Lexette™ is available in 50g cans and is dispensed as 1 or 2 cans. The WAC for the individual 50g can is $15.41 per gram, resulting in a cost of $770.50 per can. The WAC for the 100g package [supplied as (2) 50g cans] is $14.73 per gram, resulting in a cost of $1,473.00.

Recommendations

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

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

Additionally, the College of Pharmacy recommends the following:

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

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

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

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

Tier-2 Topical Corticosteroids (TCS) Approval Criteria:

1. Documented trials of all Tier-1 TCS of similar potency in the past 30 days that did not yield adequate relief; and

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

Tier-3 Topical Corticosteroids (TCS) Approval Criteria:

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

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% (**Diprolene AF®**)	**C,G**	amcinonide 0.1%	**C,L**	clobetasol propionate 0.025% (**Impoyz™**)	**C**
clobetasol propionate 0.05% (**Temovate®**)	**C,L,O, So**	augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**L,O**	clobetasol propionate 0.05% (**Clobex®**)	**Sh,Spr**
fluocinonide 0.05%	**C,O,So**	betamethasone dipropionate 0.05% (**Diprosone®**)	**C,O**	clobetasol propionate 0.05% (**Olux®, Olux-E®**)	**F**
halobetasol propionate 0.05% (**Ultravate®**)	**C**	clobetasol propionate 0.05% (**Clobex®**)	**L**	desoximetasone 0.25% (**Topicort®**)	**C,O,Spr**
		clobetasol propionate 0.05% (**Temovate®**)	**G**	diflorasone diacetate 0.05% (**Apexicon®**)	**C,O**
		desoximetasone 0.05% (**Topicort®**)	**G**	diflorasone diacetate/emollient 0.05% (**Apexicon E®**)	**C**
		fluocinonide 0.05%	**G**	halobetasol propionate 0.01% (**Bryhali™**)	**L**
		fluocinonide 0.1% (**Vanos®**)	**C**	halobetasol propionate 0.05% (**Lexette™**)	**F**

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
		flurandrenolide 0.05% (**Cordran®**)	**Tape**		
		halcinonide 0.1% (**Halog®**)	**C,O**		
		halobetasol propionate 0.05% (**Ultravate®**)	**L,O**		
		halobetasol propionate/lactic acid 0.05%/10% (**Ultravate X®**)	**C**		
Medium-High to Medium Potency					
betamethasone dipropionate 0.05%	**L**	betamethasone dipropionate/calcipotriene 0.064%/0.005% (**Taclonex®**)	**O,Spr, Sus**	betamethasone dipropionate 0.05% (**Sernivo®**)	**Spr**
betamethasone valerate 0.1% (**Beta-Val®**)	**C,L,O**	betamethasone valerate 0.12% (**Luxiq®**)	**F**	hydrocortisone valerate 0.2% (**Westcort®**)	**C,O**
fluticasone propionate 0.05% (**Cutivate®**)	**C,O**	calcipotriene/betamethasone dipropionate 0.064%/0.005% (**Enstilar®**)	**F**		
mometasone furoate 0.1% (**Elocon®**)	**C,L,O, So**	clocortolone pivalate 0.1% (**Cloderm®**)	**C**		
triamcinolone acetonide 0.025%	**O**	desoximetasone 0.05% (**Topicort LP®**)	**C,O**		
triamcinolone acetonide 0.1%	**C,L,O**	fluocinolone acetonide 0.025% (**Synalar®**)	**C,O**		
triamcinolone acetonide 0.5%	**C,O**	fluocinonide emollient 0.05% (**Lidex E®**)	**C**		
		flurandrenolide 0.05%	**C,L,O**		
		fluticasone propionate 0.05% (**Cutivate®**)	**L**		
		hydrocortisone butyrate 0.1%	**C,L,O, So**		
		hydrocortisone probutate 0.1% (**Pandel®**)	**C**		
		prednicarbate 0.1% (**Dermatop®**)	**C,O**		
		triamcinolone acetonide 0.147mg/g (**Kenalog®**)	**Spr**		
		triamcinolone acetonide 0.05% (**Trianex®**)	**O**		
Low Potency					
desonide 0.05% (**Desonate®**)	**G**	alclometasone dipropionate 0.05% (**Aclovate®**)	**C,O**	fluocinolone acetonide 0.01% (**Derma-Smoothe®; Derma-Smoothe FS®**)	**Oil**

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
fluocinolone acetonide 0.01% (**Capex®**)	**Sh**	desonide 0.05% (**Verdeso®**)	**F**	desonide 0.05%	**L**
hydrocortisone acetate 1%	**C,O**	fluocinolone acetonide 0.01% (**Synalar®**)	**C,So**	desonide emollient 0.05%	**C,O**
hydrocortisone acetate 2.5%	**C,L,O**	hydrocortisone 2.5% (**Texacort®**)	**So**		
hydrocortisone/urea 1%/10% (**U-Cort®**)	**C**	hydrocortisone/pramoxine 1%/1% (**Pramosone®**)	**C,L**		
triamcinolone acetonide 0.025%	**C,L**				

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

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Appendix F

Fiscal Year 2019 Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Herzuma® (Trastuzumab-pkrb), Kanjinti™ (Trastuzumab-anns), Ontruzant® (Trastuzumab-dttb), Piqray® (Alpelisib), Talzenna® (Talazoparib), and Trazimera™ (Trastuzumab-qyyp)

Oklahoma Health Care Authority
September 2019

Introduction[1,2,3,4]

According to the National Cancer Institute, in 2019, there will be an estimated 268,600 new cases of breast cancer, making it the second most common cancer diagnosed in women in the United States after skin cancer. Additionally, it is estimated there will be 41,760 breast cancer deaths in 2019. The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Breast cancer can also begin in the cells of the lobules and in other tissues in the breast. Invasive breast cancer is breast cancer that has spread from where it began in the ducts or lobules to surrounding tissues. About 8 of 10 invasive breast cancers are invasive ductal carcinomas. There are several different types of treatments available for patients with breast cancer, including surgery, radiation, hormone therapy, and traditional chemotherapy. Additionally, targeted therapy using drugs or other substances to identify and attack specific cancer cells without harming normal cells is being used. Types of targeted therapy used for breast cancer include monoclonal antibodies, tyrosine kinase inhibitors, cyclin-dependent kinase inhibitors, mammalian target of rapamycin (mTOR) inhibitors, and poly-ADP ribose polymerase (PARP) inhibitors.

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.

Current Prior Authorization Criteria

Approval criteria for Tecentriq® (atezolizumab) for indications other than breast cancer diagnoses can be found in the April 2019 Drug Utilization Review (DUR) Board packet. Atezolizumab approval criteria are reviewed annually with the lung cancer medications.

Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced breast cancer; and
2. Negative expression of human epidermal receptor type 2 (HER2); and
3. Hormone receptor positive; and
4. Used in combination with exemestane, fulvestrant, or tamoxifen; and

5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.

Afinitor® (Everolimus) Approval Criteria [Neuroendocrine Tumors (NET) of Pancreatic Origin (PNET) or of Gastrointestinal or Lung Origin Diagnosis]:

1. Diagnosis of unresectable, locally advanced, or metastatic NET of pancreatic (PNET), gastrointestinal, or lung origin; and
2. Progressive disease from a previous treatment.

Afinitor® (Everolimus) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of advanced RCC; and
2. Failure of treatment with sunitinib or sorafenib; and
3. Everolimus may also be approved to be used in combination with lenvatinib for advanced RCC.

Afinitor® (Everolimus) Approval Criteria [Renal Angiomyolipoma (AML) and Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of AML and tuberous sclerosis complex (TSC); and
2. Not requiring immediate surgery; and
3. Used in pediatric and adult members 1 year of age and older.

Afinitor® (Everolimus) Approval Criteria [Subependymal Giant Cell Astrocytoma (SEGA) with Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of SEGA with TSC; and
2. Requires therapeutic intervention but cannot be curatively resected.

Afinitor® (Everolimus) Approval Criteria [Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures Diagnosis]:

1. Diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and
3. Failure of at least 3 other medications commonly used for seizures; and
4. Must be used as adjunctive treatment; and
5. The member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. The member must not be taking St. John's wort concurrently with Afinitor®; and
7. The prescriber must verify that Afinitor® trough levels and adverse reactions (e.g., non-infectious pneumonitis, stomatitis, hyperglycemia, dyslipidemia, thrombocytopenia, neutropenia, febrile neutropenia) will be monitored, and dosing changes or discontinuations will correspond with recommendations in the drug labeling; and
8. Verification from the prescriber that female members are not pregnant and will use contraception while receiving Afinitor® therapy and for 8 weeks after the last dose of Afinitor® and that male members with female partners of reproductive potential will use contraception while receiving Afinitor® therapy and for 4 weeks after the last dose of Afinitor®; and

9. The member's recent body surface area (BSA) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
10. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

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

1. Diagnosis of metastatic breast cancer; and
2. Previously received at least 2 chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Halaven® (Eribulin) Approval Criteria [Liposarcoma Diagnosis]:

1. Diagnosis of unresectable or metastic liposarcoma; and
2. Previously received an anthracycline-containing chemotherapy regimen.

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

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

Ixempra® (Ixabepilone) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Usage as either:
    a. In combination with capecitabine after failure of an anthracycline and a taxane (must have failed combination taxane and anthracycline therapy unless anthracyclines not indicated); or
    b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine.

Kadcyla® (Ado-Trastuzumab) Approval Criteria [Metastatic Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and
2. Positive expression of human epidermal receptor type 2 (HER2); and
3. Previously received trastuzumab and a taxane, separately or in combination; and
4. Members should also have either:
    a. Received prior therapy for metastatic disease; or
    b. Developed disease recurrence during or within 6 months of completing adjuvant therapy.

Kisqali® (Ribociclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Hormone receptor positive; and
2. Human epidermal receptor type 2 (HER2)-negative; and
3. If used in combination with an aromatase inhibitor:
    a. Diagnosis of advanced or metastatic breast cancer, initial therapy; or
4. If used in combination with fulvestrant:

a. Diagnosis of advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on endocrine therapy; and
b. Must be used in postmenopausal women only.

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer, initial therapy; and
2. Member must be hormone receptor positive; and
3. Member must be human epidermal receptor type 2 (HER2)-negative.

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

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

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

1. Diagnosis of deleterious or suspected deleterious germline BRCA mutated (*gBRCAm*), advanced ovarian cancer; and
2. Previous treatment with 3 or more prior lines of chemotherapy. Prior chemotherapy regimens should be documented on the prior authorization request; and
3. A quantity limit based on FDA approved dosing will apply.

Lynparza® (Olaparib) Approval Criteria [Maintenance Treatment Diagnosis]:

1. Used for maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy; and
2. Completed therapy with a platinum agent in the prior 8 weeks; and
3. A quantity limit based on FDA approved dosing will apply.

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

1. For adjuvant treatment in early-stage breast cancer; and
2. Human epidermal receptor type 2 (HER2)-overexpressed breast cancer; and
3. Neratinib must be used to follow adjuvant trastuzumab-based therapy.

Ogivri™ (Trastuzumab-dkst) Approval Criteria [Breast Cancer Diagnosis]:

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

Ogivri™ (Trastuzumab-dkst) Approval Criteria [Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Diagnosis]:

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma; and

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

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

1. Positive expression of human epidermal receptor type 2 (HER2); 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 (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel); 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 age <35]:
        i. Used in combination with trastuzumab and paclitaxel following AC (doxorubicin/cyclophosphamide); or
        ii. Used in combination with trastuzumab and docetaxel following AC; or
        iii. Used in combination with TCH (docetaxel/carboplatin/trastuzumab).

Tecentriq® (Atezolizumab) Approval Criteria [Breast Cancer Diagnosis]:

1. Unresectable locally advanced or metastatic triple-negative breast cancer; and
2. Used in combination with nab-paclitaxel (Abraxane®); and
3. Positive expression of programmed death ligand-1 (PD-L1); and
4. Member has not failed other immunotherapy(ies).

Tykerb® (Lapatinib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic or recurrent breast cancer; and
2. Positive expression of human epidermal receptor type 2 (HER2); and
3. Lapatinib must be used in combination with 1 of the following:
    a. Trastuzumab; or
    b. Capecitabine; or
    c. An aromatase inhibitor (e.g., exemestane, letrozole, anastrozole) if also estrogen receptor positive.

Verzenio™ (Abemaciclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Used in 1 of the following settings:
    a. In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women; or
    b. In combination with fulvestrant with disease progression following endocrine therapy in advanced or metastatic breast cancer; or

c. As monotherapy for disease progression following endocrine therapy and prior chemotherapy in metastatic breast cancer; and

2. All the following criteria must be present:
   a. Advanced or metastatic breast cancer; and
   b. Progressed after endocrine therapy when used with fulvestrant or as initial therapy in combination with an aromatase inhibitor; and
   c. Hormone receptor positive; and
   d. Human epidermal receptor 2 (HER2)-negative.

Utilization of Breast Cancer Medications: Fiscal Year 2019

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	62	321	$3,835,500.82	$11,948.60	$417.54	13,680	9,186
2019	62	431	$5,595,180.31	$12,981.86	$460.17	16,700	12,159
% Change	**0.00%**	**34.30%**	**45.90%**	**8.60%**	**10.20%**	**22.10%**	**32.40%**
Change	**0**	**110**	**$1,759,679.49**	**$1,033.26**	**$42.63**	**3,020**	**2,973**

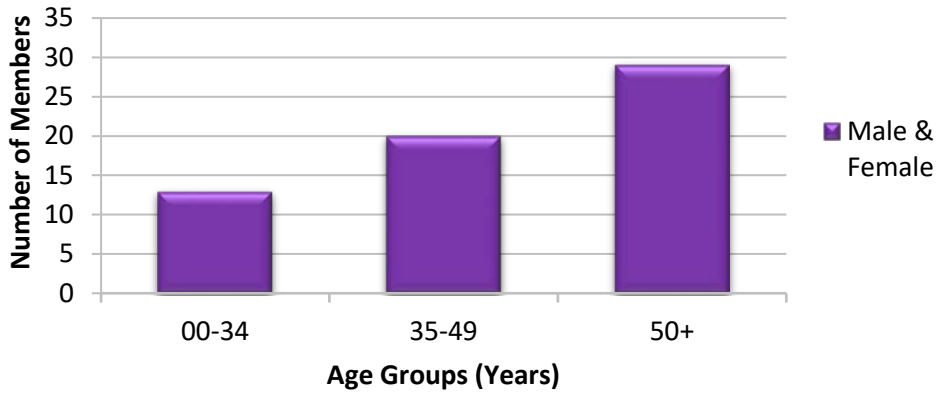
*Total number of unduplicated members.
Cost do not reflect rebated prices or net costs.
Fiscal Year 2018 = 07/01/2017 to 06/30/2018; Fiscal Year 2019 = 07/01/2018 to 06/30/2019

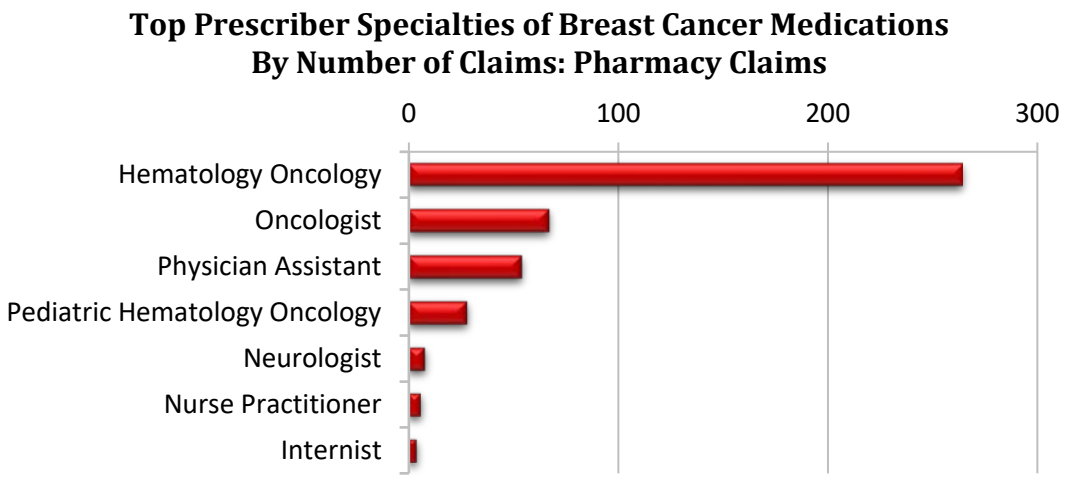
Fiscal Year Comparison: Medical Claims

Fiscal Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim	Total Units
2018	84	549	$4,311,703.46	$7,853.74	149,656
2019	84	462	$3,059,903.43	$6,623.17	161,240
% Change	**0.00%**	**-15.85%**	**-29.03%**	**-15.67%**	**7.74%**
Change	**0**	**-87**	**-$1,251,800.03**	**-$1,230.57**	**11,584**

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

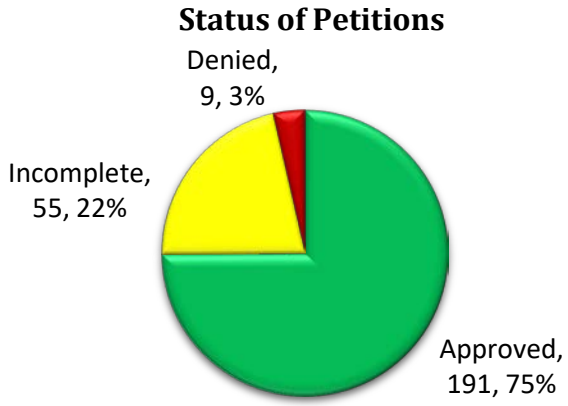
Demographics of Members Utilizing Breast Cancer Medications: Pharmacy Claims





Prior Authorization of Breast Cancer Medications

There were 255 prior authorization requests submitted for breast cancer medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



Market News and Updates[5,6,7,8,9]

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

- **October 2018:** The FDA approved Talzenna® (talazoparib), a PARP inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*), human epidermal receptor type 2 (HER2) negative, locally advanced or metastatic breast cancer.
- **December 2018:** The FDA approved Herzuma® (trastuzumab-pkrb) as a biosimilar to Herceptin® (trastuzumab) for patients with HER2-overexpressing breast cancer.
- **December 2018:** The FDA approved Lynparza® (olaparib) for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (*gBRCAm* or *sBRCAm*) advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.

- **January 2019:** The FDA approved Ontruzant® (trastuzumab-dttb), a biosimilar to Herceptin® (trastuzumab), across all eligible indications, namely adjuvant treatment of HER2-overexpressing breast cancer, metastatic breast cancer, and metastatic gastric cancer or gastroesophageal junction adenocarcinoma in patients who have not received prior treatment for metastatic disease.
- **February 2019:** The FDA approved Herceptin Hylecta™ (trastuzumab/hyaluronidase-oysk injection) for the treatment of HER2-overexpressing breast cancer. Herceptin Hylecta™ is a combination of trastuzumab, a HER2/neu receptor antagonist, and hyaluronidase, an endoglycosidase.
- **March 2019:** The FDA approved Tecentriq® (atezolizumab) for the treatment of programmed death-ligand 1 (PD-L1) positive, unresectable, locally advanced or metastatic triple-negative breast cancer. Criteria for this indication was voted on in the June 2019 DUR Board meeting.
- **March 2019:** The FDA approved Trazimera™ (trastuzumab-qyyp), a biosimilar to Herceptin® (trastuzumab), for the treatment of HER2-overexpressing breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.
- **April 2019:** The FDA approved a supplemental New Drug Application (sNDA) to expand the indications for Ibrance® (palbociclib) in combination with an aromatase inhibitor or fulvestrant to include men with hormone receptor-positive (HR+), HER2 advanced or metastatic breast cancer.
- **May 2019:** The FDA approved Kadcyla® (ado-trastuzumab) for the adjuvant treatment of patients with HER2-positive early breast cancer (EBC) who have residual, invasive disease after neoadjuvant taxane and trastuzumab-based treatment.
- **May 2019:** The FDA approved Piqray® (alpelisib) in combination with fulvestrant for the treatment of men and postmenopausal women with HR+, HER2-negative, PIK3CA-mutated, advanced or metastatic breast cancer following progression on or after an endocrine-based regimen.
- **June 2019:** The FDA approved Kanjinti™ (trastuzumab-anns) a biosimilar to Herceptin® (trastuzumab) for all approved indications of the reference product. These indications include the treatment of HER2-overexpressing adjuvant and metastatic breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Product Summaries[10,11,12,13,14,15]

Piqray® (Alpelisib):

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

Talzenna® (Talazoparib):

- **Therapeutic Class:** PARP inhibitor
- **Indication(s):** Treatment of adult patients with deleterious or suspected deleterious *gBRCAm,* HER2-negative, locally advanced or metastatic breast cancer
- **How Supplied:** 0.25mg and 1mg oral capsules
- **Dose:**
  - The recommended dose is 1mg once daily, with or without food; the 0.25mg capsule is available for dose reduction
  - Treatment is recommended until disease progression or unacceptable toxicity occurs
- **Cost:** $486.00 per 1mg capsule; $14,580.00 per month based on the recommended dose of 1mg once daily

Kanjinti™ (Trastuzumab-anns):

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

Ontruzant® (Trastuzumab-dttb):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)

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

Herzuma® (Trastuzumab-pkrb):

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

Trazimera™ (Trastuzumab-qyyp):

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

Recommendations

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

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

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

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

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

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

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

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

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

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

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

1. Diagnosis of recurrent or metastatic breast cancer; and
2. Disease is human epidermal growth factor receptor 2 (HER2)-negative; and
3. Presence of BRCA 1/2-germline mutated disease; and

4. Disease is hormone receptor negative or hormone receptor positive and endocrine therapy refractory; and
5. Patient has symptomatic visceral disease; and
6. Must be used as a single-agent.

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

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

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

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

Utilization Details of Breast Cancer Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
PALBOCICLIB PRODUCTS					
IBRANCE CAP 125MG	135	24	$1,563,532.06	5.63	$11,581.72
IBRANCE CAP 100MG	69	13	$796,188.75	5.31	$11,538.97
IBRANCE CAP 75MG	32	3	$304,634.18	10.67	$9,519.82
SUBTOTAL	**236**	**40**	**$2,664,354.99**	**5.9**	**$11,289.64**
EVEROLIMUS PRODUCTS					
AFINITOR TAB 10MG	36	9	$589,644.29	4	$16,379.01
AFINITOR TAB 7.5MG	29	3	$439,258.50	9.67	$15,146.84
AFINITOR DIS TAB 5MG	25	3	$620,640.84	8.33	$24,825.63
AFINITOR DIS TAB 2MG	12	3	$172,784.62	4	$14,398.72
AFINITOR DIS TAB 3MG	8	2	$203,024.01	4	$25,378.00
AFINITOR TAB 5MG	5	1	$57,770.16	5	$11,554.03
SUBTOTAL	**115**	**21**	**$2,083,122.42**	**5.48**	**$18,114.11**
NERATINIB PRODUCTS					
NERLYNX TAB 40MG	14	3	$151,188.94	4.67	$10,799.21
SUBTOTAL	**14**	**3**	**$151,188.94**	**4.67**	**$10,799.21**
LAPATINIB PRODUCTS					
TYKERB TAB 250MG	15	4	$106,913.33	3.75	$7,127.56
SUBTOTAL	**15**	**4**	**$106,913.33**	**3.75**	**$7,127.56**
RIBOCICLIB PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
KISQALI TAB 400MG	13	1	$126,813.29	13	$9,754.87
KISQALI FEMARA PAK	12	1	$146,532.80	12	$12,211.07
SUBTOTAL	**25**	**2**	**$273,346.09**	**12.5**	**$10,933.84**
ABEMACICLIB PRODUCTS					
VERZENIO TAB 150MG	18	6	$207,705.80	3	$11,539.21
VERZENIO TAB 100MG	1	1	$11,292.07	1	$11,292.07
SUBTOTAL	**19**	**7**	**$218,997.87**	**2.71**	**$11,526.20**
OLAPARIB PRODUCTS					
LYNPARZA TAB 100MG	5	1	$69,466.65	5	$13,893.33
LYNPARZA TAB 150MG	2	2	$27,790.02	1	$13,895.01
SUBTOTAL	**7**	**3**	**$97,256.67**	**2.33**	**$13,893.81**
TOTAL	**431**	**62***	**$5,595,180.31**	**6.95**	**$12,981.86**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS[+]	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J9355 TRASTUZUMAB INJECTION	367	68	$1,500,878.47	$4,089.59
J9306 PERTUZUMAB INJECTION	246	47	$1,014,983.15	$4,125.95
J9354 ADO-TRASTUZUMAB INJECTION	62	10	$416,251.63	$6,713.74
J9179 ERIBULIN MESYLATE INJECTION	19	6	$32,998.21	$1,736.75
J9207 IXABEPILONE INJECTION	4	2	$19,500.85	$4,875.21
J9022 ATEZOLIZUMAB INJECTION	8	2	$75,291.12	$9,411.39
TOTAL	**462[+]**	**84***	**$3,059,903.43**	**$6,623.17**

[+]Total number of unduplicated claims. Please note: Some members may be utilizing medications concomitantly.
*Total number of unduplicated members. Please note: Some members may be utilizing medications concomitantly.
Costs do not reflect rebated prices or net costs.

[1] National Cancer Institute. SEER Cancer Statistics. Available online at: https://seer.cancer.gov/statfacts/html/breast.html. Last accessed 08/08/2019.
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Appendix G

Fiscal Year 2019 Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Nubeqa™ (Darolutamide)

Oklahoma Health Care Authority
September 2019

Introduction[1,2,3]

According to the National Cancer Institute, in 2019, an estimated 174,650 men will be diagnosed with prostate cancer, making prostate cancer approximately 9.9% of all new cancer cases in the United States. Additionally, it is estimated there will be 31,620 prostate cancer deaths in 2019. Prostate cancer is the second leading cause of cancer death in men. The incidence of prostate cancer is closely correlated with trends in screening practices. Prostate specific antigen (PSA) is a protein produced by cells of the prostate gland, and elevations in PSA levels may indicate prostate cancer. PSA has been used as a screening marker for prostate cancer over the last 3 decades with its peak utilization occurring in the early 1990s and gradually declining since that time. Following the same trend, the incidence rates of prostate cancer were highest in 1992 and have slowly decreased from that date. Physicians have reduced recommending generalized PSA screening for the average risk male, primarily because the mortality associated with prostate cancer is very low with an estimated 98% survival at 5 years. Early detection of prostate cancer can lead to over-treatment of cancers that do not impact life expectancy. This may result in unwarranted side effects, reduced quality of life, and increased cost. Prostate cancer detection and progression models estimate that 23% to 42% of all screen-detected cancers are over-treated.

The most common type of prostate cancer is adenocarcinoma, which accounts for 99% of tumors in the prostate. Sarcomas, transitional, small, and squamous cell carcinomas are rare. The treatment principles for prostate cancer have largely remained the same over the past 50 years with surgery, radiation, and androgen deprivation therapy (ADT) making up the main components of therapy. Androgens, the most common of which is testosterone, promote the growth of prostate cancers. ADT involves medications that reduce the body's level of androgens or surgery to remove the testicles, which ultimately can decrease and slow the growth of prostate cancers. Early stage (stage I and II localized) prostate cancer is typically treated with either surgery, radiation therapy, or active surveillance. Stage III cancer treatment often involves a combination of radiation therapy with ADT and surgery. ADT is usually recommended for initial treatment of men with metastatic (stage IV) prostate cancer and is often combined with chemotherapy. Other treatment strategies for advanced cancers include immunotherapy and radiation. Advanced prostate cancer is incurable but treatment can help to control the tumor burden for long periods of time.

Current Prior Authorization Criteria

Erleada® (Apalutamide) Approval Criteria:

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

Jevtana® (Cabazitaxel) Approval Criteria:

1. Diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Previous treatment with a docetaxel-containing regimen; and
3. Cabazitaxel should be used in combination with prednisone.

Provenge® (Sipuleucel-T) Approval Criteria:

1. Diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Asymptomatic or minimally symptomatic; and
3. No hepatic metastases; and
4. Life expectancy of >6 months.

Xofigo® (Radium-223 Dichloride) Approval Criteria:

1. Diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Symptomatic bone metastases; and
3. No known visceral metastatic disease; and
4. Prescriber must verify radium-223 dichloride will not be used in combination with chemotherapy; and
5. Absolute neutrophil count ≥1.5 x 10^9/L, platelet count ≥100 x 10^9/L, and hemoglobin ≥10 gram/dL; and
6. Approvals will be for the duration of 3 months at which time additional authorization may be granted if the prescriber documents the following:
    a. Has not shown evidence of progressive disease while on radium-223 dichloride therapy; and
    b. Member must have an absolute neutrophil count ≥1 x 10^9/L and platelet count ≥100 x 10^9/L (radium-223 dichloride should be delayed 6 to 8 weeks otherwise).

Xtandi® (Enzalutamide) Approval Criteria:

1. Diagnosis of metastatic, castration-resistant prostate cancer (CRPC).

Yonsa® (Abiraterone Acetate) Approval Criteria:

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

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

1. Diagnosis of metastatic, CRPC; and
2. Abiraterone must be used in combination with a corticosteroid.

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

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

Utilization of Prostate Cancer Medications: Fiscal Year 2019

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	8	58	$574,794.82	$9,910.26	$330.34	6,120	1,740
2019	13	74	$789,530.00	$10,669.32	$355.64	6,810	2,220
% Change	**62.50%**	**27.60%**	**37.40%**	**7.70%**	**7.70%**	**11.30%**	**27.60%**
Change	**5**	**16**	**$214,735.18**	**$759.06**	**$25.30**	**690**	**480**

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

Fiscal Year 2019 Utilization: Medical Claims

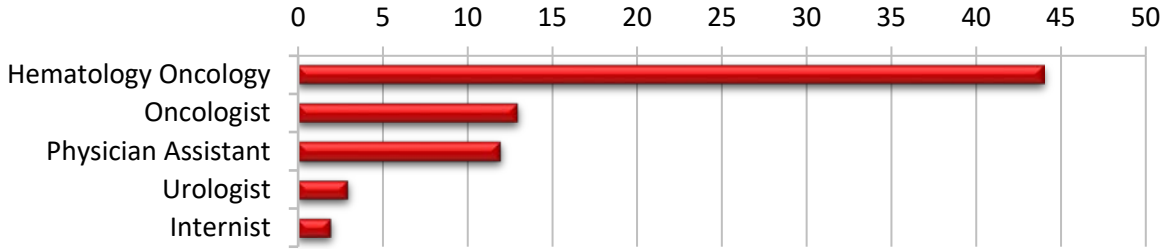
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units
2019	2	15	$153,897.04	$10,259.80	1,600

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

Demographics of Members Utilizing Prostate Cancer Medications: Pharmacy Claims

- Due to the small number of members utilizing prostate cancer medications during fiscal year 2019, detailed demographic information could not be provided. All members were male and 50 years of age or older.

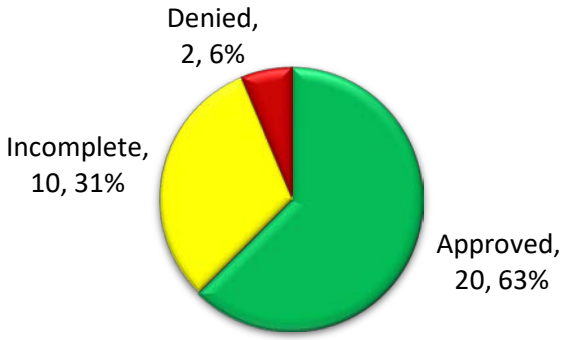
Top Prescriber Specialties of Prostate Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Prostate Cancer Medications

There were 32 prior authorization requests submitted for prostate cancer medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



Market News and Updates[4,5,6]

Anticipated Patent Expiration(s):

- Xofigo® (radium-223 dichloride): November 2022
- Xtandi® (enzalutamide): August 2027
- Zytiga® (abiraterone): August 2027
- Jevtana® (cabazitaxel): April 2031
- Erleada® (apalutamide): September 2033
- Yonsa® (abiraterone): May 2034

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

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

Nubeqa™ (Darolutamide) Product Summary[7]

Nubeqa™ (Darolutamide):

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

Recommendations

Nubeqa® (Darolutamide) Approval Criteria [Prostate Cancer Diagnosis]:

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

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

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

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

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

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

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

Utilization Details of Prostate Cancer Medications: Fiscal Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ABIRATERONE PRODUCTS					
ZYTIGA TAB 500MG	32	6	$334,789.94	5.33	$10,462.19
ZYTIGA TAB 250MG	2	1	$19,778.24	2	$9,889.12
SUBTOTAL	**34**	**7**	**$354,568.18**	**4.86**	**$10,428.48**
ENZALUTAMIDE PRODUCTS					
XTANDI CAP 40MG	40	7	$434,961.82	5.71	$10,874.05
SUBTOTAL	**40**	**7**	**$434,961.82**	**5.71**	**$10,874.05**
TOTAL	**74**	**13***	**$789,530.00**	**5.69**	**$10,669.32**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
CABAZITAXEL PRODUCTS				
JEVTANA INJECTION (J9043)	7	1	$7,030.88	$878.86
XOFIGO INJECTION (A9606)	8	1	$146,866.16	$18,358.27
TOTAL	**15**	**2***	**$153,897.04**	**$10,259.80**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] National Cancer Institute. SEER Cancer Statistics. Available online at: https://seer.cancer.gov/statfacts/html/prost.html. Last accessed 08/13/2019.
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Appendix H

Fiscal Year 2019 Annual Review of Crysvita® (Burosumab-twza)

Oklahoma Health Care Authority
September 2019

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

X-linked hypophosphatemia (XLH) is an inherited, X-linked disorder caused by mutations in the *PHEX* (phosphate-regulating endopeptidase on the X chromosome) gene. Mutations in *PHEX* result in increased concentrations of fibroblast growth factor 23 (FGF23), a protein produced by osteocytes in bones that regulates serum phosphate levels. Excess FGF23 inhibits renal sodium/phosphate cotransporters resulting in inhibition of phosphate reabsorption and causing subsequent hypophosphatemia. Chronic hypophosphatemia leads to poor bone mineralization and fractures. XLH is inherited in an X-linked dominant pattern; therefore, both males and females can develop XLH. While the majority of cases are inherited, *de novo* mutations in *PHEX* can occur in a person with no family history of the disease. It is estimated that XLH occurs in approximately 1 in 20,000 live births.

XLH is a progressive disorder; however, age of onset, disease severity, and rate of progression vary significantly among affected individuals. Some patients with XLH will only have hypophosphatemia and no bone-related symptoms while others may have more severe symptoms. In most patients, symptoms become apparent in the first 2 years of life when a child begins walking. Initial symptoms include bowing of the legs, short stature, and slowed growth. Additional findings include osteomalacia, bone pain, muscle pain and weakness, waddling gait, joint pain (a result of calcification of tendons and ligaments), abnormal tooth development, tooth abscesses, rickets, fractures, and impaired physical function. In some cases, symptoms of XLH will not appear until adulthood. Adults with XLH have overlapping symptoms including non-healing fractures, reduced mobility, pain, and functional limitations.

Diagnosis of XLH is based on clinical and laboratory findings. Clinical findings such as slow growth rate, bowing of the legs, or other skeletal abnormalities often prompt initial evaluation. Family history of XLH can also prompt evaluation. Patients with XLH will have low levels of phosphate, high levels of FGF23, and normal serum calcium and 25-hydroxy vitamin D. Genetic testing can confirm an XLH diagnosis.

Treatment of XLH focuses on reducing discomfort and correcting bone deformation. Children are generally treated from time of diagnosis until closure of growth plates. Until recently, the mainstay of pediatric treatment was oral phosphate 3 to 5 times daily in combination with high-dose calcitriol. Prepubertal children treated with this regimen can show improved radiological signs of rickets, improved growth, correction of deformities in lower limbs, and reduced bone or joint pain. Complications of this regimen may include nephrocalcinosis and hyperparathyroidism. In April 2018, the U.S. Food and Drug Administration (FDA) approved Crysvita® (burosumab-twza), an FGF23 blocking antibody, for the treatment of XLH in adult and

pediatric patients 1 year of age and older. Burosumab-twza is the first therapy directed toward correction of renal phosphate wasting and has efficacy data in repairing skeletal abnormalities, including fractures and osteomalacia. Additional therapies employed include growth hormone and epiphysiodesis (growth plate clamping) to mechanically straighten lower extremities during growth.

Treatment in adults is less established. Phosphate and calcitriol treatment is generally reserved for adults with skeletal pain, an upcoming orthopedic surgery, evidence of osteomalacia with an elevated alkaline phosphatase, or recurrent pseudofractures or stress fractures. Burosumab treatment in adults with XLH is more difficult to quantify as adult height is established and adults do not typically manifest active rickets; benefits in adults are related to potential improvement in bone and joint pain and non-healing fractures. Some patients may also require surgeries to correct bone deformities. Additionally, total hip and knee arthroplasty is sometimes required as a result of degenerative joint disease.

Current Prior Authorization Criteria

Crysvita® (Burosumab-twza) Approval Criteria:

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

9. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or be an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and
10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; and
11. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Utilization of Crysvita® (Burosumab-twza): Fiscal Year 2019[5]

Fiscal Year 2019 Utilization: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	4	21	$313,027.63	$14,906.08	$532.36	46	588

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

- Crysvita® (burosumab-twza) was approved by the FDA in April 2018. There were no SoonerCare paid pharmacy claims during fiscal year 2018.
- There were no SoonerCare paid medical claims for Crysvita® (burosumab-twza) during fiscal year 2018 or 2019.

Demographics of Members Utilizing Crysvita® (Burosumab-twza)

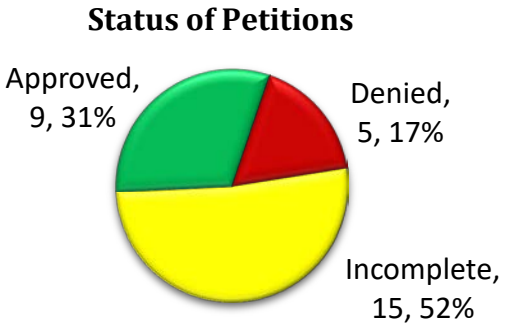
- Due to the limited number of members utilizing Crysvita® (burosumab-twza), detailed demographic information could not be provided.

Top Prescriber Specialties of Crysvita® (Burosumab-twza) by Number of Claims

- The only prescriber specialties listed on paid claims for Crysvita® (burosumab-twza) during fiscal year 2019 was medical geneticist and pediatric endocrinologist.

Prior Authorization of Crysvita® (Burosumab-twza)

There were 29 prior authorization requests submitted for Crysvita® (burosumab-twza) during fiscal year 2019 for 7 unique members. The following chart shows the status of the submitted petitions for fiscal year 2019.



Market News and Updates[7,8,9]

Pipeline:

- **Burosumab:** Burosumab (formerly known as KRN23) is being investigated in an active, open-label, Phase 2 trial to assess the efficacy and safety in subjects with tumor-induced osteomalacia (TIO) or epidermal nevus syndrome (ENS) by Ultragenyx Pharmaceutical, Inc., the company that manufactures Crysvita® (burosumab-twza). TIO is a disease characterized by typically benign tumors that produce excess levels of FGF23, including its skin lesion variant, ENS. TIO results in hypophosphatemia, osteomalacia, muscle weakness, fatigue, bone pain, and fractures. The symptoms of TIO rapidly resolve if the causal tumors can be resected; however, there are cases in which resection of the tumor is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor is inoperable, the current standard of care consists of oral phosphate and/or vitamin D replacement. The estimated study completion date is December 31, 2019.

News:

- **February 2019:** Ultragenyx Pharmaceutical, Inc. announced positive results of a 64-week efficacy and safety analysis of a randomized, active-controlled, Phase 3 study of Crysvita® (burosumab-twza) in children with XLH compared with oral phosphate and active vitamin D therapy. The new results showed that burosumab was superior to conventional therapy for all key efficacy endpoints, showing a meaningful improvement in rickets severity, lower limb deformity, growth, and physical functioning as demonstrated by increases in distance walked. The clinical study enrolled 61 patients ages 1 to 12 years, and compared the efficacy and safety of burosumab (N=29) to conventional therapy (N=32). The study's primary endpoint was the change in rickets at 40 weeks, assessed by 3 independent, blinded pediatric radiologists using the radiographic global impression of change (RGI-C) scale. Secondary endpoints included additional rickets assessments using the RGI-C scale and the Thacher Rickets Severity Scoring (RSS) system, pharmacodynamic assessments, changes in growth velocity and height, walking ability, patient-reported outcomes assessing pain, fatigue, and physical function, and safety. All endpoints were also evaluated at 64 weeks, as were the RGI-C lower limb deformity and height z-score. Prior to study enrollment, all patients received conventional therapy for an average of approximately 4 years. Patients in the

burosumab treatment group received a starting dose of 0.8mg/kg administered subcutaneously (sub-Q) every 2 weeks, with dose increases up to 1.2mg/kg implemented in 8 patients. Patients in the conventional therapy arm received the local standard regimen based on expert guidelines with ongoing optimization by each patient's physician. In May of 2018, the Phase 3 trial had met its primary endpoint demonstrating that burosumab was superior to conventional therapy in improving rickets after 40 weeks of treatment (P<0.0001). The results from the 64-week efficacy and safety analyses comparing treatment with burosumab versus conventional therapy showed the following:

- Rickets scores were superior with burosumab compared to conventional therapy, as assessed by 3 independent blinded pediatric radiologists using the RGI-C Global Score [least square (LS) mean treatment difference of +1.02, P<0.0001].
- RGI-C scores showing substantial healing of rickets (RGI-C ≥+2.0) was observed in 86.2% of patients receiving burosumab compared to 18.8% of patients receiving conventional therapy (P=0.0002).
- RSS improved more with burosumab compared to conventional therapy (LS mean treatment difference of -1.21, P<0.0001).
- Mean serum alkaline phosphatase levels as a biochemical measure of rickets were decreased by burosumab into the normal range and were superior to conventional therapy at 64 weeks (P<0.0001).
- Lower limb deformity (RGI-C score for bowing/limb deformity) was reduced more with burosumab compared with conventional therapy (LS mean treatment difference +0.97, P<0.0001).
- Growth during burosumab treatment demonstrated a statistically significant improvement as shown by a greater increase in standing height/recumbent length z-score compared with conventional therapy (LS mean treatment difference +0.14, P=0.0490).
- Walking ability as measured by the 6-minute walk test (6MWT) improved with burosumab treatment compared to conventional therapy (LS mean treatment difference +45.6 meters, P=0.0399).
- Mean serum phosphorus levels reached the lower limit of normal range with burosumab. At baseline, patients in both the burosumab and conventional therapy arms had mean serum phosphorus levels and mean renal phosphate reabsorption levels below the lower limits of normal. In the burosumab arm, mean serum phosphorus and renal phosphate reabsorption levels post-baseline through week 64 were in the normal range. In comparison, in the conventional therapy arm, mean serum phosphorus and renal phosphate reabsorption levels remained below the lower limits of normal through week 64. The treatment differences between burosumab and conventional therapy were significant (P<0.0001).
- Patients in both the burosumab and conventional therapy arms demonstrated increases in serum 1,25-dihydroxy vitamin D and maintained levels within the normal range through 64 weeks.

- The burosumab safety profile observed at week 64 was generally consistent with data from week 40 and is similar to other burosumab pediatric XLH trials.

Cost: The Wholesale Acquisition Cost (WAC) of burosumab is $3,400 per 10mg/mL single-dose vial, $6,800 per 20mg/mL single-dose vial, and $10,200 per 30mg/mL single-dose vial.

Patient Weight	Dosing Regimen	Vials Per Dose	Cost Per Dose	Cost Per Year
Pediatric Patient Dosing				
10kg	0.8 to 2mg/kg Q2W	(1) 10mg to (1) 20mg	$3,400 to $6,800	$88,400 to $176,800
20kg	0.8 to 2mg/kg Q2W	(1) 20mg to (2) 20mg	$6,800 to $13,600	$176,800 to $353,600
40kg	0.8 to 2mg/kg Q2W	(1) 30mg to (2) 30mg + (1) 20mg	$10,200 to $27,200	$265,200 to $707,200
Max	90mg Q2W	(3) 30mg	$30,600	$795,600
Adult Patient Dosing				
60kg	1mg/kg Q4W	(2) 30mg	$20,400	$265,200
70kg	1mg/kg Q4W	(2) 30mg + (1) 10mg	$23,800	$309,400
Max	90mg Q4W	(3) 30mg	$30,600	$397,800

Costs based on Wholesale Acquisition Costs (WAC) and do not reflect rebated prices or net costs.
Max = maximum recommended dose for age regardless of patient weight
Q2W = every 2 weeks; Q4W = every 4 weeks
Costs per year based on 26 injections (Q2W dosing) or 13 injections (Q4W dosing).

Specialist Recommendation(s): The College of Pharmacy received input from a geneticist regarding XLH genetic testing. The specialist recommended prior authorization of burosumab to ensure appropriate usage; however, requiring genetic testing as proof of XLH diagnosis was not recommended, but rather it could be used an option to confirm diagnosis. Laboratory evidence of elevated FGF23 was recommended as an alternative to confirm an XLH diagnosis.

Recommendations

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

Crysvita® (Burosumab-twza) Approval Criteria:

1. An FDA approved indication for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric members 1 year of age and older. Diagnosis of XLH must be confirmed by 1 of the following:
   a. Genetic testing; or
   b. Elevated serum fibroblast growth factor 23 (FGF23) level; and
2. Member's serum phosphorus level must be below the normal range for member age; and
3. ~~Member's XLH symptoms must not be adequately controlled on phosphate and calcitriol supplements. Members experiencing adverse effects related to these treatments may~~

~~also be considered for approval. Detailed information regarding adverse effects must be documented on the prior authorization request; and~~

4. Member must not have any contraindications to taking Crysvita® including the following:
    a. Concomitant use with oral phosphate and active vitamin D analogs; and
    b. Serum phosphorus within or above the normal range for member age; and
    c. Severe renal impairment or end-stage renal disease; and
5. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
    a. Crysvita® must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Crysvita® must be shipped via cold chain supply to the member's home and administered by a home health care provider and the member's caregiver must be trained on the proper storage of Crysvita®; and
6. Member must have clinical signs and symptoms of XLH (symptoms beyond hypophosphatemia alone); and
7. Every 2 week dosing will not be approved for members 18 years of age or older; and
8. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment, and thereafter as appropriate; and
9. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or be an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and
10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; and
11. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

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[2] National Institutes of Health (NIH). Genetics Home Reference: PHEX Gene. Available online at: https://ghr.nlm.nih.gov/gene/PHEX#location. Last revised 08/06/2019. Last accessed 08/12/2019.
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[4] Scheinman SJ, Drezner MK. Hereditary hypophosphatemic rickets and tumor-induced osteomalacia. *UpToDate*. Available online at: https://www.uptodate.com/contents/hereditary-hypophosphatemic-rickets-and-tumor-induced-osteomalacia?search=x+linked+hypophosphatemia&anchor=H2&language=en-US&source=preview&selectedTitle=1~15#H2. Last revised 07/12/2019. Last accessed 08/12/2019.
[5] U.S. Food and Drug Administration (FDA). FDA approves first therapy for rare inherited form of rickets, x-linked hypophosphatemia. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604810.htm. Issued 04/17/2018. Last accessed 08/12/2019.
[6] Ultragenyx Pharmaceutical, Inc. and Kyowa Hakko Kirin Co. Ltd. Ultragenyx and Kyowa Kirin Announce FDA Approval of Crysvita® (burosumab-twza) for the Treatment of Children and Adults with X–Linked Hypophosphatemia (XLH). *Globe Newswire*. Available online at: http://ir.ultragenyx.com/news-releases/news-release-details/ultragenyx-and-kyowa-kirin-announce-fda-approval-crysvitar. Issued 04/17/2018. Last accessed 08/12/2019.
[7] Ultragenyx Pharmaceutical, Inc. Study of KRN23 in Adult Subjects with Tumor-Induced Osteomalacia (TIO) or Epidermal Nevus Syndrome (ENS). U.S. National Library of Medicine. Available online at: https://clinicaltrials.gov/ct2/show/NCT02304367?term=burosumab&cond=Tumor-Induced+Osteomalacia&rank=2. Last revised 06/05/2019. Last accessed 08/12/2019.
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[9] Ultragenyx Pharmaceutical, Inc. Ultragenyx and Kyowa Kirin Announce Positive 64-Week Results for Crysvita® (burosumab) from Phase 3 Study in Children with X-linked Hypophosphatemia (XLH). *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/02/14/1725467/0/en/Ultragenyx-and-Kyowa-Kirin-Announce-Positive-64-Week-Results-for-Crysvita-burosumab-from-Phase-3-Study-in-Children-with-X-linked-Hypophosphatemia-XLH.html. Issued 02/14/2019. Last accessed 08/12/2019.

Appendix I

Fiscal Year 2019 Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Welchol® (Colesevelam Chewable Bar) and Ezallor™ Sprinkle (Rosuvastatin Capsule)

Oklahoma Health Care Authority
September 2019

Current Prior Authorization Criteria

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
DR = delayed-release; caps = capsules; tabs = tablets

Fibric Acid Derivative Medications Tier-2 Approval Criteria:

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

Juxtapid® (Lomitapide) Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least 1 of the following criteria:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least 1 of the following:
        i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
        ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; and
2. Documented trial of high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
3. Documented trial of Repatha® (evolocumab) at least 12 weeks in duration; and
4. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and

5. Prescriber must be certified with Juxtapid® REMS program.

Omega-3 Fatty Acids Approval Criteria:

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

PCSK9 Inhibitors Approval Criteria:

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

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

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

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

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

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

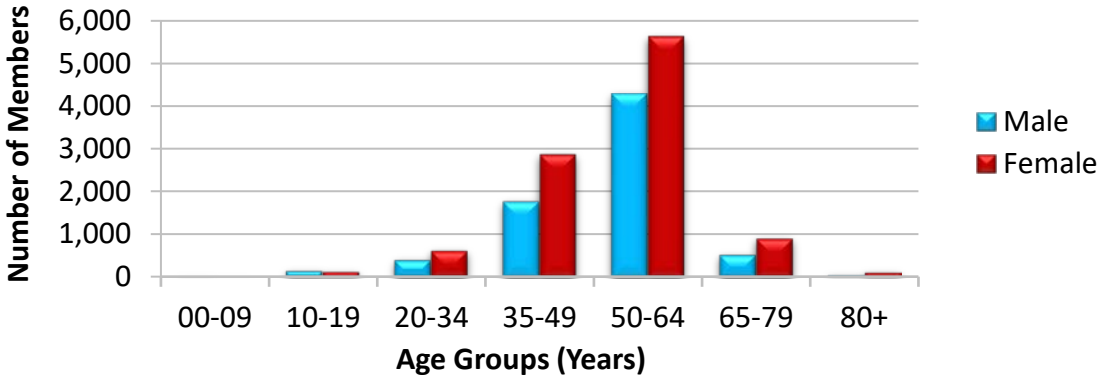
Utilization of Antihyperlipidemics: Fiscal Year 2019

Comparison of Fiscal Years

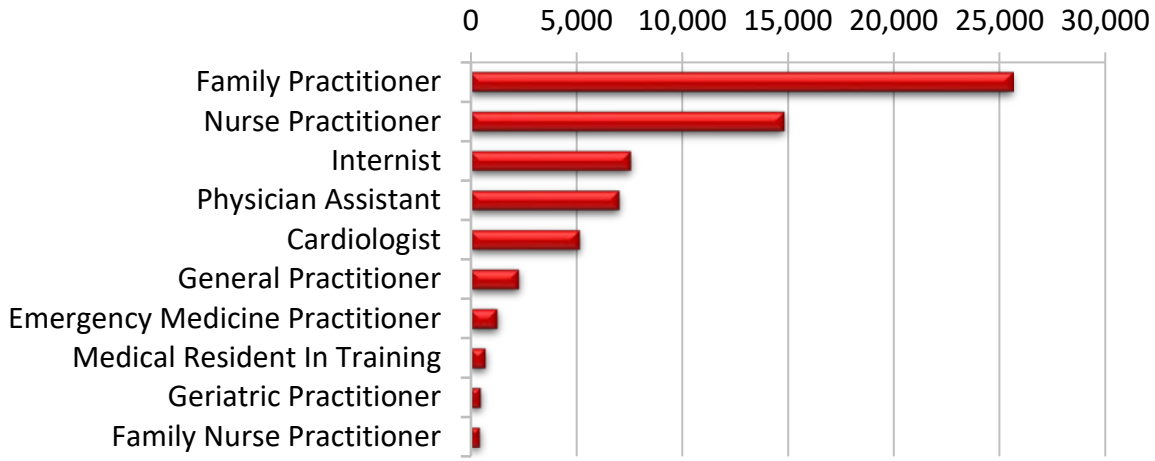
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	17,441	71,190	$1,149,332.63	$16.14	$0.33	3,615,294	3,495,078
2019	17,512	68,034	$1,060,581.25	$15.59	$0.30	3,672,296	3,554,587
% Change	**0.4%**	**-4.4%**	**-7.7%**	**-3.4%**	**-9.1%**	**1.6%**	**1.7%**
Change	**71**	**-3,156**	**-$88,751.38**	**-$0.55**	**-$0.03**	**57,002**	**59,509**

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

Demographics of Members Utilizing Antihyperlipidemics

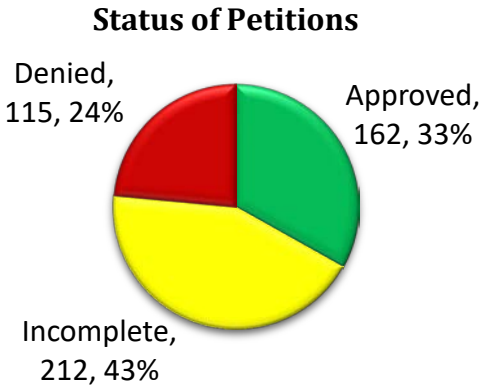


Top Prescriber Specialties of Antihyperlipidemics by Number of Claims



Prior Authorization of Antihyperlipidemics

There were 489 prior authorization requests submitted for antihyperlipidemics during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18]

Anticipated Patent Expiration(s):

- Welchol® (colesevelam chewable bar): April 2022
- Livalo® (pitavastatin calcium tablet): August 2024
- Juxtapid® (lomitapide capsule): August 2027
- FloLipid® (simvastatin oral suspension): February 2030
- Vascepa® (icosapent ethyl capsule): April 2030
- Zypitamag™ (pitavastatin magnesium tablet): January 2031
- Epanova® (omega-3-carboxylic acids): January 2033
- Antara® (fenofibrate micronized capsule): May 2033

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

- **December 2018:** The FDA approved Ezallor™ Sprinkle (rosuvastatin capsule) for the treatment of adult patients with hypertriglyceridemia as an adjunct to diet; primary dysbetalipoproteinemia (Type III hyperlipoproteinemia) as an adjunct to diet; and homozygous familial hypercholesterolemia (HoFH) to reduce LDL-cholesterol (LDL-C), total cholesterol, and apolipoprotein B (ApoB). Ezallor™ Sprinkle is not FDA approved for use in pediatric patients. The recommended dosing range for Ezallor™ Sprinkle is 5mg to 40mg once daily; the 40mg dose should only be used for patients not reaching their LDL-C goal with the 20mg dose. Ezallor™ Sprinkle is available as 5mg, 10mg, 20mg, and 40mg capsules, which may be swallowed whole or may be opened and the contents (granules) sprinkled onto 1 teaspoon of applesauce to be swallowed immediately without chewing. Ezallor™ Sprinkle capsules may be opened and the contents mixed with water for administration through a nasogastric (NG) tube (*please refer to Ezallor™ Sprinkle prescribing information for specific details regarding NG tube administration*). Ezallor™ Sprinkle recently became available on the market, and the Wholesale Acquisition Cost (WAC), regardless of strength, is $2.85 per capsule, which results in a monthly cost of $85.50, based on once daily dosing. In comparison, the State Maximum Allowable Cost (SMAC) of rosuvastatin 40mg tablets (generic Crestor®) is $0.12 per tablet, resulting in a monthly cost of $3.60 at a dose of 40mg once daily.
- **April 2019:** The FDA approved Welchol® (colesevelam chewable bar) as an adjunct to diet and exercise to reduce elevated LDL-C in adults with primary hyperlipidemia; to

reduce LDC-C levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH); and to improve glycemic control in adults with type 2 diabetes mellitus (DM). Colesevelam is a bile acid sequestrant, and the recommended dosage is 3.75 grams daily, taken with a meal. Welchol® chewable bar formulation will be available as a 3.75g chewable bar in 3 flavors: chocolate, strawberry, and caramel; the chewable bars contain approximately 80 calories per bar. The launch plans for Welchol® chewable bar are pending; cost information for Welchol® chewable bar is not yet available. Welchol® is also available, in brand and generic formulations, as a 625mg tablet and 3.75g packet for oral suspension, both of which are currently available without a prior authorization.

- **April 2019:** The FDA approved Praluent® (alirocumab) to reduce the risk of myocardial infarction (MI), stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease (CVD). This approval was based on data from the ODYSSEY OUTCOMES trial, which was published in the *New England Journal of Medicine (NEJM)* in November 2018, assessing the effect of adding alirocumab to maximally-tolerated statins on cardiovascular (CV) outcomes in 18,924 patients who had acute coronary syndrome (ACS) within 1 year of enrolling in the trial. Patients were eligible for enrollment in the trial if they were 40 years of age or older, had been hospitalized with ACS (MI or unstable angina) 1 to 12 months before randomization, and had an LDL-C level of ≥70mg/dL, a HDL-cholesterol (HDL-C) level of ≥100mg/dL, or an ApoB level of ≥80mg/dL. Patients who received alirocumab in the trial experienced a 15% reduced risk for major CV events; the primary endpoint included time to first MI, stroke, death from coronary heart disease (CHD), or unstable angina requiring hospitalization (P=0.0003). The FDA also approved alirocumab as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including HeFH) to reduce LDL-C. FDA approved in 2015, alirocumab was the first proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor approved by the FDA, and is available in a single-dose pre-filled syringe or pen in 2 strengths: 75mg/mL and 150mg/mL. The recommended dosage of alirocumab is 75mg administered subcutaneously (sub-Q) every 2 weeks, up to a maximum dosage of 150mg sub-Q every 2 weeks. Alternatively, for less frequent dosing, alirocumab may be administered at a dosage of 300mg sub-Q every 4 weeks. The WAC for Praluent® is approximately $540 per single-dose pen or syringe, regardless of strength, resulting in an annual cost of roughly $14,000.
    - **Institute for Clinical and Economic Review (ICER):** In February 2019, ICER released a final new evidence update for alirocumab, based on further analysis of the results from the ODYSSEY OUTCOMES trial, which have undergone peer review and were published in the *NEJM*. ICER is an independent, non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. Based on these new analyses, ICER revised its value-based price benchmark ranges for alirocumab to $2,300 to $3,500 per year if used to treat all patients who meet ODYSSEY trial eligibility criteria, and $2,700 to $4,000 per year if only used to treat higher-risk patients with LDL-C ≥100mg/dL despite intensive

statin therapy. ICER's value-based price benchmarks suggest a price range, net of any discounts or rebates, that aligns fairly with the treatment's added benefits for patients and the health care system; the ranges reflect commonly cited cost-effectiveness thresholds of between $100,000 and $150,000 per Quality-Adjusted Life Year (QALY) gained.

News:

- **Vascepa® (Icosapent Ethyl) REDUCE-IT CV Outcomes Study Results:** According to the results of the REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial) CV outcomes study, among statin-treated patients with elevated triglycerides (TG) and CVD or DM, multiple statistical models demonstrated that icosapent ethyl substantially reduces the burden of first, subsequent, and total ischemic events. The primary results were published in the *NEJM* in November 2018, and additional results and analysis of total recurrent events observed were subsequently published in the *Journal of the American College of Cardiology (JACC)* in March 2019. The study included 8,179 statin-treated patients with TG ≥135 and <500mg/dL, LDL-C >40 and ≤100mg/dL, and a history of atherosclerosis or DM. Patients were randomized to icosapent ethyl 4g/day or placebo, and the main outcomes were total (first and subsequent) primary composite endpoint events (CV death, nonfatal MI, nonfatal stroke, coronary revascularization, or hospitalization for unstable angina) and total key secondary composite endpoint events (CV death, nonfatal MI, or nonfatal stroke). Overall, icosapent ethyl reduced total primary endpoint events [61 vs. 89 per 1,000 patient-years for icosapent ethyl vs. placebo, respectively; rate ratio: 0.70; 95% confidence interval (CI): 0.62 to 0.78; P<0.0001]. Icosapent ethyl also reduced totals for each component of the primary composite endpoint, as well as the total key secondary endpoint events (32 vs. 44 per 1,000 patient-years; rate ratio: 0.72; 95% CI: 0.63 to 0.82; P<0.0001). Amarin, the manufacturer of Vascepa®, submitted a supplemental New Drug Application (sNDA) to the FDA in March 2019, seeking an expanded indication for Vascepa® to reduce the risk of major CV events based on the REDUCE-IT CV outcomes study results. The sNDA was given a Prescription Drug User Fee Act (PDUFA) date in January 2020; however, in May 2019, the FDA granted Priority Review designation for the sNDA, updating the PDUFA date to September 2019. Amarin recently announced that the FDA plans to hold an advisory committee meeting regarding the sNDA for Vascepa®, tentatively scheduled in mid-November, likely missing the updated PDUFA date. If approved, Vascepa® would be the first drug indicated to reduce residual CV risk in patients with statin-managed LDC-C but with persistent elevated TG.
    - **ICER:** In July 2019, ICER released a draft evidence report assessing the comparative clinical effectiveness and value of icosapent ethyl and rivaroxaban as additive CVD therapies. The draft report addresses some concerns with the REDUCE-IT study. The placebo vehicle used in the REDUCE-IT study (as well as earlier studies of icosapent ethyl) contained mineral oil to mimic the viscosity of the active agent; however, biomarker changes observed in the study add to documented concerns regarding mineral oil's potential interference with statin absorption. Additionally, a separate publication described a larger effect size for icosapent ethyl when total

ischemic events (rather than time to first event) are considered, as well as improved levels of risk reduction with each subsequent event; however, this type of analysis is controversial, given the correlation that often exists between event types (e.g., nonfatal MI followed by revascularization or death) and the consequent inflation of event rates. The authors addressed this by bundling multiple events occurring on the same day into 1 and specifying multiple statistical models. ICER does note that the results of the REDUCE-IT study stand apart from many prior studies of omega-3 preparations that showed little to no CV benefit, and that regardless of issues of study design or interpretation, the greatest uncertainty may be in how generalizable the REDUCE-IT results are and therefore what the most appropriate target population will be. Patients in the REDUCE-IT study were at very high risk of CV events and were on statin therapy; therefore, it is unclear whether icosapent ethyl would be effective in patients not treated with statins or how the benefits of treatment with icosapent ethyl would translate to an eligible population that is certain to be both broader and at lower CV risk than the study population. Compared to optimal medical management, ICER assigned an evidence rating to icosapent ethyl of B+ ("incremental or better"; moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit) for adults with established CVD or at high risk of CV events who are being treated with statins. ICER concludes that the use of icosapent ethyl (in patients receiving statins) provides clinical benefit in terms of gains in quality-adjusted survival and overall survival compared to optimal medical management alone for adults in the established CVD cohort and also for adults without known CVD but at high risk for CV events.

- **2018 Guideline on the Management of Blood Cholesterol:** A report of the American College of Cardiology (ACC)/American Heart Association (AHA) task force on clinical practice guidelines for the management of blood cholesterol was published in June 2019 in the *JACC*. Since publication of the last guidelines in 2013, a new class of non-statin drugs has become available (PCSK9 inhibitors), with evidence from 2 large randomized clinical outcome trials of secondary prevention patients. Some key updates compared to the 2013 guidelines include:
  - **Secondary prevention LDL-C threshold:** LDL-C ≥70mg/dL as threshold for non-statin drug consideration
  - **Non-statin agents:**
    - Atherosclerotic CVD (ASCVD) on maximal statin therapy: ezetimibe for clinical ASCVD and LDL-C ≥70mg/dL (Class IIb; Level of Evidence C)
    - Ezetimibe and PCSK9 inhibitor as add-on therapy for very high risk ASCVD and LDL-C ≥70mg/dL (Class IIa)
    - Ezetimibe should be initiated first, then PCSK9 inhibitor (Class I; Level of Evidence B)
    - LDL-C ≥190mg/dL on maximal statin therapy:
      - Ezetimibe if LDL-C <50% reduced on statin or remains ≥100mg/dL (Class IIa)

        - Bile acid sequestrant if LDL-C <50% reduced on statin and ezetimibe (Class IIb; Level of Evidence B)
    - PCSK9 inhibitor after statin and ezetimibe if LDL-C still ≥100mg/dL (Class IIb; Level of Evidence B-R) or if LDL-C still ≥130mg/dL and baseline LDL-C ≥220mg/dL (Class IIb; Level of Evidence C)
- **Value statement:**
    - PCSK9 inhibitor low value based on mid-2018 list prices (Level of Evidence B)
    - PCSK9 inhibitor uncertain value in primary prevention patients with familial hypercholesterolemia (FH) (Level of Evidence B)

- **2019 Guideline on the Primary Prevention of CVD:** A report of the ACC/AHA task force on clinical practice guidelines for the primary prevention of CVD was published online in March 2019 in the *JACC*. Some key recommendations from the guideline include:
    - The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.
    - Adults who are 40 to 75 years of age and are being evaluated for CVD prevention should undergo a 10-year ASCVD risk estimation and have a clinician-patient risk discussion before starting on a pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk factors can help guide decisions about preventive interventions in select patients, as can coronary artery calcium (CAC) scanning.
    - Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
    - Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated LDL-C levels ≥190mg/dL, those with DM who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician-patient risk discussion.
- **AHA Endorses Prescription Fish Oil:** According to a science advisory released in August 2019 by the AHA, prescription omega-3 fatty acids are an "effective and safe option" to lower TG levels. The AHA concluded that prescription omega-3 fatty acids at a dose of 4g/day, either as monotherapy or as an adjunct to other TG-lowering therapies, are clinically useful for reducing TG, after any underlying causes are addressed and diet and lifestyle strategies are implemented. Available prescription omega-3 fatty acids include Lovaza® [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] and Vascepa® (EPA only); Vascepa® was shown to reduce major CV events among statin-treated patients in the REDUCE-IT study (*further details included in the preceding market news*). The STRENGTH study, a CV outcomes study assessing the effects of prescription EPA/DHA in statin-treated patients with hypertriglyceridemia, is expected to be completed in September 2020. The AHA cautioned that over-the-counter (OTC) omega-3 supplements, which are not reviewed or approved by the FDA, should not be used in place of prescription medications for the long-term management of high TG.

Pipeline:

- **Bempedoic Acid:** In May 2019, Esperion filed New Drug Applications (NDAs) for bempedoic acid and a bempedoic acid/ezetimibe combination tablet, both of which

were developed to be complementary, cost-effective, convenient, once-daily oral therapies for the treatment of patients with elevated LDL-C who need additional LDL-C lowering despite the use of currently accessible therapies. Both products have a PDUFA goal date in February 2020. Bempedoic acid is a first-in-class, ATP Citrate Lyase (ACL) inhibitor that reduces cholesterol biosynthesis and lowers LDL-C by up-regulating the LDL receptor; completed Phase 3 studies with bempedoic acid have produced an additional 18% LDL-C lowering when used with moderate- and high-intensity statins and 28% LDL-C lowering when used with no background statin. The bempedoic acid/ezetimibe combination tablet has complementary mechanisms of action of inhibition of cholesterol synthesis (bempedoic acid) and inhibition of cholesterol absorption (ezetimibe); completed Phase 3 studies demonstrated that this combination resulted in a 29% LDL-C lowering when used with maximally tolerated statins and a 44% LDL-C lowering when used with no background statin.

- **Inclisiran:** The Medicines Company is developing inclisiran, a small interfering RNA (siRNA) therapy being studied to evaluate its ability to lower LDL-C; inclisiran is designed to prevent the production of PCSK9 at its primary source in the liver. Inclisiran is the first cholesterol-lowering therapy in the siRNA class and is being evaluated for the ability to lower LDL-C through twice-yearly dosing (administered as a sub-Q injection). In Phase 2 studies, inclisiran provided clinically significant LDL-C reductions greater than 50% in addition to the effects of statins and/or ezetimibe, and the LDL-C reductions were sustained through the 6-month dosing interval. The Medicines Company plans to file an NDA for inclisiran in the 4th quarter of 2019.

Recommendations

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

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

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

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

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

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

Welchol® (Colesevelam) Chewable Bar Approval Criteria:

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

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

PCSK9 Inhibitors Approval Criteria:

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

i. ~~Documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or~~
ii. ~~Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or~~

b. ~~An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of 1 of the following criteria:~~
i. ~~High cardiovascular risk confirmed by Framingham risk score; and~~
~~1.~~ ~~Supporting diagnoses/conditions signifying this risk level; or~~
ii. ~~Documented history of Coronary Heart Disease (CHD); and~~
~~1.~~ ~~Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and~~

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

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

Utilization Details of Antihyperlipidemics: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
STATIN MEDICATIONS AND EZETIMIBE						
TIER-1 MEDICATIONS						
ATORVASTATIN TAB 40MG	14,586	4,591	$202,837.11	$13.91	3.2	19.13%
ATORVASTATIN TAB 20MG	9,938	3,230	$120,796.46	$12.16	3.1	11.39%
ATORVASTATIN TAB 10MG	6,848	1,902	$78,056.14	$11.40	3.6	7.36%
ATORVASTATIN TAB 80MG	4,969	1,599	$78,743.47	$15.85	3.1	7.42%
SIMVASTATIN TAB 20MG	4,312	1,244	$40,388.97	$9.37	3.5	3.81%
PRAVASTATIN TAB 40MG	3,694	1,004	$55,453.43	$15.01	3.7	5.23%
SIMVASTATIN TAB 40MG	3,058	900	$29,924.83	$9.79	3.4	2.82%
PRAVASTATIN TAB 20MG	2,461	726	$33,110.76	$13.45	3.4	3.12%
LOVASTATIN TAB 20MG	1,834	601	$18,891.47	$10.30	3.1	1.78%
SIMVASTATIN TAB 10MG	1,344	378	$12,548.97	$9.34	3.6	1.18%
ROSUVASTATIN TAB 20MG	1,205	380	$16,562.26	$13.74	3.2	1.56%
LOVASTATIN TAB 40MG	957	283	$11,677.98	$12.20	3.4	1.10%
ROSUVASTATIN TAB 40MG	896	281	$13,973.46	$15.60	3.2	1.32%
ROSUVASTATIN TAB 10MG	844	294	$11,463.09	$13.58	2.9	1.08%
PRAVASTATIN TAB 10MG	805	219	$11,547.11	$14.34	3.7	1.09%
EZETIMIBE TAB 10MG	795	237	$15,674.00	$19.72	3.4	1.48%
PRAVASTATIN TAB 80MG	674	186	$13,403.35	$19.89	3.6	1.26%
LOVASTATIN TAB 10MG	337	135	$3,495.68	$10.37	2.5	0.33%
ROSUVASTATIN TAB 5MG	329	123	$4,407.71	$13.40	2.7	0.42%
SIMVASTATIN TAB 80MG	279	76	$3,548.33	$12.72	3.7	0.33%
SIMVASTATIN TAB 5MG	86	31	$955.65	$11.11	2.8	0.09%
ZETIA TAB 10MG	3	1	$1,780.93	$593.64	3	0.17%
TIER-1 SUBTOTAL	**60,254**	**16,589***	**$779,241.16**	**$12.93**	**3.6**	**73.47%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
LIVALO TAB 4MG	27	5	$12,434.82	$460.55	5.4	1.17%
EZET/SIMV TAB 10/40MG	24	5	$3,278.12	$136.59	4.8	0.31%
LIVALO TAB 2MG	18	5	$7,285.93	$404.77	3.6	0.69%
VYTORIN TAB 10/80MG	10	1	$4,070.38	$407.04	10	0.38%
LIVALO TAB 1MG	9	1	$2,575.41	$286.16	9	0.24%
VYTORIN TAB 10/40MG	3	1	$2,965.99	$988.66	3	0.28%
EZET/SIMV TAB 10/80MG	3	1	$627.96	$209.32	3	0.06%
SPECIAL PA SUBTOTAL	**94**	**19***	**$33,238.61**	**$353.60**	**4.9**	**3.13%**
STATINS/EZETIMIBE TOTAL	**60,348**	**16,605***	**$812,479.77**	**$13.46**	**3.6**	**76.61%**
FIBRIC ACID DERIVATIVE MEDICATIONS						
TIER-1 MEDICATIONS						
GEMFIBROZIL TAB 600MG	2,381	549	$31,953.83	$13.42	4.3	3.01%
FENOFIBRATE TAB 145MG	1,655	459	$34,052.88	$20.58	3.6	3.21%
FENOFIBRATE TAB 160MG	1,281	325	$30,763.91	$24.02	3.9	2.90%
FENOFIBRATE TAB 48MG	583	156	$11,387.68	$19.53	3.7	1.07%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FENOFIBRATE TAB 54MG	437	116	$9,228.26	$21.12	3.8	0.87%
FENOFIBRATE CAP 134MG	319	93	$10,201.23	$31.98	3.4	0.96%
FENOFIBRIC CAP 45MG DR	120	25	$3,471.69	$28.93	4.8	0.33%
FENOFIBRATE CAP 67MG	50	11	$1,188.59	$23.77	4.5	0.11%
FENOFIBRIC TAB 35MG	3	3	$232.74	$77.58	1	0.02%
TIER-1 SUBTOTAL	**6,829**	**1,679***	**$132,480.81**	**$19.40**	**4.1**	**12.49%**
TIER-2 MEDICATIONS						
FENOFIBRIC CAP 135MG DR	287	62	$20,817.35	$72.53	4.6	1.96%
FENOFIBRATE CAP 200MG	93	17	$4,383.84	$47.14	5.5	0.41%
FENOFIBRATE TAB 120MG	25	8	$23,105.40	$924.22	3.1	2.18%
FENOFIBRATE CAP 150MG	19	4	$5,715.45	$300.81	4.8	0.54%
FENOFIBRATE CAP 43MG	12	1	$454.03	$37.84	12	0.04%
FENOFIBRATE TAB 40MG	3	2	$1,238.19	$412.73	1.5	0.12%
FENOFIBRATE CAP 50MG	1	1	$247.92	$247.92	1	0.02%
FENOFIBRIC TAB 105MG	1	1	$211.63	$211.63	1	0.02%
FENOFIBRATE CAP 130MG	1	1	$77.27	$77.27	1	0.01%
TIER-2 SUBTOTAL	**442**	**96***	**$56,251.08**	**$127.26**	**4.6**	**5.30%**
FIBRIC ACIDS TOTAL	**7,271**	**1,752***	**$188,731.89**	**$25.96**	**4.2**	**17.80%**
OMEGA-3 FATTY ACIDS						
OMEGA-3-ACID CAP 1GM	367	139	$13,021.51	$35.48	2.6	1.23%
VASCEPA CAP 1GM	1	1	$298.05	$298.05	1	0.03%
OMEGA-3 FATTY ACIDS TOTAL	**368**	**140***	**$13,319.56**	**$36.19**	**2.6**	**1.26%**
PCSK9 INHIBITORS						
PRALUENT INJ 150MG/ML	25	2	$27,262.81	$1,090.51	12.5	2.57%
REPATHA AUTO-INJ 140MG/ML	16	7	$12,266.28	$766.64	2.3	1.16%
PRALUENT INJ 75MG/ML	5	2	$5,438.15	$1,087.63	2.5	0.51%
REPATHA INJ 140MG/ML	1	1	$1,082.79	$1,082.79	1	0.10%
PCSK9 INHIBITORS TOTAL	**47**	**11***	**$46,050.03**	**$979.79**	**4.3**	**4.34%**
TOTAL	**68,034**	**17,512***	**$1,060,581.25**	**$15.59**	**3.9**	**100%**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Please note, there was no SoonerCare utilization of Juxtapid® (lomitapide) in fiscal year 2019 (07/01/2018 to 06/30/2019).

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 06/2019. Last accessed 08/07/2019.

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[3] Ezallor™ Sprinkle (Rosuvastatin) Prescribing Information. Sun Pharmaceutical Industries Ltd. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208647s001lbl.pdf. Last revised 03/2019. Last accessed 08/12/2019.

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Appendix J

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

Oklahoma Health Care Authority
September 2019

Introduction[1,2,3]

Psoriasis is a common chronic, inflammatory skin disease most commonly characterized by well-demarcated, erythematous plaques with silver scale. It affects approximately 7.5 million Americans each year. There are multiple clinical subtypes of psoriasis with chronic plaque psoriasis being the most common presentation, affecting about 80% of people with psoriasis. Genetic predisposition plays a role in the development of psoriasis. Approximately 40% of patients with psoriasis or psoriatic arthritis have a family history of these disorders in first-degree relatives. In addition to genetics, multiple other exposures and characteristics have been proposed as risk factors or exacerbating factors for psoriasis. These factors include smoking, obesity, medications, infections, alcohol, vitamin D deficiency, and stress. A systematic worldwide review found the prevalence of psoriasis ranged from 0.5% to 11.4% in adults and 0% to 1.4% in children. Disease prevalence tends to increase with increasing distance from the equator. Psoriasis affects men and women equally.

Numerous topical and systemic therapies are available for the treatment of psoriasis. Treatment modalities are chosen on the basis of disease severity, relevant comorbidities, patient preference (including cost and convenience), efficacy, evaluation of individual patient response, and psychosocial needs of the patient. Patients with limited plaque psoriasis should initially be treated with topical corticosteroids and emollients. Alternatives include vitamin D analogs, such as calcipotriene and calcitriol, and topical retinoids (tazarotene). For facial or intertriginous areas, topical tacrolimus or pimecrolimus may be used as alternatives, though improvement may not be as rapid. Localized phototherapy is another option for recalcitrant disease. Combinations of potent topical corticosteroids and either calcipotriene, calcitriol, tazarotene, or phototherapy are commonly prescribed. Calcipotriene in combination with topical corticosteroids is highly effective for short-term control. Calcipotriene alone can be used continuously in combination with potent corticosteroids used intermittently for maintenance. Moderate-to-severe disease [involvement of more than 5% to 10% of the body surface area (BSA)] requires phototherapy or systemic therapies such as retinoids, methotrexate, cyclosporine, apremilast, or biologic immune modifying agents.

Sorilux® (calcipotriene 0.005% foam) was approved by the U.S. Food and Drug Administration (FDA) in 2010 for the treatment of plaque psoriasis of the scalp and body in adults. In May 2019, the FDA approved an expanded indication for Sorilux® to include adolescents, 12 years of age and older. Data from 17 patients was obtained in a follow-on open label study in patients 12 to 17 years of age with psoriasis and showed no significant effects on indices of calcium

metabolism and no quantifiable calcipotriene concentrations in patients 12 to younger than 17 years of age.

Sorilux® (Calcipotriene 0.005% Foam) Product Summary[4,5]

Indication(s): Sorilux® (calcipotriene 0.005% foam) is a vitamin-D analog indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 12 years of age and older.

Dosing:

- Sorilux® is supplied as a white, 0.005% calcipotriene topical foam available in 60g and 120g aluminum cans.
- The recommended dosing is to apply a thin layer twice daily to the affected areas. The foam should be rubbed in gently and completely.
- When applying Sorilux®, contact with the face and eyes should be avoided.

Mechanism of Action: Calcipotriene is a synthetic vitamin D_3 analog that has similar receptor binding affinity as natural vitamin D_3. However, the exact mechanism of action contributing to the clinical efficacy in the treatment of psoriasis is unknown.

Contraindication(s): Calcipotriene 0.005% foam should not be used by patients with known hypercalcemia.

Warnings and Precautions:

- Flammability: The propellant in Sorilux® is flammable. Patients should be instructed to avoid fire, flame, and smoking during and immediately following application.
- Effects on Calcium Metabolism: Transient, rapidly reversible elevation of serum calcium has occurred with use of calcipotriene. If elevation in serum calcium outside the normal range should occur, treatment should be discontinued until normal calcium levels are restored.

Adverse Reactions: Adverse reactions reported in ≥1% of patients treated with Sorilux® and at a higher incidence than patients treated with vehicle were application site erythema (2%) and application site pain (3%). The incidence of these adverse reactions was similar between the body and scalp.

Efficacy: In 2 multi-center, randomized, double-blind, vehicle-controlled clinical trials a total of 659 patients with psoriasis were randomized 2:1 to calcipotriene 0.005% foam or vehicle. The patients applied the assigned treatment twice daily for 8 weeks. Baseline disease severity was graded using a 5-point Investigator Static Global Assessment (ISGA) scale in which disease severity is rated from 0 (clear) to 4 (severe). Patients included in the studies scored either 2 (mild) or 3 (moderate) at baseline. Patients were also required to have a target lesion site (>2cm^2) on the trunk or extremities. The primary endpoint was treatment success, defined as an ISGA score of 0 or 1 (clear or almost clear) and a minimum improvement in ISGA score of at least 2 grades from baseline to week 8. In Study 1, treatment success was achieved by 14% of patients in the calcipotriene group versus 7% of patients in the vehicle group. This difference

approached statistical significance (P=0.058). In Study 2, treatment success was achieved by 27% of patients in the calcipotriene group and 16% of patients in the vehicle group (P=0.016). In the primary endpoint analysis, patients were classified as treatment failures if outcomes at week 8 were missing, regardless of the response to treatment at earlier evaluations. An additional sensitivity analysis was performed in which a last-observation-carried-forward (LOCF) approach was used for patients in the intent-to-treat (ITT) population who were missing week 8 primary endpoint evaluations. In Study 1, using the LOCF approach, 15% of patients in the calcipotriene group and 7% of patients in the vehicle group achieved treatment success at week 8 (P=0.034). Similarly in Study 2, using the LOCF approach, treatment success rates were 28% and 16% for the calcipotriene and vehicle foam groups, respectively (P=0.010).

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

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

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

Recommendations

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

Sorilux® (Calcipotriene 0.005% Foam) Approval Criteria:

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

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Appendix K

Fiscal Year 2019 Annual Review of Synagis® (Palivizumab)

Oklahoma Health Care Authority
September 2019

Current Prior Authorization Criteria

A prior authorization is required for all members who receive palivizumab in an outpatient setting. Palivizumab is approved for members who meet the established prior authorization criteria, which is based on a modified version of the American Academy of Pediatrics (AAP) 2014 guidelines for palivizumab prophylaxis.

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection:
   1. Infants younger than 12 months of age at the start of respiratory syncytial virus (RSV) season:
      a. Born before 29 weeks, 0 days gestation; or
      b. Born before 32 weeks, 0 days gestation and develop chronic lung disease (CLD) of prematurity (require >21% oxygen supplementation for at least 28 days after birth); or
      c. Have hemodynamically significant congenital heart disease [acyanotic heart disease and receiving medication to control congestive heart failure (CHF) and will require surgical procedures, or have moderate-to-severe pulmonary hypertension]; or
      d. May be considered for:
         i. Infants with neuromuscular disease or a congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough; or
         ii. Infants who undergo cardiac transplantation during RSV season; or
         iii. Infants who are profoundly immunocompromised during RSV season; or
         iv. Infants with cystic fibrosis with clinical evidence of CLD and/or are nutritionally compromised; or
   2. Infants 12 to 24 months of age at the start of RSV season:
      a. Born before 32 weeks, 0 days gestation and have CLD of prematurity (required at least 28 days of oxygen after birth) and continue to require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6 months before the start of the RSV season; or
      b. May be considered for:
         i. Infants who undergo cardiac transplantation during RSV season; or
         ii. Infants who are profoundly immunocompromised during RSV season; or
         iii. Infants with cystic fibrosis with manifestations of severe lung disease or weight for length less than the 10th percentile; and

B. Length of Treatment: Palivizumab is approved for use only during RSV season. Approval dates will be November 1st through March 31st.

C. Units Authorized: The maximum duration of therapy is 5 doses, with a dose to be administered no more often than every 30 days. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as 1 of the approved total.

D. Dose-Pooling: To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Utilization of Synagis® (Palivizumab): Fiscal Year 2019

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	264	1,156	$2,734,231.87	$2,365.25	$78.87	999	34,668
2019	288	1,143	$2,823,350.84	$2,470.12	$82.39	1,025	34,269
% Change	**9.1%**	**-1.1%**	**3.3%**	**4.4%**	**4.5%**	**2.6%**	**-1.2%**
Change	**24**	**-13**	**$89,118.97**	**$104.87**	**$3.52**	**26**	**-399**

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

Pharmacy Claim Details for Respiratory Syncytial Virus (RSV) Season 2018-2019

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Cost/ Day	Cost/ Claim
SYNAGIS INJ 100MG/ML	792	265	$2,307,362.56	2.99	$97.20	$2,913.337
SYNAGIS INJ 50MG/0.5ML	351	177	$515,988.28	1.98	$49.00	$1,470.052
Total	**1,143**	**288***	**$2,823,350.84**	**3.97**	**$82.39**	**$2,470.123**

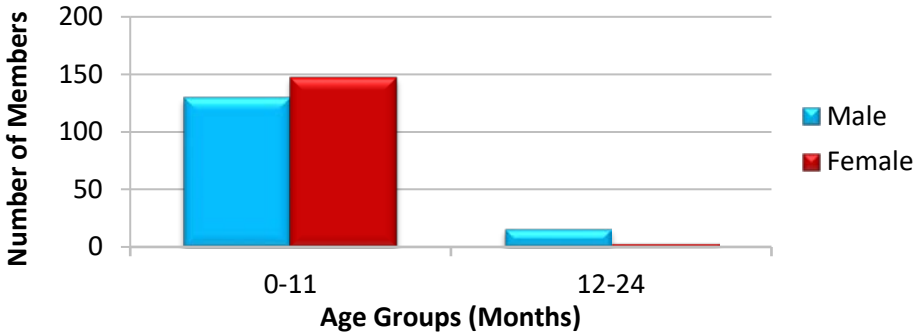
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Cost Per Vial

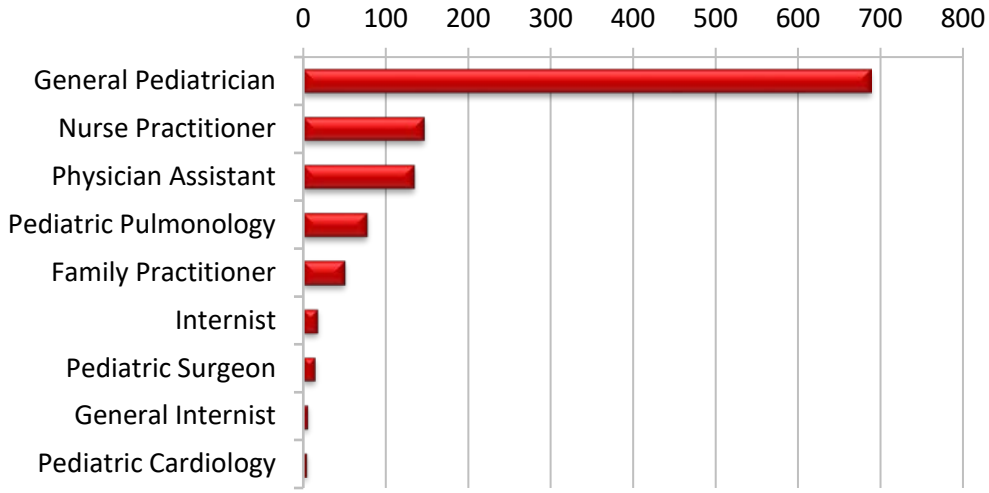
Vial Size	Cost Per Vial
Synagis® (palivizumab) 100mg/mL vial	$2,764.02
Synagis® (palivizumab) 50mg/0.5mL vial	$1,463.28

Costs do not reflect rebated prices or net costs.
Costs based on specialty pharmaceutical allowable cost (SPAC).

Demographics of Members Utilizing Synagis® (Palivizumab)



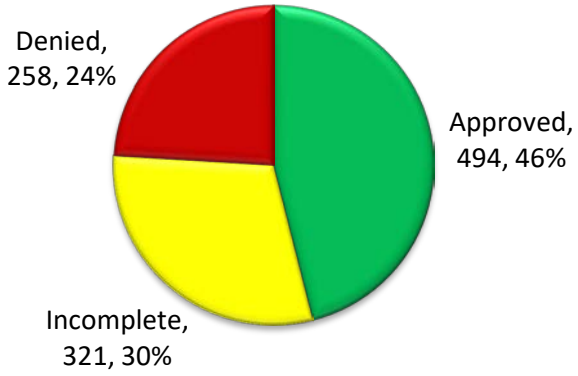
Top Prescriber Specialties of Synagis® (Palivizumab) by Number of Claims



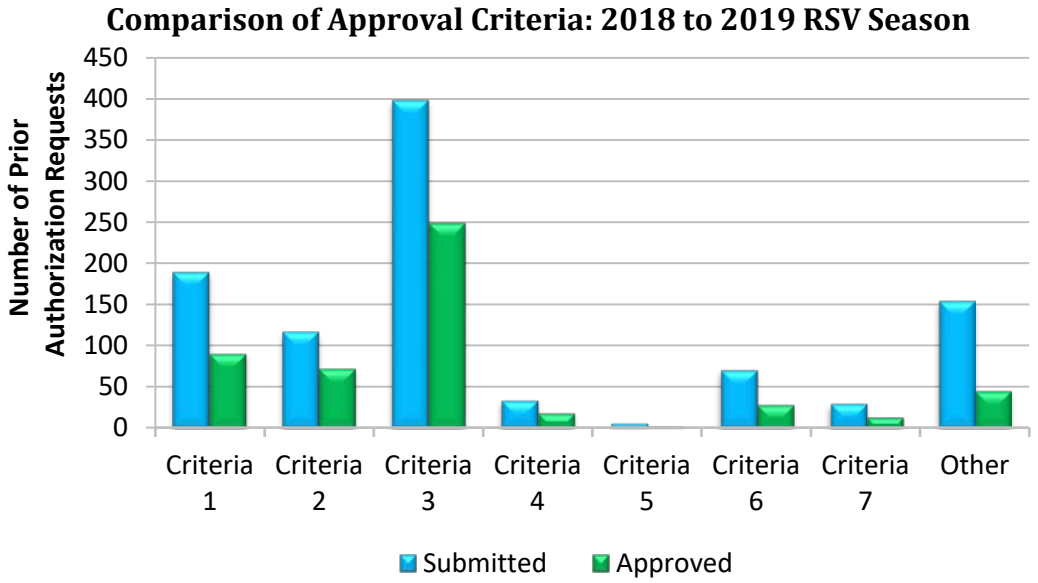
Prior Authorization of Synagis® (Palivizumab)

There were 1,073 palivizumab prior authorization requests submitted for 519 unique members during fiscal year 2019. This is an increase in both submitted petitions and number of members requesting palivizumab compared to fiscal year 2018 when there were 1,055 palivizumab prior authorization requests submitted for 482 unique members. The following chart shows the status of the submitted petitions for fiscal year 2019.

Status of Petitions



The following graph shows the number of submissions and approvals for each prior authorization criteria. The graph is followed by a numbered list in which the list number corresponds to the criteria number in the graph. The most commonly requested and approved criteria selection during the 2018 to 2019 RSV season was criteria number 3: infants born before 29 weeks, 0 days gestation. Infants born before 32 weeks, 0 days gestation and who had CLD of prematurity was also a commonly requested and approved criteria selection (criteria number 1).

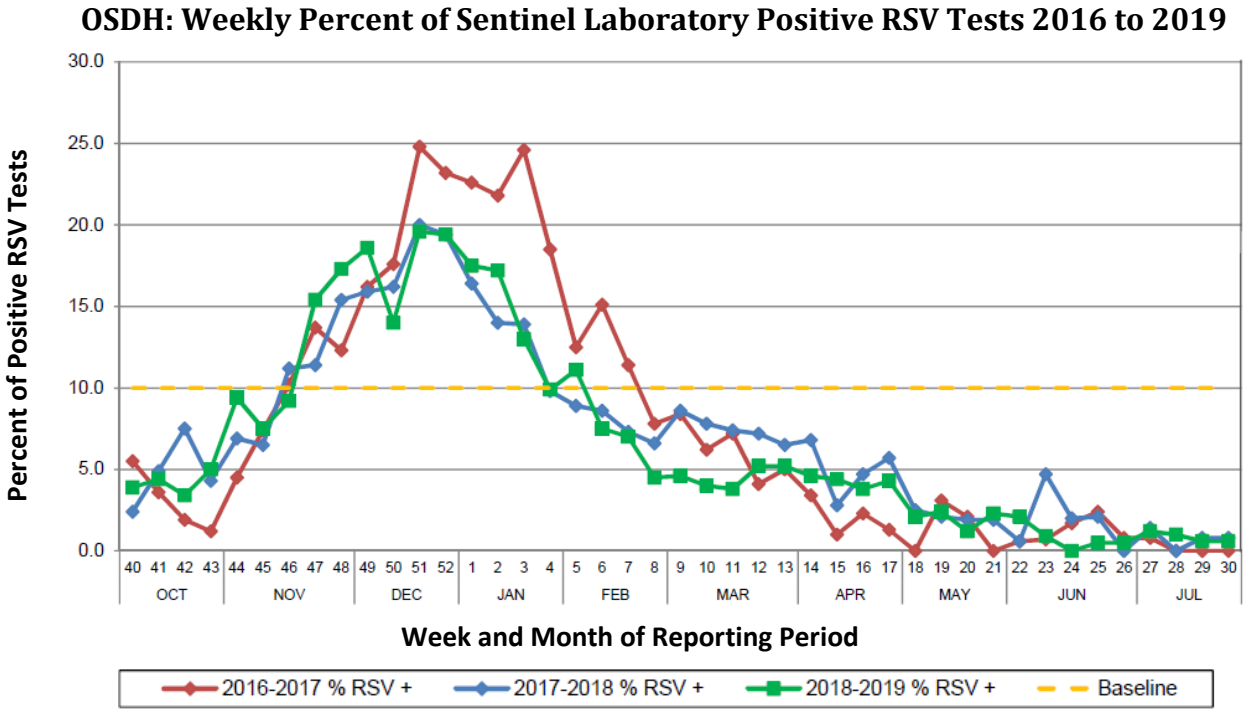


Criteria List:

1. Infants 0 to 24 months of age at the start of RSV season born before 32 weeks, 0 days gestation and have CLD of prematurity.
2. Infants who have hemodynamically significant congenital heart disease and will require surgical procedures, or have moderate-to-severe pulmonary hypertension.
3. Infants born before 29 weeks, 0 days gestation.
4. Infants with neuromuscular disease or a congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough.
5. Infants who undergo cardiac transplantation during RSV season.
6. Infants who are profoundly immunocompromised during RSV season.
7. Infants with cystic fibrosis with clinical evidence of CLD and/or are nutritionally compromised.

Season Comparison[1,2,3,4,5]

The following chart contains the weekly percent of laboratory positive RSV tests in Oklahoma as reported by the Oklahoma State Department of Health (OSDH) Viral Respiratory Illness Sentinel Surveillance System. The chart is included to compare RSV seasons since 2016. RSV is determined to be in season once the percent of positive tests is >10% for 2 consecutive weeks. Similarly, the season is determined to be at an end when the percent of positive tests is <10% for 2 consecutive weeks. RSV seasons appear to be similar with a peak typically in December or January and a season end by late March. Palivizumab prior authorization approvals are initiated with a start date of November 1st and continue to March 31st; this approval window corresponds to the following state monitoring graph as well as with state data reported by the Centers for Disease Control and Prevention (CDC). For the 2018 to 2019 RSV season for Oklahoma, the CDC determined the onset week by percentage of positive antigen detection tests was the week of October 6th with a season offset the week of February 23rd. Similarly, OSDH determined the onset week as November 26th and offset week as February 18th.



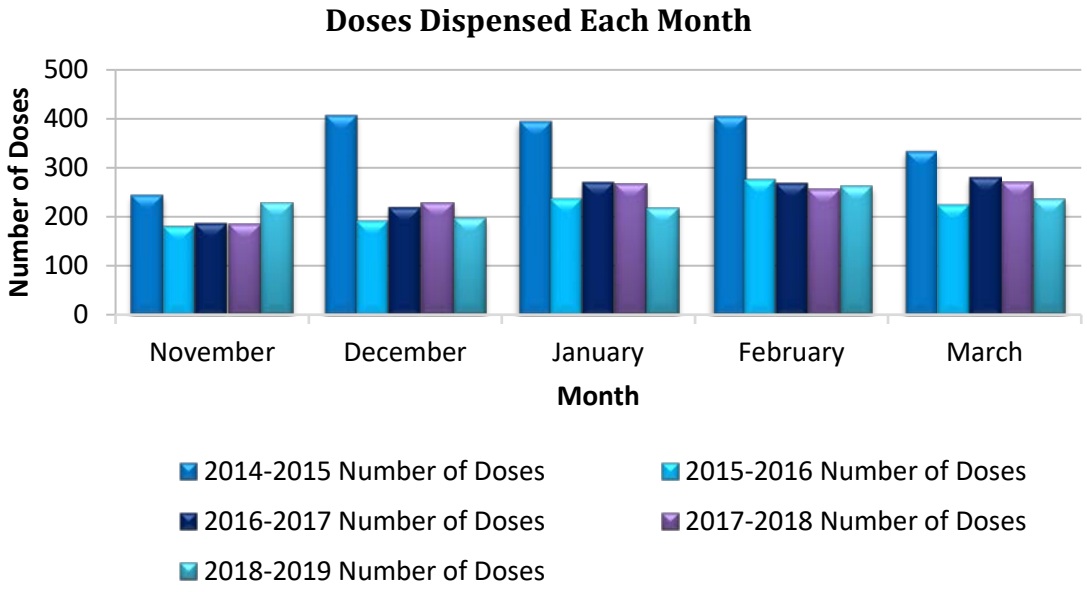
The CDC reported seasonality by using RSV polymerase chain reaction (PCR) laboratory detections. Laboratories are shifting away from antigen-based RSV testing, and since 2014 the majority of RSV detections among reporting laboratories were determined by PCR. If the Oklahoma season was based on percentage of positive PCR tests and a threshold of 10%, similar to antigen testing, season onset and offset would have occurred the week of November 24th and January 26th. If the Oklahoma season was based on percentage of positive PCR tests and a threshold of 3%, a commonly cited PCR threshold, season onset and offset would have occurred the week of October 27th and May 4th.

RSV season onset, when evaluated by PCR detections and a new statistical method determined by the CDC, is defined as the second of 2 consecutive weeks when the slope, or normalized 5-week moving average of RSV detections between subsequent weeks exceeded 10. Season offset was determined as the last week when the standardized detections exceeded the standardized detections at onset. These changes were done to reflect the adoption of a statistical method rather than a threshold or percent positive which can be influenced by volume of tests performed. For Oklahoma's region (Region 6 – Arkansas, Louisiana, New Mexico, Oklahoma, and Texas) using the CDC's statistical analysis method, the season would have had an onset the week of October 1st and an offset the week of May 6th for the 2016 to 2017 season. This is significantly longer than when determined by antigen-based RSV testing, which had an onset the week of December 3rd and an offset the week of March 11th for the 2016 to 2017 season. The CDC cautions that the statistical detection method used captures a high proportion of RSV detection for retrospectively determining seasonality but cannot be used to determine seasonal onset and offset in real time and can only be used after the season is at an end. The CDC advises that surveillance data collected by state and local health departments might be more accurate to describe local RSV circulation trends. RSV PCR testing is not currently reported by the OSDH to evaluate local trends specific to the State of Oklahoma. The Updated Guidance for Palivizumab

Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection released by the AAP in 2014 states the following with regard to RSV seasonality:

> "During the 6 RSV seasons from July 2007 to January 2013, the median duration of the RSV season ranged from 13 to 23 weeks, with median peak activity from mid-December to early February, with the exception of Florida and Alaska. Within the 10 Health and Human Services Regions, in the few regions when the RSV season began in October, the season ended in March or early April. In regions where the RSV season began in November or December, the season ended by April or early May. Because 5 monthly doses of palivizumab at 15mg/kg per dose will provide more than 6 months of serum palivizumab concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States."[3]

The following bar graph shows the number of palivizumab doses reimbursed for by SoonerCare for each month during the last 5 seasons. In 2015, SoonerCare adopted the updated guidance for palivizumab prophylaxis released by the AAP. The guidance, which was released in 2014, urged more limited use than previously recommended in children born after 29 weeks gestation or those in the second year of life. Many hospitals across the state updated their protocols at that time resulting in fewer doses dispensed in the 2014 season as well as in the 2015 season when SoonerCare adopted the updated guidance.



Market News and Updates[6,7,8,9,10,11]

Guideline Update(s):

- **October 2017:** Two groups from the AAP, the Committee on Infectious Diseases and the Subcommittee on Bronchiolitis, reviewed pertinent data regarding palivizumab and reaffirmed the recommendations from the 2014 RSV policy statement and technical report.

Pipeline:

- **MVA-BN® RSV:** In August 2018, Bavarian Nordic announced positive results from its Phase 2 extension study of MVA-BN® RSV, a universal RSV vaccine. In 2017, results of a Phase 2 study of the MVA-BN® RSV vaccine in 421 patients 55 years of age and older demonstrated that the vaccine induced antibody and T-cell responses against RSV for an entire RSV season with a single booster vaccination. The extension study re-enrolled 88 subjects 1 year later, after having received a single vaccination in the Phase 2 study and were further boosted with the same vaccine dose. The extension study demonstrated that in at least 60% of the subjects the broad antibody responses against RSV were durable and remained elevated compared to baseline, 1 year after receiving a single booster vaccination. Following a further annual booster with MVA-BN® RSV, there was an increase in serum antibody responses, including neutralizing antibodies against RSV and total IgG and IgA antibodies against RSV. The company plans to design a Phase 3 study after meeting with the U.S. Food and Drug Administration (FDA).
- **MEDI8897:** In February 2019, AstraZeneca announced that the FDA granted Breakthrough Therapy designation for MEDI88897, an extended half-life RSV F monoclonal antibody being developed for the prevention of lower respiratory tract infection caused by RSV. MEDI8897 is being developed for use in a late preterm and healthy full-term infants. Additionally, MEDI8897 is being developed so that it may only require 1 dose during a typical 5-month RSV season.
- **EPD-938:** In June 2019, Enanta Pharmaceuticals announced topline results from a Phase 2a trial of EPD-938, an N-protein inhibitor that targets RSV replication. The Phase 2a study was a randomized, double-blind, placebo-controlled, human challenge study in healthy adult subjects inoculated with RSV. A total of 115 subjects were randomized to receive either a once-daily 600mg dose, a single 500mg loading dose followed by 300mg twice daily, or placebo for 5 days. A statistically significant ($P<0.001$) reduction was observed for the area under the curve for viral load in the intent-to-treat-infected population for each of the EDP-938 dosing groups as compared with placebo. There were no serious adverse events reported and no discontinuation of study drug.
- **ResVax™:** In June 2019, Novavax, Inc. announced that the FDA has recommended the company conduct an additional Phase 3 trial of ResVax™ to confirm efficacy against medically significant RSV disease in infants born to mothers vaccinated with ResVax™. ResVax™ is an RSV F recombinant nanoparticle vaccine (RSV F Vaccine) intended for infants via maternal immunization at 28 to 36 weeks gestation. ResVax™ is being evaluated in Prepare™, a global Phase 3 clinical trial in 4,636 pregnant women, at least 3,000 of whom received the vaccine.
- **DS-Cav1:** In August 2019, an interim analysis of a Phase 1 study of DS-Cav1, an RSV vaccine candidate, found DS-Cav1 prompted large increases in RSV-neutralizing antibodies in healthy adults that were sustained for several months after only 1 dose. Final results of the trial are expected in 2020.

Recommendations

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

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Appendix L

Fiscal Year 2019 Annual Review of Sickle Cell Disease (SCD) Medications

Oklahoma Health Care Authority
September 2019

Current Prior Authorization Criteria

Endari™ (L-Glutamine) Approval Criteria:

1. An FDA approved diagnosis of sickle cell disease (SCD); and
2. Member must be 5 years of age or older; and
3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. Endari™ must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
6. Initial approvals will be for a duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Siklos® (Hydroxyurea Tablets) Approval Criteria:

1. An FDA approved indication of sickle cell anemia; and
2. Member must be 2 years of age or older; and
3. Member must have a history of moderate-to-severe, painful crises; and
4. A trial of hydroxyurea capsules or a patient-specific, clinically significant reason why hydroxyurea capsules are not appropriate for the member; and
5. Prescriber must agree to monitor blood counts every 2 weeks throughout therapy; and
6. Prescriber must agree to monitor the member for the development of secondary malignancies; and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
8. Male and female members of reproductive potential must be willing to use effective contraception during and after treatment with Siklos® for at least 6 months after therapy; and
9. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Utilization of SCD Medications: Fiscal Year 2019

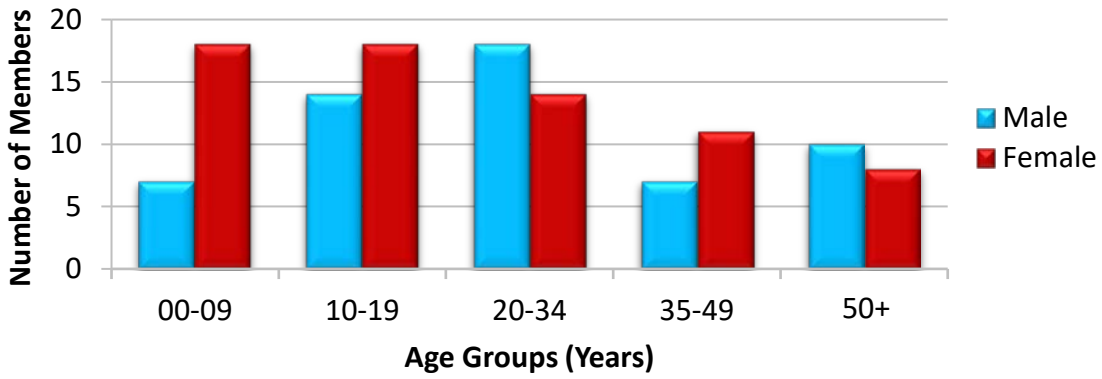
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	128	608	$21,741.86	$35.76	$1.17	52,676	18,508
2019	125	594	$19,414.75	$32.68	$1.09	50,179	17,755
% Change	**-2.30%**	**-2.30%**	**-10.70%**	**-8.60%**	**-6.80%**	**-4.70%**	**-4.10%**
Change	**-3**	**-14**	**-$2,327.11**	**-$3.08**	**-$0.08**	**-2,497**	**-753**

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

- This utilization data includes SCD medications (e.g., hydroxyurea capsules) used for all diagnoses and does not differentiate between SCD and other diagnoses for which use may be appropriate.

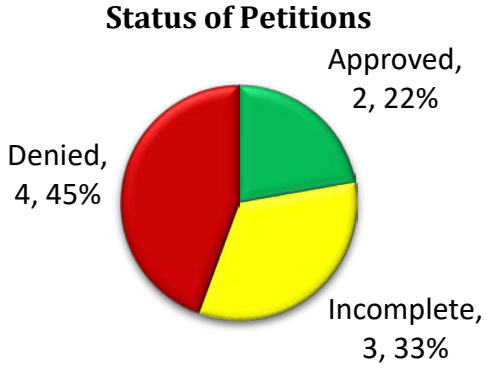
Demographics of Members Utilizing SCD Medications



Top Prescriber Specialties of SCD Medications by Number of Claims

Prior Authorization of SCD Medications

There were 9 prior authorization requests submitted for 7 unique members for SCD medications during fiscal year 2019. The following chart shows the status of the submitted petitions for fiscal year 2019.



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

Pipeline:

- **Crizanlizumab:** In July 2019, Novartis announced the U.S. Food and Drug Administration (FDA) accepted the company's Biologics License Application (BLA) for crizanlizumab and has granted the investigational medication Priority Review. If crizanlizumab is approved by the FDA, it is expected to represent the first monoclonal antibody targeting the P-selectin mediated multi-cellular adhesion in SCD. In December 2018, Novartis was granted Breakthrough Therapy designation for crizanlizumab for the prevention of vaso-occlusive crises in patients with SCD. The FDA submission is supported by Phase 2 data from the SUSTAIN study, which showed that crizanlizumab reduced the median annual rate of vaso-occlusive crises leading to health care visits by 45.3% compared with placebo (1.63 vs. 2.98, P=0.010) in patients with or without hydroxyurea. Clinically significant reductions in the frequency of vaso-occlusive crises were observed among patients regardless of SCD genotype or hydroxyurea use. The anticipated FDA decision is expected in the first half of 2020.
- **Voxelotor:** In June 2019, Global Blood Therapeutics (GBT) announced new results from its Phase 3 HOPE study of voxelotor in patients 12 years of age and older with SCD. The findings showed the HOPE study met its primary endpoint of an improvement in hemoglobin greater than 1g/dL at 24 weeks with voxelotor 1,500mg compared with placebo, with a favorable safety and tolerability profile. Voxelotor provided a statistically significant and sustained improvement in hemoglobin levels and reduced the incidence of worsening anemia and hemolysis in the study. Voxelotor is being developed as an oral, once-daily therapy for patients with SCD and works by increasing hemoglobin's affinity for oxygen. The FDA has granted voxelotor Breakthrough Therapy, Fast Track, Orphan Drug, and Rare Pediatric Disease designations for the treatment of patients with SCD. GBT is expected to initiate and complete a rolling New Drug Application (NDA) for voxelotor before the end of 2019.

- **Rivipansel:** In August 2019, Pfizer announced that the Phase 3 Rivipansel: Evaluating Safety, Efficacy, and Time to Discharge (RESET) pivotal study did not meet its primary or key secondary efficacy endpoints. The trial's objective was to evaluate the efficacy and safety of rivipansel in patients 6 years of age and older with SCD who were hospitalized for a vaso-occlusive crisis and required treatment with intravenous (IV) opioids. The primary endpoint was time to readiness-for-discharge and the key secondary efficacy endpoints were time-to-discharge, cumulative IV opioid consumption, and time to discontinuation of IV opioids.
- **Sevuparin:** In May 2019, Modus Therapeutics announced their lead therapeutic candidate for managing painful vaso-occlusive crises, sevuparin, failed to show clinically meaningful improvements in patients with SCD according to results of a Phase 2 clinical trial. Sevuparin is an investigational drug with anti-adhesive and anti-inflammatory properties that has been developed to prevent the obstruction of blood vessels and restore normal blood flow, reducing the risk of vaso-occlusive crises.
- **LentiGlobin® Gene Therapy:** In June 2019, BlueBird Bio announced new data from patients in an ongoing Phase 1/2 HGB-206 study of the company's investigational LentiGlobin® gene therapy for SCD. LentiGlobin® for SCD adds functional copies of a modified form of the β-globin gene into a patient's hematopoietic stem cells. HGB-206 is designed to evaluate the efficacy and safety of LentiGlobin® gene therapy for SCD and includes 3 treatment cohorts: Groups A, B, and C. As of March 2019, 25 patients were enrolled and a total of 13 patients had been treated with LentiGlobin® in Group C, with a median post-treatment follow-up of 9 months (1.0-15.2 months). Eight of the 13 treated patients in Group C had at least 6 months of follow-up at the time of the data cutoff. In these patients, production of gene therapy-derived hemoglobin ranged from 4.5 to 8.8g/dL and total unsupported hemoglobin levels ranged from 10.2 to 15.0g/dL at the last study visit. Among patients in Group C, at up to 15 months post-treatment with LentiGlobin®, no acute chest syndrome or serious vaso-occlusive crisis were reported. LentiGlobin® for the treatment of SCD has received Orphan Drug and Regenerative Medicine Advanced Therapy designations from the FDA. LentiGlobin® is also being evaluated for transfusion-dependent beta thalassemia (TDT) in ongoing Phase 3 studies and a long-term follow-up study. The FDA granted Orphan Drug and Breakthrough Therapy designations to LentiGlobin® for TDT.
- **CTX001:** In February 2019, CRISPR Therapeutics and Vertex Pharmaceuticals announced that the first patient had been treated with CTX001 in a Phase 1/2 clinical study of patients with TDT. The company is also investigating CTX001 for the treatment of severe SCD and announced that the first SCD patient had been enrolled in a Phase 1/2 clinical study of CTX001. CTX001 is an investigational *ex vivo* CRISPR gene-edited therapy that is being evaluated for patients with TDT or severe SCD in which a patient's hematopoietic stem cells are engineered to produce high levels of fetal hemoglobin in red blood cells. In July 2019, doctors in the United States attempted to treat a patient with SCD using CRISPR gene editing.

News:

- **March 2018:** A study published in the journal *Pediatrics* examined how many children with SCD and covered by Medicaid in Florida, Illinois, Louisiana, Michigan, South Carolina, and Texas received antibiotics for at least 300 days over the course of a year. A total of 2,821 children contributed 5,014 person-years. Overall, only 18% of children received ≥300 days of antibiotics. Each additional SCD-related outpatient visit [odds ratio (OR)=1.01, 95% confidence interval (CI): 1.01 to 1.02] and well-child visit (OR=1.08, 95% CI: 1.02 to 1.13) was associated with incrementally increased odds of receiving ≥300 days of antibiotics. According to the authors of the study, antibiotic prophylaxis rates are low among children with sickle cell anemia despite national recommendations and proven lifesaving benefits.
- **July 2019:** A secondary analysis of the Truven Health Analytics-IBM Watson Health MarketScan Medicaid database from 2009 to 2015 was published in the journal *Pediatrics*. The analysis included children 1 to 19 years of age with an International Classification of Diseases, 9th or 10th Revision diagnosis of SCD between 2009 and 2015. Changes in hydroxyurea use were measured across study years. The primary outcome was the receipt of hydroxyurea as identified through pharmacy claims. Acute care visits, including emergency department visits and hospitalizations, were extracted from billing data. A mean of 5,138 children each year were included. Hydroxyurea use increased from 14.3% in 2009 to 28.2% in 2015 (P<0.001). The acute care visit rate decreased from 1.20 acute care visits per person-year in 2009 to 1.04 acute care visits per person-year in 2015 (P<0.001). The drop in acute care visits was exclusively in the youngest and oldest age groups and was not seen when only children enrolled continuously from 2009 to 2015 were analyzed. While there was a significant increase in hydroxyurea use in children with SCD between 2009 and 2015, only approximately 1 in 4 children with SCD received hydroxyurea at least once in 2015. In addition, increases in hydroxyurea were not associated with consistently decreased acute care visits in this population-based study of children insured by Medicaid.
- **August 2019:** The Institute for Clinical and Economic Review (ICER) announced that it plans to assess the comparative clinical effectiveness of voxelotor and crizanlizumab for the treatment of SCD. ICER's evidence report will be reviewed during a public meeting of the New England Comparative Effectiveness Public Advisory Council (New England CEPAC) in March 2020.

Recommendations

The College of Pharmacy does not recommend any changes to the current prior authorization criteria for Siklos® (hydroxyurea) and Endari™ (L-glutamine) at this time.

Utilization Details of SCD Medications: Fiscal Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
HYDROXYUREA CAP 500MG	537	119	$17,274.03	$1.08	$32.17	88.97%
DROXIA CAP 300MG	26	8	$904.74	$1.10	$34.80	4.66%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
DROXIA CAP 200MG	23	9	$853.49	$1.24	$37.11	4.40%
DROXIA CAP 400MG	5	3	$232.28	$1.55	$46.46	1.20%
HYDROXYUREA POW	3	1	$150.21	$3.58	$50.07	0.77%
TOTAL	**594**	**125***	**$19,414.75**	**$1.09**	**$32.68**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] Novartis. FDA accepts file and accelerates review of Novartis sickle cell disease medicine crizanlizumab (SEG101). Available online at: https://www.novartis.com/news/media-releases/fda-accepts-file-and-accelerates-review-novartis-sickle-cell-disease-medicine-crizanlizumab-seg101. Issued 07/16/2019. Last accessed 08/12/2019.

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Appendix M

Industry News and Updates

Oklahoma Health Care Authority
September 2019

Introduction

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

News and Updates[1,2,3]

News:

- **Over-The-Counter (OTC) Oseltamivir:** Sanofi announced they reached an agreement with Roche for exclusive OTC rights to Tamiflu® (oseltamivir) to prevent and treat influenza in the United States. According to a press release, the company will be responsible for marketing, scientific engagement, distribution, and negotiating the switch to OTC with the U.S. Food and Drug Administration (FDA). Sanofi will be required to fund the studies and take responsibility for leading the clinical program necessary for the switch to OTC in the United States. The Centers for Disease Control and Prevention (CDC) found that 31 million people in the United States have influenza each year and, in 2017, 7 million patients took oseltamivir or another effective treatment. The press release stated that there is currently no effective OTC antiviral treatment for influenza in the United States; however, early treatment is essential to stop the spread of the disease.
- **Automatic Naloxone Delivery:** Researchers at Purdue University are developing a device that can automatically detect an overdose and deliver naloxone. According to the U.S. Department of Health and Human Services, approximately 130 people die in the United States each day from an opioid-related drug overdose. According to researchers, the device in development would not require someone to be aware that they were experiencing an overdose or to self-inject naloxone and could keep a person stable long enough for emergency services to arrive. The Purdue researchers have created a wearable device designed to detect when someone's respiration rate decreases to a certain level and then releases naloxone. The researchers envision the drug capsule being pre-injected under the skin in an outpatient setting. The device does not work automatically yet, but *in vitro* and *in vivo* experiments show that the setup successfully detects a low respiration rate from electrocardiogram (EKG) signals and delivers naloxone. The technology also has potential for delivering other drugs besides naloxone, including epinephrine to patients with severe allergies.
- **Side Effects:** According to a *Milwaukee Journal Sentinel* analysis, often times a drug's most dangerous side effects are not discovered until it has already been approved by the FDA and is on the market. The analysis stated that of the 21 biologic drugs that have been approved by the FDA, 13 have received a *Boxed Warning*. In the majority of those

cases, the warnings were added when new problems were identified after the drugs were on the market. According to Nathan Arnold, a spokesman for the FDA, "new safety issues can arise at any time regardless of how long a drug has been in use or its past record of safety." Arnold stated that the FDA intensely scrutinizes drugs before they are approved, but said that "much work still remains to monitor approved drugs over time" and went on to say that "no drug is risk-free, and it is not uncommon for new information to be discovered after a drug is on the market and being used by larger numbers of patients."

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[3] Fauber J. A drug's most dangerous side effects often aren't discovered until it's on the market. *Milwaukee Journal Sentinel*. Available online at: https://www.jsonline.com/story/news/investigations/2019/07/18/arthritis-psoriasis-medications-drugs-deemed-safe-get-fda-warning/1747241001/. Issued 07/18/2019. Last accessed 08/13/2019.

Appendix N

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

July 3rd, 2019

FDA approves new treatment for refractory multiple myeloma

The FDA granted accelerated approval to Xpovio™ (selinexor) tablets in combination with the corticosteroid dexamethasone for the treatment of adult patients with relapsed refractory multiple myeloma (RRMM) who have received at least 4 prior therapies and whose disease is resistant to several other forms of treatment, including at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody.

Multiple myeloma is cancer that begins in plasma cells (white blood cells that produce antibodies) and may also be referred to as plasma cell myeloma. Abnormal plasma cells build up in the bone marrow, forming tumors in many bones of the body. As more antibodies are made, it can cause blood to thicken and keep the bone marrow from making enough healthy blood cells. The exact causes of multiple myeloma are unknown, but it is more common in older people and African Americans.

Efficacy was evaluated in 83 patients with RRMM who were treated with Xpovio™ in combination with dexamethasone. At the end of the study, the overall response rate was measured at 25.3%. The median time to first response was 4 weeks, with a range of 1 to 10 weeks. The median duration of response was 3.8 months. The efficacy evaluation was supported by additional information from an ongoing, randomized trial in patients with multiple myeloma.

Common side effects of patients taking Xpovio™ in combination with dexamethasone include a low white blood cell count (leukopenia), a low count of neutrophils, a type of white blood cell (neutropenia), low count of platelets (thrombocytopenia), and low amount of red blood cells (anemia). Patients also reported vomiting, nausea, fatigue, diarrhea, fever, decreased appetite and weight, constipation, upper respiratory tract infections, and low blood sodium levels (hyponatremia).

Health care professionals are advised to monitor patients for low blood counts, platelets, and sodium levels. Patients should avoid taking Xpovio™ with other medications that may cause dizziness or confusion and avoid situations where dizziness may be a problem. Health care professionals are advised to optimize the patient's hydration status, blood counts, and other medications to avoid dizziness or confusion. The FDA advises health care professionals to tell females of reproductive age and males with a female partner of reproductive potential to use effective contraception during treatment with Xpovio™. Women who are pregnant or breastfeeding should not take Xpovio™ because it may cause harm to a developing fetus or newborn baby. Xpovio™ must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

Xpovio™ in combination with dexamethasone was granted accelerated approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on an endpoint that is reasonably likely to predict a clinical benefit to patients. Further clinical trials are required to verify and describe Xpovio™'s clinical benefit.

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

FDA NEWS RELEASE

July 17th, 2019

FDA approves new treatment for complicated urinary tract and complicated intra-abdominal infections

The FDA approved Recarbrio™ (imipenem/cilastatin/relebactam), an antibacterial drug product to treat adults with complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI).

Recarbrio™ is a 3-drug combination injection containing imipenem/cilastatin, a previously FDA-approved antibiotic, and relebactam, a new beta-lactamase inhibitor.

The determination of efficacy of Recarbrio™ was supported in part by the findings of the efficacy and safety of imipenem/cilastatin for the treatment of cUTI and cIAI. The contribution of relebactam to Recarbrio™ was

assessed based on data from *in vitro* studies and animal models of infection. The safety of Recarbrio™, administered via injection, was studied in 2 trials, 1 each for cUTI and cIAI. The cUTI trial included 298 adult patients with 99 treated with the proposed dose of Recarbrio™. The cIAI trial included 347 patients with 117 treated with the proposed dose of Recarbrio™.
The most common adverse reactions observed in patients treated with Recarbrio™ included nausea, diarrhea, headache, fever, and increased liver enzymes.
Recarbrio™ should not be used in patients taking ganciclovir unless the benefits outweigh the risks as generalized seizures have been reported. Patients should also avoid using Recarbrio™ when taking valproic acid or divalproex sodium, drugs used to manage seizures, as a reduction in valproic acid level may lead to seizures.
Recarbrio™ received the FDA's Qualified Infectious Disease Product (QIDP) designation. The QIDP designation is given to antibacterial and antifungal drug products intended to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act. As part of QIDP designation, Recarbrio™ was granted Priority Review under which the FDA's goal is to take action on an application within an expedited time frame.
The FDA granted the approval of Recarbrio™ for the treatment to Merck & Co., Inc.

FDA NEWS RELEASE

July 22nd, 2019

FDA approves first generics of Lyrica®

On July 19, the FDA approved multiple applications for first generics of Lyrica® (pregabalin) for the management of neuropathic pain associated with diabetic peripheral neuropathy, for the management of postherpetic neuralgia, as an adjunctive therapy for the treatment of partial onset seizures in patients 17 years of age and older, for the management of fibromyalgia, and for the management of neuropathic pain associated with spinal cord injury.
Pregabalin must be dispensed with a patient Medication Guide that contains important information about its uses and risks. Warnings include the risk of angioedema (swelling of the throat, head and neck), which may be associated with life-threatening respiratory compromise requiring emergency treatment. Hypersensitivity reactions such as hives, dyspnea (difficulty breathing), and wheezing can occur. Increased seizure frequency or other adverse reactions may occur if the drug is rapidly discontinued. Antiepileptic drugs, including pregabalin, increase the risk of suicidal thoughts or behavior. Additionally, pregabalin may cause peripheral edema (swelling of hands or legs) so caution should be exercised when co-administering it with thiazolidinedione antidiabetic agents. Pregabalin may cause dizziness and drowsiness and impair the ability to drive or operate machinery.
The most common side effects reported in the clinical trials for Lyrica® in adults are dizziness, somnolence, dry mouth, swelling, blurred vision, weight gain, and abnormal thinking (primarily difficulty with concentration/attention).
The FDA granted approvals for the generic versions of Lyrica® to Alembic Pharmaceuticals, Alkem Laboratories, Amneal Pharmaceuticals, Dr. Reddy's Laboratories, InvaGen Pharmaceuticals, MSN Laboratories Ltd., Rising Pharmaceuticals, Inc., Sciegen Pharmaceuticals Inc., and Teva Pharmaceuticals.

FDA NEWS RELEASE

July 24th, 2019

FDA approves first treatment for severe hypoglycemia that can be administered without an injection

The FDA approved Baqsimi™ nasal powder, the first glucagon therapy approved for the emergency treatment of severe hypoglycemia that can be administered without an injection.
Severe hypoglycemia occurs when a patient's blood sugar levels fall to a level where he or she becomes confused or unconscious or suffers from other symptoms that require assistance from another person to treat. Typically, severe hypoglycemia occurs in people with diabetes who are using insulin treatment. Baqsimi™ is approved to treat severe hypoglycemia in patients with diabetes 4 years of age and older.
Baqsimi™, which is a powder administered into the nose, will come in a single-use dispenser that can be given to someone suffering from a severe hypoglycemic episode. Baqsimi™ increases blood sugar levels in the body by stimulating the liver to release stored glucose into the bloodstream. It has the opposite effect of insulin, which lowers blood sugar levels.

Injectable glucagon has been approved for use in the United States for several decades.The efficacy and safety of Baqsimi™ nasal powder glucagon to treat severe hypoglycemia was evaluated in 2 studies of 83 and 70 adults with diabetes, comparing a single dose of Baqsimi™ to a single dose of glucagon injection in causing a blood sugar response to insulin-induced hypoglycemia. Baqsimi™ adequately increased blood sugar levels. In a pediatric study of 48 patients 4 years and older with type 1 diabetes, similar results were observed.
Baqsimi™ should not be taken by patients with pheochromocytoma, a rare tumor of adrenal gland tissue, or by patients who have insulinoma, a tumor of the pancreas. Baqsimi™ should not be taken by patients with a known hypersensitivity to glucagon or the inactive ingredients found in Baqsimi™, as allergic reactions may occur. Baqsimi™ also carries a warning that it should be used with caution by those who have been fasting for long periods, have adrenal insufficiency, or have chronic hypoglycemia because these conditions result in low levels of releasable glucose in the liver. The most common adverse reactions associated with Baqsimi™ are nausea, vomiting, headache, upper respiratory tract irritation, watery eyes, redness of eyes, and itchiness. Side effects of Baqsimi™ are similar to injectable glucagon, with the addition of nasal and eye-related symptoms, such as watery eyes and nasal congestion, because of the way the drug is administered.
The FDA granted the approval of Baqsimi™ to Eli Lilly and Company.

FDA NEWS RELEASE

August 14th, 2019

FDA approves new drug for treatment-resistant forms of tuberculosis that affects the lungs

The FDA approved Pretomanid Tablets in combination with bedaquiline and linezolid for the treatment of a specific type of highly treatment-resistant tuberculosis (TB) of the lungs.
Pretomanid in combination with bedaquiline and linezolid is approved for treating a limited and specific population of adult patients with extensively drug resistant, treatment-intolerant or nonresponsive multidrug resistant pulmonary TB. Multidrug-resistant TB and extensively drug-resistant TB are difficult to treat due to resistance to available therapies. According to the World Health Organization, in 2016, there were an estimated 490,000 new cases of multidrug-resistant TB worldwide, with a smaller portion of cases of extensively drug-resistant TB.
The safety and effectiveness of Pretomanid, taken orally in combination with bedaquiline and linezolid, was primarily demonstrated in a study of 109 patients with extensively drug-resistant, treatment intolerant or non-responsive multidrug-resistant pulmonary TB (of the lungs). Of the 107 patients who were evaluated 6 months after the end of therapy, 95 (89%) were successes, which significantly exceeded the historical success rates for treatment of extensively drug resistant TB.
The most common adverse reactions observed in patients treated with Pretomanid in combination with bedaquiline and linezolid included damage to the nerves (peripheral neuropathy), acne, anemia, nausea, vomiting, headache, increased liver enzymes (transaminases and gamma-glutamyltransferase), indigestion (dyspepsia), rash, increased pancreatic enzymes (hyperamylasemia), visual impairment, low blood sugar (hypoglycemia), and diarrhea.
Pretomanid used in combination with bedaquiline and linezolid should not be used in patients with hypersensitivity to bedaquiline or linezolid.
Pretomanid is the second drug to be approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs, or LPAD pathway, established by Congress under the 21st Century Cures Act to advance development and approval of antibacterial and antifungal drugs to treat serious or life-threatening infections in a limited population of patients with unmet need. Approval under the LPAD pathway may be supported by a streamlined clinical development program. These programs may involve smaller, shorter, or fewer clinical trials. As required for drugs approved under the LPAD pathway, labeling for Pretomanid includes certain statements to convey that the drug has been shown to be safe and effective only for use in a limited population.
Pretomanid also received the FDA's Qualified Infectious Disease Product (QIDP) designation. The QIDP designation is given to antibacterial and antifungal drug products intended to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act.
The FDA granted Pretomanid Tablets Priority Review, under which the FDA's goal is to take action on an application within an expedited time frame, and Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted the approval of Pretomanid Tablets to The Global Alliance for TB Drug Development (TB Alliance). With this approval, The Global Alliance for TB Drug Development is awarded a Tropical Disease Priority Review Voucher in accordance with a provision included in the Food and Drug Administration

Amendments Act of 2007 that aims to encourage development of new drugs and biological products for the prevention and treatment of certain tropical diseases.

FDA NEWS RELEASE

August 15th, 2019

FDA approves third oncology drug that targets a key genetic driver of cancer, rather than a specific type of tumor

The FDA granted accelerated approval to Rozlytrek™ (entrectinib), a treatment for adult and adolescent patients whose cancers have the specific genetic defect, NTRK (neurotrophic tyrosine receptor kinase) gene fusion and for whom there are no effective treatments.

This is the third time the agency has approved a cancer treatment based on a common biomarker across different types of tumors rather than the location in the body where the tumor originated. The approval marks a new paradigm in the development of cancer drugs that are "tissue agnostic." It follows the policies that the FDA developed in a guidance document released in 2018. The previous tissue agnostic indications approved by the FDA were pembrolizumab for tumors with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors in 2017 and larotrectinib for NTRK gene fusion tumors in 2018.

The ability of Rozlytrek™ to shrink tumors was evaluated in 4 clinical trials studying 54 adults with NTRK fusion-positive tumors. The proportion of patients with substantial tumor shrinkage (overall response rate) was 57%, with 7.4% of patients having complete disappearance of the tumor. Among the 31 patients with tumor shrinkage, 61% had tumor shrinkage persist for 9 months or longer. The most common cancer locations were the lung, salivary gland, breast, thyroid, and colon/rectum.

Rozlytrek™ was also approved for the treatment of adults with non-small cell lung cancer whose tumors are ROS1-positive (mutation of the ROS1 gene) and has spread to other parts of the body (metastatic). Clinical studies evaluated 51 adults with ROS1-positive lung cancer. The overall response rate was 78%, with 5.9% of patients having complete disappearance of their cancer. Among the 40 patients with tumor shrinkage, 55% had tumor shrinkage persist for 12 months or longer.

Rozlytrek™'s common side effects are fatigue, constipation, dysgeusia (distorted sense of taste), edema (swelling), dizziness, diarrhea, nausea, dysesthesia (distorted sense of touch), dyspnea (shortness of breath), myalgia (painful or aching muscles), cognitive impairment (confusion, problems with memory or attention, difficulty speaking, or hallucinations), weight gain, cough, vomiting, fever, arthralgia, and vision disorders (blurred vision, sensitivity to light, double vision, worsening of vision, cataracts, or floaters). The most serious side effects of Rozlytrek™ are congestive heart failure (weakening or damage to the heart muscle), central nervous system effects (cognitive impairment, anxiety, depression including suicidal thinking, dizziness or loss of balance, and change in sleep pattern, including insomnia and excessive sleepiness), skeletal fractures, hepatotoxicity, hyperuricemia (elevated uric acid), QT prolongation (abnormal heart rhythm), and vision disorders. Health care professionals should inform females of reproductive age and males with a female partner of reproductive potential to use effective contraception during treatment with Rozlytrek™. Women who are pregnant or breastfeeding should not take Rozlytrek™ because it may cause harm to a developing fetus or newborn baby.

Rozlytrek™ was granted accelerated approval. This approval commits the sponsor to provide additional data to the FDA. Rozlytrek™ also received Priority Review, Breakthrough Therapy, and Orphan Drug designation. The approval of Rozlytrek™ was granted to Genentech, Inc.

FDA NEWS RELEASE

August 16th, 2019

FDA approves treatment for patients with rare bone marrow disorder

The FDA approved Inrebic® (fedratinib) capsules to treat adult patients with certain types of myelofibrosis. Myelofibrosis is a chronic disorder where scar tissue forms in the bone marrow and the production of the blood cells moves from the bone marrow to the spleen and liver, causing organ enlargement. It can cause extreme fatigue, shortness of breath, pain below the ribs, fever, night sweats, itching, and bone pain. When myelofibrosis occurs on its own, it is called primary myelofibrosis. Secondary myelofibrosis occurs when there is excessive red blood cell production (polycythemia vera) or excessive platelet production (essential thrombocythemia) that evolves into myelofibrosis.

Jakafi® (ruxolitinib) was approved by the FDA in 2011. The approval of Inrebic® for intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis was based on

the results of a clinical trial where 289 patients with myelofibrosis were randomized to receive 2 different doses (400 mg or 500 mg daily by mouth) of fedratinib or placebo. The clinical trial showed that 35 of 96 patients treated with the fedratinib 400mg daily dose (the dose recommended in the approved label) experienced a significant therapeutic effect [measured by a ≥35% reduction from baseline in spleen volume at the end of cycle 6 (week 24) as measured by an MRI or CT scan with a follow-up scan 4 weeks later]. As a result of treatment with Inrebic®, 36 patients experienced a ≥50% reduction in myelofibrosis-related symptoms, such as night sweats, itching, abdominal discomfort, feeling full sooner than normal, pain under ribs on left side, and bone or muscle pain.

The prescribing information for Inrebic® includes a *Boxed Warning* to advise health care professionals and patients about the risk of serious and fatal encephalopathy (brain damage or malfunction), including Wernicke's, which is a neurologic emergency related to a deficiency in thiamine. Health care professionals are advised to assess thiamine levels in all patients prior to starting Inrebic®, during treatment, and as clinically indicated. If encephalopathy is suspected, Inrebic® should be immediately discontinued.

Common side effects for patients taking Inrebic® are diarrhea, nausea, vomiting, fatigue, and muscle spasms. Health care professionals are cautioned that patients may experience severe anemia (low iron levels) and thrombocytopenia (low level of platelets in the blood). Patients should be monitored for gastrointestinal toxicity and for hepatic toxicity (liver damage). The dose should be reduced or stopped if a patient develops severe diarrhea, nausea, or vomiting. Treatment with anti-diarrhea medications may be recommended. Patients may develop high levels of amylase and lipase in their blood and should be managed by dose reduction or stopping the mediation. Inrebic® must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

The FDA granted this application Priority Review designation. Inrebic® also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. The FDA granted the approval of Inrebic® to Impact Biomedicines, Inc., a wholly-owned subsidiary of Celgene Corporation.

FDA NEWS RELEASE

August 16th, 2019

FDA approves first of its kind device to treat pediatric patients with progressive idiopathic scoliosis

The FDA approved the first spinal tether device intended to be used in children and adolescents to correct the most common form of scoliosis, called idiopathic scoliosis, that has not responded to conservative treatment options, such as external bracing. The device, called The Tether™ – Vertebral Body Tethering System, is intended to treat growing children and adolescents whose spinal curves are approaching or have reached the range where surgical treatment is an option.

Idiopathic scoliosis is a sideways curvature of the spine whose cause is unknown. It is the most common spinal deformity in children and is most often diagnosed between 10 to 18 years of age, although it may occur at a younger age. The standard treatments for idiopathic scoliosis among children and adolescents who are still growing are conservative, non-surgical treatments such as external bracing to help correct the spinal curvature. Approximately 6,800 patients in the United States each year will develop progressive curvatures that do not respond to bracing. For these patients, spinal fusion surgery (i.e., spinal implants to correct the curvature of the spine and fusion surgery) may be used to permanently stabilize and correct spinal curvatures. While spinal fusion is often successful, this surgery permanently restricts the motion of the spine and may have long-term complications such as pain, arthritis, and future spinal deformities, which could require additional surgical treatment.

The Tether™ – Vertebral Body Tethering System provides an alternative for patients with idiopathic scoliosis that doesn't respond to bracing. As a patient grows, The Tether™ – Vertebral Body Tethering System is designed to continue to correct the curvature while maintaining a fuller range of motion when compared to spinal fusion procedures.

The Tether™ – Vertebral Body Tethering System includes anchors and vertebral body screws that are placed into the same side of each vertebra in the curved section of the spine through an incision on the side of the chest. A flexible cord, called a tether, is connected to the screws. Tension is applied to the tether during surgery to compress 1 side of the spine and to partially correct the curve. Over time, the tether slows growth on the curved side of the spine and promotes growth on the opposite side. This provides additional correction of the curve as the patient continues to grow. The Tether™ - Vertebral Body Tethering System is not intended to be removed unless certain problems, such as overcorrections, develop. Health care professionals will monitor

patients, conducting follow-up x-rays, to track the spinal curvature and identify any potential problems that might require additional surgery to revise or remove the device. For those patients whose curves are not adequately corrected by The Tether™ – Vertebral Body Tethering System, spinal fusion surgery is still possible.
The FDA reviewed data for The Tether™ – Vertebral Body Tethering System through the humanitarian device exemption (HDE) process. A Humanitarian Use Device (HUD) is a device intended to benefit to patients by treating or diagnosing a disease or condition that affects not more than 8,000 individuals in the United States per year.
The FDA reviewed clinical data supporting the safety and probable benefit of The Tether™ – Vertebral Body Tethering System from 57 patients who received the device. At 2 years, 43 patients had sufficient improvement of the curvature of their spines and did not need spinal fusion. The most common serious adverse events observed included overcorrection of the curvature, tether breakage, and pneumothorax or air leakage into the space between the lung and chest wall. General complications consistent with any spinal surgical procedure were also noted including pain, respiratory problems, nerve injuries, and bleeding.
Zimmer Biomet Spine has shared with the FDA that it will be partnering with the Harms Study Group, a cohort of surgeons dedicated to the advancement of treatment for children and adolescents with spinal deformities, to develop a patient data registry to help assess the long-term performance of The Tether™ System.
The FDA granted the approval of The Tether™ - Vertebral Body Tethering System to Zimmer Biomet Spine.

FDA NEWS RELEASE

August 19th, 2019

FDA approves new antibiotic to treat community-acquired bacterial pneumonia

The FDA approved Xenleta™ (lefamulin) to treat adults with community-acquired bacterial pneumonia (CABP). Community-acquired pneumonia occurs when someone develops pneumonia in the community (not in a hospital). Pneumonia is a type of lung infection that can range in severity from mild to severe illness and can affect people of all ages. According to data from the Centers from Disease Control and Prevention, each year in the United States, about 1 million people are hospitalized with community-acquired pneumonia and 50,000 people die from the disease.
The safety and efficacy of Xenleta™, taken either orally or intravenously, was evaluated in 2 clinical trials with a total of 1,289 patients with CABP. In these trials, treatment with Xenleta™ was compared to another antibiotic, moxifloxacin with or without linezolid. The trials showed that patients treated with Xenleta™ had similar rates of clinical success as those treated with moxifloxacin with or without linezolid.
The most common adverse reactions reported in patients taking Xenleta™ included diarrhea, nausea, reactions at the injection site, elevated liver enzymes, and vomiting. Xenleta™ has the potential to cause a change on an ECG reading (prolonged QT interval). Patients with prolonged QT interval, patients with certain irregular heart rhythms (arrhythmias), patients receiving treatment for certain irregular heart rhythms (antiarrhythmic agents), and patients receiving other drugs that prolong the QT interval should avoid Xenleta™. In addition, Xenleta™ should not be used in patients with known hypersensitivity to lefamulin or any other members of the pleuromutilin antibiotic class, or any of the components of Xenleta™. Based on findings of fetal harm in animal studies, pregnant women and women who could become pregnant should be advised of the potential risks of Xenleta™ to a fetus. Women who could become pregnant should be advised to use effective contraception during treatment with Xenleta™ and for 2 days after the final dose.
Xenleta™ received the FDA's Qualified Infectious Disease Product (QIDP) designation. The QIDP designation is given to antibacterial and antifungal drug products intended to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act. As part of QIDP designation, Xenleta™ was granted Priority Review under which the FDA's goal is to take action on an application within an expedited time frame.
The FDA granted the approval of Xenleta™ to Nabriva Therapeutics.

FDA NEWS RELEASE

August 22nd, 2019

FDA approves first therapy for rare joint tumor

The FDA granted approval to Turalio™ (pexidartinib) capsules for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not responsive to improvement with surgery.

TGCT is a rare tumor that affects the synovium (thin layer of tissue that covers the surfaces of the joint spaces) and tendon sheaths (layer of membrane that covers tendons, which are fibrous tissue that connect muscle to bone). The tumor is rarely malignant but causes the synovium and tendon sheaths to thicken and overgrow, causing damage to surrounding tissue.

The approval of Turalio™ was based on the results of a multi-center international clinical trial of 120 patients, 59 of whom received placebo. The primary efficacy endpoint was the overall response rate (ORR) analyzed after 25 weeks of treatment. The clinical trial demonstrated a statistically significant improvement in ORR in patients who received Turalio™, with an ORR of 38%, compared to no responses in patients who received placebo. The complete response rate was 15% and the partial response rate was 23%. A total of 22 out of 23 responders who had been followed for a minimum of 6 months following the initial response maintained their response for 6 or more months, and a total of 13 out of 13 responders who had been followed for a minimum of 12 months following the initial response maintained their response for 12 or more months.

The prescribing information for Turalio™ includes a *Boxed Warning* to advise health care professionals and patients about the risk of serious and potentially fatal liver injury. Health care professionals should monitor liver tests prior to beginning treatment and at specified intervals during treatment. If liver tests become abnormal, Turalio™ may need to be withheld, the dose reduced, or permanently discontinued, depending on the severity of the liver injury. Turalio™ is available only through the Turalio™ Risk Evaluation and Mitigation Strategy (REMS) Program.

Common side effects for patients taking Turalio™ were increased lactate dehydrogenase (proteins that helps produce energy in the body), increased aspartate aminotransferase (enzymes that are mostly in the liver but also in muscles), loss of hair color, increased alanine aminotransferase (enzymes that are primarily in the liver and kidney), and increased cholesterol. Additional side effects included neutropenia, increased alkaline phosphatase (enzymes that are mostly in the cells of bone and the liver), decreased lymphocytes (white blood cells that help the immune system defend against disease and infection), eye edema, decreased hemoglobin, rash, dysgeusia (altered sense of taste), and decreased phosphate (electrolytes that help with energy).

The FDA advises health care professionals to tell females of reproductive age and males with a female partner of reproductive potential to use effective contraception during treatment with Turalio™. Women who are pregnant or breastfeeding should not take Turalio™ because it may cause harm to a developing fetus or newborn baby. Turalio must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

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

FDA NEWS RELEASE

August 27th, 2019

FDA approves new add-on drug to treat off episodes in adults with Parkinson's disease

The FDA approved Nourianz™ (istradefylline) tablets as an add-on treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes. An "off" episode is a time when a patient's medications are not working well, causing an increase in PD symptoms, such as tremor and difficulty walking. According to the National Institutes of Health, PD is the second-most common neurodegenerative disorder in the United States after Alzheimer's disease. An estimated 50,000 Americans are diagnosed with PD each year, and about 1 million Americans have the condition. The neurological disorder typically occurs in people older than age 60, although it can occur earlier. It happens when cells in the brain, which produce a chemical called dopamine, become impaired or die. Dopamine helps transmit signals between the areas of the brain that produce smooth, purposeful movements – such as eating, writing, and shaving. Early symptoms of the disease are subtle and typically worsen gradually; however, the disease progresses more quickly in some people than in others.

The effectiveness of Nourianz™ in treating "off" episodes in patients with PD who are already being treated with levodopa/carbidopa was shown in (4) 12-week placebo-controlled clinical studies that included a total of 1,143 participants. In all 4 studies, patients treated with Nourianz™ experienced a statistically significant decrease from baseline in daily "off" time compared to patients receiving placebo.

The most common adverse reactions observed in patients taking Nourianz™ were involuntary muscle movement (dyskinesia), dizziness, constipation, nausea, hallucination, and sleeplessness (insomnia). Patients should be monitored for development of dyskinesia or exacerbation of existing dyskinesia. If hallucinations, psychotic behavior, or impulsive/compulsive behavior occurs, a dosage reduction or stoppage of Nourianz™

should be considered. Use of Nourianz™ during pregnancy is not recommended. Women of childbearing potential should be advised to use contraception during treatment.
The FDA granted approval of Nourianz™ to Kyowa Kirin, Inc.

Safety Announcements

FDA approves *Boxed Warning* about increased risk of blood clots and death with higher dose of arthritis and ulcerative colitis medicine tofacitinib (Xeljanz®, Xeljanz XR®)

[07/26/2019] The FDA approved new warnings about an increased risk of blood clots and death with the 10mg twice daily dose of tofacitinib (brand names Xeljanz®, Xeljanz XR®), used in patients with ulcerative colitis. The approved use of tofacitinib for ulcerative colitis will also be limited to patients who are not treated effectively or who experience severe side effects with certain other medicines. The FDA approved these changes, adding their most prominent *Boxed Warning*, after reviewing interim data from an ongoing safety clinical trial of tofacitinib in patients with rheumatoid arthritis (RA) that examined a lower and this higher dose of the medicine. The 10mg twice daily dose of tofacitinib is only approved for initial treatment of ulcerative colitis and for long-term use in limited situations. While the increased risks of blood clots and death were seen in patients taking this dose for RA, these risks may also apply to those taking tofacitinib for ulcerative colitis.
Tofacitinib was approved in 2012 to treat adult patients with RA who did not respond well to methotrexate. In 2017, the FDA approved tofacitinib to treat patients with psoriatic arthritis, who did not respond well to other medicines and in 2018, to treat ulcerative colitis.
Health care professionals should discontinue tofacitinib and evaluate patients with symptoms of thrombosis. Tofacitinib should be reserved to treat ulcerative colitis in patients who have failed or do not tolerate tumor necrosis factor (TNF) blockers. Tofacitinib should be avoided in patients who may have a higher risk of thrombosis, tofacitinib should be used at the lowest effective dose and use limited of the 10mg twice daily dosage to the shortest duration needed.
When the FDA first approved tofacitinib, the FDA required a postmarketing clinical trial in patients with RA on methotrexate, to evaluate the risk of heart-related events, cancer, and infections. An interim analysis of the trial's results found an increased occurrence of blood clots and death in patients treated with tofacitinib 10mg twice daily compared to patients treated with tofacitinib 5mg twice daily or a TNF blocker. The FDA will reassess these safety issues when the trial has completed.

Current Drug Shortages Index (as of Sept 3rd, 2019):

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

Alogliptin Tablets	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azithromycin (Azasite) Ophthalmic Solution 1%	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Buspirone HCl Tablets	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Carisoprodol Tablets, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Cysteine Hydrochloride Injection	***Currently in Shortage***

Deferoxamine Mesylate for Injection, USP	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Diltiazem Hydrochloride ER (Twice-a-Day) Capsules	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
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***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Eprosartan Mesylate Tablets	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Haloperidol Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Isocarboxazid Tablets	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Latanoprost Ophthalmic Solution 0.005%	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methocarbamol Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Susp	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***

Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nelarabine (Arranon) Injection	***Currently in Shortage***
Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***Currently in Shortage***
Pentamidine Isethionate (Nebupent) For Inhalation Solution	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Prednisolone Acetate 1% Ophthalmic Suspension	***Currently in Shortage***
Primaquine Phosphate Tablet, EQ 15mg Base	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Progesterone Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine Transdermal System	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Trifluoperazine Hydrochloride Tablets	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***
Vinblastine Sulfate Injection	***Currently in Shortage***