OKLAHOMA
Health Care Authority

Drug Utilization Review Board

OHCA Webinar
Wednesday,
May 13, 2020
4:00pm

OHCA Webinar

Register for the meeting using the following website address:
https://okhca.zoom.us/webinar/register/WN_2R6cQO1gT5afVrf5eeV2ww

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Brandy Nawaz, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – May 13, 2020

DATE: April 23, 2020

NOTE: In response to COVID-19, the May 2020 meeting will be held via OHCA webinar at 4:00pm. After registering, you will receive a confirmation email containing information about joining the webinar. Please register for the meeting using the following website address: https://okhca.zoom.us/webinar/register/WN_2R6cQO1gT5afVrf5eeV2ww

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

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet) – Appendix C

Action Item – Vote to Prior Authorize Tepezza™ (Teprotumumab-trbw) – Appendix D

Action Item – Vote to Prior Authorize Dayvigo™ (Lemborexant) – Appendix E

Action Item – Vote to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity® (Diroximel Fumarate) – Appendix F

Action Item – Vote to Prior Authorize Qternmet® XR [Dapagliflozin/Saxagliptin/Metformin Extended-Release (ER) Tablet], Riomet ER™ (Metformin ER Oral Suspension), Rybelsus® (Semaglutide Tablet), and Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet) and Update the Anti-Diabetic Medications Prior Authorization Criteria – Appendix G

Action Item – Vote to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat) – Appendix H

Action Item – Vote to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr) – Appendix I

Action Item – Vote to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™

(Bevacizumab-bvzr) – Appendix J

Annual Review of of Balversa™ (Erdafitinib) – Appendix K

Annual Review of the SoonerCare Pharmacy Benefit – Appendix L

Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Ziextenzo® (Pegfilgrastim-bmez) – Appendix M

Annual Review of Allergen Immunotherapies and 30-Day Notice to Prior Authorize Palforzia™ (Peanut Allergen Powder-dnfp) – Appendix N

Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Nourianz™ (Istradefylline) – Appendix O

Action Item – Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications – Appendix P

Annual Review of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase) – Appendix Q

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – May 13, 2020 @ 4:00pm

OHCA Webinar
Register for the meeting here:
https://okhca.zoom.us/webinar/register/WN_2R6cQO1gT5afVrf5eeV2ww

---

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Skrepnek

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. March 11, 2020 DUR Minutes – Vote
B. March 11, 2020 DUR Recommendations Memorandum
C. April 8, 2020 DUR Recommendations Memorandum

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

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

A. Pharmacy Helpdesk Activity for April 2020
B. Medication Coverage Activity for April 2020
C. Spring 2020 Pipeline Update

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

5. Action Item – Vote to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Tepezza™ (Teprotumumab-trbw) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Dayvigo™ (Lemborexant) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity® (Diroximel Fumarate) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Qternmet® XR [Dapagliflozin/Saxagliptin/Metformin Extended-Release (ER) Tablet], Riomet ER™ (Metformin ER Oral Suspension), Rybelsus® (Semaglutide Tablet), and Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet) and Update the Anti-Diabetic Medications Prior Authorization Criteria – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat) – See Appendix H

A. Introduction
B. Product Summaries
C. Recommendations

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

11. Action Item – Vote to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr) – See Appendix I

A. Introduction
B. Product Summaries
C. Recommendations

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

12. Action Item – Vote to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™ (Bevacizumab-bvzr) – See Appendix J

A. Introduction
B. Product Summaries
C. Recommendations

Non-Presentation Item; Questions Only:

13. Annual Review of Balversa™ (Erdafitinib) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Balversa™ (Erdafitinib)
C. Prior Authorization of Balversa™ (Erdafitinib)
D. Market News and Updates
E. Recommendations

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

14. Annual Review of the SoonerCare Pharmacy Benefit – See Appendix L

A. Summary
B. Medicaid Drug Rebate Program
C. Alternative Payment Models
D. Drug Approval Trends
E. Traditional Versus Specialty Pharmacy Products
F. Top 10 Therapeutic Classes by Reimbursement
G. Top 10 Medications by Reimbursement
H. Cost Per Claim
I. Conclusion
J. Top 50 Reimbursed Drugs by Fiscal Year
K. Top 50 Medications by Total Number of Claims
L. Top 10 Traditional and Specialty Therapeutic Categories by Fiscal Year

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

15. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Ziextenzo® (Pegfilgrastim-bmez) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of G-CSFs

C. Prior Authorization of G-CSFs
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of G-CSFs

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

16. Annual Review of Allergen Immunotherapies and 30-Day Notice to Prior Authorize Palforzia™ (Peanut Allergen Powder-dnfp) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Allergen Immunotherapies
C. Prior Authorization of Allergen Immunotherapies
D. Market News and Updates
E. Palforzia™ (Peanut Allergen Powder-dnfp) Product Summary
F. College of Pharmacy Recommendations

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

17. Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Nourianz™ (Istradefylline) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of PD Medications
C. Prior Authorization of PD Medications
D. Market News and Updates
E. Nourianz™ (Istradefylline Tablet) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of PD Medications

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

18. Action Item – Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications – See Appendix P

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

Non-Presentation Item; Questions Only:

19. Annual Review of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase) – See Appendix Q

A. Current Prior Authorization Criteria
B. Utilization of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase)
C. Prior Authorization of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase)
D. College of Pharmacy Recommendations

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

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

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

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

A. Attention deficit/hyperactivity disorder (ADHD) and Narcolepsy Medications
B. Atypical Antipsychotic Medications
C. Various Special Formulations
D. Ophthalmic Anti-Inflammatories

**Future business subject to change.*

22. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MARCH 11, 2020

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
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
Amy Miller, Operations Coordinator		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Grant H. Skrepnek, Ph.D.; Associate Professor; Interim Director	x	
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Tri Van, Pharm.D.; Pharmacy Resident	x	
Graduate Students: Matthew Dickson, Pharm.D.	x	
Michael Nguyen, Pharm.D.	x	
Corby Thompson, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): Justin Wilson	x	

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

OTHERS PRESENT:		
Randi Lewandowski, EMD Serono	Leann Fryer, Biogen	Evie Knisley, Novartis
Emily Oliphant, OUHSC	Elizabeth Goetaing, OUHSC	Nima Nabavi, Amgen
Burl Beasley, EGID Health Choice	Brian Maves, Pfizer	John Omick

PRESENT FOR PUBLIC COMMENT:
N/A

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

ACTION: NONE REQUIRED

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

3A: FEBURARY 12, 2020 DUR MINUTES – VOTE

3B: FEBRUARY 12, 2020 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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: PHARMACY HELPDESK ACTIVITY FOR FEBRUARY 2020

4B: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2020

4C: SOONERPSYCH PROGRAM UPDATE

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE XCOPRI® (CENOBAMATE)

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE TOSYMRA™ (SUMATRIPTAN NASAL SPRAY), REYVOW™ (LASMIDITAN), AND UBRELVY™ (UBROGEPANT)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ESPEROCT® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), GLYCOPEGYLATED-EXEI]

7A: INTRODUCTION

7B: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ratterman

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE PROAIR® DIGIHALER™ (ALBUTEROL SULFATE INHALATION POWDER)

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE EVENITY® (ROMOSOZUMAB-AQQG)

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Van

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE ASPARLAS™ (CALASPARGASE PEGOL-MKNL), DAURISMO™ (GLASDEGIB), IDHIFA® (ENASIDENIB), LUMOXITI® (MOXETUMOMAB PASUDOTOX-TDFK), TIBSOVO® (IVOSIDENIB), AND XOSPATA® (GILTERITINIB)

10A: INTRODUCTION

10B: PRODUCT SUMMARIES

10C: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Schmidt

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE AZEDRA® (IOBENGUANE I-131)

11A: INTRODUCTION

11B: AZEDRA® (IOBENGUANE I-131) PRODUCT SUMMARY

11C: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Schmidt

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF LYMPHOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ALIQOPA™ (COPANLISIB), BRUKINSA™ (ZANUBRUTINIB), POLIVY™ (POLATUZUMAB VEDOTIN-PIIQ), AND RUXIENCE™ (RITUXIMAB-PVVR)

12A: INTRODUCTION

12B: CURRENT PRIOR AUTHORIZATION CRITERIA

12C: UTILIZATION OF LYMPHOMA MEDICATIONS

12D: PRIOR AUTHORIZATION OF LYMPHOMA MEDICATIONS

12E: MARKET NEWS AND UPDATES

12F: PRODUCT SUMMARIES

12G: RECOMMENDATIONS

12H: UTILIZATION DETAILS OF LYMPHOMA MEDICATIONS

Materials included in agenda packet; presented by Dr. Schmidt

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF LUTATHERA® (LUTETIUM LU-177 DOTATATE) AND VITRAKVI® (LAROTRECTINIB)

13A: INTRODUCTION

13B: CURRENT PRIOR AUTHORIZATION CRITERIA

13C: UTILIZATION OF LUTATHERA® (LUTETIUM LU-177 DOTATATE) AND VITRAKVI® (LAROTRECTINIB)

13D: PRIOR AUTHORIZATION OF LUTATHERA® (LUTETIUM LU-177 DOTATATE) AND VITRAKVI® (LAROTRECTINIB)

13E: MARKET NEWS AND UPDATES
13F: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF MULTIPLE SCLEROSIS (MS) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MAYZENT® (SIPONIMOD), MAVENCLAD® (CLADRIBINE), AND VUMERITY® (DIROXIMEL FUMARATE)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF MS MEDICATIONS
14C: PRIOR AUTHORIZATION OF MS MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: MAYZENT® (SIPONIMOD) PRODUCT SUMMARY
14F: MAVENCLAD® (CLADRIBINE) PRODUCT SUMMARY
14G: VUMERITY® (DIROXIMEL FUMARATE) PRODUCT SUMMARY
14H: COLLEGE OF PHARMACY RECOMMENDATIONS
14I: UTILIZATION DETAILS OF MS MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: 30-DAY NOTICE TO PRIOR AUTHORIZE TEPEZZA™ (TEPROTUMUMAB-TRBW)
15A: INTRODUCTION
15B: MARKET NEWS AND UPDATES
15C: TEPEZZA™ (TEPROTUMUMAB-TRBW) PRODUCT SUMMARY
15D: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF ANTI-EMETIC MEDICATIONS
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF ANTI-EMETIC MEDICATIONS
16C: PRIOR AUTHORIZATION OF ANTI-EMETIC MEDICATIONS
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS
16F: UTILIZATION DETAILS OF ANTI-EMETIC MEDICATIONS
Materials included in agenda packet; presented by Dr. Van
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
18A: ANNUAL REVIEW OF PHARMACY BENEFIT
18B: ANTI-DIABETIC MEDICATIONS
18C: ANTIHYPERTENSIVE MEDICATIONS
18D: LUNG CANCER MEDICATIONS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: ADJOURNMENT
The meeting was adjourned at 5:03pm.

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

Memorandum

Date: March 12, 2020

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

Terry Cothran, D.Ph.
Pharmacy Director
OHCA

From: Michyla Adams, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of March 11, 2020

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Xcopri® (Cenobamate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Xcopri® (cenobamate) with the following criteria:

Xcopri® (Cenobamate) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants.

Additionally, the College of Pharmacy recommends updating the current approval criteria for Sabril® (vigabatrin) based on the expanded FDA approved indication (changes noted in red):

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
   a. Refractory complex seizures in adults and pediatric patients ~~10~~ 2 years of age or older; or
   b. Infantile spasms in children 1 month to 2 years of age; and
2. Authorization of generic vigabatrin (in place of brand Sabril®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
3. Members with refractory complex seizures must have previous trials of at least 3 other anticonvulsants; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the Vigabatrin REMS Program and maintain enrollment throughout therapy.

Recommendation 3: Vote to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Anti-Migraine Medications Product Based Prior Authorization (PBPA) category:

1. The placement of Tosymra™ (sumatriptan nasal spray), Reyvow™ (lasmiditan), and Ubrelvy™ (ubrogepant) into the Special Prior Authorization (PA) Tier with the following criteria (changes shown in red in the following Tier Chart and Special PA criteria)
2. Updating the current approval criteria for Emgality® (galcanezumab-gnlm) based on the new FDA approved indication (changes shown in red in the following criteria)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan (Relpax®) – **brand only**	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)			eletriptan (Relpax®) – **generic**
sumatriptan/naproxen (Treximet®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan (Reyvow™)
			sumatriptan injection (Imitrex®)
			sumatriptan injection (Zembrace® SymTouch®)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan nasal spray (Tosymra™)
			ubrogepant (Ubrelvy™)

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

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response or a patient-specific, clinically significant reason why a Tier-1 product is not appropriate for the member; or
2. Documented adverse effect(s) to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response or a patient-specific, clinically significant reason why a lower tiered product is not appropriate for the member; or
2. Documented adverse effect(s) to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days; and
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Anti-Migraine Medications Special Prior Authorization (PA) Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zembrace® SymTouch® or Tosymra™ will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
5. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent CYP 3A4 inhibitor, women who are or may become pregnant, peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, sepsis, hypersensitivity to any of the components); and

b. A quantity limit of 20 tablets per 28 days will apply.

6. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
7. Use of Reyvow™ (lasmiditan) or Ubrelvy™ (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications.

Emgality® (Galcanezumab-gnlm) Approval Criteria [Episodic Cluster Headache Diagnosis]:

1. An FDA approved indication for the treatment of episodic cluster headache in adults; and
2. Member must be 18 years of age or older; and
3. Member has a diagnosis of episodic cluster headache as defined by the International Headache Society (IHS) International Classification of Headache Disorders (ICHD) guideline and meets the following criteria:
   a. Member has a history of episodic cluster headache with at least 2 cluster periods lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥1 month; and
4. Member is not frequently taking medications that 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
5. The member has failed prophylactic therapy with at least 1 other medication (e.g., verapamil, select anticonvulsants, glucocorticoids); and
6. Member must have been evaluated within the last 6 months by a neurologist for cluster headaches and the requested medication (e.g., Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and
7. Member will not use Emgality® concurrently with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
8. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
9. Initial approvals will be for the duration of 3 months. Continuation approvals will be granted until the end of the cluster period if the prescriber documents that the member is responding well to treatment as indicated by a reduction in cluster headache attack frequency; and
10. A quantity limit of (3) 100mg/mL syringes per 30 days will apply.

Recommendation 4: Vote to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei]

MOTION CARRIED by unanimous approval.

The Oklahoma Health Care Authority recommends the prior authorization of Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei] with the following criteria (changes noted in red):

Eloctate®, Adynovate®, Afstyla®, Jivi®, Esperoct®, Alprolix®, Idelvion®, and Rebinyn® Approval Criteria:

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
   a. Hemophilia A: Advate® or current factor VIII replacement product; or
   b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of 1 year.

Recommendation 5: Vote to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of ProAir® Digihaler™ (albuterol sulfate inhalation powder) into Tier-2 of the Short-Acting Beta$_2$ Agonists Product Based Prior Authorization (PBPA) category with the following criteria (changes noted in red):

Short-Acting Beta$_2$ Agonists	
Tier-1	**Tier-2**
albuterol HFA (ProAir® HFA)*	albuterol HFA (generic)
albuterol HFA (Proventil® HFA)*	**albuterol inhalation powder (ProAir® Digihaler™)¥**
albuterol HFA (Ventolin® HFA)*	levalbuterol HFA (generic)
albuterol inhalation powder (ProAir® RespiClick®)	
levalbuterol HFA (Xopenex® HFA)*	

*Brand preferred.
¥Additional criteria applies.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC is unavailable.

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

Short-Acting Beta$_2$ Agonists Tier-2 Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member cannot use all available Tier-1 medications must be provided.

ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member requires the ProAir® Digihaler™ formulation over all available Tier-1 medications must be provided; and
3. The prescriber agrees to closely monitor member adherence; and
4. The member should be capable and willing to use the Companion Mobile App and follow the *Instructions for Use* and ensure the ProAir® Digihaler™ Companion Mobile App is compatible with their specific smartphone; and
5. The member's phone camera must be functional and able to scan the inhaler QR code and register the ProAir® Digihaler™ inhaler; and
6. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance greater than 80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

Recommendation 6: Vote to Prior Authorize Evenity® (Romosozumab-aqqg)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Evenity® (romosozumab-aqqg) into the Special Prior Authorization (PA) Tier of the Osteoporosis Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Evenity® (Romosozumab-aqqg) Approval Criteria:

1. An FDA approved diagnosis of osteoporosis in postmenopausal women at high risk for fracture; and
2. Member meets 1 of the following:
   a. History of osteoporotic fracture; or
   b. Multiple risk factors for fracture (e.g., T-score ≤-2.5 at the total hip or femoral neck, smoking, corticosteroid use, rheumatoid arthritis); or
   c. Failed or are intolerant to other available osteoporosis therapies; and
3. Prescriber must verify member has not had a myocardial infarction or stroke within the preceding year; and
4. Prescriber must verify calcium levels will be monitored and pre-existing hypocalcemia will be corrected prior to starting therapy; and
5. Prescriber must verify that the member will take adequate calcium and vitamin D supplements during treatment with Evenity® to reduce the risk of hypocalcemia; and
6. Evenity® must be administered by a health care provider; and
7. Approvals will be for a maximum total duration of 1 year of therapy.

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax Plus D®)	abaloparatide inj (Tymlos®)
calcium + vitamin D*	risedronate tabs (Actonel®)	alendronate effervescent tabs (Binosto®)
ibandronate tabs (Boniva®)		alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)		alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		romosozumab-aqqg (Evenity®)
		teriparatide inj (Forteo®)

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization

*Must be used in combination with a bisphosphonate to count as a trial.

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

Recommendation 7: Vote to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti™ (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib)

MOTION CARRIED by unanimous approval.

- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations; changes can be seen in the following criteria listed in red (only criteria with updates listed)
- The prior authorization of Asparlas™ (calaspargase pegol-mknl), Daurismo™ (glasdegib), Idhifa® (enasidenib), Lumoxiti® (moxetumomab pasudotox-tdfk), Tibsovo® (ivosidenib), and Xospata® (gilteritinib) with the following criteria listed in red

Asparlas™ (Calaspargase Pegol-mknl) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. A patient-specific, clinically significant reason why the member cannot use pegaspargase must be provided; and
2. Member must be 1 month to 21 years of age.

Calquence® (Acalabrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As a single-agent ~~in members who have received ≥1 prior therapy~~.

Calquence® (Acalabrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As a single-agent ~~in relapsed/refractory disease~~.

Daurismo™ (Glasdegib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have significant comorbidities that preclude use of intensive chemotherapy [severe cardiac disease, ECOG performance status ≥2, or serum creatinine (SCr) >1.3]; and
2. In combination with low-dose cytarabine (LDAC).

Gazyva® (Obinutuzumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As a single-agent for relapsed/refractory disease; or
2. In combination with chlorambucil, bendamustine, ibrutinib, or venetoclax for first-line therapy; and
3. When obinutuzumab is used in combination with venetoclax, maximum approval duration will be 6 treatment cycles of obinutuzumab.

Idhifa® (Enasidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. IDH2 mutation; or
2. Relapsed/refractory AML; and
    a. As a single-agent; and
    b. IDH2 mutation.

Lumoxiti® (Moxetumomab Pasudotox-tdfk) Approval Criteria [Hairy Cell Leukemia (HCL) Diagnosis]:

1. Treatment of relapsed or refractory HCL in adults; and
2. Member has received at least 2 prior systemic therapies, including treatment with a purine nucleoside analog (PNA); and
3. Creatinine clearance (CrCl) ≥30mL/minute/1.73m^2; and
4. As a single-agent.

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

1. Member must have 1 of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Philadelphia Chromosome Positive (Ph+) CML chronic phase (CP) resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy; or
    c. Post-hematopoietic stem cell transplantation.

Tibsovo® (Ivosidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. IDH1 mutation; or
2. Relapsed/refractory AML; and

a. As a single-agent; and
b. IDH1 mutation.

Venclexta® (Venetoclax) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. Untreated disease in combination with obinutuzumab for a maximum duration of 12 months; or
2. Relapsed/refractory disease in combination with rituximab or as a single-agent.

Xospata® (Gilteritinib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Relapsed/refractory AML; and
2. FLT3 mutation; and
3. As a single-agent.

Recommendation 8: Vote to Prior Authorize Azedra® (Iobenguane I-131)

MOTION CARRIED by unanimous approval.

Azedra® (Iobenguane I-131) Approval Criteria [Pheochromocytoma or Paraganglioma (PPGL) Diagnosis]:

1. Adult and pediatric members 12 years of age and older; and
2. Iobenguane scan positive; and
3. Unresectable, locally advanced or metastatic pheochromocytoma or PPGL requiring systemic anticancer therapy.

Recommendation 9: Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity™ (Diroximel Fumarate)

NO ACTION REQUIRED.

Recommendation 12: 30-Day Notice to Prior Authorize Tepezza™ (Teprotumumab-trbw)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Anti-Emetic Medications

NO ACTION REQUIRED.

Recommendation 14: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 15: Future Business

NO ACTION REQUIRED.

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

Memorandum

Date: April 09, 2020

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

Terry Cothran, D.Ph.
Pharmacy Director
OHCA

From: Wendi Chandler, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: Drug Utilization Review (DUR) Board Recommendations from Packet Meeting of April 08, 2020

Recommendation 1: Prenatal Vitamin (PV) Utilization Update

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Anti-Diabetic Medications and 30-Day Notice to Prior Authorize Qternmet® XR [Dapagliflozin/Saxagliptin/Metformin Extended-Release (ER) Tablet], Riomet ER™ (Metformin ER Oral Suspension), Rybelsus® (Semaglutide Tablet), and Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet)

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet)

NO ACTION REQUIRED.

Recommendation 4: 30-Day Notice to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™ (Bevacizumab-bvzr)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Dayvigo™ (Lemborexant)

NO ACTION REQUIRED.

Recommendation 7: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

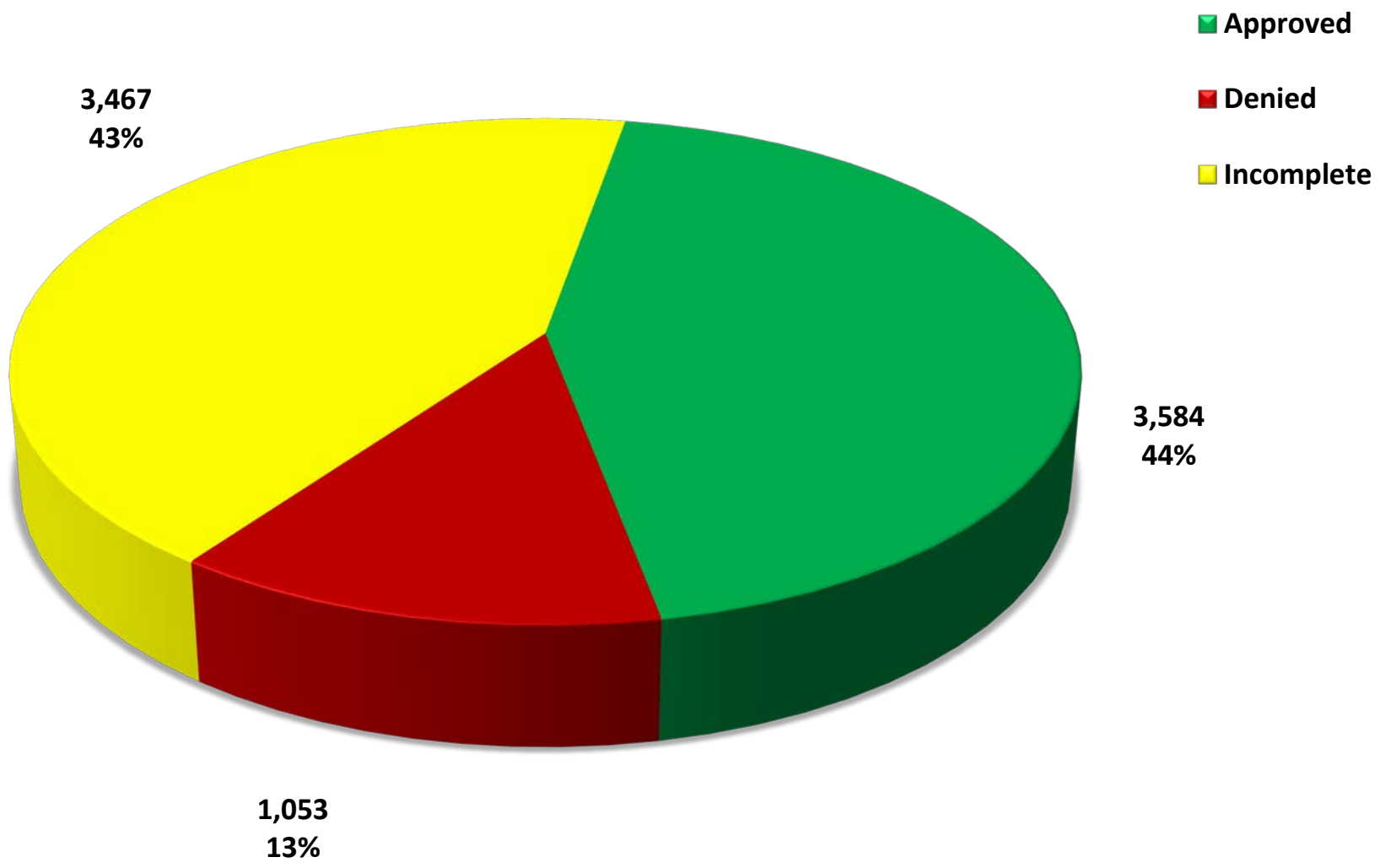
NO ACTION REQUIRED.

Recommendation 8: Future Business

NO ACTION REQUIRED.

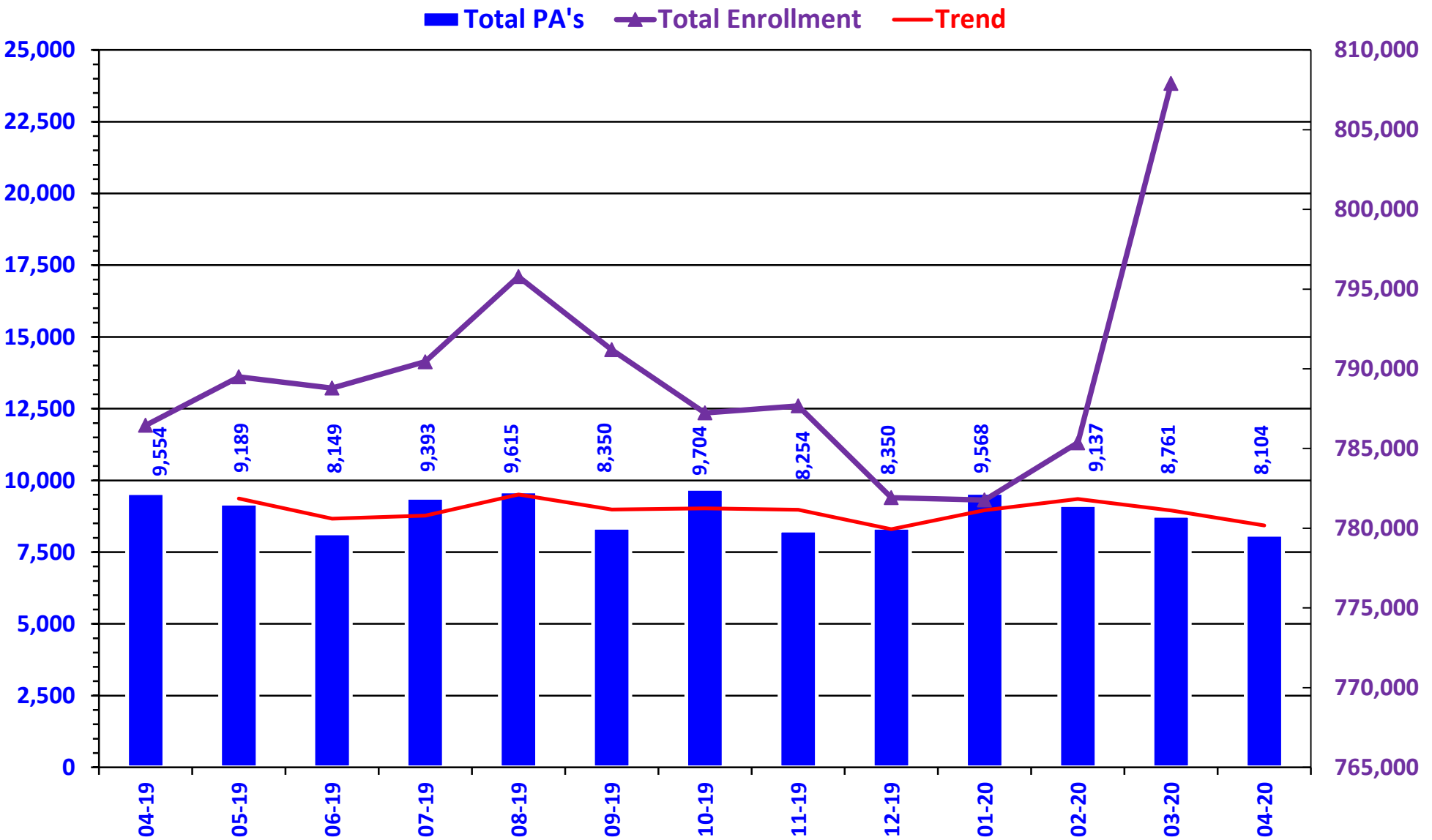
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: APRIL 2020



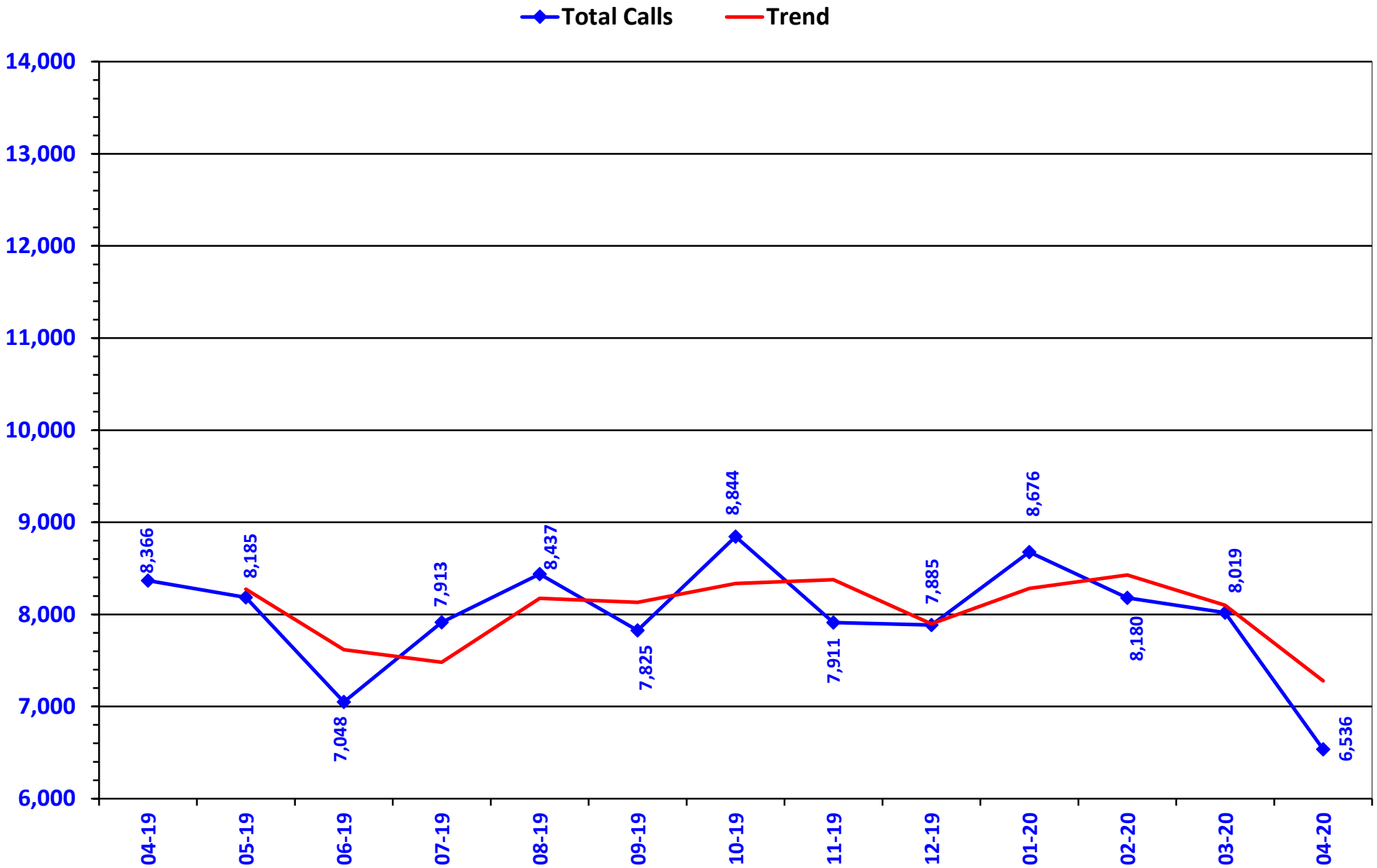
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: APRIL 2019 – APRIL 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
APRIL 2019 – APRIL 2020



Prior Authorization Activity

4/1/2020 Through 4/30/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	91	11	16	64	359
Analgesic - NonNarcotic	26	0	2	24	0
Analgesic, Narcotic	328	119	43	166	155
Angiotensin Receptor Antagonist	13	3	2	8	359
Antiasthma	92	22	26	44	267
Antibiotic	18	5	3	10	232
Anticonvulsant	145	62	16	67	329
Antidepressant	183	38	30	115	327
Antidiabetic	259	91	51	117	355
Antihistamine	24	8	7	9	256
Antimalarial Agent	122	72	15	35	318
Antimigraine	167	19	63	85	168
Antineoplastic	81	50	6	25	166
Antiparasitic	16	1	5	10	23
Antiulcers	92	23	22	47	161
Anxiolytic	19	2	1	16	222
Atypical Antipsychotics	314	147	30	137	358
Biologics	157	79	24	54	307
Bladder Control	47	6	17	24	359
Blood Thinners	301	170	22	109	342
Botox	27	19	2	6	323
Buprenorphine Medications	80	13	3	64	73
Calcium Channel Blockers	17	4	2	11	284
Cardiovascular	79	23	16	40	297
Chronic Obstructive Pulmonary Disease	125	22	34	69	331
Constipation/Diarrhea Medications	166	33	51	82	233
Contraceptive	24	9	3	12	355
Corticosteroid	10	1	5	4	25
Dermatological	273	80	60	133	112
Diabetic Supplies	750	361	64	325	231
Endocrine & Metabolic Drugs	77	42	9	26	176
Erythropoietin Stimulating Agents	16	8	2	6	100
Fibromyalgia	11	1	3	7	358
Fish Oils	21	2	5	14	359
Gastrointestinal Agents	126	23	32	71	194
Genitourinary Agents	18	9	4	5	230
Glaucoma	13	4	1	8	282
Growth Hormones	105	74	9	22	128
Hematopoietic Agents	19	12	1	6	187
Hepatitis C	114	69	8	37	10
HFA Rescue Inhalers	83	36	1	46	37
Insomnia	53	3	14	36	177
Insulin	174	54	13	107	354
Multiple Sclerosis	38	17	0	21	202
Muscle Relaxant	39	8	12	19	137
Nasal Allergy	87	13	30	44	127
Neurological Agents	76	27	12	37	188
NSAIDs	33	1	7	25	84
Ocular Allergy	34	4	8	22	154
Osteoporosis	3	3	0	0	359

* 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	23	2	2	19	18
Pediculicide	11	0	1	10	0
Respiratory Agents	55	39	0	16	166
Statins	12	1	6	5	78
Stimulant	567	261	50	256	342
Testosterone	53	16	16	21	326
Topical Antifungal	14	0	3	11	0
Topical Corticosteroids	70	1	28	41	85
Vitamin	49	14	19	16	221
Pharmacotherapy	107	98	1	8	287
Emergency PAs	0	0	0	0	
Total	**6,394**	**2,402**	**980**	**3,012**	
Overrides					
Brand	42	24	3	15	259
Compound	3	3	0	0	29
Cumulative Early Refill	1	1	0	0	16
Diabetic Supplies	16	14	1	1	176
Dosage Change	292	271	2	19	13
High Dose	1	1	0	0	360
Ingredient Duplication	19	14	0	5	29
Lost/Broken Rx	56	55	1	0	19
MAT Override	207	153	2	52	77
NDC vs Age	297	173	23	101	241
NDC vs Sex	4	2	1	1	63
Nursing Home Issue	32	29	0	3	8
Opioid MME Limit	117	57	5	55	107
Opioid Quantity	36	29	1	6	169
Other*	51	41	4	6	13
Quantity vs. Days Supply	463	272	24	167	230
STBS/STBSM	29	11	6	12	48
Step Therapy Exception	2	0	0	2	0
Stolen	14	11	0	3	13
Third Brand Request	28	21	0	7	31
Overrides Total	**1,710**	**1,182**	**73**	**455**	
Total Regular PAs + Overrides	**8,104**	**3,584**	**1,053**	**3,467**	

Denial Reasons	
Unable to verify required trials.	2,747
Does not meet established criteria.	1,096
Lack required information to process request.	712
Other PA Activity	
Duplicate Requests	887
Letters	13,741
No Process	8
Changes to existing PAs	666
Helpdesk Initiated Prior Authorizations	689
PAs Missing Information	17

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

Spring 2020 Pipeline Update

Oklahoma Health Care Authority
May 2020

Introduction

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

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

Anticipated Indication(s): Treatment of spinal muscular atrophy (SMA).

Clinical Trial(s): The efficacy and safety of risdiplam is supported by 2 pivotal, Phase 2/3 trials: FIREFISH (ages 1 to 7 months) and SUNFISH (ages 2 to 25 years). FIREFISH is an open-label, single-arm trial in infants with Type 1 SMA, ages 1 to 7 months. The primary endpoint is the percentage of infants able to sit without support for at least 5 seconds at 12 months. After 12 months of treatment, 86% of patients were event-free and did not need permanent ventilation, and 59% of infants had a CHOP-INTEND score ≥40. Among the milestone achievements, 53% were able to maintain upright head control and 41% could sit independently for at least 5 seconds. While no treatment-related safety trends were identified, pneumonia was reported in 4 infants, and respiratory tract infection and acute respiratory failure/distress each were reported in 2 infants. SUNFISH is a double-blind, placebo-controlled trial in children and young adults (2 to 25 years of age) with Type 2 or 3 SMA. The primary endpoint was the change from baseline in the Motor Function Measure 32 (MFM-32) scale after 1 year of treatment. The trial showed that change from baseline in the primary endpoint of the MFM-32 was significantly greater in participants treated with risdiplam, compared to placebo (1.55 point mean difference; P=0.0156). The Revised Upper Limb Module (RULM) also showed an improvement (1.59 point difference; P=0.0028). Safety for risdiplam in the SUNFISH trial was consistent with its known safety profile.

Place in Therapy: SMA is a rare, debilitating genetic disease characterized by progressive motor function decline and muscular atrophy while sparing cognitive abilities. SMA involves the loss of motor neurons leading to progressive muscle weakness and atrophy. It is caused by deletion or mutation of the survival motor neuron (SMN) gene 1 (*SMN1*), resulting in a lack of SMN protein needed to maintain motor neurons in the spinal cord and lower brain stem and in the symptoms of muscle weakness. SMN gene 2 (*SMN2*) is a backup of *SMN1* gene and produces

only 10% functional SMN protein. *SMN2* is considered a prognostic indicator for disease type and severity due to copy number variations. In general, fewer copies of *SMN2* result in more severe disease, but this does not always hold true. FDA-approved treatments for SMA in the United States include the biologic agents nusinersen (Spinraza®; December 2016), an *SMN2*-directed antisense oligonucleotide indicated to treat all SMA types in patients from birth to adulthood, and onasemnogene abeparvovec-xioi (Zolgensma®; May 2019), a gene replacement therapy indicated for all types of SMA in patients younger than 2 years of age. If approved, risdiplam will be the third disease modifying therapy approved by the FDA for this condition. Risdiplam is an *SMN2* splicing modifier for which approval is being sought for infants with type 1 SMA and patients age 2 to 25 years of age with types 2 and 3 SMA. Risdiplam is designed to provide sustained increase in SMN protein centrally and peripherally by helping the *SMN2* gene produce more functional SMN protein throughout the body. Risdiplam's oral, once-daily dosing will potentially provide a significant advantage as it allows for self- or caregiver-administration, circumventing the administration issues of the other 2 treatments currently available.

Projected FDA Decision: May 24, 2020

SoonerCare Impact: During calendar year 2019, 3 SoonerCare members qualified for treatment with Zolgensma® for whom SoonerCare is the primary payer and 18 SoonerCare members qualified for treatment with Spinraza®.

Obeticholic acid (Ocaliva®)[1,2,6,7,8]

Anticipated Indication(s): Treatment of patients with fibrosis due to nonalcoholic steatohepatitis (NASH).

Clinical Trial(s): The FDA submission of obeticholic acid was evaluated in the REGENERATE trial, a randomized, double-blind, placebo-controlled trial of 2,400 adult patients with NASH and METAVIR fibrosis stage F1, F2, or F3. Patients were randomized 1:1:1 to receive placebo or obeticholic acid (10 or 25mg). The primary objective was improvement in fibrosis with no worsening of NASH or resolution of NASH as determined by liver biopsy at the 18th month interim analysis. For the end-of-trial assessments, clinical benefit was confirmed by evaluating composite endpoints. At 18 months, the proportion of patients who achieved fibrosis improvement (≥1 stage) with no worsening of NASH was 18% (P=0.045) and 23% (P=0.0002) with oral once-daily obeticholic acid 10mg and 25mg, respectively, and 12% with placebo. However, the co-primary endpoint of NASH resolution with no worsening of fibrosis did not meet statistical significance in any group. More than half of the patients on the 25mg dose experienced pruritus; 9% of patients discontinued treatment due to severe pruritus. The 10mg dose was better tolerated but was also less effective. Of note, treatment with obeticholic acid was associated with an early increase in low-density lipoprotein (LDL) cholesterol levels which peaked at 4 weeks of therapy and subsequently declined approaching baseline at month 18.

Place in Therapy: NASH is a chronic, progressive, and severe form of nonalcoholic fatty liver disease (NAFLD) with non-specific symptomatology. Pathophysiology involves fat accumulation (steatosis), inflammation, and, variably, fibrosis. Steatosis results from hepatic triglyceride accumulation. Possible mechanisms for steatosis include reduced synthesis of very low density

lipoprotein (VLDL) and increased hepatic triglyceride synthesis (possibly due to decreased oxidation of fatty acids or increased free fatty acids being delivered to the liver). Inflammation may result from lipid peroxidative damage to cell membranes. These changes can stimulate hepatic stellate cells, resulting in fibrosis. NASH is a very prevalent conditions in the United States and is estimated to be 1 of the leading causes for liver transplantation. The only widely accepted treatment goal is to eliminate potential causes and risk factors. Such a goal may include discontinuation of drugs or toxins, weight loss, treatment for dyslipidemia, or treatment for hyperglycemia. Preliminary evidence suggests that thiazolidinediones and vitamin E can help correct biochemical and histologic abnormalities in NASH, but do not improve fibrosis. Obeticholic acid is a farnesoid X receptor agonist which suppresses *de novo* synthesis of bile acids from cholesterol, increases transport of bile acids out of the hepatocytes which limits the overall size of the circulating bile acid pool, and promotes choleresis. If approved, obeticholic acid will become the first medication approved in the United States by the FDA to treat NASH. Lower dose oral formulations of obeticholic acid are currently available under the brand name Ocaliva® for the treatment of primary biliary cholangitis (PBC).

Projected FDA Decision: June 26, 2020

SoonerCare Impact: During calendar year 2019, there were 489 SoonerCare members with a diagnosis of NASH for whom SoonerCare is the primary payer.

Viltolarsen[1,2,9,10,11]

Anticipated Indication(s): Treatment of Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping.

Clinical Trial(s): The safety and efficacy of viltolarsen was evaluated in a Phase 2 trial that enrolled 16 male patients ages 4 to younger than 10 years of age with confirmed DMD amenable to exon 53 skipping. Patients were randomized into 2 cohorts, each comprising of 8 participants treated with weekly intravenous (IV) infusions of viltolarsen for 24 weeks. Two patients in each cohort received placebo in place of viltolarsen for the first 4 weeks. The primary endpoints were the induction of dystrophin protein in muscle after 20 to 24 weeks of treatment measured by the Western blot assessment of muscle tissue samples prior to treatment and following week 24 of treatment. After 24 weeks, a drug-induced increase in the percentage of dystrophin protein in muscle was seen in both groups, with a dystrophin increase of 5.7% in the 40mg/kg cohort and 5.9% in the 80mg/kg cohort. Compared to historical data, viltolarsen-treated patients showed significant improvements in ambulation as measured by the time to stand from supine, climb 4 steps, and run/walk 10 meters, as well as in the distance walked in 6 minutes. All adverse effects were mild and none led to treatment discontinuation.

Place in Therapy: DMD is a progressive form of muscular dystrophy that occurs primarily in males, though in rare cases may affect females. It is caused by a genetic mutation in the DMD gene on the X-chromosome which can disrupt the reading frame of the dystrophin primary transcript and thus interferes with the production of dystrophin. When dystrophin is missing the muscle cells become damaged more easily. In response to the damage, inflammation occurs which only worsens the process. The onset of symptoms occurs between 3 and 5 years of age

and progressively worsens. Over time the muscle cells without dystrophin weaken and die leading to the muscle weakness and heart problems seen in DMD. Viltolarsen is an antisense oligonucleotide which can induce exon 53 mutation skipping during pre-mRNA splicing and restore the reading frame of the DMD primary transcript. The resulting dystrophin protein is internally deleted but partially functional. Current FDA approved treatments for DMD in the United States are eteplirsen (Exondys 51®), which targets exon 51, and golodirsen (Vyondys 53™), which targets exon 53. Both viltolarsen and golodirsen require weekly IV infusion; however, unlike golodirsen, viltolarsen has not yet reported an increased risk of IV infusion port infection and renal toxicity.

Projected FDA Decision: October 2, 2020

SoonerCare Impact: Only an estimated 8% of patients with DMD have a mutation amendable to exon 53. During calendar year 2019, there was a total of 2 SoonerCare members with paid claims for Emflaza® or Exondys 51™ accounting for 13 claims totaling $142,381.89 in drug spending and an average cost per claim of $10,952.45.

Pipeline Table[1,2]

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
dasotraline	Sunovion	Binge eating disorder	PO	Filed NDA	05/14/2020
apomorphine	Sunovion	Parkinson's disease	PO	Filed NDA	05/21/2020
risdiplam	Roche/PTC Therapeutics	Spinal muscular atrophy	PO	Filed NDA	05/24/2020
L-lactic acid/citric acid/potassium bitartrate (Amphora®)	Evofem Biosciences	Pregnancy prevention	VG	Filed NDA	05/25/2020
minocycline	Foamix	Rosacea	TOP	Filed NDA	06/02/2020
elagolix (Orilissa®)	Abbvie	Uterine fibroids	PO	Filed sNDA	06/05/2020
ketotifen	Eton	Allergic conjunctivitis	OP	Filed NDA	06/11/2020
fosfomycin (Contepo™)	Nabriva Therapeutics	Bacterial infections	IV	Filed NDA	06/19/2020
metoclopramide	Evoke Pharma	Diabetic gastroparesis	IN	Filed NDA	06/19/2020
obeticholic acid (Ocaliva®)	Intercept Pharmaceuticals	NASH	PO	Filed NDA	06/26/2020
octreotide (Mycapssa™, Octreolin®)	Chiasma	Acromegaly	PO	Filed NDA	06/2020
ofatumumab	Novartis	Multiple sclerosis	SC	Filed BLA	06/2020
mannitol (Bronchitol®)	Pharmaxis	Cystic fibrosis	INH	Filed NDA	2Q 2020
cantharidin 0.7% solution	Verrica	Molluscum	TOP	Filed NDA	07/13/2020
oxymetazoline	Osmotica/ Vertical Pharmaceuticals	Acquired blepharoptosis	OP	Filed NDA	07/16/2020
capsaicin (Qutenza®)	Grünenthal	Diabetic peripheral neuropathy	TOP	Filed sNDA	07/19/2020
calcipotriene/ betamethasone	MC2 Therapeutics	Psoriasis	TOP	Filed NDA	07/20/2020

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
sodium oxybate ER	Jazz	Narcolepsy	PO	Filed NDA	07/21/2020
donepezil transdermal system (Adlarity®)	Corium International	Alzheimer's disease	TOP	Filed NDA	07/30/2020
fluticasone furoate/ umeclidinium bromide/ vilanterol (Trelegy® Ellipta®)	GlaxoSmithKline	Asthma (adults)	INH	Filed sNDA	07/31/2020
triheptanoin	Ultragenyx	Glucose transport type 1 deficiency syndrome	PO	Filed NDA	07/31/2020
decitabine and E7727	Astex Pharmaceuticals	Myelodysplastic syndrome	PO	Filed NDA	07/2020-08/2020
Viaskin™ Peanut	DBV Technologies	Peanut allergy	TOP	Filed BLA	08/05/2020
fostemsavir	Bristol-Myers Squibb	HIV	PO	Filed NDA	08/05/2020
ustekinumab (Stelara®)	Janssen	Psoriasis (ages 6 to 11 years)	IV, SC	Filed sBLA	08/07/2020
oliceridine	Trevena	Pain	IV	Filed NDA	08/10/2020
berotralstat	BioCryst	Hereditary angioedema	PO	Filed NDA	08/11/2020
sodium thiosulfate (Pedmark™)	Fennec	Hearing loss	IV	Filed NDA	08/11/2020
dolutegravir/lamivudine (Dovato®)	GlaxoSmithKline	HIV-1 treatment (switch therapy in virologically suppressed adults)	PO	Filed sNDA	08/16/2020
filgotinib	Gilead	Rheumatoid arthritis	PO	Filed NDA	08/18/2020
veverimer	Tricida	Chronic kidney disease	PO	Filed NDA	08/22/2020
valoctocogene roxaparvovec	BioMarin	Hemophilia A	IV	Filed BLA	08/23/2020
clascoterone (Winlevi®)	Cassiopea	Acne vulgaris	TOP	Filed NDA	08/27/2020
satralizumab	Roche	Neuromyelitis optica	SC	Filed BLA	08/2020 - 09/2020
somapacitan	Novo Nordisk	Growth hormone deficiency	SC	Filed BLA	09/21/2020
artesunate	La Jolla Pharmaceutical	Malaria	Undisclosed	Filed NDA	09/25/2020
diazepam (Libervant™)	Aquestive Therapeutics	Seizures	PO	Filed NDA	09/27/2020
remestemcel-L (Prochymal®)	Mesoblast	Graft versus host disease	IV	Filed BLA	09/30/2020
hydrocortisone (Infacort®)	Diurnal Group	Adrenal insufficiency	PO	Filed NDA	10/02/2020
viltolarsen	Nippon Shinyaku	Duchenne muscular dystrophy	IV	Filed BLA	10/02/2020
tramadol	Avenue Therapeutics	Pain	IV	Filed NDA	10/09/2020
zolmitriptan (Qtrypta®)	Zosano	Acute migraines	TOP	Filed NDA	10/20/2020
eflapegrastim	Spectrum/Hanmi	Neutropenia	SC	Filed BLA	10/24/2020

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
viloxazine	Supernus	Attention deficit/hyperactivity disorder	PO	Filed NDA	11/08/2020
olanzapine/samidorphan	Alkermes	Schizophrenia/Bipolar disorder	PO	Filed NDA	11/15/2020
daxibotulinumtoxinA	Revance Therapeutics	Glabellar lines	IM	Filed BLA	11/25/2020
treprostinil	Liquidia Technologies	Pulmonary arterial hypertension	INH	Filed NDA	11/27/2020
nifurtimox	Bayer	Chagas disease	PO	Filed NDA	11/30/2020
roxadustat	FibroGen/ AstraZeneca	Anemia	PO	Filed NDA	12/23/2020
ansofaxine	Luye Pharma	Major depressive disorder	PO	Filed NDA	12/26/2020
vibegron	Urovant Sciences	Overactive bladder	PO	Filed NDA	12/29/2020

NDA = New Drug Application; BLA = Biologic License Application; sBLA = supplemental Biologic License Application; sNDA = supplemental New Drug Application; Admin = administration; SC = subcutaneous; PO = oral; TOP = topical; IV = intravenous; IO = intraocular; IM = intramuscular; IN = intranasal; INH = inhaled; VG = vaginal; OP: opthalmic 2Q = 2nd quarter 2; ER = extended-release; HIV = human immunodeficiency virus;
*Most biosimilars and oncology medications are excluded from the table. Medications known to have received a Complete Response Letter (CRL) from the FDA that have not resubmitted were also excluded.

---

[1] OptumRx. RxOutlook® 1st Quarter 2020. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/outlook/ORX6204_200224_B2B-NEWSLETTER_RxOutlook_2020Q1_FINAL.pdf. Issued 02/26/2020. Last accessed 04/08/2020.
[2] MagellanRx Management. MRx Pipeline. Available online at: https://www1.magellanrx.com/documents/2020/01/mrx-pipeline-january-2020.pdf/. Issued 01/2020. Last accessed 04/08/2020.
[3] PTC Therapeutics, Inc. Data from Pivotal FIREFISH and SUNFISH Studies Demonstrate Clinical Benefit of Risdiplam in Type 1, 2, & 3 Spinal Muscular Atrophy Patients. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/data-from-pivotal-firefish-and-sunfish-studies-demonstrate-clinical-benefit-of-risdiplam-in-type-1-2--3-spinal-muscular-atrophy-patients-300844863.html. Issued 05/07/2019. Last accessed 04/08/2020.
[4] National Institute of Health. Spinal muscular atrophy. Available online at: https://ghr.nlm.nih.gov/condition/spinal-muscular-atrophy. Issued 03/31/2020. Last accessed 04/09/2020.
[5] SMA News Today. Risdiplam (Formerly RG7916). Available online at: https://smanewstoday.com/rg7916-rg7800-roche-ptc-smaf. Issued 02/27/2020. Last accessed 04/09/2020.
[6] American Association for the Advancement of Science (AAAS). Obeticholic acid improves liver fibrosis and other histological features of NASH. *EurekAlert*. Available online at: https://www.eurekalert.org/pub_releases/2019-04/sh-oai040819.php. Issued 04/11/2019. Last accessed 04/09/2020.
[7] Jennison E, Patel J, Scorletti E, et al. Diagnosis and management of non-alcoholic fatty liver disease. *Postgraduate Medical Journal* 2019; 95:314-322.
[8] Ocaliva® Prescribing Information. Intercept Pharmaceuticals, Inc, Available online at: https://www.interceptpharma.com/wp-content/uploads/2020/02/US-Package_Insert-07Feb2020_VV-REG-030820.pdf. Last revised 02/2020. Last accessed 04/09/2020.
[9] Clemens P, Rao V, Connolly A, et al. A Phase II, Dose Finding Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of NS-065/NCNP-01 (Viltolarsen) in Boys with Duchenne Muscular Dystrophy (DMD). Available online at: http://www.nspharma.com/pdf/Poster_slides_WMS_Final.pdf. Last accessed 04/09/2020.
[10] National Institute of Health. Duchenne muscular dystrophy. Available online at: https://rarediseases.info.nih.gov/diseases/6291/duchenne-muscular-dystrophy. Last revised 09/28/2017. Last accessed 04/09/2020
[11] U.S. Food and Drug Administration. FDA grants accelerated approval to first targeted treatment for rare Duchenne muscular dystrophy mutation. *FDA News Release*. Available online at: https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation. Last revised 12/12/2019. Last accessed 04/09/2020.

Appendix C

Vote to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet)

Oklahoma Health Care Authority
May 2020

Introduction[1,2]

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

- **Katerzia™ (Amlodipine Oral Suspension):** Katerzia™ (amlodipine oral suspension), FDA approved July 2019, is a calcium channel blocker (CCB) and may be used alone or in combination with other antihypertensive and antianginal agents for the treatment of hypertension (HTN) in adults and children 6 years of age and older to lower blood pressure (BP); lowering BP reduces the risk of fatal and nonfatal cardiovascular (CV) events, primarily stroke and myocardial infarction (MI). Katerzia™ is also indicated to treat coronary artery disease (CAD) in adults including chronic stable angina, vasospastic angina (Prinzmetal's or variant angina), and angiographically documented CAD in patients without heart failure (HF) or with an ejection fraction (EF) <40%. Katerzia™ oral suspension contains 1mg/mL of amlodipine (equivalent to 1.3mg of amlodipine benzoate) and is supplied as 150mL in a 185mL high-density polyethylene (HDPE) bottle with a child-resistant cap and tamper-evident seal. The pediatric starting dose for Katerzia™ is 2.5mg to 5mg once daily. The Katerzia™ recommended starting dose for adults is 5mg once daily with a maximum dose of 10mg once daily. Based on the maximum FDA recommended dose of amlodipine 10mg daily, the cost per year for Katerzia™ 1mg/mL is $11,916.00 compared to the annual cost of $7.20 for generic amlodipine 10mg tablets.
- **Conjupri® (Levamlodipine Tablet):** Conjupri® (levamlodipine tablet), FDA approved December 2019, is a CCB and may be used alone or in combination with other antihypertensive agents for the treatment of HTN. Levamlodipine is the pharmacologically active isomer of amlodipine. Conjupri® is supplied as 1.25mg, 2.5mg (functionally scored), and 5mg (functionally scored) tablets. Conjupri® cost and launch date information is currently unavailable.

Recommendations

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

1. Moving Cardene® (nicardipine) from Tier-1 to Tier-2 of the CCB Antihypertensive Medications PBPA tier chart based on the National Average Drug Acquisition Cost (NADAC). Current Tier-2 criteria will apply.
2. Placement of Katerzia™ (amlodipine oral suspension) and Conjupri® (levamlodipine tablet) into the Special Prior Authorization (PA) Tier of the CCB Antihypertensive Medications PBPA tier chart with the following criteria:

Katerzia™ (Amlodipine Oral Suspension) Approval Criteria:

1. An FDA approved diagnosis of hypertension or coronary artery disease; and
2. A patient-specific, clinically significant reason why the member cannot use amlodipine oral tablets even when crushed must be provided; and
3. A quantity limit of 300mL per 30 days will apply.

Conjupri® (Levamlodipine Tablet) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use amlodipine oral tablets, which are available without prior authorization, must be provided.

The recommended changes are shown in red in the following CCB PBPA Tier Chart:

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
amlodipine (Norvasc®)	amlodipine/atorvastatin (Caduet®)	amlodipine/celecoxib (Consensi™)
diltiazem (Cardizem®)	diltiazem LA (Cardizem® LA, Matzim® LA)	**amlodipine oral suspension (Katerzia™)**
diltiazem (Tiazac®, Taztia XT®)	diltiazem SR (Cardizem® SR)	diltiazem CD 360mg (Cardizem® CD)
diltiazem CD (Cardizem® CD)*	isradipine (Dynacirc®, Dynacirc CR®)	**levamlodipine (Conjupri®)**
diltiazem ER (Cartia XT®, Diltia XT®)	**nicardipine (Cardene®)**	
diltiazem XR (Dilacor® XR)	nicardipine SR (Cardene® SR)	
felodipine (Plendil®)	nisoldipine (Sular®)	
nifedipine (Adalat®, Procardia®)	verapamil (Covera-HS®)	
nifedipine ER (Adalat® CC)	verapamil ER (Verelan®, Verelan® PM)	
nifedipine XL (Nifedical XL®, Procardia XL®)		
nimodipine (Nimotop®)		
verapamil (Calan®, Isoptin®)		
verapamil SR (Calan® SR, Isoptin® SR)		

XR, XL, ER = extended-release; SR = sustained-release; LA = long-acting; CD = controlled-delivery; PA = prior authorization
*All strengths other than 360mg.

[1] Katerzia™ (Amlodipine Oral Suspension) Prescribing Information. Silvergate Pharmaceuticals, Inc. Available online at: https://katerzia.com/Katerzia-Prescribing-Info.pdf. Last revised 07/2019. Last accessed 03/15/2020.
[2] Conjupri® (Levamlodipine Tablet) Prescribing Information. CSPC Ouyi Pharmaceutical Co., Ltd. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212895s000lbl.pdf. Last revised 12/2019. Last accessed 03/15/2020.

Appendix D

Vote to Prior Authorize Tepezza™ (Teprotumumab-trbw)

Oklahoma Health Care Authority
May 2020

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

In January 2020, the U.S. Food and Drug Administration (FDA) approved Tepezza™ (teprotumumab-trbw), the first FDA-approved treatment for thyroid eye disease. Thyroid eye disease, also known as Graves' eye disease, is caused by retro-orbital inflammation to which orbital fibroblast activation is a key contributor; fibroblast activation is presumed to occur secondary to stimulatory auto-antibodies [anti-thyroid stimulating hormone (TSH) receptor (anti-TSHR) and anti-insulin-like growth factor-1 (anti-IGF-1)]. Inflammation of the extraocular muscles can lead to restricted eye movements and proptosis, and the optic nerve can be compressed, which can cause optic neuropathy resulting in permanent vision loss. Thyroid function control should be the primary approach to treatment, as normal thyroid function is associated with a reduction in the severity of thyroid eye disease.

Teprotumumab is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the IGF-1 receptor (IGF-1R) indicated for the treatment of thyroid eye disease in adult patients. Teprotumumab should be administered by intravenous (IV) infusion every 3 weeks, and the recommended dosage of teprotumumab is 10mg/kg for the initial dose, followed by 20mg/kg for 7 additional infusions. Teprotumumab may cause infusion reactions. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid, and/or administering all subsequent infusions at a slower infusion rate. The Wholesale Acquisition Cost (WAC) of Tepezza™ (teprotumumab-trbw) is $14,900 per 500mg single-dose vial. Treatment cost will vary depending on patient weight. The cost of treatment for a 70kg patient would be $342,700 for the recommended 8 total infusions.

Recommendations

The College of Pharmacy recommends the prior authorization of Tepezza™ (teprotumumab-trbw) with the following criteria with changes noted in red based on recommendations by the Drug Utilization Review (DUR) Board at the March 2020 DUR Board meeting:

Tepezza™ (Teprotumumab-trbw) Approval Criteria:

1. An FDA approved indication for the treatment of thyroid eye disease in adult members 18 years of age and older; and
    a. Member must be experiencing eye symptoms related to thyroid eye disease; and
    b. Member must have thyroid blood levels in the normal range or must be undergoing active treatment working toward normal range; and
2. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and

3. Female members of reproductive potential must be willing to use effective contraception prior to initiation, during treatment with Tepezza™, and for at least 6 months after the last dose of Tepezza™; and
4. Member must not have had prior surgical treatment for thyroid eye disease; or
    a. A prior authorization request with patient-specific information may be submitted for consideration of Tepezza™ for members who have had prior surgical treatment for thyroid eye disease, including but not limited to patient-specific, clinically significant information regarding the member's prior surgery and the need for Tepezza™; and
5. Medical supervision by an ophthalmologist in conjunction with an endocrinologist for the treatment of thyroid eye disease; and
    a. The name of the ophthalmologist and endocrinologist recommending treatment with Tepezza™ must be provided on the prior authorization request; and
6. Tepezza™ must be administered as an intravenous (IV) infusion at the recommended infusion rate per package labeling, with appropriate pre-medication(s) based on the member's risk of infusion reactions; and
7. Tepezza™ must be administered by a health care professional. Prior authorization requests must indicate how Tepezza™ will be administered; and
    a. Tepezza™ must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Tepezza™ must be shipped via cold chain supply to the member's home and administered by a home health care provider and the member (or the member's caregiver) must be trained on the proper storage of Tepezza™; and
8. The member's current weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
9. Approvals will be for a maximum of 8 total infusions.

---

[1] McAlinden C. An Overview of Thyroid Eye Disease. *Eye Vis* 2014; 1:9. doi: 10.1186/s40662-014-0009-8.
[2] Davies TF, Burch HB. Treatment of Graves' Orbitopathy (Ophthalmopathy). *UpToDate*. Available online at: https://www.uptodate.com/contents/treatment-of-graves-orbitopathy-ophthalmopathy. Last revised 04/03/2020. Last accessed 04/06/2020.
[3] U.S. Food and Drug Administration (FDA) News Release: FDA Approves First Treatment for Thyroid Eye Disease. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease. Issued 01/21/2020. Last accessed 04/06/2020.
[4] Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. *N Engl J Med* 2020; 382: 341-352. doi: 10.1056/NEJMoa1910434.
[5] Tepezza™ (Teprotumumab-trbw) Prescribing Information. Horizon Therapeutics. Available online at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Last revised 01/2020. Last accessed 04/06/2020.

Appendix E

Vote to Prior Authorize Dayvigo™ (Lemborexant)

Oklahoma Health Care Authority
May 2020

Introduction[1,2,3]

- **Dayvigo™ (Lemborexant):** The U.S. Food and Drug Administration (FDA) approved Dayvigo™ (lemborexant), an orexin receptor antagonist, in December 2019 for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. Lemborexant is available as 5mg and 10mg oral tablets, and the recommended dosage is 5mg taken no more than once per night, immediately before going to bed, with at least 7 hours remaining before the planned time of awakening. Dosage may be increased to 10mg based on clinical response and tolerability; the maximum recommended dosage is 10mg once per night. In randomized, controlled clinical studies, the most common adverse reactions (occurred ≥2% and more frequently than placebo) following treatment with lemborexant were somnolence or fatigue, headache, and nightmare or abnormal dreams. Cost information for Dayvigo™ (lemborexant) is not yet available, as lemborexant is currently pending controlled substance scheduling by the U.S. Drug Enforcement Administration (DEA). Dayvigo™ will be commercially available following scheduling by the DEA.
- **Non-24-Hour Sleep-Wake Disorder (Non-24 or N24SWD) Treatment Guidelines:** Non-24 is a circadian rhythm sleep disorder that affects the normal 24-hour synchronization of circadian rhythms; therefore, patients with Non-24 will typically find their sleep time gradually delaying by minutes to hours every day. Non-24 is most common in totally blind patients; however, this disorder also occurs among sighted patients. A diagnosis of Non-24 requires at least 14 days of documentation of progressively shifting sleep-wake times with sleep diaries and/or actigraphy. In October 2015, the American Academy of Sleep Medicine (AASM) published an update to the clinical practice guideline for the treatment of intrinsic circadian rhythm sleep-wake disorders, including Non-24. A key recommendation from the AASM guideline update in regards to Non-24 includes the recommendation that clinicians use strategically timed melatonin for the treatment of Non-24 in blind adults (versus no treatment). Hetlioz® (tasimelteon), a melatonin receptor agonist, was approved by the FDA in 2014 as the first FDA-approved treatment for Non-24; the effectiveness of tasimelteon was evaluated in 2 clinical trials of totally blind patients with Non-24.

Recommendations

The College of Pharmacy recommends the following changes to the Insomnia Medications Product Based Prior Authorization (PBPA) category (changes noted in red in the following Tier chart and criteria):

1. Placement of Dayvigo™ (lemborexant) into Tier-3; current Tier-3 approval criteria will apply

2. Updating the current approval criteria for Hetlioz® (tasimelteon) based on current clinical practice guidelines for Non-24

Insomnia Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA***
estazolam (ProSom®) eszopiclone (Lunesta®) flurazepam (Dalmane®) ramelteon (Rozerem®) – *Brand Preferred* temazepam (Restoril®) 15mg and 30mg triazolam (Halcion®) zaleplon (Sonata®) zolpidem (Ambien®)	zolpidem CR (Ambien® CR)	**lemborexant (Dayvigo™)** suvorexant (Belsomra®)	doxepin (Silenor®) tasimelteon (Hetlioz®)+ temazepam (Restoril®) 7.5mg and 22.5mg zolpidem oral spray (Zolpimist®) zolpidem SL tablet (Edluar®) zolpidem SL tablet (Intermezzo®)

PA = prior authorization; CR = controlled-release; SL = sublingual
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Unique dosage formulations require a special reason for use in place of Tier-1 formulations.
+Individual criteria specific to tasimelteon applies.

- Tier-1 medications are available without a prior authorization for all members older than 18 years of age.
- Members 18 years of age or younger will be required to submit a prior authorization for consideration.
- All medications have a quantity limit of 30 units per 30 days.

Insomnia Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A minimum of a 30-day trial with at least 2 Tier-1 medications and clinical documentation of attempts to correct any primary cause for insomnia; and
3. No concurrent anxiolytic benzodiazepine therapy greater than 3 times daily dosing; and
4. Approvals will be granted for the duration of 6 months.

Insomnia Medications Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. A minimum of a 30-day trial with at least 2 Tier-1 medications and clinical documentation of attempts to correct any primary cause for insomnia; and
3. A minimum of a 30-day trial with at least 2 Tier-2 medications; and

    a. If only 1 Tier-2 medication is available, a minimum of a 30-day trial with 1 Tier-2 medication will be required; and
4. No concurrent anxiolytic benzodiazepine therapy greater than 3 times daily dosing; and
5. Approvals will be granted for the duration of 6 months.

Hetlioz® (Tasimelteon) Approval Criteria:

1. An FDA approved diagnosis of Non-24-Hour Sleep-Wake Disorder (Non-24) confirmed by a sleep specialist; and
2. Member must be 18 years of age or older; and
3. ~~Member must be totally blind; and~~
4. A failed trial of appropriately timed doses of melatonin; and
5. ~~A failed trial of Rozerem® (ramelteon); and~~
6. Initial approvals will be for the duration of 12 weeks. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
7. A quantity limit of 30 capsules for 30 days will apply.

[1] Eisai. U.S. FDA Approves Eisai's Dayvigo™ (Lemborexant) for the Treatment of Insomnia in Adult Patients. Available online at: http://eisai.mediaroom.com/2019-12-23-U-S-FDA-Approves-Eisais-DAYVIGO-TM-lemborexant-for-the-Treatment-of-Insomnia-in-Adult-Patients. Issued 12/23/2019. Last accessed 04/06/2020.

[2] Dayvigo™ (Lemborexant) Prescribing Information. Eisai Inc. Available online at: https://us.eisai.com/-/media/Files/Eisai/PrescribingInformation.pdf. Last revised 12/2019. Last accessed 04/06/2020.

[3] Auger RR, Burgess HJ, Emens JS, et al. Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder (DSWPD), Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD). An Update for 2015. *J Clin Sleep Med* 2015; 11(10):1199–1236. doi: 10.5664/jcsm.5100.

Appendix F

Vote to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity® (Diroximel Fumarate)

Oklahoma Health Care Authority
May 2020

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

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

- **Mayzent® (Siponimod):** In January 2019, the FDA approved Mayzent® (siponimod) for the treatment of adults with relapsing forms of multiple sclerosis (MS), including secondary progressive multiple sclerosis (SPMS) with active disease, relapsing-remitting multiple sclerosis (RRMS), and clinically isolated syndrome (CIS). CIS is defined as a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination in the central nervous system (CNS). SPMS is a debilitating form of MS characterized by progressive and irreversible neurological disability. Mayzent® is a selective sphingosine-1-phosphate (S1P) receptor modulator that selectively binds to S1P1 and S1P5 receptors. In relation to the S1P1 receptor, it prevents the lymphocytes from egressing the lymph nodes and as a consequence, from entering the CNS of patients with MS. This leads to the anti-inflammatory effects of siponimod. Mayzent® also enters the CNS and directly binds to the S1P5 and S1P1 sub-receptors on specific cells in the CNS (oligodendrocytes and astrocytes) to promote remyelination and prevent inflammation. Mayzent® is supplied as 0.25mg and 2mg oral tablets. Assessments should be done prior to the initiation of treatment with Mayzent® which include CYP2C9 genotype determination, complete blood count (CBC), ophthalmic evaluation, cardiac evaluation, review of current or prior medications, vaccinations, and liver function tests (LFTs). A 4- or 5- day titration is required for treatment initiation. If 1 titration dose is missed for more than 24 hours, treatment needs to be reinitiated with day 1 of the titration regimen. The recommended maintenance dosage of Mayzent® is 2mg once daily. The recommended maintenance dosage in patients with CYP2C9*1/*3 or *2/*3 genotype is 1mg once daily. The estimated cost per year of Mayzent® 2mg once daily is $92,088.00.
- **Mavenclad® (Cladribine):** In March 2019, the FDA approved Mavenclad® (cladribine) to treat relapsing forms of MS in adults, to include RRMS and active SPMS. Mavenclad® is not recommended for MS patients with CIS. Because of its safety profile, the use of Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Mavenclad® has a *Boxed Warning* for an increased risk of malignancy and fetal harm. Mavenclad® is not to be used in patients with current malignancy. Mavenclad® is supplied as a 10mg oral tablet. Assessments should be done prior to the initiation of treatment with Mavenclad® which include cancer screening, pregnancy test, CBC, ruling out certain infections, and LFTs. The recommended cumulative dosage of Mavenclad® is 3.5mg/kg administered orally and divided into 2 treatment courses (1.75mg/kg per

treatment course). Each treatment course is divided into 2 treatment cycles. Following the administration of 2 treatment courses, Mavenclad® should not be administered during the next 2 years. Treatment during these 2 years may further increase the risk of malignancy. The safety and efficacy of reinitiating Mavenclad® >2 years after completing 2 treatment courses has not been studied. The cost of Mavenclad® for the maximum dose of 10 tablets per cycle for 2 courses containing 2 cycles each is $284,285.60.

- **Vumerity® (Diroximel Fumarate):** In October 2019, the FDA approved Vumerity® (diroximel fumarate) for the treatment of relapsing forms of MS, to include CIS, RRMS, and active SPMS. Once in the body, Vumerity® rapidly converts to monomethyl fumarate (MMF), the same active metabolite of dimethyl fumarate (Tecfidera®). The FDA approval of Vumerity® was based on a New Drug Application (NDA) submitted under the 505(b)(2) filing pathway, which included data from pharmacokinetic bridging studies comparing Vumerity® and Tecfidera® to establish bioequivalence, and relied, in part, on the FDA's findings of safety and efficacy for Tecfidera®. Vumerity® is supplied as a 231mg delayed-release capsule. A CBC (including lymphocyte count) and serum aminotransferase, alkaline phosphatase, and total bilirubin should be obtained prior to treatment with Vumerity®. The starting dosage for Vumerity® is 231mg orally twice daily (BID) for 7 days. After 7 days, the maintenance dose is 462mg [(2) 231mg capsules] orally BID. If taken with food, a high-fat, high-calorie meal/snack should be avoided with the administration of Vumerity®. The meal/snack should contain ≤700 calories and ≤30 grams of fat. The cost per year of Vumerity® based on the maintenance dose of 462mg [(2) 231mg capsules] BID is $86,788.80.

Recommendations

The College of Pharmacy recommends the prior authorization of Mayzent® (siponimod), Mavenclad® (cladribine), and Vumerity® (diroximel fumarate) with the following criteria:

Mayzent® (Siponimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and
2. Member must have been assessed for CYP2C9 genotype:
    a. Members with a CYP2C9*3/*3 genotype will not generally be approved; or
    b. Members with a CYP2C9*1/*3 or *2/*3 genotype will not be approved for doses exceeding 1mg per day; or
    c. All other genotypes (CYP2C9*1/*1, *1/*2, or *2/*2) will be approved for 2mg per day; and
3. Member must not have any contraindication for use of siponimod including:
    a. CYP2C9*3/*3 genotype; or
    b. Experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or class III/IV HF in the last 6 months; or
    c. Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless member has a functioning pacemaker; and

4. Member must not have received prior treatment with alemtuzumab; and
5. Verification from the prescriber that member has no active infection(s); and
6. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
7. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
8. Ophthalmic evaluation and verification that member will be monitored for changes in vision throughout therapy; and
9. Verification from the prescriber that the member has been assessed for medications and conditions that cause reduction in heart rate (HR) or AV conduction delays and that the member will be followed with appropriate monitoring per package labeling; and
10. Verification from the prescriber that the member has been assessed for previous confirmed history of chickenpox or vaccination against varicella. Members without history of chickenpox or varicella vaccination should receive a full course of the varicella vaccine prior to commencing treatment with Mayzent®; and
11. Verification from the prescriber that members with sinus bradycardia (HR <55 beats per minute), first- or second-degree AV block (Mobitz type I), or a history of HF or MI will be monitored following the first dose for a minimum of 6 hours; and
12. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
13. Female members of reproductive potential must be willing to use effective contraception during treatment with Mayzent® and for at least 10 days after discontinuing treatment; and
14. Member must have had an inadequate response to Gilenya® (fingolimod) or a patient-specific, clinically significant reason why fingolimod is not appropriate for the member must be provided; and
15. Compliance will be checked for continued approval every 6 months; and
16. Quantity limits according to package labeling will apply.

Mavenclad® (Cladribine) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease in adults; and
2. Requests for use in patients with clinically isolated syndrome will not generally be approved; and
3. Member must have had at least 1 relapse in the previous 12 months; and
4. Member must have had an inadequate response to 2 or more medications indicated for the treatment of MS; and
5. Prescriber must confirm that the member does not have any contraindications for use of cladribine; and
6. Prescriber must confirm that the member does not have an active malignancy; and
7. Prescriber must confirm that females members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and

8. Prescriber must attest that female and male members of reproductive potential plan to use effective contraception during cladribine dosing and for 6 months after the last dose in each treatment course; and
9. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
10. Verification from the prescriber that member has no active infection(s); and
11. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
12. 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
13. Quantity limits according to package labeling will apply.

Vumerity® (Diroximel Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no serious active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Verification from the prescriber that member does not have moderate or severe renal impairment; and
7. Verification from the prescriber that the member has been counseled on proper administration of Vumerity® including caloric and fat intake limits at the time of dosing; and
8. Compliance will be checked for continued approval every 6 months; and
9. A quantity limit of 120 capsules per 30 days will apply.

[1] Novartis. Novartis Receives FDA Approval for Mayzent® (Siponimod), the First Oral Drug to Treat Secondary Progressive MS with Active Disease. Available online at: https://novartis.gcs-web.com/Novartis-receives-FDA-approval-for-Mayzent-siponimod-the-first-oral-drug-to-treat-secondary-progressive-MS-with-active-disease. Issued 03/26/2019. Last accessed 04/15/2020.

[2] Mayzent® Prescribing Information. Novartis Pharmaceuticals Corporation. Available online at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/mayzent.pdf. Last revised 03/2019. Last accessed 04/15/2020.

[3] U.S. Food and Drug Administration. FDA Approves New Oral Treatment for Multiple Sclerosis. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-oral-treatment-multiple-sclerosis. Issued 03/29/2019. Last accessed 04/15/2020.

[4] Mavenclad® Prescribing Information. Merck KGaA. Available online at: https://www.mavenclad.com/content/dam/web/healthcare/neurology/united-states/pdfs/Prescribing%20Information.pdf. Last revised 04/2019. Last accessed 04/15/2020.

[5] Biogen Inc. Biogen and Alkermes Announce FDA Approval of Vumerity™ (Diroximel Fumarate) for Multiple Sclerosis. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/30/1937769/0/en/Biogen-and-Alkermes-Announce-FDA-Approval-of-VUMERITY-diroximel-fumarate-for-Multiple-Sclerosis.html. Issued 10/30/2019. Last accessed 04/15/2020.

[6] Vumerity® Prescribing Information. Biogen, Inc. Available online at: https://www.vumerityhcp.com/content/dam/commercial/vumerity/hcp/en_us/pdf/vumerity-prescribing-information.pdf. Last revised 03/2020. Last accessed 04/15/2020.

Appendix G

Vote to Prior Authorize Qternmet® XR [Dapagliflozin/ Saxagliptin/Metformin Extended-Release (ER) Tablet], Riomet ER™ (Metformin ER Oral Suspension), Rybelsus® (Semaglutide Tablet), and Trijardy™ XR (Empagliflozin/Linagliptin/ Metformin ER Tablet) and Update the Anti-Diabetic Medications Prior Authorization Criteria

Oklahoma Health Care Authority
May 2020

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

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

- **Qternmet® XR (Dapagliflozin/Saxagliptin/Metformin ER Tablet):** In May 2019, the FDA approved Qternmet® XR (dapagliflozin/saxagliptin/metformin ER tablet) as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM). Qternmet® XR initiation is intended only for patients currently taking metformin. Qternmet® XR is a once-daily, oral drug compromised of dapagliflozin [a sodium-glucose cotransporter-2 (SGLT-2) inhibitor], saxagliptin [a dipeptidyl peptidase-4 (DPP-4) inhibitor], and metformin (a biguanide). Dapagliflozin and saxagliptin plus metformin has been studied in adult patients with T2DM inadequately controlled on metformin. Treatment with dapagliflozin and saxagliptin plus metformin (combination or add-on therapy) at all doses produced statistically significant improvements in hemoglobin A1c (HbA1c) compared to the active comparators (dapagliflozin/ placebo/metformin ER or placebo/saxagliptin/metformin ER) or placebo trial arms in combination with metformin. Qternmet® XR is supplied as an oral ER tablet in 4 strengths: 2.5mg/2.5mg/1,000mg, 5mg/2.5mg/1,000mg, 5mg/5mg/1,000mg, and 10mg/5mg/1,000mg dapagliflozin/saxagliptin/metformin ER tablet. Qternmet® XR should be taken orally, once daily in the morning with food. For patients not currently taking dapagliflozin, the recommended starting total daily dose of Qternmet® XR is 5mg dapagliflozin/5mg saxagliptin/1,000mg or 2,000mg metformin once daily. The maximum recommended daily dose is 10mg dapagliflozin/5mg saxagliptin/2,000mg metformin. Qternmet® XR cost and launch date information is not available at this time.
- **Riomet ER™ (Metformin ER Oral Suspension):** In August 2019, the FDA approved Riomet ER™ (metformin ER oral suspension) as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with T2DM. Riomet ER™ is the first ER oral suspension formulation of metformin. Other formulations of metformin are currently available, including immediate-release (IR) and ER tablets and an IR oral solution. Riomet ER™ is supplied as an ER oral suspension containing 47.31g of metformin for reconstitution in a 473mL bottle pack. The reconstituted suspension is 500mg/5mL. Riomet ER™ is available in strawberry and grape flavors. The starting dose is 500mg (5mL) orally once daily, with the evening meal.

The dose should be increased in increments of 500mg (5mL) weekly, up to a maximum dose of 2,000mg (20mL) once daily, with the evening meal. In patients with renal impairment, renal function with estimated glomerular filtration rate (eGFR) should be assessed prior to initiation. The estimated cost per year of Riomet ER™ oral suspension at the maximum dose of 2,000mg per day is $9,000.00. Comparatively, generic metformin 1,000mg IR oral tablet is estimated to cost $14.40 per year at the maximum dose of 2,000mg per day.

- **Rybelsus® (Semaglutide Tablet):** In September 2019, the FDA approved Rybelsus® (semaglutide tablet) as an adjunct to diet and exercise to improve glycemic control in adults with T2DM. Rybelsus® is the first and only glucagon-like peptide-1 (GLP-1) analog available as an oral tablet and is a new option for adults with T2DM who are not achieving their HbA1c goal with current anti-diabetic treatment. The approval of Rybelsus® is based on results from 10 PIONEER clinical trials, which enrolled 9,543 patients and included head-to-head studies of Rybelsus® vs. sitagliptin, empagliflozin, and liraglutide. In the trials, Rybelsus® reduced HbA1c and, as a secondary endpoint, showed reductions in body weight. The most common adverse reactions in the PIONEER trials, reported in ≥5% of patients, were nausea, abdominal pain, diarrhea, decreased appetite, vomiting, and constipation. Rybelsus® is supplied as an oral tablet in the following strengths: 3mg, 7mg, and 14mg. Patients should be instructed to take Rybelsus® at least 30 minutes before the first food, beverage, or other oral medications of the day with no more than 4 ounces of plain water only. Waiting <30 minutes, or taking with food, beverages (other than plain water), or other oral medications will lessen the effects of Rybelsus®. Waiting >30 minutes to eat may increase the absorption of Rybelsus®. The recommended starting dose is 3mg once daily for 30 days. After 30 days on the 3mg dose, the dose should be increased to 7mg once daily. The dose may be increased to 14mg once daily if additional glycemic control is needed after at least 30 days on the 7mg dose. Patients treated with once weekly Ozempic® (semaglutide subcutaneous injection) 0.5mg can be transitioned to Rybelsus® 7mg or 14mg. Patients can start Rybelsus® up to 7 days after their last injection of Ozempic®. There is no equivalent dose of Rybelsus® for Ozempic® 1mg. The estimated cost of Rybelsus® per year is $8,859.60 at the maximum dose of 14mg per day.
- **Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet):** In January 2020, the FDA approved Trijardy™ XR (empagliflozin/linagliptin/metformin ER tablet) as an adjunct to diet and exercise to improve glycemic control in adults with T2DM. Trijardy™ XR provides 3 T2DM medications in 1 tablet, including Jardiance® (empagliflozin), Tradjenta® (linagliptin), and metformin ER. The FDA approval of Trijardy™ XR is based on 2 randomized open-label trials that assessed the bioequivalence of empagliflozin, linagliptin, and metformin ER fixed-dose combination tablets and their individual components in healthy adults. The safety profile of Trijardy™ XR was found to be consistent with its individual components. Trijardy™ XR is not for patients who have severe kidney problems, end stage renal disease (ESRD), are on dialysis, have metabolic acidosis or diabetic ketoacidosis, or are allergic to empagliflozin, linagliptin, metformin, or any of the ingredients in Trijardy™ XR. There have been postmarketing reports of acute pancreatitis, including fatal pancreatitis, in patients taking linagliptin, a

component of Trijardy™ XR. Trijardy™ XR is supplied as an ER oral tablet in the following 4 strengths: 5mg/2.5mg/1,000mg, 10mg/5mg/1,000mg, 12.5mg/2.5mg/1,000mg, and 25mg/5mg/1,000mg empagliflozin/linagliptin/metformin ER tablet. Renal function should be assessed prior to the initiation of Trijardy™ XR and periodically thereafter. Trijardy™ XR starting dose should be individualized based on the patient's current regimen. The maximum recommended dose of Trijardy™ XR is 25mg empagliflozin/5mg linagliptin/2,000mg metformin ER. The estimated cost per year of Trijardy™ XR is $6,721.20 based on the maximum FDA recommended dose of Trijardy™ XR 25mg empagliflozin/5mg linagliptin/2,000mg metformin ER [(2) Trijardy™ XR 12.5mg/2.5mg/1,000mg ER tablets] once daily.

New FDA Approved Indication(s):

- **Invokana® (Canagliflozin Tablet):** In September 2019, the FDA approved Invokana® (canagliflozin tablet) to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine (sCr), cardiovascular (CV) death, and hospitalization for heart failure (HF) in adults with T2DM and diabetic nephropathy with albuminuria >300mg/day. Invokana® is also approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM and to reduce the risk of major adverse CV events [CV death, non-fatal myocardial infarction (MI), and non-fatal stroke] in adults with T2DM and established CV disease. The approval of Invokana® for the new indication was based on CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation), a randomized, double-blind trial in 4,401 patients with T2DM, an eGFR ≥30 to <90mL/min/1.73m^2, and albuminuria who were receiving standard of care. Patients received Invokana® or placebo. The primary composite endpoint was the time to first occurrence of ESKD (defined as an eGFR <15mL/min/1.73m^2, initiation of chronic dialysis, or renal transplant), doubling of sCr, and renal or CV death. Invokana® significantly reduced the risk of the primary composite endpoint based on a time-to-event analysis [hazard ratio (HR): 0.70; 95% confidence interval (CI): 0.59, 0.82; P<0.0001]. The treatment effect reflected a reduction in progression to ESKD, doubling of sCr, and CV death. Invokana® also significantly reduced the risk of hospitalization for HF (HR: 0.61; 95% CI: 0.47, 0.80; P<0.001). In addition to the approval of this new indication, the warning for increases in low-density lipoprotein cholesterol (LDL-C) was removed from the *Warnings and Precautions* section of the Invokana® label. The Invokana® label carries a *Boxed Warning* for lower limb amputation. The recommended dose of Invokana® for all indications is based on eGFR. In patients with eGFR ≥60mL/min/1.73m^2, the recommended initial dose is 100mg once daily, taken before the first meal of the day. The dose can be increased to 300mg once daily for additional glycemic control. In patients with eGFR 30 to <60mL/min/1.73m^2, the recommended dose is 100mg once daily.
- **Farxiga® (Dapagliflozin Tablet):** In October 2019, the FDA approved Farxiga® (dapagliflozin tablet) to reduce the risk of hospitalization for HF in adults with T2DM and multiple CV risk factors or established CV disease. The decision is based on the results from the DECLARE (Dapagliflozin Effect on Cardiovascular Events)-TIMI 58 trial, the largest CV outcomes trial (CVOT) conducted in a broad patient population for an SGLT-2

inhibitor to date. DECLARE-TIMI 58 showed that Farxiga® significantly reduced the risk of the primary composite endpoint of hospitalization for HF or CV death versus placebo by 17% (4.9% vs. 5.8%; HR: 0.83; 95% CI: 0.73-0.95, P=0.005). This finding was driven by a significant 27% reduction in the risk of hospitalization for HF (2.5% vs. 3.3%; HR: 0.73; 95% CI: 0.61, 0.88). The treatment benefit was consistent across patient subgroups. The full results of the DECLARE-TIMI 58 trial were published in *The New England Journal of Medicine* in January 2019.

Recommendations

The College of Pharmacy recommends the following changes to the Anti-Diabetic Medications Product Based Prior Authorization (PBPA) category:

1. Update the Anti-Diabetic Medications Approval Criteria as shown in red to reflect the recent FDA approved indications
2. Place Rybelsus® (semaglutide tablet) into Tier-3 of the Anti-Diabetic Medications PBPA category
    a. Current Tier-3 criteria will apply
3. Place Qternmet® XR (dapagliflozin/saxagliptin/metformin ER tablet), Riomet ER™ (metformin ER oral suspension), and Trijardy™ XR (empagliflozin/linagliptin/metformin ER tablet) in the Special Prior Authorization (PA) Tier of the Anti-Diabetic Medications PBPA category
    a. Current Special PA Tier criteria will apply

Anti-Diabetic Medications Tier-2 Approval Criteria:

1. A trial of 1 Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier-2 medications may be approved based on current American Association of Clinical Endocrinologists (AACE) or American Diabetes Association (ADA) guidelines.
3. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (T2DM) and CV disease for patients with the diagnosis of T2DM at high risk for CV events. Tier structure rules for this indication will apply.
4. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of end-stage kidney disease, worsening of kidney function, CV death, and hospitalization for heart failure (HF) in adults with T2DM and diabetic kidney disease. Tier structure rules for this indication will apply.
5. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of hospitalization for HF in adults with T2DM and other CV risk factors. Tier structure rules for this indication will apply.

Anti-Diabetic Medications Tier-3 Approval Criteria:

1. Member must have tried 1 Tier-2 medication in the same category and have a documented clinical reason why the Tier-2 medication is not appropriate (for Tier-3

medications that do not have a similar category in Tier-2, a medication from any category in Tier-2 may be used).

2. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (T2DM) and CV disease for patients with the diagnosis of T2DM at high risk for CV events. Tier structure rules for this indication will apply.
3. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of end-stage kidney disease, worsening of kidney function, CV death, and hospitalization for heart failure (HF) in adults with T2DM and diabetic kidney disease. Tier structure rules for this indication will apply.
4. A clinical exception will apply for medications with an FDA approved indication to reduce the risk of hospitalization for HF in adults with T2DM and other CV risk factors. Tier structure rules for this indication will apply.

Anti-Diabetic Medications Special Prior Authorization (PA) Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least 3 other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member; and
2. Use of Invokamet® XR [canagliflozin/metformin extended-release (ER)] or Jentadueto® XR (linagliptin/metformin ER) will require a patient-specific, clinically significant reason why the member cannot take the immediate-release formulation(s); and
3. Use of Bydureon® BCise™ (exenatide ER autoinjector pen) will require a patient-specific, clinically significant reason the member cannot use the vial or pen formulation.

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors			
acarbose (**Precose®**)		miglitol (**Glyset®**)	
Biguanides			
metformin (**Glucophage®**)			metformin ER (**Fortamet®**, **Glumetza®**)
metformin SR (**Glucophage XR®**)			metformin solution (**Riomet®**)
metformin/glipizide (**Metaglip®**)			**metformin ER suspension (Riomet ER™)**
metformin/glyburide (**Glucovance®**)			
DPP-4 Inhibitors			
	linagliptin (**Tradjenta®**)	alogliptin (**Nesina®**)	linagliptin/metformin ER (**Jentadueto® XR**)
	linagliptin/metformin (**Jentadueto®**)	alogliptin/metformin (**Kazano®**)	
	sitagliptin (**Januvia®**)	alogliptin/pioglitazone (**Oseni®**)	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
	sitagliptin/metformin (**Janumet®**)	saxagliptin (**Onglyza®**)	
	sitagliptin/ metformin ER (**Janumet XR®**)	saxagliptin/metformin (**Kombiglyze®**, **Kombiglyze XR®**)	
DPP-4/SGLT-2 Inhibitors			
	empagliflozin/ linagliptin (**Glyxambi®**)	dapagliflozin/saxagliptin (**Qtern®**)	
		ertugliflozin/sitagliptin (**Steglujan™**)	
Dopamine Agonists			
		bromocriptine (**Cycloset®**)	
Glinides			
repaglinide (**Prandin®**)	nateglinide (**Starlix®**)		
	repaglinide/ metformin (**Prandimet®**)		
GLP-1 Agonists			
	exenatide (**Byetta®**)	albiglutide (**Tanzeium™**)	exenatide ER autoinjector (**Bydureon® BCise™**)
	exenatide ER (**Bydureon®**)	dulaglutide (**Trulicity®**)	
	liraglutide (**Victoza®**)	lixisenatide (**Adlyxin®**)	
		semaglutide sub-Q injection (**Ozempic®**)	
		semaglutide oral tablet (Rybelsus®)	
GLP-1 Agonists/Insulin			
		insulin degludec/ liraglutide (**Xultophy® 100/3.6**)+	
		insulin glargine/ lixisenatide (**Soliqua® 100/33**)+	
SGLT-2 Inhibitors			
	dapaglifilozin (**Farxiga®**)	canagliflozin (**Invokana®**)	canagliflozin/metformin ER (**Invokamet® XR**)
	dapaglifilozin/ metformin ER (**Xigduo® XR**)	canagliflozin/metformin (**Invokamet®**)	
	empagliflozin (**Jardiance®**)	ertugliflozin (**Steglatro™**)	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
	empagliflozin/ metformin (**Synjardy®**)	ertugliflozin/metformin (**Segluromet™**)	
	empagliflozin/ metformin ER (**Synjardy® XR**)		
SGLT-2/DPP-4 Inhibitors/Biguanides			
			dapagliflozin/saxagliptin/ metformin ER (Qternmet® XR)
			empagliflozin/linagliptin/ metformin ER (Trijardy™ XR)
Sulfonylureas			
chlorpropamide (**Diabinese®**)			
glimepiride (**Amaryl®**)			
glipizide (**Glucotrol®**)			
glipizide SR (**Glucotrol XL®**)			
glyburide (**Diabeta®**)			
glyburide micronized (**Micronase®**)			
tolbutamide (**Orinase®**)			
Thiazolidinediones			
pioglitazone (**Actos®**)		pioglitazone/glimepiride (**Duetact®**)	
		pioglitazone/metformin (**Actoplus Met®**, **Actoplus Met XR®**)	
		rosiglitazone (**Avandia®**)	
		rosiglitazone/glimepiride (**Avandaryl®**)	
		rosiglitazone/metformin (**Avandamet®**)	

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

[+]Unique criteria applies.

PA = prior authorization; SR = sustained-release; ER = extended-release; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium-glucose cotransporter-2; Sub-Q = subcutaneous

[1] Qternmet® XR Prescribing Information. AstraZeneca. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210874s000lbl.pdf. Last revised 05/2019. Last accessed 04/15/2020.
[2] Qternmet® XR (dapagliflozin/saxagliptin/metformin) - New Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_qternmetxr_2019-0506.pdf. Issued 2019. Last accessed 04/15/2020.
[3] Riomet ER™ Prescribing Information. Sun Pharmaceutical Industries, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212595s000lbl.pdf. Last revised 08/2019. Last accessed 04/15/2020.
[4] Riomet ER™ (metformin) - New Formulation Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_riometer_2019-0830.pdf. Issued 2019. Last accessed 04/15/2020.
[5] Rybelsus™ Prescribing Information. Novo Nordisk. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/213051s000lbl.pdf. Last revised 09/2019. Last accessed 04/15/2020.
[6] Rybelsus® (semaglutide) – New Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_rybelsus_2019-0920.pdf. Issued 2019. Last accessed 04/15/2020.
[7] Trijardy™ XR Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc. Available online at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Trijardy%20XR/Trijardy%20XR.pdf?DMW_FORMAT=pdf. Last revised 01/2020. Last accessed 04/15/2020.
[8] Trijardy™ XR (empagliflozin/linagliptin/metformin) – New Drug Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_trijardyxr_2020-0129.pdf. Issued 2020. Last accessed 04/15/2020.
[9] Invokana® (canagliflozin) - New Indication. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/clinical-updates/clinicalupdates_Invokana_2019-0930.pdf. Issued 2019. Last accessed 04/15/2020.
[10] AstraZeneca. Farxiga Approved in the US to Reduce the Risk of Hospitalization for Heart Failure in Patients with Type 2 Diabetes. Available online at: https://www.astrazeneca-us.com/content/az-us/media/press-releases/2019/farxiga-approved-in-the-US-to-reduce-the-risk-of-hospitalization-for-heart-failure-in-patients-with-type-2-diabetes-10212019.html. Issued 10/21/2019. Last accessed 04/15/2020.

Appendix H

Vote to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat)

Oklahoma Health Care Authority
May 2020

Introduction[1,2]

- **January 2020:** The U.S. Food and Drug Administration (FDA) approved Ayvakit™ (avapritinib) for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumors (GIST) harboring a platelet-derived growth factor receptor alpha (*PDGFRA*) exon 18 mutation, including D842V mutations.
- **January 2020:** The FDA granted accelerated approval to Tazverik™ (tazemetostat) for the treatment of adults and pediatric patients 16 years of age or older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
- **January 2020:** The FDA approved Bynfezia Pen™ (octreotide) for the treatment of adult patients with severe diarrhea and flushing episodes associated with metastatic carcinoid tumors, for the treatment of adult patients with profuse watery diarrhea associated with vasoactive intestinal peptide-secreting tumors (VIPomas), and to reduce blood levels of growth hormone and insulin-like growth factor 1 (somatomedin C) in adult patients with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.

Product Summaries[3,4,5]

Ayvakit™ (Avapritinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adults with unresectable or metastatic GIST harboring a *PDGFRA* exon 18 mutation, including *PDGFRA* D842V mutations
- **How Supplied:** 100mg, 200mg, and 300mg oral tablets
- **Dose:** 300mg taken orally once daily; alternative strengths available for dose reductions/modifications if adverse reactions occur
- **Cost:** Wholesale Acquisition Cost (WAC) of $1,066.67 per tablet for all available strengths (100mg, 200mg, and 300mg); $32,000.10 per 30 days based on the FDA recommended dose of 300mg once daily

Bynfezia Pen™ (Octreotide):

- **Therapeutic Class:** Somatostatin analogue
- **Indication(s):**
  - Treatment of adults with severe diarrhea/flushing episodes associated with metastatic carcinoid tumors
  - Treatment of adult patients with profuse watery diarrhea associated with VIPomas

    - To reduce blood levels of growth hormone and insulin-like growth factor 1 (somatomedin C) in adult patients with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses
- **How Supplied:** 2,500mcg/mL octreotide as a 2.8mL single-patient-use pen for subcutaneous (sub-Q) injection
- **Dose:**
    - Acromegaly: Initiate dosage at 50mcg 3 times daily; typical dosage is 100mcg 3 times daily
    - Carcinoid Tumors: 100-600mcg daily in 2-4 divided doses for first 2 weeks
    - VIPomas: 200-300mcg daily in 2-4 divided doses for first 2 weeks
- **Cost:** Cost information for Bynfezia Pen™ is not yet available

Tazverik™ (Tazemetostat):

- **Therapeutic Class:** Methyltransferase inhibitor
- **Indication(s):** Treatment of adults and pediatric patients 16 years of age or older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection
- **How Supplied:** 200mg oral tablets
- **Dose:** 800mg taken orally twice daily
- **Cost:** WAC of $64.58 per 200mg tablet; $15,499.20 per 30 days based on the FDA recommended dose of 800mg twice daily

Recommendations

- The prior authorization of Ayvakit™ (avapritinib), Tazverik™ (tazemetostat), and Bynfezia Pen™ (octreotide) with the following criteria listed in red:

Ayvakit™ (Avapritinib) Approval Criteria [Gastrointestinal Stromal Tumor (GIST) Diagnosis]:

1. A diagnosis of unresectable or metastatic GIST in adult members; and
2. Member has a *PDGFRA* exon 18 mutation (including *PDGFRA* D842V mutations).

Tazverik™ (Tazemetostat) Approval Criteria [Epithelioid Sarcoma Diagnosis]:

1. A diagnosis of metastatic or locally advanced epithelioid sarcoma; and
2. Member is not eligible for complete resection; and
3. Member must be 16 years of age or older.

Bynfezia Pen™ (Octreotide) Approval Criteria [Metastatic Carcinoid Tumor or Vasoactive Intestinal Peptide-Secreting Tumors (VIPoma) Diagnosis]:*

1. A diagnosis of advanced metastatic carcinoid tumor or VIPoma; and
2. Presence of severe diarrhea or flushing; and
3. A patient-specific, clinically significant reason why the member cannot use other available short-acting injectable formulations of octreotide must be provided.

Bynfezia Pen™ (Octreotide) Approval Criteria [Acromegaly Diagnosis]:*

1. A diagnosis of acromegaly; and

2. Documentation of inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses; and
3. A patient-specific, clinically significant reason why the member cannot use other available short-acting injectable formulations of octreotide must be provided.

[*The College of Pharmacy will monitor Bynfezia Pen™ (octreotide) pricing as it becomes available and assess prior authorization status based on cost-effectiveness compared to other available short-acting octreotide formulations.]

[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 04/06/2020. Last accessed 04/07/2020.

[2] Bynfezia Pen™ (Octreotide Acetate) – New drug approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_bynfezia_2020-0203.pdf. Issued 01/2020. Last accessed 04/07/2020.

[3] Ayvakit™ Prescribing Information. Blueprint Medicines Corporation. Available online at: https://www.blueprintmedicines.com/uspi/AYVAKIT.pdf. Last revised 01/2020. Last accessed 04/07/2020.

[4] Bynfezia Pen™ Prescribing Information. Sun Pharmaceutical Industries, Inc. Available online at: https://bynfeziapen.com/BYNFEZIAPEN_PI.pdf. Last revised 01/2020. Last accessed 04/07/2020.

[5] Tazverik™ Prescribing Information. Epizyme, Inc. Available online at: https://www.tazverik.com/prescribing-information.pdf. Last revised 01/2020. Last accessed 04/07/2020.

Appendix I

Vote to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr)

Oklahoma Health Care Authority
May 2020

Introduction[1,2]

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

- **September 2017:** The FDA granted accelerated approval to Aliqopa™ (copanlisib) for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least 2 prior systemic therapies.
- **June 2019:** The FDA granted accelerated approval to Polivy™ (polatuzumab vedotin-piiq), a CD79b-directed antibody-drug conjugate indicated in combination with bendamustine and a rituximab product for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least 2 prior therapies.
- **July 2019:** The FDA approved Ruxience™ (rituximab-pvvr), a biosimilar to Rituxan® (rituximab), for the treatment of adult patients with non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).
- **November 2019:** The FDA granted accelerated approval to Brukinsa™ (zanubrutinib) for the treatment of mantle cell lymphoma (MCL) for adult patients who have received at least 1 prior therapy.

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

- **January 2020:** The FDA approved Keytruda® (pembrolizumab) for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Product Summaries[3,4,5,6]

Aliqopa™ (Copanlisib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with relapsed FL who have received at least 2 prior systemic therapies
- **How Supplied:** 60mg lyophilized solid in a single-dose vial (SDV)
- **Dose:** 60mg intravenously (IV) on days 1, 8, and 15 of a 28-day treatment cycle on an intermittent schedule (3 weeks on, 1 week off)
- **Cost:** Wholesale Acquisition Cost (WAC) of $4,665.28 per SDV; $13,995.84 per 28 days based on FDA recommended dosing

Brukinsa™ (Zanubrutinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with MCL who have received at least 1 prior therapy
- **How Supplied:** 80mg oral capsules
- **Dose:** 160mg orally twice daily or 320mg orally once daily
- **Cost:** WAC of $107.79 per 80mg capsule; $12,934.80 per 30 days based on FDA recommended dosing of 160mg twice daily or 320mg once daily

Polivy™ (Polatuzumab Vedotin-piiq):

- **Therapeutic Class:** CD79b-directed antibody-drug conjugate
- **Indication(s):** For use in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, after at least 2 prior therapies
- **How Supplied:** 140mg lyophilized powder in a SDV
- **Dose:** 1.8mg/kg IV every 21 days for 6 cycles
- **Cost:** WAC of $15,000 per SDV; cost will vary due to weight-based dosing

Ruxience™ (Rituximab-pvvr):

- **Therapeutic Class:** CD20-directed cytolytic antibody; biosimilar to Rituxan® (rituximab)
- **Indication(s):** Treatment of adult patients with NHL, CLL, and GPA/MPA
- **How Supplied:** 100mg/10mL or 500mg/50mL solution for IV infusion in a SDV
- **Dose:**
  - NHL: 375mg/m^2 IV infusion; *refer to Ruxience™ Prescribing Information for dosing schedules specific to type of NHL being treated*
  - CLL: 375mg/m^2 in the first cycle and 500mg/m^2 in cycles 2 through 6, in combination with fludarabine and cyclophosphamide (FC), administered every 28 days
  - GPA and MPA: For induction, 375mg/m^2 once weekly for 4 weeks with glucocorticoids; then (2) 500mg IV infusions separated by 2 weeks; then 500mg every 6 months thereafter
- **Cost:** WAC of $71.68 per mL; cost will vary depending on patient weight, diagnosis, and treatment duration

Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications; changes can be seen in the following criteria listed in red (only criteria with updates are listed)
- The prior authorization of Aliqopa™ (copanlisib), Brukinsa™ (zanubrutinib), Polivy™ (polatuzumab vedotin-piiq), and Ruxience™ (rituximab-pvvr) with the following criteria listed in red

Aliqopa™ (Copanlisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of relapsed/refractory FL; and
2. Member must have failed at least 2 prior systemic therapies.

Brukinsa™ (Zanubrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. Adult members with a diagnosis of MCL; and
2. Member must have received at least 1 prior therapy.

Keytruda® (Pembrolizumab) Approval Criteria [Non-Muscle Invasive Bladder Cancer (NMIBC) Diagnosis]:

1. A diagnosis of high-risk, NMIBC; and
2. Member must have failed therapy with Bacillus Calmette-Guerin (BCG)-therapy; and
3. Member must be ineligible for or has elected not to undergo cystectomy.

Polivy™ (Polatuzumab Vedotin-piiq) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade B-Cell Lymphoma Diagnosis]:

1. Relapsed/refractory DLBCL or high grade B-cell lymphoma after at least 2 prior therapies; and
2. Used in combination with bendamustine and rituximab; and
3. Member is not a candidate for transplant.

Ruxience™ (Rituximab-pvvr) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Rituxan® (rituximab) must be provided.

---

[1] U.S. Food and Drug Administration (FDA): Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 04/06/2020. Last accessed 04/07/2020.

[2] Pfizer. FDA Approves Pfizer's Biosimilar, Ruxience™ (rituximab-pvvr), for Certain Cancers and Autoimmune Conditions. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/fda_approves_pfizer_s_biosimilar_ruxience_rituximab_pvvr_for_certain_cancers_and_autoimmune_conditions. Issued 07/23/2019. Last accessed 04/07/2020.

[3] Aliqopa™ Prescribing Information. Bayer Healthcare Pharmaceuticals. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Aliqopa_PI.pdf. Last revised 02/2020. Last accessed 04/07/2020.

[4] Brukinsa™ Prescribing Information. BeiGene. Available online at: https://www.brukinsa.com/prescribing-information.pdf. Last revised 11/2019. Last accessed 04/07/2020.

[5] Polivy™ Prescribing Information. Genentech. Available online at: https://www.gene.com/download/pdf/polivy_prescribing.pdf. Last revised 06/2019. Last accessed 04/07/2020.

[6] Ruxience™ Prescribing Information. Pfizer. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=12090. Last revised 07/2019. Last accessed 04/07/2020.

Appendix J

Vote to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™ (Bevacizumab-bvzr)

Oklahoma Health Care Authority
May 2020

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

New U.S. Food and Drug Administration (FDA) Approvals and Label Update(s):

- **March 2019:** The FDA approved Zykadia® (ceritinib) tablet formulation for the treatment of adults with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive. Zykadia® capsule formulation was approved by the FDA in 2014 for the same indication. The approval of the Zykadia® tablet formulation was based on studies conducted with Zykadia® capsules. The recommended dosing for the tablet formulation is the same as the capsule formulation, 450mg orally once daily. The Zykadia® capsule formulation has been discontinued.
- **June 2019:** The FDA approved Zirabev™ (bevacizumab-bvzr), a biosimilar to Avastin® (bevacizumab), for the treatment of 5 types of cancer: metastatic colorectal cancer; unresectable, locally advanced, recurrent, or metastatic non-squamous NSCLC; recurrent glioblastoma; metastatic renal cell carcinoma (RCC); and persistent, recurrent, or metastatic cervical cancer.
- **August 2019:** The FDA approved Rozlytrek® (entrectinib) for the treatment of adults with NSCLC whose tumors are *ROS1*-positive. Additionally, Rozlytrek® was granted accelerated approval by the FDA for the treatment of adults and pediatric patients 12 years of age and older with solid tumors that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have progressed following treatment or have no satisfactory standard therapy.
- **December 2019:** The FDA approved Tecentriq® (atezolizumab) in combination with paclitaxel (protein-bound) and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no epidermal growth factor receptor (EGFR) or ALK genomic tumor aberrations.
- **February 2020:** The FDA approved Pemfexy™ (pemetrexed), a branded alternative to Alimta®, for the treatment of locally advanced or metastatic non-squamous NSCLC in combination with cisplatin; locally advanced or metastatic non-squamous NSCLC whose disease has not progressed after 4 cycles of platinum-based first-line chemotherapy, as maintenance treatment; locally advanced or metastatic non-squamous NSCLC after prior chemotherapy as a single agent; and malignant pleural mesothelioma in patients with unresectable disease or who are otherwise not candidates for curative surgery in combination with cisplatin. The FDA gave tentative approval for Pemfexy™ in 2018, but due to litigation over patent issues (with the manufacturer of Alimta®), a settlement was not reached until December 2019. The final FDA approval in 2020 allows for initial

limited entry of Pemfexy™ into the market on February 1, 2022, with an uncapped entry on April 1, 2022.

- **March 2020:** The FDA approved Imfinzi® (durvalumab) in combination with etoposide and either carboplatin or cisplatin as first-line treatment of patients with extensive-stage small cell lung cancer (SCLC).

Product Summaries[6,7,8]

Pemfexy™ (Pemetrexed):

- **Therapeutic Class:** Folate analog metabolic inhibitor
- **Indication(s):**
  - In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic non-squamous NSCLC
  - As a single agent for the maintenance treatment of patients with locally advanced or metastatic non-squamous NSCLC whose disease has not progressed after 4 cycles of platinum-based first-line chemotherapy
  - As a single agent for the treatment of patients with recurrent, metastatic non-squamous NSCLC after prior chemotherapy
  - In combination with cisplatin for the initial treatment, of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery
- **How Supplied:** 500mg/20mL intravenous (IV) solution in a single-dose vial (SDV)
- **Dose:** 500mg/m^2 as an IV infusion on day 1 of each 21-day cycle; *refer to Pemfexy™ Prescribing Information for diagnosis-specific dosing regimens*
- **Cost:** Cost information for Pemfexy™ is not yet available

Rozlytrek® (Entrectinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Treatment of adult patients with metastatic NSCLC whose tumors are *ROS1*-positive
  - Treatment of adults and pediatric patients 12 years of age and older with solid tumors that have a NTRK gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have progressed following treatment or have no satisfactory standard therapy
- **How Supplied:** 100mg and 200mg oral capsules
- **Dose:**
  - *ROS1*-positive NSCLC: 600mg orally once daily
  - NTRK gene fusion-positive solid tumors:
    - Adults: 600mg orally once daily
    - Pediatric Patients 12 Years of Age and Older: Dosing based on body surface area (BSA):
      - BSA >1.5m^2: 600mg once daily

        - BSA 1.11 to 1.5m^2: 500mg once daily
        - BSA 0.91 to 1.10m^2: 400mg once daily
    - **Cost:** Wholesale Acquisition Cost (WAC) of $186.67 for either 100mg or 200mg capsule; cost will vary based on diagnosis

Zirabev™ (Bevacizumab-bvzr):

- **Therapeutic Class:** Vascular endothelial growth factor inhibitor; a biosimilar to Avastin®
- **Indication(s):**
    - The treatment of metastatic colorectal cancer
    - The treatment of unresectable, locally advanced, recurrent, or metastatic non-squamous NSCLC
    - Treatment of recurrent glioblastoma
    - Treatment of metastatic RCC
    - Treatment of persistent, recurrent, or metastatic cervical cancer
- **How Supplied:** 100mg/4mL or 400mg/16mL solution for IV infusion in SDVs
- **Dose:** Recommended dosing ranges from 5mg/kg every 2 weeks to 15mg/kg every 3 weeks; *refer to Zirabev™ Prescribing Information for diagnosis-specific dosing regimens*
- **Cost:** WAC of $153.35 per milliliter resulting in a cost of $613.40 for a 100mg/4mL SDV and $2,453.60 for a 400mg/16mL SDV; cost of total regimen will vary based on weight and diagnosis

Recommendations

- The prior authorization of Pemfexy™ (pemetrexed), Rozlytrek® (entrectinib), and Zirabev™ (bevacizumab-bvzr) with the following criteria listed in red
- Updating the prior authorization criteria for Imfinzi® (durvalumab) and Tecentriq® (atezolizumab) to reflect new FDA approved indications; changes and new criteria noted in red (only criteria with updates are listed)

Pemfexy™ (Pemetrexed) Approval Criteria:[¥]

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason the member cannot use Alimta® (pemetrexed) must be provided.

[¥The College of Pharmacy will monitor Pemfexy™ (pemetrexed) pricing as it becomes available and assess prior authorization status based on cost-effectiveness compared to Alimta® (pemetrexed).]

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

1. Diagnosis of metastatic NSCLC; and
2. *ROS1*-positive.

Rozlytrek® (Entrectinib) Approval Criteria [Solid Tumor Diagnosis]:

1. Diagnosis of solid tumors; and
2. Member must be 12 years of age or older; and
3. Neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation; and

4. Metastatic or not a surgical candidate; and
5. Progressed following treatment or have no satisfactory alternative therapy.

Zirabev™ (Bevacizumab-bvzr) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Avastin® (bevacizumab) must be provided.

Imfinzi® (Durvalumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of extensive-stage SCLC; and
2. In combination with etoposide and either cisplatin or carboplatin followed by single-agent maintenance.

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

1. A diagnosis of non-squamous NSCLC; and
    a. First-line therapy for metastatic disease; and
    b. The member does not have epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutations; and
    c. In combination with bevacizumab, paclitaxel, and carboplatin (maximum of 6 cycles) or in combination with paclitaxel (protein bound) and carboplatin; and
    d. Atezolizumab and bevacizumab may be continued after the above combination in members without disease progression (applies to the bevacizumab/paclitaxel/ carboplatin regimen); or
2. A diagnosis of NSCLC; and
    a. Subsequent therapy for metastatic disease; and
    b. As a single-agent only.

---

[1] Zykadia® (Ceritinib) – New Formulation Approval. *OptumRx*. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_zykadia_2019-0320.pdf. Issued 03/2019. Last accessed 04/08/2020.

[2] Pfizer. Pfizer Receives U.S. FDA Approval for Its Oncology Biosimilar, Zirabev™ (bevacizumab-bvzr). Available online at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer_receives_u_s_fda_approval_for_its_oncology_biosimilar_zirabev_bevacizumab_bvzr. Issued 06/28/2019. Last accessed 04/08/2020.

[3] U. S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Last revised 04/06/2020. Last accessed 04/09/2020.

[4] Eagle Pharmaceuticals. Eagle Pharmaceuticals Receives Final FDA Approval for Pemfexy™ (Pemetrexed for Injection). *Business Wire*. Available online at: https://www.businesswire.com/news/home/20200210005518/en/Eagle-Pharmaceuticals-Receives-Final-FDA-Approval-PEMFEXY%E2%84%A2. Issued 02/10/2020. Last accessed 04/08/2020.

[5] Terry M. After Settlement with Lilly, Eagle Pharma Gets Pemfexy Go-Ahead from FDA. *BioSpace*. Available online at: https://www.biospace.com/article/fda-greenlights-eagle-pharma-s-pemfexy-for-lung-cancer/. Issued 02/11/2020. Last accessed 04/08/2020.

[6] Pemfexy™ Prescribing Information. Eagle Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209472s000lbl.pdf. Last revised 02/2020. Last accessed 04/08/2020.

[7] Rozlytrek® Prescribing Information. Genentech. Available online at: https://www.gene.com/download/pdf/rozlytrek_prescribing.pdf. Last revised 08/2019. Last accessed 04/08/2020.

[8] Zirabev™ Prescribing Information. Pfizer. Available online at: https://labeling.pfizer.com/ShowLabeling.aspx?id=11860. Last revised 01/2020. Last accessed 04/08/2020.

Appendix K

Calendar Year 2019 Annual Review of Balversa™ (Erdafitinib)

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria

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.

Utilization of Balversa™ (Erdafitinib): Calendar Year 2019

There was no SoonerCare utilization of Balversa™ (erdafitinib) during calendar year 2019.

Prior Authorization of Balversa™ (Erdafitinib)

There were no prior authorization requests submitted for Balversa™ (erdafitinib) during calendar year 2019.

Market News and Updates[1,2]

Anticipated Patent Expiration(s):

- Balversa™ (erdafitinib): March 2035

Pipeline:

- **Infigratinib:** In January 2020, QED Therapeutics began enrollment in a Phase 3 trial designed to investigate the efficacy and safety of infigratinib versus placebo as adjuvant therapy in patients with high-risk invasive urothelial carcinoma and fibroblast growth factor receptor 3 (*FGFR3*) alterations. This Phase 3 trial, PROOF 302, is a randomized, double-blind, placebo-controlled trial. Adult patients with high-risk invasive upper tract urothelial carcinoma (UTUC) or urothelial bladder carcinoma (UBC) with *FGFR3* genetic alterations who are ≤120 days following surgical resection and ineligible for cisplatin-based adjuvant chemotherapy or with residual disease after cisplatin-based neoadjuvant therapy (NAT) are eligible for the trial. Those who received non cisplatin-based NAT are eligible if they have residual disease and are ineligible for adjuvant cisplatin. Eligible patients will receive oral infigratinib 125mg or placebo (1:1 ratio) once daily on days 1 through 21 every 28 days for up to 52 weeks or until disease recurrence, unacceptable toxicity, or death. The primary endpoint is centrally reviewed disease-free survival (DFS).

Recommendations

No changes are recommended to the current Balversa™ (erdafitinib) prior authorization criteria at this time.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 04/2020. Last accessed 04/08/2020.
[2] Pal SK, Daneshmand S, Matin SF, et al. PROOF 302: A Randomized, Double-Blind, Placebo-Controlled, Phase III Trial of Infigratinib as Adjuvant Therapy in Patients with Invasive Urothelial Carcinoma Harboring FGFR3 Alterations. *Journal of Clinical Oncology* 2020; 38(6):TPS600-TPS600.

Appendix L

Fiscal Year 2019 Annual Review of the SoonerCare Pharmacy Benefit

Oklahoma Health Care Authority
May 2020

Summary[1,2,3,4]

During State Fiscal Year (SFY) 2019 (July 1, 2018 to June 30, 2019), prescription drugs accounted for $555 million of the approximate $5.47 billion in total SoonerCare funding. According to the Centers for Medicare and Medicaid Services (CMS), the national health expenditure is projected to grow at an average rate of 5.4% annually, and Medicaid expenditures are expected to grow at a rate of 5.7% annually. Comparing SoonerCare pharmacy data from SFY 2018, the total reimbursement increased 2.2% from SFY 2018 to SFY 2019, less than the CMS-estimated Medicaid expenditure increases. The pharmacy cost per member per year (PMPY; total pharmacy cost per total members) increased from $532.52 in SFY 2018 to $556.64 in 2019, a 4.6% increase. Reimbursement increases per member can largely be attributed to the increase in cost per claim for specialty medications as well as an increase in the number of claims for specialty mediations. The specialty pharmaceutical products total pharmacy reimbursement has been on the incline as a result of orphan drug approvals for rare diseases and the high costs associated with these therapies. During SFY 2018, SoonerCare spent 42.6% of total pharmacy expenditures on 0.92% of claims for medications costing greater than $1,000 per claim and in SFY 2019, spent 45.3% of total pharmacy expenditures on 1.1% of claims for medications costing greater than $1,000 per claim. Claims costing greater than $1,000 per claim are largely specialty medications but may include some traditional claims.

Indian Health Service (IHS) reimbursement was updated in 2017 to the Federal Office of Management and Budget (OMB) encounter rate. In order to more accurately compare SFY 2019 with previous fiscal years, IHS data was excluded from the analysis.

Costs in this report do not reflect the federal and state supplemental rebates that are provided by medication manufacturers. Many products, particularly the anti-infective medications, attention-deficit/hyperactivity disorder (ADHD) medications, antipsychotic medications, endocrine medications, and pain medications are heavily influenced by supplemental rebates, and net costs are substantially lower than the total reimbursement to pharmacies included in this analysis.

Total Pharmacy State Fiscal Year (SFY) Comparison							
SFY	**Claims**	**Members**	**Utilizers***	**Reimbursement**	**Cost/Claim**	**Cost/Member**	**Cost/Day**
2017	5,897,218	1,014,983	541,021	$514,062,768	$87.17	$506.47	$3.40
2018	5,802,025	1,020,726	535,823	$543,569,067	$93.70	$532.62	$3.61
2019	5,508,417	998,209	516,569	$555,643,845	$100.87	$556.64	$3.80

*Total number of unduplicated utilizers.
Reimbursement does not reflect rebated costs or net costs.
State Fiscal Year = July 1 to June 30

The per member per year (PMPY) value reflects the total pharmacy cost divided by the unduplicated number of members (total enrollees) for each time period. In order to reflect an accurate PMPY value, average monthly enrollment is used in place of annual enrollment, and dual eligible (members eligible for Medicare and Medicaid) and IHS members are excluded. The PMPY value is used across benefit plans with similar populations to accurately assess health care spending. The following table contains the PMPY values for the past few years. Calendar year (CY) 2019 saw a 6.6% increase from CY 2018 in overall PMPY.

Calendar Year	CY 2017	CY 2018	CY 2019
Overall PMPY	$735	$803	$856

Oklahoma uses a fee-for-service (FFS) pharmacy benefit for the SoonerCare program, while many other states contract out the management of their Medicaid programs under capitated payment arrangements with managed care organizations (MCOs). Medicaid MCOs frequently subcontract the management of the pharmacy benefit to a separate pharmacy benefit manager (PBM); PBMs are also used by some states for their FFS pharmacy programs, contracting out services such as claims processing and payment, prior authorization processing, drug utilization review, and formulary management. The Oklahoma Health Care Authority (OHCA) currently contracts with Pharmacy Management Consultants (PMC), a department within the University of Oklahoma College of Pharmacy, for many of these services.

To measure the success of the SoonerCare pharmacy benefit management, Oklahoma's Medicaid statistics were compared to the Medicaid statistics of the largest PBM in the United States, Express Scripts (ESI). For CY 2018, ESI's Medicaid PMPY was $1,342 making it 67% higher than OHCA's $803. If OHCA had experienced the same PMPY as ESI for CY 2018, it would have cost over $371 million more than the $543 million OHCA spent in CY 2018. Similarly, for CY 2019, ESI's Medicaid PMPY was $1,373 making it 60% higher than OHCA's $856. At the ESI PMPY rate, it would have cost the OHCA over $373 million more than the $555 million spent during CY 2019 for pharmacy reimbursement.

Calendar Year	ESI	OHCA	Percent Difference
2017	$1,241	$735	69%
2018	$1,342	$803	67%
2019	$1,373	$856	60%

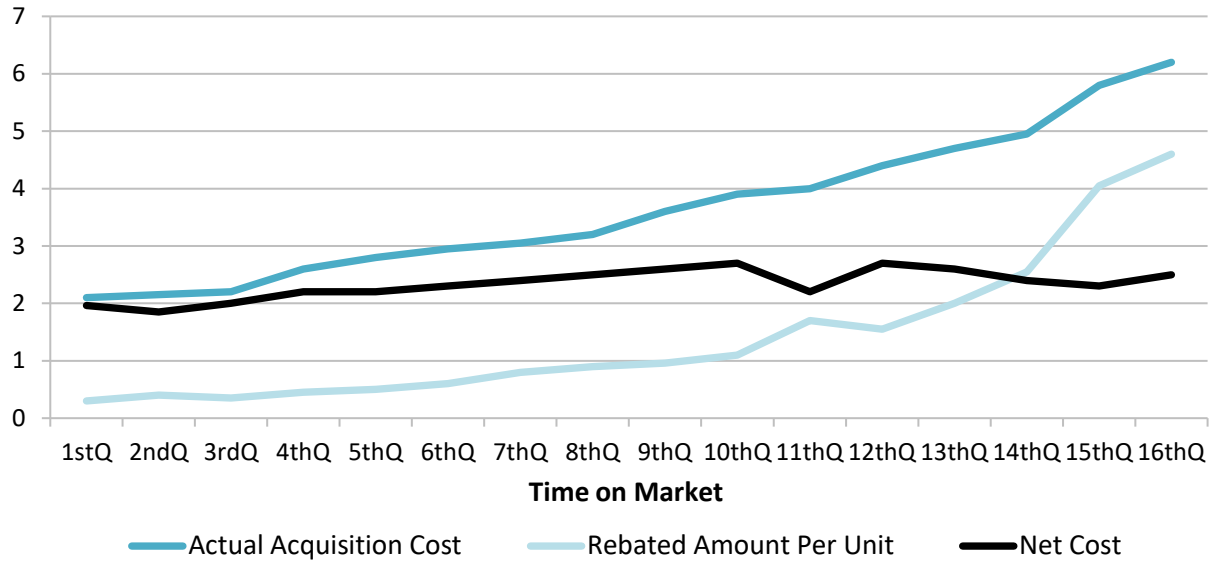
SoonerCare prior authorization policies, coupled with quantity limits and monthly prescription limits, yield better than average results while still providing a comprehensive pharmacy benefit for approximately 900,000 SoonerCare members. Looking at the cost to manage the pharmacy benefit, the OHCA pharmacy department has a cost of about $1 million. OHCA's partner, PMC, spent approximately $4.4 million of their contract in SFY 2019. As a return on investment (ROI), using the overage generated by the ESI PMPY rate, for CY 2018 the ROI is $74 to $1 and for CY 2019 it is $73 to $1.

Medicaid Drug Rebate Program[5,6,7]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Participation in the federal drug rebate

program requires Medicaid coverage with limited exceptions (e.g., cosmetic medications, fertility medications). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any commercial payer. Best prices are reported to CMS by the manufacturer, but are not publicly available.

If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices. Until the first quarter of 2017, the CPI penalty only applied to brand medications; following a Senate vote in October 2015, the Medicaid CPI penalty was extended to generic drugs with an effective date of January 1, 2017. Generic drugs became a concern of Congress after a letter to the Office of Inspector General noted that between July 2013 and June 2014, half of all generic drugs increased in price, 10% of which doubled during that time period. The cost increases found in this report do not reflect net cost increases. The following graph is an example of Medicaid net cost of a drug over time. As average wholesale price (AWP) increases, the rebated amount per unit (RAPU) increases as well resulting in minimal effect on net cost.



Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. In SFY 2019, OHCA collected $350 million in federal and state supplemental rebates, resulting in a total decrease from SFY 2018 ($351 million in federal and state rebates). These rebates are collected after reimbursement for the medication and are not reflected in this report.

Alternative Payment Models[8,9,10,11,12,13]

The introduction of a greater number of costly specialty medications, finite Medicaid budgets, Medicaid policy, and access requirements has resulted in alternative payment arrangements as particularly compelling opportunities. Medicaid programs must provide comprehensive care to vulnerable individuals while operating under limited budgets and regulatory requirements. An alternative payment model (APM) is an agreement between a payer and manufacturer that is

intended to provide improved patient care or increased access to evidence-based therapies while lowering costs or improving health outcomes. In general, there are 2 types of APMs:

- **Financial APM:** Caps or discounts are used to provide predictability or limit spending; these type of contracts are intended to lower costs and expand access. Data collection for financial APMs is minimal, making them easier to administer.
    - Examples: Price volume agreements, market share, patient level utilization caps, manufacturer funded treatment initiation
- **Health Outcome-Based APM:** Payments for medications are tied to clinical outcomes or measurements; these type of contracts are often referred to as "value-based contracts." Health outcome-based APMs require additional planning and data collection, but do have the potential to increase the quality and value of treatments.
    - Examples: Outcomes guarantee, conditional coverage, PMPY guarantees, event avoidance (e.g., hospitalizations)

Until recently, prescription drug value-based payment arrangements have not been initiated in Medicaid. Since October 2016, PMC and OHCA have been engaged in negotiations with pharmaceutical manufacturers regarding pharmacy value-based contracts. PMC and OHCA have initiated talks with more than 25 companies regarding APMs and have established APM contracts with 4 companies following CMS approval to participate in value-based payment arrangements in June 2018. Oklahoma was the first Medicaid state to receive approval from CMS to participate in value-based payment arrangements. Future considerations include the expectation that initial value-based contracts will set the precedent for further collaboration among manufacturers and state Medicaid agencies.

Overview of Executed Contracts	
Manufacturer	**Details**
Alkermes	Long-acting injectable antipsychotic; focus on adherence
Eisai	Antiepileptic medication; focus on reduction in hospitalizations
Janssen	Long-acting injectable antipsychotic; focus on population adherence (phase 1); phase 2 will include additional clinical outcomes
Collaboration Agreements: Amgen and Otsuka	Focus on population characterization to inform future value-based contracts

Drug Approval Trends[14,15,16]

During SFY 2019, the U.S. Food and Drug Administration (FDA) approved the first generic product of several key medications that may have a significant effect on SoonerCare reimbursement. The first generic for Onfi® (clobazam) was FDA approved in October 2018. Other key first-time generic approvals during SFY 2019 include Butrans® (buprenorphine transdermal patch) in November 2018, Elidel® (pimecrolimus 1% cream) and Advair® (fluticasone/salmeterol inhalation powder) in January 2019, and Latuda® (lurasidone tablet) in January 2019.

A total of 48 novel drugs were approved by the FDA during CY 2019. The active ingredient or ingredients in a novel drug have never before been approved in the United States. Of the novel

drugs approved, 19 were considered first-in-class and 34 were approved to treat rare or "orphan" diseases.

Select Novel Drugs Approved During Calendar Year 2019			
Drug Name	**Date Approved**	**FDA-Approved Indication**	**Estimated Annual Cost***
Ubrelvy™ (ubrogepant)	12/23/2019	Treatment of acute migraine with or without aura	$16,320
Vyondys 53® (golodirsen)	12/12/2019	Treatment of Duchenne muscular dystrophy	$499,200 for 19kg
Oxbryta® (voxelotor)	11/25/2019	Treatment of sickle cell disease	$124,999
Adakveo® (crizanlizumab-tmca)	11/15/2019	Treatment of pain due to sickle cell disease	$122,569 for 70kg
Trikafta® (elexacaftor/ivacaftor/tezacaftor)	10/21/2019	Treatment of cystic fibrosis in patients 12 years of age and older	$310,652
Zolgensma® (onasemnogene abeparvovec-xioi)	05/24/2019	Treatment of pediatric patients younger than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene	$2,125,000
Mayzent® (siponimod)	03/26/2019	Treatment of relapsing forms of multiple sclerosis	$92,088

*Costs do not include rebated or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.

Traditional Versus Specialty Pharmacy Products

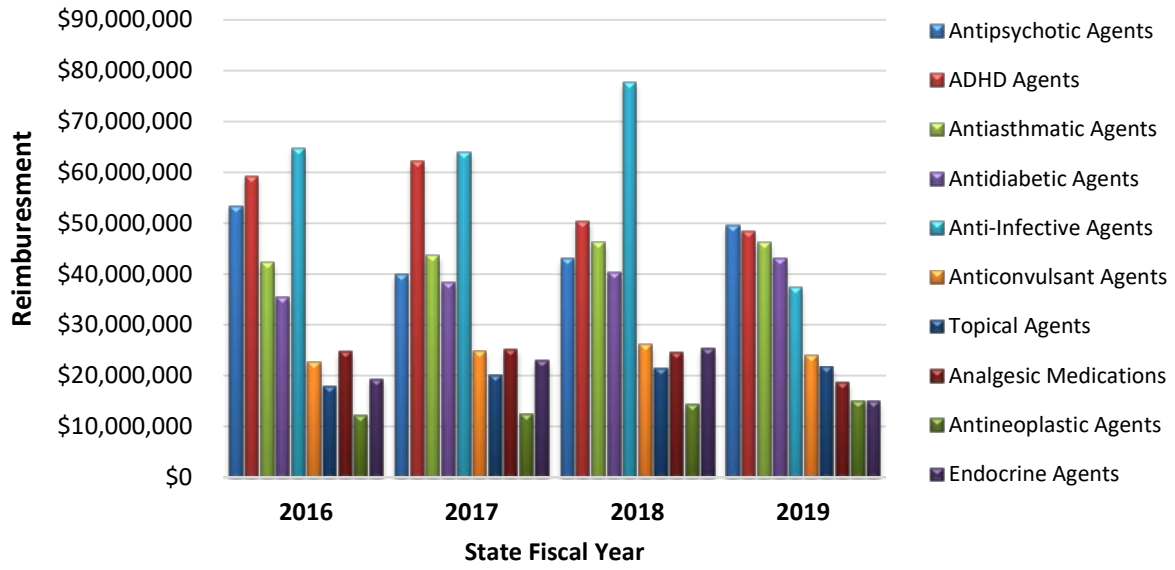
Traditional pharmaceuticals include products that are typically non-injectable and do not require special transportation, storage, administration, and are not typically indicated for rare diseases requiring unique management. These products treat many common chronic diseases such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). Traditional pharmaceuticals carried the bulk of the reimbursement costs accounting for 69.7% of the total pharmacy reimbursement and more than 99% of utilizers in SFY 2019. Specialty products, in contrast, are typically injectable and require special handling such as refrigerated transport and special administration techniques or are indicated for rare diseases requiring unique management. These products include treatments for cystic fibrosis (CF), hemophilia, rheumatoid arthritis (RA), and genetic deficiencies, for example. Specialty pharmaceuticals have become a larger part of reimbursement over the last 5 years, now comprising close to 17% of the total expenditures. Newly FDA approved therapies for RA and dermatological conditions led to an increase in specialty pharmaceutical expenditures for SFY 2019.

Top 10 Therapeutic Classes by Reimbursement: Fiscal Year 2019

Traditional Top 10 Classes by Reimbursement				
2016	2017	2018	2019	Therapeutic Class
$53,434,190	$39,977,374	$43,111,772	**$49,593,892**	**Antipsychotic Agents**
$59,210,124	$62,118,533	$50,326,685	**$48,455,174**	**ADHD Agents**
$42,407,875	$43,565,926	$46,258,925	**$46,164,626**	**Anti-Asthmatic Agents**
$35,416,629	$38,298,122	$40,247,671	**$43,181,023**	**Anti-Diabetic Agents**
$64,753,193	$63,996,676	$77,754,042	**$37,513,036**	**Anti-Infective Agents**
$22,587,039	$24,851,122	$26,190,057	**$24,002,605**	**Anticonvulsants**
$17,927,089	$20,067,381	$21,345,644	**$21,824,974**	**Topical Agents**
$24,729,391	$25,210,044	$24,633,644	**$18,731,633**	**Analgesic Agents**
$19,378,355	$22,954,966	$25,402,170	**$15,037,750**	**Endocrine Agents**
$12,125,906	$12,518,084	$14,310,913	**$15,025,287**	**Antineoplastic Agents**

ADHD = attention-deficit/hyperactivity disorder
Reimbursement does not reflect rebated costs or net costs.

Top 10 Traditional Therapy Classes by Reimbursement



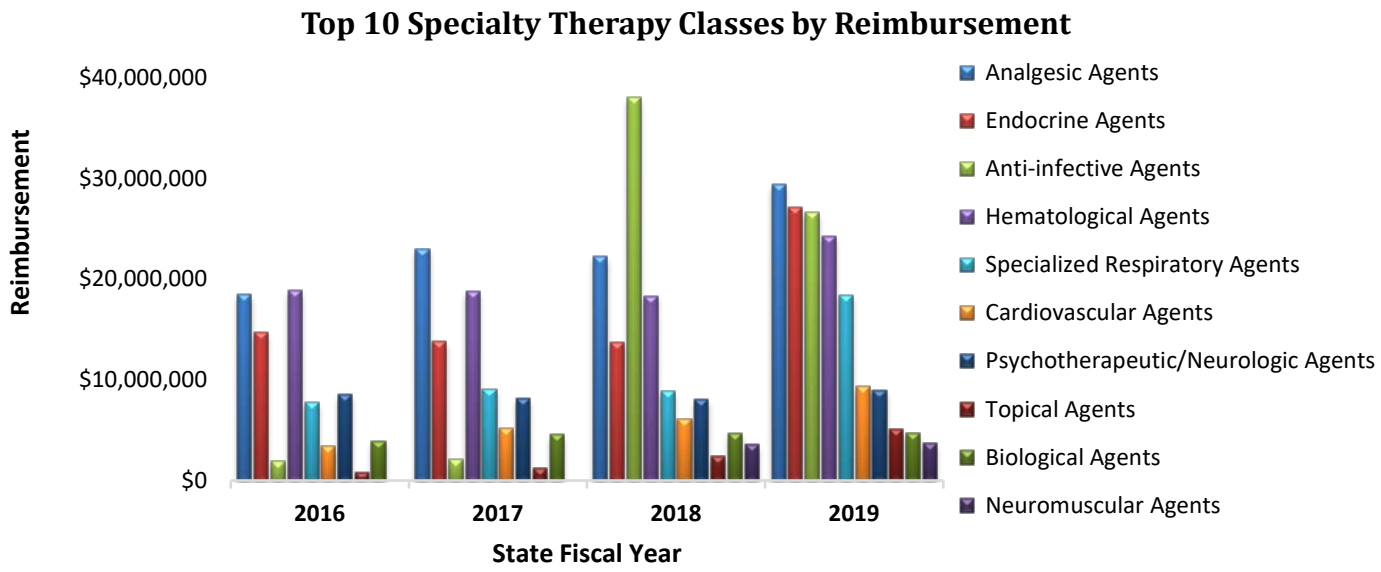
The top 10 traditional pharmaceutical classes that show the most significant change include the antipsychotic agents and endocrine agents. Other classes saw more minor fluctuations and are accounted for in the following analysis.

- Reimbursement decreased by more than $10 million in the endocrine agents including a $2 million decrease in progestin.
- Antipsychotic agents' reimbursement increases can be accounted for by increased utilization of long-acting injectable antipsychotics as well as utilization of brand formulation oral medications. It is important to note that many medications in this class have supplemental rebates in place with Oklahoma Medicaid and net cost increases are not reflected in this analysis.

- The anti-diabetic agents saw a $2.9 million spending increase from SFY 2018. These products have significant federal rebates designed to keep the Medicaid net cost relatively flat; however, rebates are not accounted for in this analysis.
- Analgesic agents saw a $6 million decline in reimbursement from SFY 2018 to SFY 2019 as a result of numerous opioid anlagesic initiatives and the 90 morphine milligram equivalent (MME) limit that was slowly implemented.
- Costs in this report do not reflect the federal and state supplemental rebates that are provided by medication manufacturers. Many branded products, particularly the anti-infective agents, ADHD agents, antipsychotic agents, endocrine agents, and analgesic agents are heavily influenced by supplemental rebates and net costs are substantially lower than the total reimbursement paid to pharmacies shown in this analysis.

Specialty Top 10 Classes by Reimbursement				
2016	2017	2018	2019	Therapeutic Class
$18,481,116	$22,988,676	$22,236,627	**$29,408,297**	**Analgesic Agents**
$14,684,343	$13,782,182	$23,738,382	**$27,100,383**	**Endocrine Agents**
$1,865,601	$2,060,760	$38,069,135	**$26,584,509**	**Anti-Infective Agents**
$18,852,788	$18,813,132	$22,339,418	**$24,294,488**	**Hematological Agents**
$7,754,987	$9,093,408	$13,860,036	**$18,430,265**	**Specialized Respiratory Agents**
$3,387,174	$5,143,843	$6,071,976	**$9,324,548**	**Cardiovascular Agents**
$8,540,617	$8,139,124	$8,035,140	**$8,928,529**	**Psychotherapeutic/Neurologic Agents**
$793,104	$1,253,685	$2,380,074	**$5,049,950**	**Topical Agents**
$3,935,198	$4,581,237	$4,745,569	**$4,676,353**	**Biological Agents**
N/A	N/A	$3,571,542	**$3,642,244**	**Neuromuscular Agents**

Reimbursement do not reflect rebated prices or net costs.



Specialty therapeutic products costs are high largely in part due to biologic therapies and the therapies focused on rare diseases including CF, hemophilia, and pulmonary arterial hypertension (PAH). Continuous review and management of biological agents and gastrointestinal agents has promoted minimal reimbursement increases other than expected

yearly price increases by product manufacturers and declines in reimbursement for analgesic agents, hematological agents, endocrine agents, specialized respiratory agents, and neurologic agents.

- The cost of specialty analgesic products increased this year with a $5 million increase in anti-inflammatory agents and a decrease in narcotic agents. Reimbursement in this class is largely attributed to targeted immunomodulatory agents such as Humira® (adalimumab), Enbrel® (etanercept), Ilaris® (canakinumab), Orencia® (abatacept), Simponi® (golimumab), Xeljanz® (tofacitinib), Otezla® (apremilast), and Kineret® (anakinra). The majority of utilization was seen in Tier-2 medications (Humira® and Enbrel®), which are supplementally rebated medications. The supplementally rebated prices and net costs are not reflected in this analysis.
- Cardiovascular agents again saw a significant increase in reimbursement from SFY 2018 to SFY 2019. Reimbursement for the specialty cardiovascular agents is largely comprised of medications indicated to treat PAH.
- Respiratory agents saw a $6 million increase in reimbursement from SFY 2018 to SFY 2019. This class includes medications indicated for the treatment of CF. Symdeko® (tezacaftor/ivacaftor and ivacaftor) was FDA approved in February 2018 which contributed to the SFY 2019 increase.

Top 10 Medications by Reimbursement: Fiscal Year 2019

Many of the top 10 medications by reimbursement are still branded at this time and not available in a generic formulation. Only 3 of the top 10 medications from last year have not changed in ranking: lisdexamfetamine, paliperidone injection, and albuterol. The top products typically come from highly utilized classes such as atypical antipsychotics, ADHD therapies, respiratory medications, including rescue and maintenance therapies, and the anti-infective class, including antiviral medications for hepatitis C. Top drug reimbursement rankings only slightly change from year to year for several reasons: high use, broad use between age demographics, and high costs of new therapies such as those indicated for hepatitis C.

Top 10 Medications by Reimbursement*				
Rank	**2016**	**2017**	**2018**	**2019**
1	lisdexamfetamine	lisdexamfetamine	lisdexamfetamine	**lisdexamfetamine**
2	aripiprazole	ledipasvir/sofosbuvir	paliperidone inj	**paliperidone inj**
3	ledipasvir/sofosbuvir	paliperidone inj	ledipasvir/sofosbuvir	**adalimumab**
4	methylphenidate	methylphenidate	albuterol	**albuterol**
5	albuterol	albuterol	adalimumab	**ledipasvir/sofosbuvir**
6	paliperidone inj	adalimumab	oseltamivir	**lurasidone**
7	atomoxetine	atomoxetine	methylphenidate	**somatropin injection**
8	adalimumab	insulin glargine	lurasidone	**fluticasone**
9	insulin glargine	oseltamivir	sofosbuvir/velpatasvir	**insulin glargine**
10	sofosbuvir	somatropin inj	insulin glargine	**methylphenidate**

*Includes brand and generic where applicable.
Rank does not reflect rebated prices or net costs.
Medications are listed by generic name, but may include both generic and brand formulations.
inj = injection

Cost Per Claim

Claims for generic medications made up 83.6% of the volume while only accounting for 25.4% of the reimbursement amount. The SoonerCare cost per claim of traditional medications decreased by 9.7% in SFY 2019 in comparison to SFY 2018, and the cost per specialty claim increased by 32.8%. As mentioned previously, specialty costs are largely driven by the significant cost associated with medications for rare diseases. The list of specialty drugs had not been updated in several years, so OHCA and PMC collaborated for SFY 2019 to update the list. The specialty cost per claim increase can be attributed in large part to the update.

Cost per Claim			
Drug Class	**SFY 2017**	**SFY 2018**	**SFY 2019**
Traditional	$72.13	$78.16	$70.55
Specialty	$5,321.87	$5,485.05	$7,285.07

Reimbursement does not reflected rebated costs or net costs.

Conclusion

New prior authorization categories and continuous evaluation of categories such as cancer and hemophilia medications, along with new respiratory and anti-diabetic medications that continue to be FDA approved, ensure the most clinically appropriate, cost-effective measures are taken. Modifications to tier structure and other generic categories reduced elevated spending on high-priced generic products. When new drugs are FDA approved and available on the market, a cost-effective analysis is performed to minimize spending while ensuring appropriate clinical care. The goal of the SoonerCare program is to provide members with the most appropriate health care in a fiscally responsible manner. For the pharmacy benefit, this is accomplished using prior authorization, limiting the number of total prescriptions and the number of brand name prescriptions allowed each month for non-institutionalized adult members, continuous product pricing maintenance, and provider outreach and education. Constant market review and response to changes, such as evolving gene therapies, growth of the specialty market, and introduction of biosimilars, is necessary. SoonerCare will continue to strive to bring value-based pharmacy services to its members.

Top 50 Reimbursed Drugs by Fiscal Year

Top 50 Reimbursed Drugs By Fiscal Year		SFY 2019		SFY 2018	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Lisdexamfetamine	Vyvanse	**1**	**$24,702,189.32**	1	$25,084,930.85
Paliperidone Injection	Invega Trinza	**2**	**$20,204,721.44**	2	$17,612,374.59
Adalimumab	Humira	**3**	**$18,125,313.72**	5	$14,163,188.51
Albuterol	Multiple Products	**4**	**$14,376,869.65**	4	$14,894,214.27
Sofosbuvir/Velpatasvir	Epclusa	**5**	**$11,657,679.93**	9	$9,545,422.66

Lurasidone	Latuda	**6**	**$11,377,055.06**	8	$9,745,294.36
Somatropin	Multiple Products	**7**	**$9,885,546.47**	11	$8,860,134.27
Fluticasone Inhalation	Flovent	**8**	**$9,596,952.53**	12	$8,711,905.91
Insulin Glargine	Toujeo	**9**	**$9,503,963.79**	10	$8,989,182.95
Methylphenidate	Multiple Products	**10**	**$9,260,002.26**	7	$10,302,222.28
Fluticasone/Salmeterol	Multiple Products	**11**	**$8,680,497.91**	13	$7,724,105.71
Ledipasvir/Sofosbuvir	Harvoni	**12**	**$8,505,742.36**	3	$15,933,872.05
Insulin Aspart	Novolog	**13**	**$7,890,670.53**	14	$7,680,727.71
Anti-Inhibitor Coagulant Complex For IV Solution 2500 Unit	Feiba	**14**	**$7,805,229.42**	19	$5,780,915.33
Dexmethylphenidate	Focalin	**15**	**$7,090,329.34**	22	$4,940,696.71
Etanercept	Enbrel	**16**	**$7,046,175.88**	17	$6,489,067.66
Tezacaftor/Ivacaftor	Symdeko	**17**	**$7,036,713.78**	N/A	N/A
Hydroxyprogesterone Caproate	Makena	**18**	**$6,604,586.84**	16	$6,642,750.22
Oseltamivir	Tamiflu	**19**	**$6,530,713.00**	6	$11,640,456.94
Aripiprazole	Multiple Products	**20**	**$5,827,434.03**	27	$4,301,119.40
Ciprofloxacin/Dexamethasone Otic	Ciprodex	**21**	**$5,798,413.04**	18	$5,814,284.09
Buprenorphine/Naloxone	Multiple Products	**22**	**$5,421,614.38**	25	$4,712,276.44
Insulin Detemir	Levemir	**23**	**$5,156,240.65**	24	$4,859,296.17
Insulin Lispro	Humalog	**24**	**$4,929,585.59**	23	$4,884,230.20
Lumacaftor/Ivacaftor	Orkambi	**25**	**$4,785,304.80**	15	$6,824,219.89
Lacosamide	Vimpat	**26**	**$4,667,200.69**	33	$3,974,274.79
Pregabalin	Lyrica	**27**	**$4,530,026.85**	32	$4,037,343.89
Glucose Blood Test Strip	Multiple Products	**28**	**$4,189,353.15**	26	$4,453,184.21
Sildenafil Citrate Tablet 20MG	Revatio	**29**	**$4,025,618.14**	39	$2,911,996.07
Nusinersen Intrathecal Solution 12MG/5ML (2.4MG/ML)	Spinraza	**30**	**$3,769,588.47**	34	$3,571,541.65
Oxycodone	Oxycontin	**31**	**$3,657,063.87**	20	$5,500,196.87
Antihemophilic Factor (Recombinant)	Kogenate	**32**	**$3,381,886.64**	35	$3,361,476.60
Tiotropium	Spiriva	**33**	**$3,370,092.85**	37	$3,155,794.85

Dornase Alfa	Pulmozyme	**34**	**$3,210,745.02**	38	$3,054,487.66
Ivermectin Lotion	Sklice	**35**	**$3,062,449.25**	40	$2,894,794.20
Antihemophilic Factor rAHF-PFM	Kovaltry	**36**	**$3,042,836.99**	47	$2,406,813.96
Atomoxetine	Strattera	**37**	**$3,035,324.29**	30	$4,070,448.25
Pancrelipase	Zenprep	**38**	**$3,029,521.15**	44	$2,594,038.12
Sitagliptin	Januvia	**39**	**$2,876,570.35**	43	$2,667,189.78
Glecaprevir/Pibrentasvir	Mavyret	**40**	**$2,851,695.49**	28	$4,173,662.90
Palivizumab	Synagis	**41**	**$2,824,554.94**	42	$2,734,231.87
Ivacaftor	Kalydeco	**42**	**$2,824,125.42**	51	$2,271,323.67
Liraglutide Solution	Victoza	**43**	**$2,809,892.51**	46	$2,419,030.61
Vigabatrin	Sabril	**44**	**$2,774,112.97**	58	$1,910,975.75
Amphetamine/Dextroamphetamine	Multiple Products	**45**	**$2,699,958.82**	31	$4,070,235.76
Palbociclib	Ibrance	**46**	**$2,664,354.99**	60	$1,786,146.82
Amoxicillin	Amoxicillin	**47**	**$2,658,753.44**	45	$3,236,041.02
Epinephrine Solution (1:1000)	Multiple Products	**48**	**$2,410,805.72**	36	$2,387,510.67
Cetirizine	Zyrtec	**49**	**$2,326,568.13**	48	$1,981,912.60
Sapropterin	Kuvan	**50**	**$2,252,871.50**	57	$1,981,912.60

*Includes brand and generic where applicable.
SFY = state fiscal year
NA = not applicable; IV = intravenous
Reimbursement does not reflect rebated costs or net costs.

Top 50 Medications by Total Number of Claims: Fiscal Year 2019

Top 50 Medications by Total Number of Claims									
Rank	Generic Name	Brand Name	Claims	Members	Cost	Units/ Day	Claims/ Member	Cost/ Claim	% Cost+
1	albuterol	Multiple	210,420	89,389	$14,375,632.03	2.15	2.35	$68.32	2.60%
2	cetirizine	Multiple	207,296	90,876	$2,326,568.13	2.97	2.28	$11.22	0.42%
3	amoxicillin	Amoxil*	203,895	150,178	$2,658,741.69	11.9	1.36	$13.04	0.48%
4	montelukast	Singulair*	142,587	40,229	$2,180,714.55	1	3.54	$15.29	0.39%
5	hydrocodone-acetaminophen	Multiple	125,255	50,547	$2,050,613.36	3.95	2.48	$16.37	0.37%
6	azithromycin	Zithromax*	95,623	73,372	$1,714,359.22	2.95	1.3	$17.93	0.31%
7	fluticasone propionate nasal	Flonase*	95,125	50,873	$1,368,515.29	0.42	1.87	$14.39	0.25%
8	gabapentin	Neurontin*	94,851	19,475	$1,539,460.49	3.14	4.87	$16.23	0.28%
9	lisdexamfetamine	Vyvanse	89,104	15,725	$24,702,189.32	1	5.67	$277.23	4.47%
10	clonidine	Catapres*	82,090	14,815	$874,907.27	1.46	5.54	$10.66	0.16%
11	methylphenidate	Multiple	76,327	11,800	$9,260,002.26	1.31	6.47	$121.32	1.67%
12	sertraline hcl	Zoloft*	75,027	19,219	$921,481.60	1.16	3.9	$12.28	0.17%
13	ondansetron	Zofran*	72,692	56,837	$1,027,325.49	2.32	1.28	$14.13	0.19%
14	fluoxetine	Prozac*	63,615	14,910	$761,879.13	1.24	4.27	$11.98	0.14%
15	ibuprofen	Motrin*	63,390	43,150	$738,832.79	3.04	1.47	$11.66	0.13%
16	cefdinir	Omnicef*	62,309	48,361	$1,406,540.23	6.63	1.29	$22.57	0.25%
17	trazodone	Desyrel*	62,098	14,941	$732,962.53	1.21	4.16	$11.80	0.13%
18	prednisone	Multiple	60,770	44,627	$698,737.56	2.1	1.36	$11.50	0.13%
19	omeprazole	Multiple	59,558	19,258	$694,330.01	1.13	3.09	$11.66	0.13%
20	amoxicillin/clavulanate	Augmentin*	59,262	49,554	$1,545,690.79	8.26	1.2	$26.08	0.28%
21	oseltamivir	Tamiflu*	57,777	55,125	$6,527,612.61	11.06	1.05	$112.98	1.18%
22	guanfacine extended-release	Intuniv*	52,737	8,807	$1,208,054.01	1	5.99	$22.91	0.22%
23	cephalexin	Keflex*	51,580	44,874	$940,694.61	9.59	1.15	$18.24	0.17%
24	lisinopril	Multiple	48,975	14,058	$470,369.25	1.09	3.48	$9.60	0.09%
25	levothyroxine	Multiple	48,551	10,507	$1,239,464.82	1	4.62	$25.53	0.22%
26	loratadine	Multiple	48,058	21,949	$590,967.40	2.77	2.19	$12.30	0.11%
27	quetiapine	Seroquel*	47,930	8,602	$779,474.34	1.44	5.57	$16.26	0.14%
28	amphetamine/dextroamphetamine	Multiple	47,617	7,664	$2,699,848.04	1.45	6.21	$56.70	0.49%
29	triamcinolone topical	Multiple	43,888	31,879	$647,320.63	4.43	1.38	$14.75	0.12%
30	prednisolone sodium phosphate	Multiple	43,734	32,888	$858,898.87	6.48	1.33	$19.64	0.16%
31	fluticasone propionate inhalation	Flovent	43,327	16,875	$9,596,952.53	0.33	2.57	$221.50	1.74%

Top 50 Medications by Total Number of Claims									
Rank	**Generic Name**	**Brand Name**	**Claims**	**Members**	**Cost**	**Units/ Day**	**Claims/ Member**	**Cost/ Claim**	**% Cost+**
32	sulfamethoxazole/trimethoprim	Bactrim*	42,711	34,572	$929,404.78	7.27	1.24	$21.76	0.17%
33	alprazolam	Xanax*	41,550	7,175	$432,625.43	2.26	5.79	$10.41	0.08%
34	aripiprazole	Abilify*	41,470	8,788	$5,827,421.17	0.96	4.72	$140.52	1.05%
35	oxycodone	Multiple	41,041	17,231	$938,728.55	3.69	2.38	$22.87	0.17%
36	mupirocin	Bactroban*	40,831	34,993	$620,796.29	2.27	1.17	$15.20	0.11%
37	risperidone	Risperdal*	39,588	6,674	$558,613.22	1.53	5.93	$14.11	0.10%
38	escitalopram	Lexapro*	39,293	10,355	$503,737.72	1.06	3.79	$12.82	0.09%
39	metformin	Multiple	37,678	10,707	$395,532.98	2.03	3.52	$10.50	0.07%
40	hydroxyzine hcl	Atarax*	36,933	16,634	$504,724.76	3.81	2.22	$13.67	0.09%
41	atorvastatin	Lipitor*	36,376	10,629	$480,902.23	1	3.42	$13.22	0.09%
42	cyclobenzaprine	Flexeril*	35,672	16,395	$354,230.63	2.39	2.18	$9.93	0.06%
43	ranitidine	Zantac*	35,253	14,993	$467,641.64	3.49	2.35	$13.27	0.08%
44	buspirone	Buspar*	34,769	9,617	$531,643.23	2.26	3.62	$15.29	0.10%
45	levetiracetam	Keppra*	32,550	5,023	$955,336.04	5.41	6.48	$29.35	0.17%
46	dexmethylphenidate hcl	Multiple	32,118	4,600	$7,090,329.34	1.2	6.98	$220.76	1.28%
47	citalopram	Celexa*	31,900	8,930	$318,469.81	1.02	3.57	$9.98	0.06%
48	atomoxetine	Strattera*	30,982	6,122	$3,034,720.18	1.1	5.06	$97.95	0.55%
49	prednisolone syrup	Prelone*	30,661	24,981	$375,454.10	6.55	1.23	$12.25	0.07%
50	topiramate	Multiple	30,249	6,839	$856,733.88	1.89	4.42	$28.32	0.15%

*Includes brand and generic where applicable.

Top 10 Traditional and Specialty Therapeutic Categories by Fiscal Year

Top 10 Traditional Therapeutic Categories by Fiscal Year*				
Attention Deficit Hyperactivity Disorder (ADHD) Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREXIANTS	330,767	$48,455,174.06	340,534	$50,324,050.47
Total	**330,767**	**$48,455,174.06**	**340,534**	**$50,324,050.47**
Antipsychotics and Antimanic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTIPSYCHOTICS	213,130	$49,593,892.43	214,357	$42,888,211.18
Total	**213,130**	**$49,593,892.43**	**214,357**	**$42,888,211.18**
Anti-Asthmatic and Bronchodilator Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTI-ASTHMATIC AND BRONCHODILATOR AGENTS	468,000	$46,164,625.55	487,624	$46,213,224.91
Total	**468,000**	**$46,164,625.55**	**487,624**	**$46,213,224.91**
Anti-Diabetic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTI-DIABETIC	127,576	$43,181,023.30	134,254	$40,246,024.44
Total	**127,576**	**$43,181,023.30**	**134,254**	**$40,246,024.44**
Anti-Infective Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTIVIRAL	79,084	$18,793,819.84	98,878	$22,958,583.51
MISC. ANTI-INFECTIVES	81,901	$4,781,952.77	88,903	$5,011,406.24
PENICILLINS	272,467	$4,505,625.13	284,131	$4,569,077.58
CEPHALOSPORINS	120,672	$2,755,920.19	126,429	$3,273,670.04
MACROLIDE ANTIBIOTICS	98,422	$2,441,250.85	111,745	$2,749,182.42
ANTIFUNGALS	25,519	$2,372,747.84	25,903	$1,048,859.44
ANTHELMINTIC	2,492	$851,368.46	2,888	$971,938.10
TETRACYCLINES	23,735	$491,595.22	23,308	$561,516.31
ANTIMALARIAL	4,140	$254,664.53	4,130	$156,611.96
FLUOROQUINOLONES	15,559	$211,336.71	17,320	$216,888.63
ANTIMYCOBACTERIAL AGENTS	382	$27,013.06	416	$27,162.22

AMINOGLYCOSIDES	320	$22,455.66	394	$21,566.35
SULFONAMIDES	6	$2,483.96	30	$1,837.58
AMEBICIDES	3	$802.24	0	$0.00
Total	**724,702**	**$37,513,036.46**	**784,475**	**$41,568,300.38**
Anticonvulsant Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTICONVULSANT	315,942	$24,002,604.94	326,119	$24,280,002.62
Total	**315,942**	**$24,002,604.94**	**326,119**	**$24,280,002.62**
Topical Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
DERMATOLOGICAL	195,183	$13,131,566.90	200,134	$11,706,437.59
OTIC	27,512	$5,982,613.18	29,866	$6,046,624.72
OPHTHALMIC	59,712	$2,259,509.83	62,034	$2,233,099.86
MOUTH/THROAT/DENTAL AGENTS	22,505	$362,440.28	25,057	$398,276.39
ANORECTAL	1,300	$88,844.20	1,304	$105,604.66
Total	**306,212**	**$21,824,974.39**	**318,395**	**$20,490,043.22**
Analgesic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANALGESICS - Narcotic	281,567	$16,152,773.39	352,465	$19,258,321.74
ANALGESICS - Anti-Inflammatory	135,594	$1,891,545.95	137,185	$1,864,033.38
MIGRAINE PRODUCTS	11,146	$314,147.44	11,658	$291,187.66
ANALGESICS - NonNarcotic	7,359	$194,921.49	8,535	$306,470.75
GOUT	5,593	$176,423.19	5,818	$185,631.43
LOCAL ANESTHETICS - Parenteral	123	$1,821.71	120	$1,592.07
Total	**441,382**	**$18,731,633.17**	**515,781**	**$21,907,237.03**
Endocrine Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
CONTRACEPTIVES	93,510	$5,630,714.64	99,093	$5,817,996.59
MISC. ENDOCRINE	17,444	$3,313,566.91	18,864	$3,391,465.37
CORTICOSTEROIDS	169,457	$2,634,177.72	177,064	$2,714,949.59
THYROID	52,765	$1,402,932.87	55,014	$1,427,848.51

PROGESTINS	5,594	$1,063,072.52	5,556	$1,490,996.17
ESTROGENS	8,194	$791,129.15	8,993	$868,834.23
ANDROGEN - Anabolic	685	$136,434.31	613	$134,507.97
OXYTOCICS	162	$65,721.65	197	$46,221.64
Total	**347,811**	**$15,037,749.77**	**365,394**	**$15,892,820.07**
Antineoplastic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTINEOPLASTICS	10,320	$15,025,287.18	10,627	$13,319,997.73
Total	**10,320**	**$15,025,287.18**	**10,627**	**$13,319,997.73**

Top 10 Specialty Therapeutic Categories by Fiscal Year*

Anti-Infective Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANTIVIRAL	1,081	$24,788,087.08	1,574	$36,175,385.41
AMINOGLYCOSIDES	403	$1,193,029.85	370	$1,141,262.14
MISC. ANTI-INFECTIVES	71	$598,361.68	91	$748,211.08
ANTIFUNGALS	1	$5,030.31	1	$4,276.26
Total	**1,556**	**$26,584,508.92**	**2,036**	**$38,069,134.89**
Analgesic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ANALGESICS - Anti-Inflammatory	5,194	$29,384,093.46	4,784	$24,927,017.11
ANALGESICS - Narcotic	81	$65,151.73	74	$33,891.65
MIGRAINE PRODUCTS	110	$65,058.42	N/A	N/A
LOCAL ANESTHETICS - Parenteral	102	$2,507.36	119	$2,909.93
Total	**5,487**	**$29,516,810.97**	**4,977**	**$24,963,818.69**
Endocrine Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
MISC. ENDOCRINE	3,761	$21,513,970.52	3,478	$17,879,858.30
PROGESTINS	2,033	$5,734,955.88	1,770	$5,358,097.86
Total	**5,794**	**$27,248,926.40**	**5,248**	**$23,237,956.16**
Hematological Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**

MISC. HEMATOLOGICAL	741	$23,360,951.16	752	$19,926,104.70
HEMATOPOIETIC AGENTS	575	$2,121,480.77	595	$2,389,000.76
Total	**1,316**	**$25,482,431.93**	**1,347**	**$22,315,105.46**
Specialized Respiratory Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
MISC. RESPIRATORY	1,736	$18,430,265.48	1,466	$13,813,179.81
Total	**1,736**	**$18,430,265.48**	**1,466**	**$13,813,179.81**
Psychotherapeutic/Neurologic Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
MISC PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENTS	1,461	$8,928,529.46	1,441	$8,854,503.22
Total	**1,461**	**$8,928,529.46**	**1,441**	**$8,854,503.22**
Cardiovascular Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
MISC. CARDIOVASCULAR	1,454	$9,190,447.38	1,231	$6,554,965.10
VASOPRESSORS	9	$134,578.75	1	$1,012.91
ANTIHYPERLIPIDEMIC	47	$46,050.03	10	$11,006.64
ANTIHYPERTENSIVE	24	$1,543.09	65	$4,073.60
Total	**1,534**	**$9,372,619.25**	**1,307**	**$6,571,058.25**
Biological Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
PASSIVE IMMUNIZING AGENTS	2,196	$4,456,877.69	2,202	$4,286,210.56
BIOLOGICALS MISC	6	$250,000.26	13	$534,809.15
Total	**2,202**	**$4,706,877.95**	**2,215**	**$4,821,019.71**
Topical Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
DERMATOLOGICAL	795	$5,171,077.30	447	$3,150,005.78
Total	**795**	**$5,171,077.30**	**447**	**$3,150,005.78**
Neuromuscular Agents	**2019**		**2018**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
NEUROMUSCULAR AGENTS	33	$3,769,588.47	26	$3,571,541.65
Total	**33**	**$3,769,588.47**	**26**	**$3,571,541.65**

Grand Total	2019		2018	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Top 10 Traditional and Specialty Therapeutic Categories	**3,306,020**	**$476,969,566**	**3,999,021**	**$457,435,605**

*Table contains top 10 traditional and specialty therapeutic categories and is not an all-inclusive list.
Reimbursement does not reflect rebated costs or net costs.

IHS Trends									
Unduplicated Member Count 2018	Unduplicated Member Count 2019	American Indian Count 2018	American Indian Count 2019	Total Reimbursement 2018	Total Reimbursement 2019	Total American Indian Members 2018	Total American Indian Members 2019	% Filling Prescriptions 2018	% Filling Prescriptions 2019
9,921	**9,601**	**8,421**	**8,168**	**$5,785,762.41**	**$5,770,808.97**	**130,943**	**81,610**	**6%**	**10%**

IHS = Indian Health Service

[1] Centers for Medicare and Medicaid Services (CMS). National Health Expenditure Projections 2019-2028. Available online at: https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00094. Issued 03/24/2020. Last accessed 04/20/2020.

[2] CMS. National Health Expenditure Projections 2019-2028. Available online at: https://www.cms.gov/files/document/nhe-projections-2019-2028-forecast-summary.pdf. Last accessed 04/20/2020.

[3] Express Scripts. 2019 Drug Trend Report. Available online at: https://www.express-scripts.com/corporate/drug-trend-report#focusing-on-patient-care-for-better-health-and-savings. Issued 02/2020. Last accessed 04/15/2020.

[4] Centers for Medicare and Medicaid Services (CMS). National Health Expenditure Projections 2017-2026, Forecast summary. Available online at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/nhe-fact-sheet.html. Last revised 02/10/2010. Last accessed 04/15/2020.

[5] Peters CP. The Basics: The Medicaid Drug Rebate Program. *National Health Policy Forum*. Available Online at: https://www.nhpf.org/library/the-basics/Basics_MedicaidDrugRebate_04-13-09.pdf. Issued 04/13/2009. Last accessed 04/20/2020.

[6] Office of Inspector General (OIG): Department of Health and Human Services. States' Collection of Offset and Supplemental Medicaid Rebates. Available online at: http://oig.hhs.gov/oei/reports/oei-03-12-00520.pdf. Issued 12/2014. Last accessed 04/15/2020.

[7] Gibbons DC, Kirschenbaum AM. Bipartisan Budget Bill Extends Medicaid Drug Rebate Program Price Increase Penalty to Generic Drugs. *FDA Law Blog*. Available online at: http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/11/bipartisan-budget-bill-extends-medicaid-drug-rebate-program-price-increase-penalty-to-generic-drugs.html. Issued 11/02/2015. Last accessed 04/15/2020.

[8] Stuard S, Beyer J, Bonetto M, et al. State Medicaid Alternative Reimbursement and Purchasing Test for High-Cost Drugs (SMART-D): Summary Report. Center for Evidence-Based Policy. Available online at: http://smart-d.org/research-and-reports/. Issued 09/2016. Last accessed 04/15/2020.

[9] Social Security Administration. Payment for Covered Outpatient Drugs. Available online at: https://www.ssa.gov/OP_Home/ssact/title19/1927.htm. Last accessed 03/22/2020.

[10] National Association of Medicaid Directors (NAMD). The Role of State Medicaid Programs in Improving the Value of the Health Care System. Bailit Health. Available online at: http://medicaiddirectors.org/wp-content/uploads/2016/03/NAMD_Bailit-Health_Value-Based-Purchasing-in-Medicaid.pdf. Issued 03/22/2016. Last accessed 04/15/2020.

[11] Goodman C, Daniel R, Balch A, Doyle J. Value-Based Health Care for Patients, Providers & Payers – Summary from AMCP Foundation Research Symposium Highlights Webinar. *AMCP Foundation*. Webinar recorded 11/30/2017. Last accessed 04/22/2020.

[12] Kenney JT. The Outcome of it All – The Impact and Value of Outcomes Based Contracts. Academy of Managed Care Pharmacy Nexus 2017. October 16-19, 2017. Dallas, TX

[13] CMS. CMS Approves State Proposal to Advance Specific Medicaid Value-Based Arrangements with Drug Makers. Available online at: https://www.cms.gov/newsroom/press-releases/cms-approves-state-proposal-advance-specific-medicaid-value-based-arrangements-drug-makers. Issued 06/27/2018. Last accessed 04/22/2020.

[14] U.S. Food and Drug Administration (FDA). First Generic Drug Approvals. Available online at:. https://www.fda.gov/drugs/first-generic-drug-approvals/2018-first-generic-drug-approvals. Last revised 01/11/2019. Last accessed 04/22/2020.

[15] FDA. Novel Drug Approvals for 2018. Available online at: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm592464.htm. Last revised 03/23/2020. Last accessed 04/23/2020.

[16] FDA. 2018 New Drug Therapy Approvals Report. Available online at: https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM629290.pdf. Issued 03/2020. Last accessed 04/22/2020.

Appendix M

Calendar Year 2019 Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Ziextenzo® (Pegfilgrastim-bmez)

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria

Granix® (Tbo-filgrastim), Nivestym™ (Filgrastim-aafi), and Zarxio® (Filgrastim-sndz) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Neupogen® (filgrastim) must be provided.

Fulphila® (Pegfilgrastim-jmdb) and Udenyca™ (Pegfilgrastim-cbqv) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Neulasta® (pegfilgrastim) or Neupogen® (filgrastim) must be provided.

Utilization of G-CSFs: Calendar Year 2019

Comparison of Calendar Years for G-CSFs: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	57	241	$1,185,495.01	$4,919.07	$258.28	1,626	4,590
2019	45	174	$766,853.53	$4,407.20	$243.76	983	3,146
% Change	**-21.10%**	**-27.80%**	**-35.30%**	**-10.40%**	**-5.60%**	**-39.50%**	**-31.50%**
Change	**-12**	**-67**	**-$418,641.48**	**-$511.87**	**-$14.52**	**-643**	**-1,444**

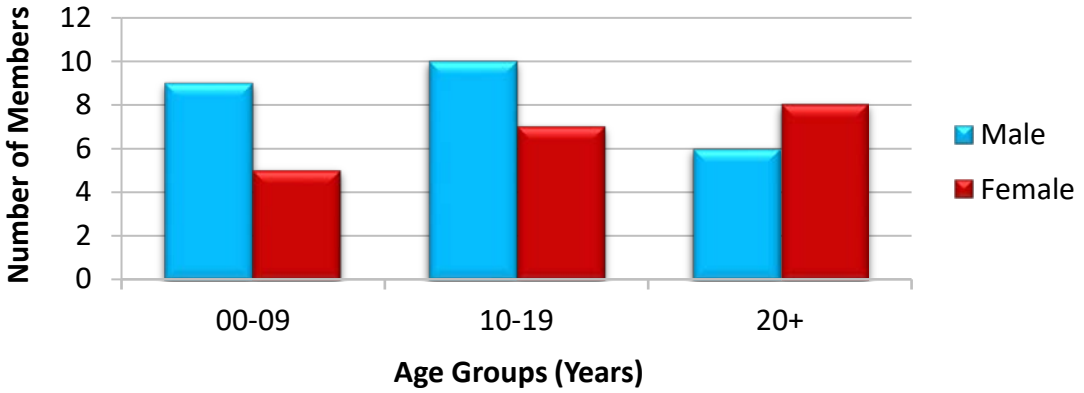
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Calendar Years for G-CSFs: Medical Claims

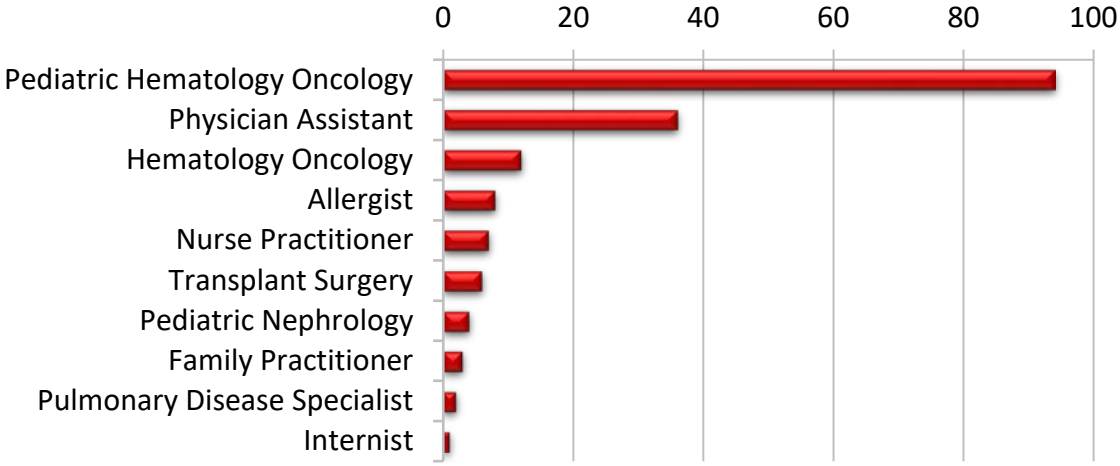
Calendar Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2018	234	750	$3,039,174.61	$4,052.23	3.2
2019	218	737	$3,139,993.27	$4,260.51	3.4
% Change	**-6.84%**	**-1.73%**	**3.32%**	**5.14%**	**5.65%**
Change	**-16**	**-13**	**$100,818.66**	**$208.28**	**0.2**

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

Demographics of Members Utilizing G-CSFs: Pharmacy Claims



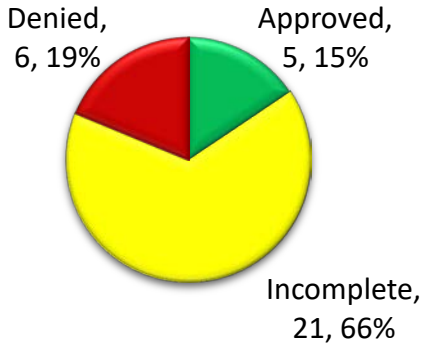
Top Prescriber Specialties of G-CSFs by Number of Claims: Pharmacy Claims



Prior Authorization of G-CSFs

There were 32 prior authorization requests submitted for G-CSFs during calendar year 2019. Currently, Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are available without prior authorization. The following chart shows the status of the submitted petitions for calendar year 2019.

Status of Petitions



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

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

- **November 2019:** The FDA approved Ziextenzo® (pegfilgrastim-bmez) as a biosimilar to Neulasta® (pegfilgrastim). Ziextenzo® is indicated for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy. Neulasta® was first FDA approved in 2002 and is also indicated for hematopoietic subsyndrome of acute radiation syndrome, in addition to the above listed indication for prophylaxis of febrile neutropenia. Pegfilgrastim is a pegylated derivative of filgrastim and has a longer elimination half-life compared to filgrastim. Ziextenzo® has been approved and marketed in Europe since 2018.

Pipeline:

- **PF-06881894 (Proposed Pegfilgrastim Biosimilar):** Pfizer is developing PF-06881894 as a proposed biosimilar to Neulasta® (pegfilgrastim); however, Pfizer's potential biosimilar product is currently the subject of litigation for patent infringement with Amgen, the manufacturer of Neulasta®.

Recommendations

The College of Pharmacy recommends the prior authorization of Ziextenzo® (pegfilgrastim-bmez) with the following criteria (changes shown in red):

Fulphila® (Pegfilgrastim-jmdb), Udenyca™ (Pegfilgrastim-cbqv), and Ziextenzo® (Pegfilgrastim-bmez) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Neulasta® (pegfilgrastim) or Neupogen® (filgrastim) must be provided.

Utilization Details of G-CSFs: Calendar Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FILGRASTIM PRODUCTS						
NEUPOGEN INJ 300/ML	73	13	$238,411.92	$3,265.92	5.6	31.09%
NEUPOGEN INJ 480/0.8ML	16	9	$62,760.96	$3,922.56	1.8	8.18%
NEUPOGEN INJ 300/0.5ML	6	5	$32,857.76	$5,476.29	1.2	4.28%
SUBTOTAL	**95**	**27**	**$334,030.64**	**$3,516.11**	**3.5**	**43.56%**
PEGFILGRASTIM PRODUCTS						
NEULASTA INJ 6/0.6ML	79	23	$432,822.89	$5,478.77	3.4	56.44%
SUBTOTAL	**79**	**23**	**$432,822.89**	**$5,478.77**	**3.4**	**56.44%**
TOTAL	**174**	**45***	**$766,853.53**	**$4,407.20**	**3.9**	**100%**

*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	CLAIMS/ MEMBER	% COST
PEGFILGRASTIM PRODUCTS						
PEGFILGRASTIM INJ J2505	682	210	$3,117,824.15	$4,571.59	3.2	99.29%
SUBTOTAL	**682**	**210**	**$3,117,824.15**	**$4,571.59**	**3.2**	**99.29%**
FILGRASTIM PRODUCTS						
FILGRASTIM INJ J1442	51	11	$21,026.72	$412.29	4.6	0.67%
TBO-FILGRASTIM INJ J1447	2	1	$556.80	$278.40	2	0.02%
FILGRASTIM-SNDZ INJ Q5101	2	1	$585.60	$292.80	2	0.02%
SUBTOTAL	**55**	**13**	**$22,169.12**	**$403.07**	**4.2**	**0.71%**
TOTAL	**737+**	**218***	**$3,139,993.27**	**$4,260.51**	**3.4**	**100%**

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

[1] Novartis. Sandoz Receives U.S. FDA Approval for Long-Acting Oncology Supportive Care Biosimilar Ziextenzo® (Pegfilgrastim-bmez). Available online at: https://www.novartis.com/news/media-releases/sandoz-receives-us-fda-approval-long-acting-oncology-supportive-care-biosimilar-ziextenzo-pegfilgrastim-bmez. Issued 11/05/2019. Last accessed 04/07/2020.
[2] Ziextenzo® (Pegfilgrastim-bmez) Prescribing Information. Novartis. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7dada041-6528-4acf-809c-62d271538c9a. Last revised 11/11/2019. Last accessed 04/07/2020.
[3] Pfizer. Pfizer Oncology Pipeline: Pipeline and Clinical Trials. Available online at: https://www.pfizer.com/science/oncology-cancer/pipeline. Last revised 01/28/2020. Last accessed 04/07/2020.
[4] Cipriano L. Amgen Sues Pfizer Over Proposed Neulasta® Biosimilar. *Big Molecule Watch*. Available online at: https://www.bigmoleculewatch.com/2020/02/12/amgen-sues-pfizer-over-proposed-neulasta-biosimilar/. Issued 02/12/2020. Last accessed 04/07/2020.

Appendix N

Calendar Year 2019 Annual Review of Allergen Immunotherapies and 30-Day Notice to Prior Authorize Palforzia™ (Peanut Allergen Powder-dnfp)

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria*

Grastek® (Timothy Grass Pollen Allergen Extract) Approval Criteria:

1. Member must be 5 to 65 years of age; and
2. Member must have a positive skin test (labs required) or *in vitro* testing for pollen specific IgE antibodies for Timothy grass or cross-reactive grass pollen (cool season grasses); and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of 2 different products for 14 days each during a previous season; and
    ~~b. **Montelukast:** (1) 14-day trial during a previous season in combination with an antihistamine; and~~
    c. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and
6. Treatment must begin ≥12 weeks prior to the start of the grass pollen season (November 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) Approval Criteria:

1. Member must be 5 to 65 years of age; and

2. Member must have a positive skin test or *in vitro* testing for pollen specific IgE antibodies to 1 of the 5 grass pollens contained in Oralair®; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of 2 different products for 14 days each during a previous season; and
    ~~b. **Montelukast:** (1) 14-day trial during a previous season in combination with an antihistamine; and~~
    c. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and
6. Treatment must begin ≥16 weeks prior to the start of the grass pollen season (October 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 months of therapy to include 16 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Ragwitek® (Short Ragweed Pollen Allergen Extract) Approval Criteria:

1. Member must be 18 to 65 years of age; and
2. Member must have a positive skin test or *in vitro* testing for pollen specific IgE antibodies to short ragweed pollen; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of 2 different products for 14 days each during a previous season; and
    ~~b. **Montelukast:** (1) 14-day trial during a previous season in combination with an antihistamine; and~~
    c. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each during a previous season; and
6. Treatment must begin ≥12 weeks prior to the start of ragweed pollen season (May 15th) and continue throughout the season; and

7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of 1 tablet daily will apply; and
9. Initial approvals will be for the duration of 6 months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Odactra® (House Dust Mite Allergen Extract) Approval Criteria:

1. Member must be 18 to 65 years of age; and
2. Member must have a positive skin test (labs required) to licensed house dust mite allergen extracts or *in vitro* testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of 2 different products for 14 days each; and
    ~~b. **Montelukast:** (1) 14-day trial in combination with an antihistamine; and~~
    c. **Intranasal corticosteroids:** Trials of 2 different products for 21 days each; and
6. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
7. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
8. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
9. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist; and
10. A quantity limit of 1 tablet daily will apply; and
11. Initial approvals will be for the duration of 6 months of therapy, at which time the prescriber must verify the patient is responding well to Odactra™ therapy. Additionally, compliance will be evaluated for continued approval.

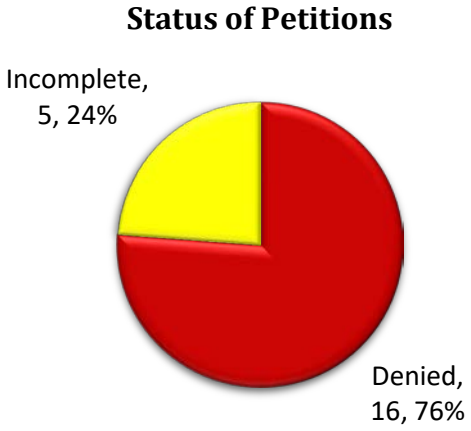
*Current prior authorization criteria is only applicable to allergen immunotherapies with a current federal drug rebate agreement. All criteria, regardless of coverage, are provided in this report for informational purposes.

Utilization of Allergen Immunotherapies: Calendar Year 2019

There was no SoonerCare utilization of allergen immunotherapies during calendar year 2019.

Prior Authorization of Allergen Immunotherapies

There were a total of 21 prior authorization requests submitted for allergen immunotherapies during calendar year 2019. The following chart shows the status of submitted petitions for calendar year 2019.



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

New U.S. Food and Drug Administration (FDA) Approvals and Label Update(s):

- **June 2019:** The FDA approved a supplemental Biologics License Application (sBLA) for Ragwitek® (short ragweed pollen allergen extract), to update the *Postmarketing Experience* section of the package labeling to include dysphonia (an impairment or change in voice quality) as a possible adverse reaction. This adverse reaction was reported voluntarily during post-exposure use of Ragwitek® in a population of uncertain size. The estimated frequency of this adverse reaction and casual relationship to drug exposure have not been established.
- **January 2020:** Aimmune Therapeutics announced that the FDA approved Palforzia™ (peanut allergen powder-dnfp). Palforzia™ is the first FDA approved treatment for patients with a peanut allergy and it is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, which may occur with accidental exposure to peanuts. Palforzia™ is approved for use in patients with a confirmed diagnosis of peanut allergy and is to be used in conjunction with a peanut-avoidant diet.
- **February 2020:** The FDA approved an sBLA for Odactra® (house dust mite allergen extract), to update the *Postmarketing Experience* section of the package labeling to include erythema as a possible adverse reaction.
- **March 2020:** The FDA announced that it is requiring a *Boxed Warning* for montelukast (sold under the brand name Singulair® and in generic form) to strengthen an existing warning about the risk of neuropsychiatric events associated with the drug, which is used to treat asthma and allergic rhinitis. The *Boxed Warning* advises health care providers to avoid prescribing montelukast for patients with mild symptoms, particularly those with allergic rhinitis. The warning follows the FDA's review of available data regarding continued reports of neuropsychiatric events with montelukast, such as agitation, depression, sleeping problems, and suicidal thoughts and actions. As part of

its review, the FDA re-evaluated the benefits and risks of montelukast as the treatment landscape has evolved since the drug was first approved in 1998. Based upon this assessment, the FDA determined the risks of montelukast may outweigh the benefits in some patients, particularly when the symptoms of the disease are mild and can be adequately treated with alternative therapies. For allergic rhinitis in particular, the FDA has determined that montelukast should be reserved for patients who have not responded adequately to other therapies or who cannot tolerate these therapies.

Guideline Updates:

- **May 2019:** The European Academy of Allergy and Clinical Immunology (EAACI) has developed a clinical practice guideline providing evidence-based recommendations for the use of house dust mites (HDM) allergen immunotherapy (AIT) as add-on treatment for HDM-driven allergic asthma. HDM sublingual AIT (SLIT) tablet is recommended as an add-on to regular asthma therapy for adults with controlled or partially controlled HDM-driven allergic asthma. HDM subcutaneous AIT (SCIT) is recommended for adults and children, and SLIT drops are recommended for children with controlled HDM-driven allergic asthma as the add-on to regular asthma therapy to decrease symptoms and medication needs.

Pipeline:

- **Dupixent® (Dupilumab):** Dupilumab, a monoclonal antibody against the interleukin 4 (IL-4) receptor, is currently FDA-approved to treat atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyps (CRSwNP). It is also being studied for peanut allergy, grass allergy, chronic obstructive pulmonary disease (COPD), and eosinophilic esophagitis. Dupilumab is being studied with a grass pollen SCIT to determine if the antibody can enhance the patient's response to the SCIT. A Phase 2 trial was recently completed with 103 patients in the United States and Canada studying dupilumab alone and as an adjunct therapy to Timothy Grass SCIT. After 16 weeks of treatment, allergic rhinitis symptoms were measured after nasal allergen challenge; however, no results have been reported and there has been no word from the company of when a Phase 3 trial is expected.
- **Ragwitek® (Short Ragweed Pollen Allergen Extract):** In November 2019, ALK presented Phase 3 data on Ragwitek® at the American College of Allergy, Asthma & Immunology (ACAAI) 2019 Annual Scientific Meeting. The data included efficacy and safety findings from the largest allergy immunotherapy clinical trial in children with ragweed allergic rhinitis with or without conjunctivitis (AR/C). The data demonstrated that Ragwitek® SLIT significantly improved AR/C symptoms in children 5 to 17 years of age and decreased medication use compared to placebo. Overall, treatment was well tolerated and discontinuation rates due to adverse events were low.
- **Viaskin® Peanut:** In August 2019, DBV Technologies submitted an updated Biologics License Application (BLA) to the FDA for Viaskin® Peanut for the treatment of peanut-allergic children 4 to 11 years of age. The company had initially submitted a BLA for Viaskin® Peanut in October 2018 but withdrew the application in order to address data needed on manufacturing procedures and quality controls. Viaskin® Peanut is an

epicutaneous immunotherapy (EPIT) that delivers small amounts of peanut protein through a wearable patch to induce desensitization. The BLA is supported by data from 2 Phase 3 trials (PEPITES and REALISE). The FDA accepted the BLA and set a prescription drug user fee act (PDUFA) target action date of August 5, 2020.

Palforzia™ (Peanut Allergen Powder-dnfp) Product Summary[10,11]

Indication(s): Palforzia™ (peanut allergen powder-dnfp) is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, which may occur with accidental exposure to peanut. Palforzia™ is approved for use in patients with a confirmed diagnosis of peanut allergy.

Dosing:

- Palforzia™ is supplied as 0.5mg, 1mg, 10mg, 20mg, and 100mg capsules or 300mg sachets containing powder for oral administration.
- The capsule or sachet should be opened and the entire contents emptied into a few spoonfuls of refrigerated or room temperature semisolid food (e.g., applesauce, yogurt, pudding) and mixed well.
- The entire volume of the prepared mixture should be consumed promptly.
- The capsules should not be swallowed nor the powder inhaled.
- Treatment with Palforzia™ is administered in 3 sequential phases: initial dose escalation, up-dosing, and maintenance.
- The Initial Dose Escalation Kit has designated levels (A through E) and contains: (1) 0.5mg capsule, (1) 1mg capsule, (1) 0.5mg capsule & (1) 1mg capsule, (3) 1mg capsules, and (6) 1mg capsules.
- Initial dose escalation is administered in sequential order on a single day (day 1) beginning at Level A and progressing through Level E as tolerated.
- Initial dose escalation is administered on a single day under the supervision of a health care professional in a health care setting with the ability to manage potentially severe allergic reactions, including anaphylaxis.
- Each dose should be separated by an observation period of 20 to 30 minutes with a 60-minute observation after the last dose and prior to discharge.
- The Up-Dosing kits contain 2-week kits of capsules or sachets with doses ranging from 3mg to 300mg.
- The day following completion of initial dosing, if possible, the patient should begin the Up-Dosing Kit; dosing should start at level 1 and progress through level 11 as tolerated in 2 week intervals.
- The first dose of each new up-dosing level should be administered under the supervision of a health care professional in a health care setting. The patient should be monitored for 60 minutes after administering the first dose of a new up-dosing level.
- If the patient tolerates the first dose of the increased dose level, the patient may continue that dose level at home.
- Office Dose Kits are available for in-office administration and observation of new up-dosing levels.

- The Maintenance Dose Kit contains (30) 300mg sachets and should begin after the completion of all up-dosing levels. The recommended maintenance dose is 300mg once daily.

Contraindication(s):

- Uncontrolled asthma
- History of eosinophilic esophagitis and other eosinophilic gastrointestinal (GI) disease

Warnings and Precautions:

- GI reactions: GI adverse reactions, including abdominal pain, vomiting, nausea, oral pruritus, and oral paresthesia, were commonly reported in Palforzia™-treated patients in the placebo-controlled clinical trial population. Dose modification should be considered for patients who report these reactions. For severe or persistent GI symptoms, a diagnosis of eosinophilic esophagitis should be considered.

Adverse Reactions: The most common adverse reactions reported in subjects treated with Palforzia™ (incidence ≥ 5% and at least 5% greater than that reported in subjects treated with placebo) are abdominal pain, vomiting, nausea, oral pruritus, oral paresthesia, throat irritation, cough, rhinorrhea, sneezing, throat tightness, wheezing, dyspnea, pruritus, urticaria, anaphylactic reaction, and ear pruritus.

Use in Specific Populations:

- Pregnancy: No human or animal data are available to establish the presence or absence of the risks due to Palforzia™ in pregnant women. Palforzia™ may cause anaphylaxis. Anaphylaxis can cause a dangerous decrease in blood pressure, which could result in compromised placental perfusion and significant risk to a fetus. A pregnancy exposure registry is available that monitors pregnancy outcomes in women exposed to Palforzia™ during pregnancy.
- Lactation: There are no data available on the presence of Palforzia™ in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of Palforzia™ have not been established in patients younger than 4 years of age.

Boxed Warning: Anaphylaxis

- Palforzia™ can cause anaphylaxis, which may be life-threatening and can occur at any time during therapy.
- Injectable epinephrine should be prescribed and patients should be instructed and trained on its appropriate use. Patients should be instructed to seek immediate medical care upon its use.
- Palforzia™ should not be administered to patients with uncontrolled asthma.
- Dose modifications may be necessary following an anaphylactic reaction.
- Patients should be observed during and after administration of the initial dose escalation and the first dose of each up-dosing level, for at least 60 minutes.
- Because of the risk of anaphylaxis, Palforzia™ is available only through the Palforzia™ Risk Evaluation and Mitigation Strategy (REMS) program.

Efficacy: The efficacy of Palforzia™ for the mitigation of allergic reactions, including anaphylaxis, in patients with a peanut allergy was investigated in a Phase 3, randomized, double-blind, placebo-controlled trial. The primary analysis population consisted of 496 patients (Palforzia™, N=372; placebo, N=124) 4 to 17 years of age in the intent-to-treat (ITT) population who received at least 1 dose of study treatment. After an initial dose escalation ranging from 0.5mg to 6mg on day 1 and confirmation of tolerability of the 3mg dose on day 2, patients underwent up-dosing for 20 to 40 weeks starting at 3mg until the 300mg dose was reached. The up-dosing period varied for each patient depending on how the dose was tolerated. Patients then underwent 24 to 28 weeks of maintenance immunotherapy with 300mg Palforzia™ until the end of the study. At the end of the maintenance period, subjects completed an exit double-blind, placebo-controlled food challenge (DBPCFC) to approximate an accidental exposure to peanut and to assess their ability to tolerate increasing amounts of peanut protein without dose-limiting symptoms. The median maximum tolerated dose of peanut protein at the screening food challenge, prior to receiving Palforzia™, was 10mg.

- The primary efficacy endpoint was the percentage of patients tolerating a single dose of 600mg peanut protein in the exit DBPCFC without dose-limiting symptoms after 6 months of maintenance treatment. Dose-limiting symptoms, in the setting of the DBPCFC, were any symptoms that, in the investigator's assessment, indicated poor tolerability of the last challenge dose administered, and precluded safe advancement to the next challenge dose. Mild symptoms of the skin (e.g., localized hives, limited skin flushing), respiratory system (e.g., occasional sneezing, nasal congestion), and GI system (e.g., mild nausea) may not have been considered dose-limiting unless these symptoms required pharmacological treatment. Of the 372 patients who received active treatment, 250 (67.2%) were able to ingest a dose of 600mg or more of peanut protein, without dose-limiting symptoms at the exit DBPCFC. Of the 124 patients who received placebo, 5 (4.0%) were able to ingest a dose of 600mg or more of peanut protein, without dose-limiting symptoms, at the exit DBPCFC [difference, 63.2%; 95% confidence interval (CI), 53.0 to 73.3; $P<0.001$].
- The key secondary end points included the proportion of patients who could tolerate single doses of 300mg and 1,000mg at the exit DBPCFC and the maximum severity of symptoms that occurred at any dose level of peanut protein during the exit DBPCFC. For the key secondary end points of tolerating the 300mg dose and the 1,000mg dose during the exit DBPCFC, the response rates in the active-drug group were 76.6% and 50.3%, respectively, as compared with 8.1% and 2.4%, respectively, in the placebo group ($P<0.001$ for both comparisons). During the exit DBPCFC, the maximum severity of symptoms was moderate in 25% of the participants in the active-drug group and 59% of those in the placebo group and severe in 5% and 11%, respectively ($P<0.001$ for both between-group differences).

Cost: The Wholesale Acquisition Cost (WAC) of the initial dose escalation kit is $30.03 which includes 13 capsules of various strengths for dosing of levels A through E and is administered in a single day (day 1 of treatment). The WAC for the up-dosing kits ranges from $444.60 to $445.20 (per 2-week supply), with a total cost to complete the 11 levels of up-dosing of

$4,895.10. The WAC for the maintenance dose kit is $890.10 per 30-day supply; resulting in a yearly maintenance dose cost of $10,681.20.

Recommendations

The College of Pharmacy recommends updating the current Allergen Immunotherapies approval criteria to remove the montelukast trial requirement based on the recent FDA *Boxed Warning*. The changes are shown in red in the *Current Prior Authorization Criteria* section.

Additionally, the College of Pharmacy recommends the prior authorization of Palforzia™ (peanut allergen powder-dnfp) with the following criteria:

Palforzia™ (Peanut Allergen Powder-dnfp) Approval Criteria:

1. Member must be 4 to 17 years of age to initiate initial dose escalation (maintenance dosing may be continued for members 4 years of age and older); and
2. Member must have a diagnosis of peanut allergy confirmed by a positive skin test, positive *in vitro* test for peanut-specific IgE, or positive clinician-supervised oral food challenge; and
3. Prescriber must confirm member will use Palforzia™ with a peanut-avoidant diet; and
4. Member must not have severe uncontrolled asthma; and
5. Member must not have a history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease; and
6. Member must not have had severe or life-threatening anaphylaxis within the previous 60 days; and
7. Member or caregiver must be trained in the use of an auto-injectable epinephrine device and have such a device available for immediate use at all times; and
8. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist; and
9. Prescriber, health care setting, and pharmacy must be certified in the Palforzia™ Risk Evaluation and Mitigation Strategy (REMS) program; and
10. Member must be enrolled in the Palforzia™ REMS program; and
11. Palforzia™ must be administered under the direct observation of a health care provider in a REMS certified health care setting with an observation duration in accordance with the prescribing information; and
12. Initial approvals will be for 6 months. For continued approval, the member must be compliant and prescriber must verify the member is responding well to treatment.

[1] Fink DL. U.S. Food and Drug Administration (FDA) Supplement Approval. Available online at: https://www.fda.gov/media/127818/download. Issued 06/07/2019. Last accessed 04/14/2020.
[2] Ragwitek® Prescribing Information. ALK. Available online at: https://ragwitek.com/app/uploads/sites/4/2020/02/USPI_US_RAG2019final.pdf. Last revised 06/2019. Last accessed 04/14/2020.
[3] Aimmune Therapeutics. FDA Approves Aimmune's Palforzia™ as First Treatment for Peanut Allergy. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20200131005593/en/. Issued 01/31/2020. Last accessed 04/14/2020.
[4] Fink DL. FDA Supplement Approval. Available online at https://www.fda.gov/media/135594/download. Issued 02/26/2020. Last accessed 04/14/2020.
[5] U.S. Food and Drug Administration (FDA). Drugs. FDA Requires Boxed Warning About Serious Mental Health Side Effects for Asthma and Allergy Drug Montelukast (Singulair); Advises Restricting Use for Allergic Rhinitis. Available online at: https://www.fda.gov/drugs/fda-requires-boxed-warning-about-serious-mental-health-side-effects-asthma-and-allergy-drug. Issued 03/11/2020. Last accessed 05/01/2020.
[6] Agache I, Lau S, Akdis CA, et al. EAACI Guidelines on Allergen Immunotherapy: House Dust Mite-Driven Allergic Asthma. *Allergy* 2019; 74(5):855-873.
[7] Burke CW. Allergy Immunotherapy: Relief that is Nothing to Sneeze at. *BioSpace*. Available online at: https://www.biospace.com/article/allergy-immunotherapy-relief-that-is-nothing-to-sneeze-at/. Issued 02/27/2020. Last accessed 04/14/2020.
[8] ALK. ALK to Present New Phase 3 Data Demonstrating the Efficacy and Safety of Ragwitek® (short ragweed pollen allergen extract tablet for sublingual use 12 Amb a 1-U) Sublingual Allergy Immunotherapy (SLIT)-Tablets in Pediatric Patients at ACAAI 2019 Annual Scientific Meeting. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/alk-to-present-new-phase-3-data-demonstrating-the-efficacy-and-safety-of-ragwitek-short-ragweed-pollen-allergen-extract-tablet-for-sublingual-use-12-amb-a-1-u-sublingual-allergy-immunotherapy-slit-tablets-in-pediatric-patient-300954202.html. Issued 11/08/2019. Last accessed 04/14/2020.
[9] Park B. FDA to Review Epicutaneous Immunotherapy for Peanut Allergy. *MPR*. Available online at: https://www.empr.com/home/news/drugs-in-the-pipeline/fda-to-review-epicutaneous-immunotherapy-for-peanut-allergy/. Issued 10/07/2019. Last accessed 04/14/2020.
[10] Palforzia™ Prescribing Information. Aimmune Therapeutics. Available online at: https://www.palforzia.com/static/pi_palforzia.pdf. Last revised 01/2020. Last accessed 04/14/2020.
[11] Vickery BP, Vereda A, Casale TB, et al. AR101 Oral Immunotherapy for Peanut Allergy. *N Engl J Med* 2018; 379:1991-2001.

Appendix O

Calendar Year 2019 Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Nourianz™ (Istradefylline Tablet)

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria

Duopa™ (Carbidopa/Levodopa Enteral Suspension) Approval Criteria:

1. An FDA approved diagnosis of advanced Parkinson's disease (PD); and
2. For long-term administration, member or caregivers must be willing and able to administer Duopa™ through a percutaneous endoscopic gastrostomy; and
3. Patients must be experiencing 3 hours or more of "off" time on their current PD drug treatment and they must have demonstrated a clear responsiveness to treatment with levodopa; and
4. Approvals will be for a quantity of 1 cassette per day.

Gocovri® [Amantadine Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication for the treatment of dyskinesia in patients with Parkinson's disease (PD) receiving levodopa-based therapy; and
2. Member must use Gocovri® concomitantly with levodopa therapy; and
3. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m^2]; and
4. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
5. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
6. A patient-specific, clinically significant reason why Osmolex ER™ (amantadine ER) cannot be used must be provided; and
7. A quantity limit of (1) 68.5mg capsule or (2) 137mg capsules per day will apply.

Inbrija™ (Levodopa Inhalation Powder) Approval Criteria:

1. An FDA approved indication for the treatment of "off" episodes in patients with Parkinson's disease (PD) treated with carbidopa/levodopa; and
2. Member must be taking carbidopa/levodopa in combination with Inbrija™. Inbrija™ has been shown to be effective only in combination with carbidopa/levodopa; and
3. The member must be experiencing motor fluctuations with a minimum of 2 hours of "off" time and demonstrate levodopa responsiveness; and
4. Member must not be taking nonselective monoamine oxidase inhibitors (MAOIs) concomitantly with Inbrija™ or within 2 weeks prior to initiating Inbrija™; and
5. A previous failed trial of immediate-release (IR) carbidopa/levodopa formulations alone or in combination with long-acting carbidopa/levodopa formulations or a reason why

supplementation with IR carbidopa/levodopa formulations is not appropriate for the member must be provided; and
6. A quantity limit of 10 capsules for inhalation per day will apply.

Neupro® (Rotigotine Transdermal System) Approval Criteria:

1. For the diagnosis of Parkinson's disease (PD) the following criteria apply:
    a. An FDA approved indication for the treatment of signs and symptoms of PD; and
    b. Member must be 18 years of age or older; and
    c. Failed treatment, intolerance, or a patient-specific, clinically significant reason why the member cannot use oral dopamine agonists must be provided.
2. For the diagnosis of restless leg syndrome (RLS) the following criteria apply:
    a. An FDA approved indication of RLS; and
    b. Member must be 18 years of age or older; and
    c. Documented treatment attempts at recommended dose with at least 2 of the following that did not yield adequate relief:
        i. Carbidopa/levodopa; or
        ii. Pramipexole; or
        iii. Ropinirole.

Nuplazid® (Pimavanserin) Approval Criteria:

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease (PD) psychosis; and
2. Member must have a concomitant diagnosis of PD; and
3. Member must not be taking concomitant medications known to prolong the QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin); and
4. The member must not have a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia, hypomagnesemia, and the presence of congenital prolongation of the QT interval; and
5. Nuplazid® will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD psychosis; and
6. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
7. A quantity limit of 1 tablet per day will apply.

Osmolex ER™ [Amantadine Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication for the treatment of Parkinson's disease (PD) or drug-induced extrapyramidal reactions in adults patients; and
2. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m^2]; and

3. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
4. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
5. A quantity limit will apply based on FDA approved dosing regimen(s).

Requip XL® [Ropinirole Extended-Release (ER)] and Mirapex ER® (Pramipexole ER) Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease (PD); and
2. A patient-specific, clinically significant reason why the immediate-release products cannot be used must be provided.

Rytary® [Carbidopa/Levodopa Extended-Release (ER) Capsule] Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease (PD), post-encephalitic parkinsonism, or parkinsonism that may follow carbon monoxide intoxication or manganese intoxication; and
2. A patient-specific, clinically significant reason why the member cannot use other generic carbidopa/levodopa combinations including Sinemet® CR (carbidopa/levodopa ER tablet) must be provided.

Xadago® (Safinamide) Approval Criteria:

1. An FDA approved indication as adjunctive treatment to carbidopa/levodopa in patients with Parkinson's disease (PD) experiencing "off" episodes; and
2. Member must be taking carbidopa/levodopa in combination with safinamide (safinamide has not been shown to be effective as monotherapy for the treatment of PD); and
3. A patient-specific, clinically significant reason why the member cannot use rasagiline or other lower cost monoamine oxidase type B (MAO-B) inhibitors must be provided; and
4. Member must not have severe hepatic impairment; and
5. Member must not be taking any of the following medications concomitantly with safinamide:
    a. Monoamine oxidase inhibitors (MAOIs); or
    b. Linezolid; or
    c. Opioid analgesics (including tramadol); or
    d. Selective norepinephrine reuptake inhibitors (SNRIs); or
    e. Tri- or tetra-cyclic or triazolopyridine antidepressants; or
    f. St. John's wort; or
    g. Cyclobenzaprine; or
    h. Methylphenidate and its derivatives; or
    i. Amphetamine and its derivatives; or
    j. Dextromethorphan; and
6. Prescriber must verify member has been counseled on avoiding foods that contain a large amount of tyramine while taking safinamide; and
7. A quantity limit of 1 tablet per day will apply.

Utilization of PD Medications: Calendar Year 2019

The following utilization data includes PD medications used for all diagnoses and does not differentiate between PD diagnoses and other diagnoses, for which use may be appropriate.

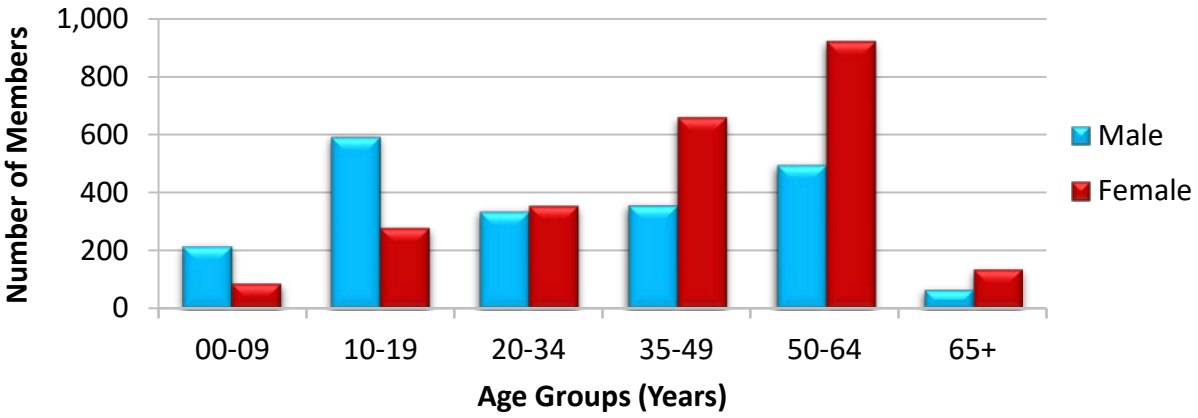
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	4,595	25,797	$845,086.51	$32.76	$1.02	1,656,648	827,830
2019	4,497	25,838	$884,369.41	$34.23	$1.07	1,628,169	823,109
% Change	**-2.10%**	**0.20%**	**4.60%**	**4.50%**	**4.90%**	**-1.70%**	**-0.60%**
Change	**-98**	**41**	**$39,282.90**	**$1.47**	**$0.05**	**-28,479**	**-4,721**

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

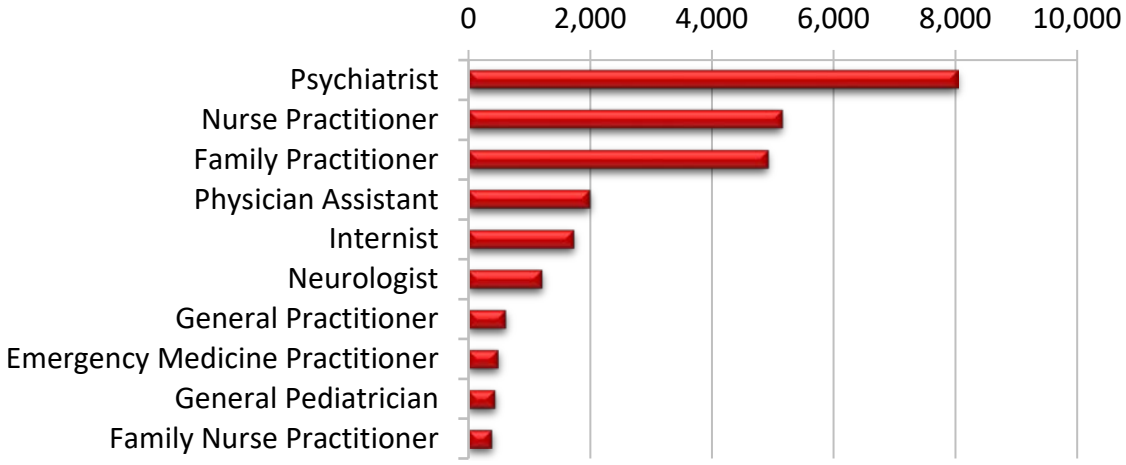
- There were no SoonerCare paid medical claims for Duopa™ (carbidopa/levodopa enteral suspension) during calendar year 2019.

Demographics of Members Utilizing PD Medications



- The utilization data includes PD medications used for all diagnoses and does not differentiate between PD diagnoses and other diagnoses, for which use may be appropriate. Utilization of PD medications in the pediatric population can be accounted for by the inclusion of amantadine in the utilization data. Amantadine is indicated for the prophylaxis and treatment of the signs and symptoms of infection caused by various strains of the influenza A virus.

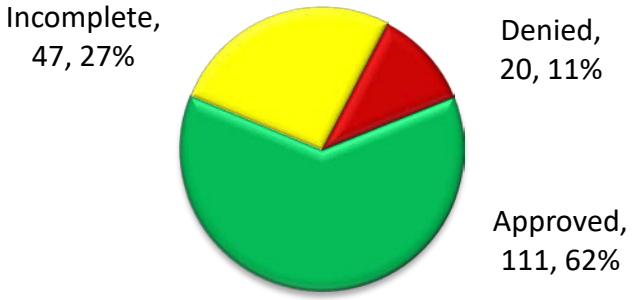
Top Prescriber Specialties of PD Medications by Number of Claims



Prior Authorization of PD Medications

There were 178 prior authorization requests submitted for PD medications during calendar year 2019. The following chart shows the status of the submitted petitions for calendar year 2019.

Status of Petitions



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

Patent Expiration(s):

- Duopa™ (carbidopa/levodopa enteral suspension): There are no unexpired patents for Duopa™; however, exclusivity expiration is anticipated in January 2022
- Azilect® (rasagiline tablet): August 2027
- Nourianz™ (istradefylline tablet): September 2027
- Rytary® [carbidopa/levodopa extended-release (ER) capsule]: December 2028
- Xadago® (safinamide tablet): December 2028
- Neupro® (rotigotine transdermal patch): March 2032
- Inbrija™ (levodopa inhalation powder): November 2032
- Gocovri® (amantadine ER capsule): December 2034
- Osmolex ER™ (amantadine ER tablet): February 2038
- Nuplazid® (pimavanserin tablet): August 2038

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

- **August 2019:** The FDA approved Nourianz™ (istradefylline tablet) as an add-on treatment to carbidopa/levodopa in adult patients with 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. The effectiveness of Nourianz™ was shown in (4) 12-week, placebo-controlled, clinical studies that included a total of 1,143 patients. In all 4 studies, patients treated with Nourianz™ experienced a statistically significant decrease from baseline in daily "off" time compared to patients receiving a placebo. The most common adverse reactions observed in patients taking Nourianz™ were dyskinesia, dizziness, constipation, nausea, hallucination, and insomnia. Patients taking Nourianz™ should be monitored for the development of dyskinesia or exacerbation of existing dyskinesia. If hallucinations, psychotic behavior, or impulsive/compulsive behavior occurs, a dosage reduction or discontinuation 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 with Nourianz™.

News:

- **November 2019:** A study evaluating the possible association between high exposure to antibiotics and the onset of PD was published in *Movement Disorders*. Investigators from Helsinki University Hospital in Finland carried out a nationwide case-control study to compare antibiotic exposure in a large group of patients with and without PD. The study population consisted of 13,976 PD cases and 40,697 control cases. The strongest connection with PD risk was found for oral exposure to macrolides and lincosamides (adjusted odds ratio up to 1.416; 95% confidence interval, 1.053–1.904). After correction for multiple comparisons, exposure to antianaerobics and tetracyclines 10 to 15 years before the index date, sulfonamides and trimethoprim 1 to 5 years before the index date, and antifungal medications 1 to 5 years before the index date were positively associated with PD risk. In post hoc analyses, further positive associations were found for broad-spectrum antibiotics. The study concluded, exposure to certain types of oral antibiotics seems to be associated with an elevated risk of PD with a delay that is consistent with the proposed duration of a prodromal period. The pattern of associations supports the hypothesis that effects on gut microbiota could link antibiotics to PD, but further studies are needed to confirm this.
- **April 2020:** A report highlighting the potential negative impact caused by the SARS-CoV-2 virus (and the COVID-19 pandemic) on PD patients, including increased stress and limits on physical activity which could worsen their symptoms, was published in the *Journal of Parkinson's Disease*. Social distancing may be a particular burden to people with PD due to the ability to rapidly adapt to new circumstances being largely dependent on brain systems involving the neurotransmitter dopamine. Such drastic changes require a flexible adaptation to new circumstances, which is a cognitive operation that depends on normal dopaminergic functioning. A large body of literature has shown that many PD patients experience cognitive and motor inflexibility, as a result of nigrostriatal dopamine depletion that forms the pathophysiological substrate of PD. Importantly, increased levels of stress during the COVID-19 pandemic may have

several short-term as well as long-term adverse consequences for individuals with PD. First, increased psychological stress can temporarily worsen various motor symptoms, such as tremor, freezing of gait, or dyskinesias, while it reduces the efficacy of dopaminergic medication. Second, increased stress may unmask a latent hypokinetic rigid syndrome, possibly by depleting compensatory mechanisms. This could lead to an increase in numbers of new PD diagnoses during the pandemic. In a year from now, it might be worthwhile to investigate incidence levels of PD during this time of crisis, as compared to the period before. Third, animal studies have shown that prolonged episodes of chronic stress may worsen the rate of dopaminergic cell loss in response to a toxin. Comparable studies in human patients are lacking, so it remains presently unclear whether chronic stress can actually accelerate PD.

Another hidden but potentially highly disconcerting consequence of the pandemic is a marked reduction in physical activities. Many people are now largely stuck at home, being unable to go out for a regular walk, let alone to see their physiotherapist or attend a fitness class. Recent evidence has shown that physical exercise may attenuate clinical symptom progression in PD. However, there are also emerging opportunities. This crisis calls for the rapid introduction of better self-management strategies that can help patients to better deal with the challenges of social distancing and the other consequences of this crisis. The COVID-19 pandemic is an external stressor that is aligned in time for large groups of people. This provides a unique opportunity for researchers to test how the pandemic influences the course of PD in existing longitudinal cohorts (e.g., by taking advantage of wearable sensors or biological biomarkers). It also allows researchers to test which factors protect patients from the detrimental consequences of this crisis, increasing our insight into the resilience in PD. The report concluded that the COVID-19 pandemic crisis, as deleterious as the crisis may be, may also bring some long-term positive outcomes for the many people living with PD worldwide.

Pipeline:

- **Apomorphine Sublingual (SL) Film (APL-130277):** In December 2019, Sunovion announced the FDA has accepted its second submission of its New Drug Application (NDA) for apomorphine SL film (APL-130277) to treat motor fluctuations ("off" episodes) experienced by people living with PD. In late January 2019, Sunovion announced that the FDA declined to approve APL-130277; Sunovion did not disclose specific reasons why the drug was not approved. Apomorphine SL film is a novel formulation of apomorphine, a dopamine agonist, being developed as a fast-acting on-demand treatment of "off" episodes associated with PD. Apomorphine SL film is designed to offer a potential option that may be used to treat "off" episodes associated with PD up to 5 times throughout the day. It may help patients with PD rapidly convert from the "off" to the "on" state. Results of the pivotal Phase 3 study (CTH-300) of apomorphine SL film were recently published in *Lancet Neurology.* The expected action date by the FDA under the Prescription Drug User Fee Act (PDUFA) is May 21, 2020.
- **AXO-Lenti-PD:** In June 2019, Axovant Gene Therapies reported 6-month follow-up data from the first dose cohort in the open-label, dose-escalation portion of the ongoing SUNRISE-PD Phase 2 study of AXO-Lenti-PD for the treatment of PD. AXO-Lenti-PD is an

investigational gene therapy for the treatment of PD that is designed to deliver 3 genes (tyrosine hydroxylase, cyclohydrolase 1, and aromatic L-amino acid decarboxylase) via a single lentiviral vector to encode a set of critical enzymes required for dopamine synthesis with the goal of reducing variability and restoring steady levels of dopamine in the brain. The investigational gene therapy aims to provide patient benefit for years following a single administration. AXO-Lenti-PD was observed to be generally well tolerated with no serious adverse events related to the product or procedure, and patients showed continued improvement from baseline across multiple measurements.

- **Foliglurax:** In March 2020, Lundbeck announced the development program for foliglurax, a small molecule modulator that acts on mGluR4 glutamate receptors under investigation for the treatment of PD, has been terminated after the Phase 2 clinical study AMBLED failed to show sufficient efficacy. There was no statistically significant difference in change from baseline in "off" time versus placebo after a 4-week treatment period. The difference in change from baseline versus placebo was 0.27 hours and 0.44 hours for the 10mg and 30mg doses (twice daily), respectively, as assessed by the Hauser diary. Neither of the foliglurax doses separated from placebo on dyskinesia (secondary endpoint). The study showed an acceptable clinical safety and tolerability profile in patients with PD. Lundbeck is conducting additional analyses to understand the totality of the foliglurax data. The results from the study will be published in the near future following international publication guidelines.
- **Mesdopetam (IRL790):** In August 2018, Integrative Research Laboratories (IRLAB) announced that the in-depth analysis of the data from the recently concluded Phase 2a study of mesdopetam in PD patients with L-dopa induced dyskinesia (LIDs) brings further evidence of the drug candidate's ability to significantly and meaningfully improve daytime movement quality. IRLAB has therefore decided to prioritize the LIDs indication in the development of mesdopetam. A Phase 2b/3 study in this patient group is planned to start in the first half of 2020, as part of a pivotal clinical program towards market approval. The planned study in PD psychosis will be performed in parallel with the pivotal program in LIDs. In February 2020, IRLAB announced the decision to use the name mesdopetam for its drug candidate IRL790 following the recommendation for International Nonproprietary Name (INN) by the World Health Organization (WHO). WHO concluded that IRL790 is wholly unique in its mechanism of action and has, therefore, assigned IRL790 a new INN that can become a new substance class in the existing classification system for pharmaceutical substances. The INN will serve to identify the active pharmaceutical substance mesdopetam (IRL790) worldwide.
- **Opicapone:** In July 2019, Neurocrine Biosciences announced the FDA accepted an NDA for opicapone, a once-daily, oral, selective catechol-O-methyltransferase (COMT) inhibitor as an adjunctive treatment to carbidopa/levodopa in patients with PD experiencing "off" episodes. The NDA for opicapone is supported by data from 38 clinical studies, including 2 Phase 3 studies (BIPARK-1 and BIPARK-2), with more than 1,000 patients with PD treated with opicapone. BIPARK-1 was a Phase 3, randomized, double-blind, placebo- and active-controlled study of opicapone as an adjunct to levodopa therapy in which approximately 600 patients with PD and motor fluctuations

received once-daily opicapone (5mg, 25mg, or 50mg), placebo, or 200mg doses of the COMT inhibitor entacapone for 14 to 15 weeks. BIPARK-2 was a Phase 3, randomized, double-blind, placebo-controlled study of opicapone as an adjunct to levodopa therapy in which approximately 400 patients with PD and motor fluctuations received once-daily opicapone (25mg or 50mg) or placebo for 14 to 15 weeks. The primary endpoint in both studies was the change from baseline in absolute time in the "off" state, as assessed by patient diaries. In June 2016, BIAL Pharmaceuticals received approval from the European Commission for Ongentys® (opicapone) as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCIs) in adult patients with PD and end-of-dose motor fluctuations who cannot be stabilized on those combinations; BIAL currently markets Ongentys® in Germany, United Kingdom, Spain, Portugal, and Italy. Neurocrine Biosciences in-licensed opicapone from BIAL in 2017 and has exclusive development and commercialization rights in the United States and Canada. The FDA has set a standard 12-month review process for opicapone with a PDUFA target action date of April 26, 2020.

- **Pimavanserin (Nuplazid®):** Acadia Pharmaceuticals announced the topline results of HARMONY, a Phase 3, double-blind, placebo-controlled, relapse prevention study in 392 patients evaluating pimavanserin for the treatment of dementia-related psychosis in December 2019. HARMONY was designed to evaluate the efficacy and safety of pimavanserin for the treatment of delusions and hallucinations associated with dementia-related psychosis across a broad population of patients with the most common clinically diagnosed subtypes of dementia including: PD dementia, Alzheimer's dementia, dementia with Lewy bodies, vascular dementia, and frontotemporal dementia spectrum disorders. Pimavanserin was stopped at the pre-planned interim analysis and met the primary endpoint of the study by significantly reducing risk of relapse of psychosis by 2.8 fold compared to placebo [hazard ratio (HR) = 0.353; one-sided P=0.0023]. In addition, pimavanserin met the key secondary endpoint by significantly reducing risk of discontinuation for any reason by 2.2 fold (HR = 0.452; one-sided P=0.0024). Acadia is planning to meet with the FDA in the first half of 2020 regarding a supplemental NDA (sNDA) submission. The FDA previously granted pimavanserin Breakthrough Therapy designation for the treatment of dementia-related psychosis. Currently, no drug is approved by the FDA for the treatment of dementia-related psychosis. Pimavanserin was approved for the treatment of hallucinations and delusions associated with PD psychosis by the FDA in April 2016 under the trade name Nuplazid®. Nuplazid® is not approved for dementia-related psychosis, schizophrenia, or major depressive disorder.
- **PR001:** In March 2020, Prevail Therapeutics announced an update on the clinical advancement of its gene therapy program PR001 for patients with PD with *GBA1* mutations (PD-GBA). Enrollment in the PR001 Phase 1/2 PROPEL clinical study is progressing, patient dosing continues, and the company is on track to report interim data on a subset of patients in the second half of 2020. The PROPEL study is a randomized, double-blind Phase 1/2 clinical study evaluating the safety and tolerability of 2 escalating dose levels of PR001 in up to 16 patients with moderate-to-severe PD-GBA. The trial also evaluates the effect of PR001 on biomarkers of disease activity and

on PD clinical efficacy measures. PR001 utilizes an adeno-associated virus vector to deliver the *GBA1* gene to a patient's cells, correcting the lysosomal enzyme deficiency caused by PD-GBA patients' *GBA1* mutations. *GBA1* encodes the lysosomal enzyme, beta-glucocerebrosidase, or GCase, which is required for the disposal and recycling of glycolipids. PD-GBA patients have a mutation in at least 1 chromosomal copy of *GBA1*. In addition to the PROPEL clinical study for patients with PD-GBA, PR001 is also being developed for neuronopathic Gaucher disease, a devastating disorder that shares the same underlying genetic mechanism. In December 2019, Prevail announced that its Investigational New Drug (IND) application for PR001 for the treatment of neuronopathic Gaucher disease is active.

- **Prasinezumab (PRX002/RG7935):** Roche is currently conducting a randomized double-blind, placebo-controlled, 52-week, Phase 2 study of prasinezumab, an investigational, intravenous (IV) monoclonal antibody that targets α-synuclein, a protein that is believed to misfold and aggregate to form the protein structures that are implicated in PD pathology. The study enrolled 316 adult patients with early PD. The study's primary outcome measure is the change from baseline in the Movement Disorder Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) Total Score at week 52. The estimated study completion date is February 2021.

Nourianz™ (Istradefylline Tablet) Product Summary[16]

Indication(s): Nourianz™ (istradefylline) is an adenosine receptor antagonist indicated as adjunctive treatment to carbidopa/levodopa in adult patients with PD experiencing "off" episodes.

Dosing:

- Nourianz™ is available as an oral tablet in 2 strengths: 20mg and 40mg.
- Nourianz™ may be taken with or without food.
- The recommended dosage of Nourianz™ is 20mg orally once daily. The dose may be increased to a maximum of 40mg once daily.
- The maximum recommended dosage with moderate hepatic impairment is 20mg once daily. Use of Nourianz™ in patients with severe hepatic impairment should be avoided.
- For patients who smoke 20 or more cigarettes per day (or the equivalent of another tobacco product), the recommended dosage is 40mg once daily.

Mechanism of Action: The precise mechanism by which istradefylline exerts its therapeutic effect in PD is unknown. In *in vitro* studies and *in vivo* animal studies, istradefylline was demonstrated to be an adenosine A_{2A} receptor antagonist.

Contraindication(s): None.

Warnings and Precautions:

- Dyskinesia: Nourianz™ in combination with levodopa may cause or exacerbate pre-existing dyskinesia. In controlled clinical studies (Studies 1, 2, 3, and 4), the incidence of dyskinesia was 15% for Nourianz™ 20mg, 17% for Nourianz™ 40mg, and 8% for placebo, in combination with levodopa. One percent of patients treated with either Nourianz™

20mg or 40mg discontinued treatment because of dyskinesia, compared to 0% for placebo.

- Hallucinations/Psychotic Behavior: Because of the potential risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Nourianz™. Dosage reduction or discontinuation should be considered if a patient develops hallucinations or psychotic behaviors while taking Nourianz™. In controlled clinical studies (Studies 1, 2, 3, and 4), the incidence of hallucinations was 2% for Nourianz™ 20mg, 6% for Nourianz™ 40mg, and 3% for placebo. In patients treated with Nourianz™ 40mg, 1% discontinued because of hallucinations, compared to 0% for placebo and 0% for patients treated with Nourianz™ 20mg. The incidence of "abnormal thinking and behavior" (paranoid ideation, delusions, confusion, mania, disorientation, aggressive behavior, agitation, or delirium) reported as an adverse reaction was 1% for Nourianz™ 20mg, 2% for Nourianz™ 40mg, and 1% for placebo.
- Impulse Control/Compulsive Behaviors: Patients treated with Nourianz™ and 1 or more medication(s) for the treatment of PD (including levodopa) may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges. In controlled clinical studies (Studies 1, 2, 3, and 4), 1 patient treated with Nourianz™ 40mg was reported to have impulse control disorder, compared to no patients on placebo or Nourianz™ 20mg. In some post marketing cases, these urges were reported to have stopped when the dose was reduced or when the medication was discontinued. Because patients may not recognize these behaviors as abnormal, it is recommended that prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, binge or compulsive eating, or other urges while being treated with Nourianz™. Dose reduction or discontinuation should be considered if a patient develops such urges while taking Nourianz™.

Drug Interactions:

- Strong CYP3A4 Inhibitors: The recommended maximum dosage of Nourianz™ with concomitant use of strong CYP3A4 inhibitors is 20mg once daily.
- Strong CYP3A4 Inducers: Concomitiant use of Nourianz™ with strong CYP3A4 inducers should be avoided.

Adverse Reactions: The most common adverse reactions (≥5% and more frequent than placebo) were dyskinesia, dizziness, constipation, nausea, hallucinations, and insomnia.

Efficacy: The efficacy of Nourianz™ for the adjunctive treatment to carbidopa/levodopa in patients with PD experiencing "off" episodes was demonstrated in 4 randomized, multicenter, double-blind, 12-week, placebo-controlled studies. The studies enrolled patients with a mean duration of PD of 9 years (range: 1 month to 37 years) that were Hoehn and Yahr Stage II to IV, experiencing at least 2 hours (mean approximately 6 hours) of "off" time per day, and were treated with levodopa for at least 1 year, with stable dosage for at least 4 weeks before screening. Patients continued levodopa treatment with or without concomitant PD medications, including dopamine agonists (85%), COMT inhibitors (38%), MAO-B inhibitors

(40%), anticholinergics (13%), and/or amantadine (33%), provided the medications were stable for at least 4 weeks before screening and throughout the study period. The primary efficacy endpoint was the change from baseline in the daily awake percentage of "off" time or the change from baseline in total daily "off" time, based on 24-hour diaries completed by patients. A change from baseline in "on" time without troublesome dyskinesia (i.e., "on" time without dyskinesia plus "on" time with non-troublesome dyskinesia) was a secondary efficacy endpoint.

- Study 1 was conducted in the United States and Canada, and Study 2 was conducted in the United States. In these studies, patients were randomized to once-daily treatment with Nourianz™ 20mg, 40mg, or placebo. Patients treated with Nourianz™ 20mg or Nourianz™ 40mg once daily experienced a statistically significant decrease from baseline in percentage of daily awake "off" time, compared with patients on placebo. Compared with patients on placebo, patients treated with Nourianz™ experienced an additional increase from baseline in "on" time without troublesome dyskinesia of 0.96 hours (nominal p=0.026) in Study 1 and of 0.55 hours (nominal P=0.135) in Study 2.
- Study 3 and Study 4 were conducted in Japan. In these studies, patients were randomized equally to treatment with Nourianz™ 20mg, 40mg, or placebo. Patients treated with Nourianz™ 20mg or Nourianz™ 40mg once daily experienced a statistically significant decrease from baseline in "off" time compared with patients on placebo. In Study 3, compared with placebo, an additional increase from baseline in "on" time without troublesome dyskinesia of 0.57 hours (nominal P=0.085) and of 0.65 hours (nominal P=0.048) was observed in patients treated with Nourianz™ 20mg or Nourianz™ 40mg, respectively. In Study 4, the corresponding increases in "on" time without troublesome dyskinesia were 0.83 hours (nominal P=0.008) for Nourianz™ 20mg and 0.81 hours (nominal p=0.008) for Nourianz™ 40mg.

Cost Comparison:

Medication	Cost Per Tablet	Cost Per Month	Cost Per Year
Nourianz™ (istradefylline) 20mg and 40mg tablet	**$50.00**	**$1,500.00⁺**	**$18,000.00⁺**
carbidopa/levodopa 25mg/250mg tablet	$0.13	$15.60*	$187.20*

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
⁺Costs based on Nourianz™ dosed once daily.
*Costs based on carbidopa/levodopa 25mg/250mg dosed 4 times daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Nourianz™ (istradefylline tablet) with the following criteria:

Nourianz™ (Istradefylline Tablet) Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease (PD); and
2. Member must be taking carbidopa/levodopa in combination with istradefylline (istradefylline has not been shown to be effective as monotherapy for the treatment of PD); and

3. Prescriber must verify that the dose is appropriate for the member based on degree of hepatic impairment, concomitant strong CYP3A4 inhibitors, and smoking status of the member; and
4. Member must be experiencing at least 2 hours of "off" time per day; and
5. A quantity limit of 1 tablet per day will apply.

Utilization Details of PD Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
AMANTADINE PRODUCTS						
AMANTADINE CAP 100MG	3,262	567	$112,262.25	5.75	$1.15	$34.42
AMANTADINE TAB 100MG	1,576	323	$92,974.32	4.88	$1.96	$58.99
AMANTADINE SYP 50MG/5ML	236	70	$4,030.32	3.37	$0.67	$17.08
GOCOVRI CAP 137MG	7	1	$17,991.25	7	$85.67	$2,570.18
SUBTOTAL	**5,081**	**961**	**$227,258.14**	**5.29**	**$1.50**	**$44.73**
BENZTROPINE PRODUCTS						
BENZTROPINE TAB 1MG	5,744	1,116	$79,635.46	5.15	$0.46	$13.86
BENZTROPINE TAB 2MG	2,317	398	$35,820.86	5.82	$0.50	$15.46
BENZTROPINE TAB 0.5MG	2,089	401	$27,821.92	5.21	$0.45	$13.32
SUBTOTAL	**10,150**	**1,915**	**$143,278.24**	**5.30**	**$0.47**	**$14.12**
ROPINIROLE PRODUCTS						
ROPINIROLE TAB 1MG	1,312	387	$16,108.80	3.39	$0.31	$12.28
ROPINIROLE TAB 0.5MG	1,192	358	$14,824.01	3.33	$0.34	$12.44
ROPINIROLE TAB 2MG	816	221	$9,952.32	3.69	$0.33	$12.20
ROPINIROLE TAB 0.25MG	620	216	$7,517.97	2.87	$0.36	$12.13
ROPINIROLE TAB 4MG	325	84	$4,489.16	3.87	$0.34	$13.81
ROPINIROLE TAB 3MG	211	60	$2,898.21	3.52	$0.35	$13.74
ROPINIROLE TAB 5MG	112	26	$1,913.07	4.31	$0.43	$17.08
SUBTOTAL	**4,588**	**1,352**	**$57,703.54**	**3.39**	**$0.34**	**$12.58**
TRIHEXYPHENIDYL PRODUCTS						
TRIHEXYPHENIDYL TAB 5MG	1,093	187	$16,029.46	5.84	$0.48	$14.67
TRIHEXYPHENIDYL TAB 2MG	960	229	$11,596.11	4.19	$0.40	$12.08
TRIHEXYPHENIDYL ELXIR 0.4MG/ML	144	25	$4,252.60	5.76	$1.02	$29.53
SUBTOTAL	**2,197**	**441**	**$31,878.17**	**4.98**	**$0.48**	**$14.51**
CARBIDOPA/LEVODOPA PRODUCTS						
CARB/LEVO TAB 25-100MG	789	149	$13,909.47	5.3	$0.57	$17.63
CARB/LEVO TAB 25-250MG	242	34	$5,626.04	7.12	$0.77	$23.25
CARB/LEVO TAB 10-100MG	207	41	$4,135.21	5.05	$0.61	$19.98
CARB/LEVO ER TAB 50-200MG	129	21	$5,413.65	6.14	$1.25	$41.97
CARB/LEVO ER TAB 25-100MG	49	10	$1,801.19	4.9	$1.24	$36.76
RYTARY CAP 245MG	13	2	$8,970.26	6.5	$23.00	$690.02
RYTARY CAP 95MG	9	1	$4,175.11	9	$15.46	$463.90
CARB/LEVO ODT 25-100MG	1	1	$35.01	1	$1.17	$35.01
SUBTOTAL	**1,439**	**259**	**$44,065.94**	**5.56**	**$0.98**	**$30.62**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
CARBIDOPA/LEVODOPA/ENTACAPONE PRODUCTS						
CARB/LEVO/ENTACA TAB 25/100/200MG	28	5	$3,276.21	5.6	$4.04	$117.01
CARB/LEVO/ENTACA TAB 37.5/150/200MG	19	3	$3,012.19	6.33	$5.44	$158.54
CARB/LEVO/ENTACA TAB 50/200/200MG	9	3	$765.51	3	$3.20	$85.06
CARB/LEVO/ENTACA TAB 31.25/125/200MG	4	1	$465.34	4	$4.65	$116.34
CARB/LEVO/ENTACA TAB 12.5/50/200MG	1	1	$35.50	1	$1.18	$35.50
SUBTOTAL	**61**	**13**	**$7,554.75**	**4.69**	**$4.36**	**$123.85**
LEVODOPA PRODUCTS						
INBRIJA CAP 42MG	1	1	$2,857.37	1	$158.74	$2,857.37
SUBTOTAL	**1**	**1**	**$2,857.37**	**1**	**$158.74**	**$2,857.37**
PRAMIPEXOLE PRODUCTS						
PRAMIPEXOLE TAB 0.5MG	437	106	$4,993.92	4.12	$0.31	$11.43
PRAMIPEXOLE TAB 0.125MG	376	120	$4,418.02	3.13	$0.33	$11.75
PRAMIPEXOLE TAB 1MG	369	79	$4,623.93	4.67	$0.32	$12.53
PRAMIPEXOLE TAB 0.25MG	275	84	$2,867.40	3.27	$0.28	$10.43
PRAMIPEXOLE TAB 1.5MG	46	14	$534.61	3.29	$0.27	$11.62
PRAMIPEXOLE TAB 0.75MG	36	9	$465.30	4	$0.43	$12.93
SUBTOTAL	**1,539**	**412**	**$17,903.18**	**3.74**	**$0.31**	**$11.63**
BROMOCRIPTINE PRODUCTS						
BROMOCRIPTINE TAB 2.5MG	377	82	$41,792.78	4.6	$3.80	$110.86
BROMOCRIPTINE CAP 5MG	266	47	$76,511.33	5.66	$9.86	$287.64
SUBTOTAL	**643**	**129**	**$118,304.11**	**4.98**	**$6.31**	**$183.99**
ENTACAPONE PRODUCTS						
ENTACAPONE TAB 200MG	13	2	$1,338.58	6.5	$3.80	$102.97
SUBTOTAL	**13**	**2**	**$1,338.58**	**6.5**	**$3.80**	**$102.97**
RASAGILINE PRODUCTS						
RASAGILINE TAB 0.5MG	12	1	$2,182.85	12	$6.06	$181.90
RASAGILINE TAB 1MG	11	2	$2,046.43	5.5	$6.20	$186.04
SUBTOTAL	**23**	**3**	**$4,229.28**	**7.67**	**$6.13**	**$183.88**
ROTIGOTINE PRODUCTS						
NEUPRO 8MG/24HR	8	1	$6,478.70	8	$21.60	$809.84
SUBTOTAL	**8**	**1**	**$6,478.70**	**8**	**$21.60**	**$809.84**
SELEGILINE PRODUCTS						
SELEGILINE CAP 5MG	9	2	$686.10	4.5	$2.54	$76.23
SELEGILINE TAB 5MG	4	1	$321.86	4	$2.68	$80.47
SUBTOTAL	**13**	**3**	**$1,007.96**	**4.33**	**$2.58**	**$77.54**
PIMAVANSERIN PRODUCTS						
NUPLAZID TAB 34MG	79	7	$216,510.06	11.29	$104.19	$2,740.63
NUPLAZID TAB 10MG	2	1	$1,212.52	2	$20.21	$606.26
NUPLAZID TAB 17MG	1	1	$2,788.87	1	$92.96	$2,788.87
SUBTOTAL	**82**	**9**	**$220,511.45**	**9.11**	**$101.71**	**$2,689.16**
TOTAL	**25,838**	**4,497***	**$884,369.41**	**5.75**	**$1.07**	**$34.23**

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

[1] U.S. Food and Drug Administration (FDA) News Release. FDA Approves New Add-On Drug to Treat off Episodes in Adults with Parkinson's Disease. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-add-drug-treat-episodes-adults-parkinsons-disease. Issued 08/27/2019. Last accessed 03/25/2020.

[2] Carvalho J. High Exposure to Antibiotics May Increase Risk of Parkinson's, Study Suggests. *Parkinson's News Today*. Available online at: https://parkinsonsnewstoday.com/2019/11/27/high-exposure-to-antibiotics-increases-risk-of-parkinsons/. Issued 11/27/2019. Last accessed 04/09/2020.

[3] Mertsalmi TH, Pekkonen E, Scheperjans F. Antibiotic Exposure and Risk of Parkinson's Disease in Finland: A Nationwide Case-Control Study. *Movement Disorders* 2020; Vol. 35 (3). DOI: 10.1002/mds.27924.

[4] Helmich, Rick C. and Bloem, Bastiaan R. The Impact of the COVID-19 Pandemic on Parkinson's Disease: Hidden Sorrows and Emerging Opportunities. *Journal of Parkinson's Disease* 2020; 351–354.

[5] Wexler M. COVID-19 Presents Distinct Challenges, and Opportunities, with Parkinson's. *Parkinson's News Today*. Available online at: https://parkinsonsnewstoday.com/2020/04/08/challenges-opportunities-evident-with-covid-19/. Issued 04/08/2020. Last accessed 04/10/2020.

[6] Sunovion Pharmaceuticals, Inc. Sunovion Announces FDA Filing Acceptance of Resubmitted New Drug Application for Apomorphine Sublingual Film. Available online at: https://news.sunovion.com/press-releases/press-releases-details/2019/Sunovion-Announces-FDA-Filing-Acceptance-of-Resubmitted-New-Drug-Application-for-Apomorphine-Sublingual-Film/default.aspx. Issued 12/20/2019. Last accessed 04/10/2020.

[7] DeAngelis A. FDA Rejects Sunovion's Experimental Drug to Treat Parkinson's. *Boston Business Journal*. Available online at: https://www.bizjournals.com/boston/news/2019/01/31/fda-rejects-sunovions-experimental-drug-to-treat.html. Issued 01/31/2019. Last accessed 04/10/2020.

[8] Axovant Gene Therapies, Ltd. Axovant Announces 6-Month Follow-Up Data from First Cohort of Sunrise-PD Phase 2 Trial of AXO-Lenti-PD and Pipeline Update. *Globe Newswire*. Available online at: http://investors.axovant.com/news-releases/news-release-details/axovant-announces-6-month-follow-data-first-cohort-sunrise-pd. Issued 06/06/2019. Last accessed 04/13/2020.

[9] Lundbeck. Lundbeck Reports Headline Results from Phase IIa AMBLED Study of Foliglurax in Parkinson's Disease. Available online at: https://investor.lundbeck.com/news-releases/news-release-details/lundbeck-reports-headline-results-phase-iia-ambled-study. Issued 03/27/2020. Last accessed 04/10/2020.

[10] IRLAB. IRLAB to Advance Clinical Development of IRL790 in LIDs Based on In-Depth Analysis of Positive Phase IIa Results. Available online at: https://www.irlab.se/irlab-to-advance-clinical-development-of-irl790-in-lids-based-on-in-depth-analysis-of-positive-phase-iia-results/. Issued 08/28/2019. Last accessed 04/10/2020.

[11] IRLAB. IRLAB's IRL790 Receives New Name 'Mesdopetam'. Available online at: https://www.irlab.se/irlabs-irl790-receives-new-name-mesdopetam/. Issued 02/04/2020. Last accessed 04/10/2020.

[12] Neurocrine Biosciences, Inc. Neurocrine Biosciences Announces FDA Acceptance of New Drug Application for Opicapone as an Adjunctive Treatment for Patients with Parkinson's Disease. *PR Newswire*. Available online at: https://neurocrine.gcs-web.com/news-releases/news-release-details/neurocrine-biosciences-announces-fda-acceptance-new-drug. Issued 07/10/2019. Last accessed 04/13/2020.

[13] Acadia Pharmaceuticals. ACADIA Pharmaceuticals Presents Positive Top-line Results from Pivotal Phase 3 HARMONY Trial of Pimavanserin in Patients with Dementia-Related Psychosis at 12th Clinical Trials on Alzheimer's Disease (CTAD) Meeting. Available online at: https://ir.acadia-pharm.com/news-releases/news-release-details/acadia-pharmaceuticals-presents-positive-top-line-results. Issued 12/04/2019. Last accessed 04/10/2020.

[14] Prevail Therapeutics. Prevail Therapeutics Provides Clinical Advancement Update on PR001 for the Treatment of Parkinson's Disease with GBA1 Mutations. *Globe Newswire*. Available online at: https://ir.prevailtherapeutics.com/news-releases/news-release-details/prevail-therapeutics-provides-clinical-advancement-update-pr001. Issued 03/03/2020. Last accessed 04/13/2020.

[15] Hoffmann-La Roche. Prasinezumab. *Alzforum*. Available online at: https://www.alzforum.org/therapeutics/prasinezumab. Last revised 03/19/2020. Last accessed 04/10/2020.

[16] Nourianz™ Prescribing Information. Kyowa Kirin, Inc. Available online at: https://nourianz.com/assets/pdf/nourianz-full-prescribing-information.pdf. Last revised 08/2019. Last accessed 04/03/2020.

Appendix P

Calendar Year 2019 Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by, or in consultation with, a pulmonologist or pulmonary specialist; and
4. A quantity limit of 270 capsules or tablets per 30 days will apply for the 267mg strength capsules and tablets, and a quantity limit of 90 tablets per 30 days will apply for the 801mg strength tablets.

Ofev® (Nintedanib) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by, or in consultation with, a pulmonologist or pulmonary specialist; and
4. A quantity limit of 60 capsules per 30 days will apply.

Utilization of IPF Medications: Calendar Year 2019

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	3	10	$65,894.75	$6,589.48	$219.65	1,944	300
2019	8	40	$338,488.99	$8,462.22	$268.64	6,114	1,260
% Change	**166.7%**	**300.0%**	**413.7%**	**28.4%**	**22.3%**	**214.5%**	**320.0%**
Change	**5**	**30**	**$272,594.24**	**$1,872.74**	**$48.99**	**4,170**	**960**

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

Demographics of Members Utilizing IPF Medications

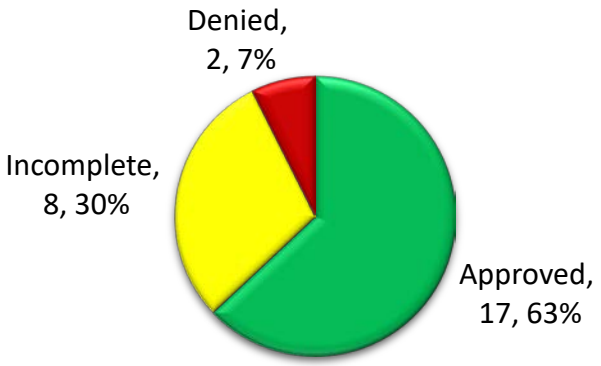
- All members utilizing IPF medications during calendar year 2019 were adults. Detailed demographic information cannot be provided due to the limited number of members using IPF medications during calendar year 2019.

Top Prescriber Specialties of IPF Medications by Number of Claims

- The prescriber specialties listed on paid claims for IPF medications during calendar year 2019 were pulmonary disease specialist, internist, family practitioner, and physician assistant. Upon further research, all prior authorization requests for IPF medications during calendar year 2019 were submitted by or in consultation with a pulmonary disease specialist.

Prior Authorization of IPF Medications

There were 27 prior authorization requests submitted for IPF medications during calendar year 2019. The following chart shows the status of the submitted petitions for calendar year 2019.



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

Anticipated Patent Expiration(s):

- Ofev® (nintedanib): June 2029
- Esbriet® (pirfenidone): March 2037

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

- **September 2019:** The FDA approved Ofev® (nintedanib) oral capsules to slow the rate of decline in pulmonary function in adults with interstitial lung disease associated with systemic sclerosis or scleroderma (SSc-ILD). The effectiveness of Ofev® to treat SSc-ILD was studied in a randomized, double-blind, placebo-controlled trial of 576 patients ages 20 to 79 years of age with the SSc-ILD. Patients received treatment for 52 weeks, with some patients treated up to 100 weeks. The primary test for efficacy measured the forced vital capacity (FVC), which is a measure of lung function. Ofev® treated patients had less lung function decline compared to those on placebo.
- **March 2020:** The FDA approved Ofev® (nintedanib) oral capsules to treat patients with progressive fibrosing interstitial lung disease (PF-ILD). The safety and effectiveness of Ofev® to treat chronic fibrosing ILD with a progressive phenotype in adults was evaluated in a randomized, double-blind, placebo-controlled trial of 663 adults, where patients received either 150mg of Ofev® twice a day or placebo. The primary test for effectiveness was the FVC. After 52 weeks, patients who received Ofev® had less lung function decline compared to those on the placebo.

News:

- **July 2019:** The prescribing information for Esbriet® (pirfenidone) was updated to include a warning about risk of elevated liver enzymes, drug-induced liver injury (DILI), and a recommendation to conduct liver function tests (LFTs) prior to the initiation of therapy with Esbriet®, monthly for the first 6 months, every 3 months thereafter, and as clinically indicated. Incidences of elevations in LFTs, non-serious and serious DILI and have been reported in clinical trials and in the postmarketing period.
- **September 2019:** The prescribing information for Ofev® (nintedanib) was updated to include a recommendation to conduct LFTs in all patients and a pregnancy test in females of reproductive potential prior to initiating treatment with Ofev®. Cases of DILI have been observed with Ofev® treatment in the clinical trials and postmarketing period. Patients with a low body weight (<65kg) and Asian, elderly, and female patients may have a higher risk of elevations in liver enzymes. Regarding embryo-fetal toxicity, findings from animal studies and its mechanism of action demonstrate that Ofev® can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to avoid becoming pregnant while receiving treatment with Ofev® and to use highly effective contraception during treatment and at least 3 months after the last dose of Ofev®.
- **January 2020:** A study published in the journal *PharmacoEconomics* that compared the cost-effectiveness of nintedanib to pirfenidone found nintedanib to be more cost-saving than pirfenidone for the treatment of IPF. The study utilized a Markov model to conduct an economic analysis that calculated outcomes over a patient's lifetime. Researchers used a network meta-analysis to collect data for loss of lung function, acute exacerbation events, and safety and treatment discontinuation. The health-state utility estimates in the model were calculated from quality of life data in nintedanib studies. The author concluded that the treatment with nintedanib resulted in an estimated total cost of $111,208, which was less than the total cost of treatment with pirfenidone ($123,176). Given the similarities in the survival and progression outcomes obtained with nintedanib and pirfenidone, the model predicted near equivalence in total quality-adjusted life-years (QALYs) (3.353 QALYs for the nintedanib arm and 3.318 for the pirfenidone arm).
- **February 2020:** An analysis of the United States Pulmonary Fibrosis Foundation Patient Registry showed that 61% of patients with IPF are prescribed FDA approved anti-fibrotic therapies, namely Ofev® (nintedanib) and Esbriet® (pirfenidone). Among the individuals taking anti-fibrotic medication, only 71 (9.6%) had an FVC >90%. Meanwhile, 107 (14.5%) had an FVC <50% which corresponds to a severe decline in lung function. The authors suggested that the lack of treatment may be due to providers and patients deferring anti-fibrotic initiation in patients with less severe disease, which goes against evidences that showed anti-fibrotic use prevents irreversible lung function loss at all levels of disease severity.

Pipeline:

- **Saracatinib:** The FDA has granted Orphan Drug designation (ODD) for saracatinib, a potential new medication for the treatment of IPF. Saracatinib is a small molecule, highly-potent and selective inhibitor of src tyrosine kinase. Saracatinib was previously in

clinical development in oncology. Pre-clinical trials of saracatinib showed that it inhibits fibroblast activity and collagen deposition, which are key features of lung fibrosis. Phase 2 trials for saracatinib in IPF have not yet commenced.

- **PRM-151:** The FDA has granted Breakthrough Therapy designation (BMD) to PRM-151. PRM-151 is a recombinant version of the endogenous human innate immunity protein pentraxin-2 (PTX-2), which is specifically active at the site of tissue damage. PRM-151 is an agonist that acts as a macrophage polarization factor to prevent and potentially reverse fibrosis. The FDA's decision was based on the success of a double-blind, multicenter Phase 2 clinical trial that compared PRM-151 treatment with a placebo in 117 IPF patients. Patients who received PRM-151 had slower lung function decline of 2.5% FVC, whereas those who received the placebo had a FVC decrease of 4.8% after 28 weeks. Additionally, patients treated with PRM-151 had better exercise capacity as demonstrated by an average 0.5 meters decrease in change in the 6-minute walk distance (6MWD) test compared to an average decrease of 31.8 meters in distance walked for placebo patients ($P<0.001$).
- **GKT831:** The FDA has approved the Investigational New Drug (IND) application allowing the initiation of a Phase 2 trial of GKT831 in patients with IPF. The investigator-initiated Phase 2 trial will be a placebo-controlled, double-blind, randomized, parallel group study to evaluate the safety and efficacy of oral GKT831 in patients with IPF receiving standard of care therapies. A total of 60 patients will be allocated to a 24-week treatment with oral GKT831 or matching placebo. The primary endpoint of the IPF trial will be the change in plasma levels at the end of the 24-week treatment period of o,o'-dityrosine, which is an oxidized covalent modification of protein tyrosine residues that has been shown to be a marker of pulmonary oxidative stress and is markedly elevated in patients with interstitial lung disease. Key secondary endpoints include changes in 6MWD, FVC, and high-resolution CT imaging.
- **PBI-4050:** A 12-week open-label trial that explored the safety, efficacy, and pharmacokinetics of daily oral doses of PBI-4050 800mg in patients with IPF showed that PBI-4050 alone or in combination with nintedanib or pirfenidone was well tolerated with no safety concerns. Similar pharmacokinetics profiles were seen for patients given PBI-4050 alone or in combination with Ofev®, but a reduced absorption rate and a faster metabolization rate were seen when it was paired with Esbriet®. Patients in the group taking PBI-4050 alone or combined with Ofev® at the end of the trial showed no decline in lung function, as measured by FVC. In contrast, patients on PBI-4050 plus Esbriet® had a mean FVC reduction of 2.69% at the end of 12 weeks.
- **Pamrevlumab:** A study published in *The Lancet Respiratory Medicine* reported data from PRAISE, a Phase 2, randomized, double-blind, placebo-controlled trial. Pamrevlumab is a fully human, lab-made antibody that blocks connective tissue growth factor (CTGF), which is a secreted protein that has a central role in the process of fibrosis. The data from the Phase 2 trial showed that pamrevlumab reduced the decline in percentage of predicted FVC by 60.3% and reduced the proportion of patients with disease progression by two-thirds at week 48. Pamrevlumab was well tolerated, with a safety profile similar to that of placebo.

Recommendations

The College of Pharmacy recommends the following changes to the Esbriet® (pirfenidone) and Ofev® (nintedanib) approval criteria to reflect the new FDA approved indications and updates in the prescribing information (changes shown in red):

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored prior to the initiation of Esbriet®, monthly for the first 6 months of treatment, and every 3 months thereafter, and as clinically indicated; and
4. Medication must be prescribed by, or in consultation with, a pulmonologist or pulmonary specialist (or an advanced care practitioner with a supervising physician who is a pulmonologist or pulmonary specialist); and
5. A quantity limit of 270 capsules or tablets per 30 days will apply for the 267mg strength capsules and tablets, and a quantity limit of 90 tablets per 30 days will apply for the 801mg strength tablets.

Ofev® (Nintedanib) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Treatment of idiopathic pulmonary fibrosis (IPF); or
    b. Treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype; or
    c. Slowing the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD); and
2. Member must be 18 years of age or older; and
3. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored prior to initiation of Ofev® treatment, at regular intervals during the first 3 months of treatment, and periodically thereafter or as clinically indicated; and
4. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Female members of reproductive potential must be willing to use effective contraception while on therapy and for at least 3 months after therapy completion; and
5. Medication must be prescribed by, or in consultation with, a pulmonologist or pulmonary specialist (or an advanced care practitioner with a supervising physician who is a pulmonologist or pulmonary specialist); and
6. A quantity limit of 60 capsules per 30 days will apply.

Utilization Details of IPF Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
ESBRIET TAB 267MG	24	1	$180,117.63	$7,504.90	4.80
OFEV CAP 150MG	10	4	$98,982.64	$9,898.26	2.50
OFEV CAP 100MG	6	1	$59,388.72	$9,898.12	6.00
TOTAL	**40**	**8***	**$338,488.99**	**$8,462.22**	**5.00**

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

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 04/2020. Last accessed 04/08/2020.

[2] FDA. FDA approves first treatment for patients with rare type of lung disease. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-patients-rare-type-lung-disease. Issued 09/06/2019. Last accessed 04/08/2020.

[3] U.S. Food and Drug Administration (FDA). FDA Approves First Treatment for Group of Progressive Interstitial Lung Diseases. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-group-progressive-interstitial-lung-diseases. Issued 03/09/2020. Last accessed 04/08/2020.

[4] Esbriet® (Pirfenidone) Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/esbriet_prescribing.pdf. Last revised 07/2019. Last accessed 04/08/2020.

[5] Ofev® (Nintedanib) Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc. Available online at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Ofev/ofev.pdf. Last revised 03/2020. Last accessed 04/09/2020.

[6] Rinciog C, Diamantopoulos A, Gentilini A. *et al.* Cost-Effectiveness Analysis of Nintedanib versus Pirfenidone in Idiopathic Pulmonary Fibrosis in Belgium. *PharmacoEconomics Open* 2020. Available online at: https://doi.org/10.1007. Issued 01/14/2020. Last accessed 04/08/2020.

[7] Holtze CH, Freiheit EA, Limb SL et al. Patient and Site Characteristics Associated with Pirfenidone and Nintedanib use in the United States; an Analysis of Idiopathic Pulmonary Fibrosis Patients Enrolled in the Pulmonary Fibrosis Foundation Patient Registry. *Respir Res* 2020; 21 (48). Available online at: https://doi.org/10.1186/s12931-020-1315-4. Issued 02/10/2020. Last accessed 04/08/2020.

[8] AstraZeneca PLC. US FDA Grants Saracatinib Orphan Drug Designation for Idiopathic Pulmonary Fibrosis. Available online at: https://www.astrazeneca.com/media-centre/press-releases/2019/us-fda-grants-saracatinib-orphan-drug-designation-for-idiopathic-pulmonary-fibrosis-18032019.html. Issued 03/18/2019. Last accessed 04/08/2020.

[9] Promedior. Promedior Received Breakthrough Therapy Designation from FDA for PRM-151 in Idiopathic Pulmonary Fibrosis. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/promedior-received-breakthrough-therapy-designation-from-fda-for-prm-151-in-idiopathic-pulmonary-fibrosis-300818229.html. Issued 03/26/2019. Last accessed 04/08/2020.

[10] Genkyotex. Genkyotex Announces FDA Approval of Phase 2 Investigator-Initiated Trial with GKT831 in IPF. *Globe Newswire*. Available online at: https://www.globenewswire.com/news-release/2019/07/17/1883758/0/en/Genkyotex-Announces-FDA-Approval-of-Phase-2-Investigator-Initiated-Trial-with-GKT831-in-IPF.html. Issued 07/17/2019. Last accessed 04/08/2020.

[11] Khalil N, Manganas H, Ryerson CJ,et al. Phase 2 Clinical Trial of PBI-4050 in Patients with Idiopathic Pulmonary Fibrosis. *European Respiratory Journal*. Available online at: https://erj.ersjournals.com/content/53/3/1800663?ctkey=shareline. Issued 03/18/2019. Last accessed 04/08/2020.

[12] Richeldi L, Fernández Pérez ER, Costabel U, et al. Pamrevlumab, an Anti-Connective Tissue Growth Factor Therapy, For Idiopathic Pulmonary Fibrosis (PRAISE): a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial. *Lancet Respir Med* 2020; 8(1):25-33. doi: 10.1016/S2213-2600(19)30262-0.

Appendix Q

Calendar Year 2019 Annual Review of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase)

Oklahoma Health Care Authority
May 2020

Current Prior Authorization Criteria

Aldurazyme® (Laronidase) Approval Criteria:

1. An FDA approved diagnosis of Hurler, Hurler-Scheie, or Scheie syndrome (mucopolysaccharidosis type I; MPS I) confirmed by:
    a. Enzyme assay demonstrating a deficiency of alpha-L-iduronidase (IDUA) enzyme activity; or
    b. Molecular genetic testing to confirm pathogenic mutations in the *IDUA* gene; and
2. For Scheie syndrome, the provider must document that the member has moderate-to-severe symptoms; and
3. Aldurazyme® must be administered by a health care professional prepared to manage anaphylaxis; and
4. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
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.

Naglazyme® (Galsulfase) Approval Criteria:

1. An FDA approved diagnosis of Maroteaux-Lamy syndrome (mucopolysaccharidosis type VI; MPS VI) confirmed by:
    a. Enzyme assay demonstrating a deficiency of arylsulfatase B (ASB) enzyme activity; or
    b. Genetic testing to confirm diagnosis of MPS VI; and
2. Naglazyme® must be administered by a health care professional prepared to manage anaphylaxis; and
3. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
4. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Utilization of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase): Calendar Year 2019

There was no SoonerCare utilization of Aldurazyme® (laronidase) or Naglazyme® (galsulfase) during calendar year 2019.

Prior Authorization of Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase)

There were no prior authorization requests submitted for Aldurazyme® (laronidase) or Naglazyme® (galsulfase) during calendar year 2019.

Recommendations

The College of Pharmacy does not recommend any changes to the current Aldurazyme® (laronidase) and Naglazyme® (galsulfase) prior authorization criteria at this time.

Appendix R

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

FDA NEWS RELEASE

For Immediate Release: April 22, 2020

FDA Approves New Therapy for Triple Negative Breast Cancer That Has Spread, Not Responded to Other Treatments

The FDA granted accelerated approval to Trodelvy (sacituzumab govitecan-hziy) for the treatment of adult patients with triple-negative breast cancer that has spread to other parts of the body. Patients must have received at least 2 prior therapies before taking Trodelvy. Trodelvy is a Trop-2-directed antibody and topoisomerase inhibitor drug conjugate, meaning that the drug targets the Trop-2 receptor that helps the cancer grow, divide and spread, and is linked to topoisomerase inhibitor, which is a chemical compound that is toxic to cancer cells. Approximately 2 of every 10 breast cancer diagnoses worldwide are triple-negative. Triple-negative breast cancer is a type of breast cancer that tests negative for estrogen receptors, progesterone receptors, and human epidermal growth factor receptor 2 (HER2) protein. Therefore, triple-negative breast cancer does not respond to hormonal therapy medicines or medicines that target HER2.

The FDA approved Trodelvy based on the results of a clinical trial of 108 patients with metastatic triple-negative breast cancer who had received at least 2 prior treatments for metastatic disease. The efficacy of Trodelvy was based on the overall response rate (ORR) – which reflects the percentage of patients that had a certain amount of tumor shrinkage. The ORR was 33.3%, with a median duration of response of 7.7 months. Of the patients with a response to Trodelvy, 55.6% maintained their response for 6 or more months and 16.7% maintained their response for 12 or more months.

The prescribing information for Trodelvy includes a *Boxed Warning* to advise health care professionals and patients about the risk of severe neutropenia and severe diarrhea. Health care professionals should monitor patient's blood cell counts periodically during treatment with Trodelvy and consider treatment with a type of therapy called granulocyte-colony stimulating factor (G-CSF), which stimulates the bone marrow to produce white blood cells called granulocytes and stem cells and releases them into the bloodstream, to help prevent infection, and should initiate anti-infective treatment in patients with febrile neutropenia (development of fever when white blood cell are abnormally low). Additionally, health care professionals should monitor patients with diarrhea and give fluid, electrolytes, and supportive care medications, as needed. Trodelvy may need to be withheld, dose reduced or permanently discontinued for neutropenia or diarrhea. Trodelvy can cause hypersensitivy reactions including severe anaphylactic reactions. Patients should be monitored for infusion-related reactions and health care professionals should discontinue Trodelvy if severe or life-threatening reactions occur. If patients experience nausea or vomiting while taking Trodelvy, health care professionals should use antiemetic preventive treatment, to prevent nausea and vomiting. Patients with reduced uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) activity are at increased risk for neutropenia following initiation of Trodelvy treatment. The most common side effects for patients taking Trodelvy were nausea, neutropenia, diarrhea, fatigue, anemia, vomiting, alopecia (hair loss), constipation, decreased appetite, rash and abdominal pain. Women who are pregnant should not take Trodelvy because it may cause harm to a developing fetus or newborn baby. The FDA advises health care professionals to inform females of reproductive age to use effective contraception during treatment with Trodelvy and for 6 months after the last dose. Male patients with female partners of reproductive potential should also use effective contraception during treatment with Trodelvy and for 3 months after the last dose.

Trodelvy was granted accelerated approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. Further clinical trials are required to verify and describe Trodelvy's clinical benefit. The FDA granted Trodelvy Priority Review, Breakthrough Therapy, and Fast Track designations.

FDA NEWS RELEASE

For Immediate Release: April 17, 2020

FDA Approves First New Drug Under International Collaboration, A Treatment Option for Patients with HER2-Positive Metastatic Breast Cancer

As part of Project Orbis, the FDA approved Tukysa (tucatinib) in combination with chemotherapy (trastuzumab and capecitabine) for the treatment of adult patients with advanced forms of HER2-positive breast cancer that can't be removed with surgery, or has spread to other parts of the body, including the brain, and who have received 1 or more prior treatments. The FDA collaborated with the Australian Therapeutic Goods Administration (TGA), Health Canada, Health Sciences Authority (HSA, Singapore), and Swissmedic (SMC, Switzerland) on this review. This is the first Project Orbis partnership between the FDA, HSA, and Swissmedic. While the FDA approved Tukysa today, the application is still under review at the other agencies. Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions, regardless of whether the product has received FDA approval. Early availability of new therapies and adoption as standard of care around the world may have an impact on the increasingly international conduct of cancer clinical trials, potentially accelerating the development of anticancer products. With a framework for concurrent submission and review of oncology drugs, Project Orbis facilitates a collaborative review to identify any regulatory divergence across review teams.

HER2-positive breast cancer, which makes up approximately one-fifth of breast cancers, has too much of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. More than 25% of women with metastatic HER2-positive breast cancer will develop brain metastases. Tukysa is a kinase inhibitor and is approved for treatment after patients have taken 1 or more anti-HER2-based regimens in the metastatic setting. The FDA approved Tukysa based on the results of a clinical trial enrolling 612 patients who had HER2-positive advanced unresectable or metastatic breast cancer and had prior treatment with trastuzumab, pertuzumab, and ado-trastuzumab emtansine (T-DM1). Patients with previously treated and stable brain metastases, as well as those with previously treated and growing or untreated brain metastases, were eligible for the clinical trial, and 48% of enrolled patients had brain metastases at the start of the trial.

The primary endpoint was progression-free survival (PFS), or the amount of time when there was no growth of the tumor. The median PFS in patients who received Tukysa, trastuzumab, and capecitabine was 7.8 months compared to 5.6 months in those patients who received placebo, trastuzumab, and capecitabine. Overall survival and PFS in patients with brain metastases at baseline were key secondary endpoints. The median overall survival in patients who received Tukysa, trastuzumab, and capecitabine was 21.9 months compared to 17.4 months in patients who received placebo, trastuzumab, and capecitabine. The median PFS in patients with brain metastases at baseline who received Tukysa, trastuzumab and capecitabine was 7.6 months compared to 5.4 months in patients who received placebo, trastuzumab and capecitabine.

Common side effects for patients taking Tukysa were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia and rash. Tukysa can cause serious side effects including severe diarrhea associated with dehydration, acute kidney injury, and death. Health care professionals should advise patients to notify their health care provider and start antidiarrheals as clinically indicated if diarrhea occurs. If patients are experiencing severe diarrhea, Tukysa should be interrupted or the dosage reduced. Tukysa can also cause severe hepatotoxicity. Health care professionals should monitor liver tests in patients taking Tukysa every 3 weeks while the patient is on treatment or as clinically indicated. Women who are pregnant or breastfeeding should not take Tukysa because it may cause harm to a developing fetus or newborn baby. The FDA advises health care professionals to tell females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Tukysa and for at least 1 week after the last dose.

In addition to the international collaboration, this review used the Real-Time Oncology Review (RTOR) pilot program, which can streamline the submission of data prior to the completion and submission of the

entire clinical application. RTOR, as well as the Assessment Aid, facilitated discussions among the regulatory agencies and regulatory review. The FDA granted Tukysa Priority Review, Breakthrough Therapy, Fast Track, and Orphan Drug designations.

FDA NEWS RELEASE

For Immediate Release: April 16, 2020

Coronavirus (COVID-19) Update: FDA Encourages Recovered Patients to Donate Plasma for Development of Blood-Related Therapies

As part of the all-of-America approach to fighting the COVID-19 pandemic, the FDA has been working with partners across the U.S. government, academia, and industry to expedite the development and availability of critical medical products to treat this novel virus. The FDA is providing an update on 1 potential treatment called convalescent plasma and encouraging those who have recovered from COVID-19 to donate plasma to help others fight this disease.

Convalescent plasma is an antibody-rich product made from blood donated by people who have recovered from the disease caused by the virus. Prior experience with respiratory viruses and limited data that have emerged from China suggest that convalescent plasma has the potential to lessen the severity or shorten the length of illness caused by COVID-19. It is important that we evaluate this potential therapy in the context of clinical trials, through expanded access, as well as facilitate emergency access for individual patients, as appropriate.

The response to the agency's recently announced national efforts to facilitate the development of and access to convalescent plasma has been tremendous. More than 1,040 sites and 950 physician investigators nationwide have signed on to participate in the Mayo Clinic-led expanded access protocol. A number of clinical trials are also taking place to evaluate the safety and efficacy of convalescent plasma, and the FDA has granted numerous single patient emergency investigational new drug (eIND) applications as well.

As this work moves forward, the key to ensuring the availability of convalescent plasma to those in greatest need is getting recovered COVID-19 patients to donate plasma. The FDA has launched a new webpage (https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/donate-covid-19-plasma) to guide recovered COVID-19 patients to local blood or plasma collection centers to discuss their eligibility and potentially schedule an appointment to donate. The webpage also provides information for those interested in participating in the expanded access protocol, conducting clinical trials, or submitting eIND applications. The American Red Cross has also set up a website for interested donors (www.redcross.org/plasma4covid) and the FDA continues to work with others in this area to help encourage additional donations.

During this challenging time, many people are asking what they can do to contribute to the COVID-19 response. Those individuals who have recovered from COVID-19 could have an immediate impact in helping others who are severely ill. In fact, 1 donation has the potential to help up to 4 patients. Convalescent plasma can also be used to manufacture a biological product called hyperimmune globulin, which can similarly be used to treat patients with COVID-19. People who have fully recovered from COVID-19 for at least 2 weeks can contact their local blood or plasma collection center today to schedule an appointment. We encourage individuals to consider donating and hope this information will serve as a helpful resource to facilitate this important act of kindness.

FDA NEWS RELEASE

For Immediate Release: April 10, 2020

FDA Approves First Therapy for Children with Debilitating and Disfiguring Rare Disease

The FDA approved Koselugo (selumetinib) for the treatment of pediatric patients, 2 years of age and older, with neurofibromatosis type 1 (NF1), a genetic disorder of the nervous system causing tumors to grow on nerves. Koselugo is the first drug approved by the FDA to treat this debilitating, progressive, and often disfiguring rare disease that typically begins early in life. Koselugo is approved specifically for patients who

have symptomatic, inoperable plexiform neurofibromas (PN), which are tumors involving the nerve sheaths (coating around nerve fibers) and can grow anywhere in the body, including the face, extremities, areas around the spine, and deep in the body where they may affect organs. Koselugo is a kinase inhibitor, meaning it functions by blocking a key enzyme, which results in helping to stop the tumor cells from growing.

NF1 is a rare, progressive condition caused by a mutation or flaw in a particular gene. NF1 is usually diagnosed in early childhood and appears in an estimated 1 out of every 3,000 infants. It is characterized by changes in skin coloring (pigmentation), neurologic, and skeletal impairments and risk for development of benign and malignant tumors throughout life. Between 30% and 50% of patients born with NF1 develop 1 or more PNs.

The FDA approved Koselugo based on a clinical trial conducted by the National Cancer Institute of pediatric patients who had NF1 and inoperable PN (defined as a PN that could not be completely removed without risk for substantial morbidity to the patient). The efficacy results were from 50 of the patients who received the recommended dose and had routine evaluations of changes in tumor size and tumor-related morbidities during the trial. Patients received Koselugo 25mg/m^2 orally twice a day until disease progression or until they experienced unacceptable adverse reactions. The clinical trial measured the overall response rate (ORR), defined as the percentage of patients with a complete response and those who experienced more than a 20% reduction in PN volume on MRI that was confirmed on a subsequent MRI within 3-6 months. The ORR was 66% and all patients had a partial response, meaning that no patients had complete disappearance of the tumor. Of these patients, 82% had a response lasting 12 months or longer.

Other clinical outcomes for patients during Koselugo treatment including changes in PN-related disfigurement, symptoms and functional impairments. Although the sample sizes of patients assessed for each PN-related morbidity (such as disfigurement, pain, strength and mobility problems, airway compression, visual impairment and bladder or bowel dysfunction) were small, there appeared to be a trend of improvement in PN-related symptoms or functional deficits during treatment.

Common side effects for patients taking Koselugo were vomiting, rash, abdominal pain, diarrhea, nausea, dry skin, fatigue, musculoskeletal pain (pain in the body affecting bones, muscles, ligaments, tendons and nerves), fever, acneiform rash (acne), stomatitis (inflammation of the mouth and lips), headache, paronychia (infection in the skin that surrounds a toenail or fingernail) and pruritus (itching). Koselugo can also cause serious side effects including heart failure (manifested as ejection fraction decrease, or when the muscle of the left ventricle of the heart is not pumping as well as normal) and ocular toxicity (acute and chronic damage to the eye) including retinal vein occlusion, retinal pigment epithelial detachment and impaired vision. Patients should have cardiac and ophthalmic assessments performed prior to initiating Koselugo and at regular intervals during treatment. Koselugo can also cause increased creatinine phosphokinase (CPK). CPK is an enzyme found in the heart, brain and skeletal muscles. When muscle tissue is damaged, CPK leaks into a person's blood. CPK elevation in a patient receiving Koselugo should prompt an evaluation for rhabdomyolysis (breakdown of skeletal muscle due to direct or indirect muscle injury). Koselugo should be withheld, dosage reduced or dosage permanently discontinued based on the severity of adverse reactions. Further, Koselugo contains vitamin E, and patients are at an increased risk of bleeding if their daily intake of vitamin E exceeds the recommended or safe limits.

Based on findings from animal studies, Koselugo may cause harm to a newborn baby when administered to a pregnant woman. The FDA advises health care professionals to tell females of reproductive age, and males with female partners of reproductive potential, to use effective contraception during treatment with Koselugo, and for 1 week after the last dose.

The FDA granted Koselugo Priority Review, Breakthrough Therapy, Orphan Drug, and Rare Pediatric Disease designations.

FDA NEWS RELEASE

For Immediate Release: April 1, 2020

FDA Approves Additional Treatment for Adults and Adolescents with Hemophilia A or B and Inhibitors

The FDA approved Sevenfact [coagulation factor VIIa (recombinant)-jncw] for the treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with hemophilia A or B with inhibitors (neutralizing antibodies). Sevenfact contains an active ingredient expressed in genetically engineered rabbits. The active ingredient of Sevenfact is a recombinant analog of human Coagulation Factor (F) VII (FVII), which is expressed in the mammary gland of genetically engineered rabbits and secreted into the rabbits' milk. During purification and processing of the milk, FVII is converted into activated FVII (FVIIa).

Hemophilia A or B is a congenital bleeding disorder caused by a dysfunction or deficiency of FVIII or FIX, respectively. People with hemophilia may bleed for a longer time than others after injury or surgery. They may also have spontaneous bleeding in muscles, joints and organs, which may be life-threatening. Individuals with inhibitors may not respond to factor replacement therapy. According to the Centers for Disease Control and Prevention (CDC), there are an estimated 20,000 people living with hemophilia in the United States. Bleeding episodes in these individuals are managed by either on-demand treatment or prophylaxis using products containing FVIII or FIX. However, when inhibitors to FVIII or FIX develop in these individuals, treatment of bleeding episodes with FVIII or FIX products may no longer be effective. In these situations, the administration of products such as Sevenfact, which bypass the Factor VIII and Factor IX reactions, promotes clot formation and controls bleeding.

The safety and efficacy of Sevenfact were determined using data from a clinical study that evaluated 27 patients with hemophilia A or B with inhibitors, which included treatment of 465 mild or moderate, and three severe bleeding episodes. The study assessed the efficacy of treatment 12 hours after the initial dose was given. The proportion of mild or moderate bleeding episodes treated successfully both with the lower dose of 75mcg/kg and higher dose of 225mcg/kg (requiring no further treatment for the bleeding episode, no administration of blood products and no increase in pain beyond 12 hours from initial dose) was approximately 86%. The study also included 3 severe bleeding episodes that were treated successfully with the higher dose. Another study evaluated the safety and pharmacokinetics of 3 escalating doses of Sevenfact in 15 patients with severe hemophilia A or B with or without inhibitors. Results from this study were used to select the 2 doses, 75mcg/kg and 225mcg/kg, that were evaluated in the study described above.

The most common side effects of Sevenfact were headache, dizziness, infusion site discomfort, infusion related reaction, infusion site hematoma, and fever. Sevenfact is contraindicated in patients with known allergy or hypersensitivity to rabbits or rabbit proteins. Patients with hemophilia A or B with inhibitors who have other risk factors for thrombosis may be at increased risk of serious arterial and venous thrombotic events. Hypersensitivity reactions, including anaphylaxis, are possible. Should symptoms of a thrombotic event or hypersensitivity reaction occur, patients should discontinue Sevenfact and seek appropriate medical intervention.

FDA NEWS RELEASE

For Immediate Release: April 1, 2020

FDA Requests Removal of All Ranitidine Products (Zantac) from the Market

The FDA announced it is requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine drugs from the market immediately. This is the latest step in an ongoing investigation of a contaminant known as N-Nitrosodimethylamine (NDMA) in ranitidine medications (commonly known by the brand name Zantac). The agency has determined that the impurity in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity. As a result of this immediate market withdrawal request, ranitidine products will not be available for new or existing prescriptions or OTC use in the United States.

NDMA is a probable human carcinogen (a substance that could cause cancer). In the summer of 2019, the FDA became aware of independent laboratory testing that found NDMA in ranitidine. Low levels of NDMA are commonly ingested in the diet, for example NDMA is present in foods and in water. These low levels would not be expected to lead to an increase in the risk of cancer. However, sustained higher levels of exposure may increase the risk of cancer in humans. The FDA conducted thorough laboratory tests and found

NDMA in ranitidine at low levels. At the time, the agency did not have enough scientific evidence to recommend whether individuals should continue or stop taking ranitidine medicines, and continued its investigation and warned the public in September 2019 of the potential risks and to consider alternative OTC and prescription treatments.

New FDA testing and evaluation prompted by information from third-party laboratories confirmed that NDMA levels increase in ranitidine even under normal storage conditions, and NDMA has been found to increase significantly in samples stored at higher temperatures, including temperatures the product may be exposed to during distribution and handling by consumers. The testing also showed that the older a ranitidine product is, or the longer the length of time since it was manufactured, the greater the level of NDMA. These conditions may raise the level of NDMA in the ranitidine product above the acceptable daily intake limit.

With this announcement, the FDA is sending letters to all manufacturers of ranitidine requesting they withdraw their products from the market. The FDA is also advising consumers taking OTC ranitidine to stop taking any tablets or liquid they currently have, dispose of them properly and not buy more; for those who wish to continue treating their condition, they should consider using other approved OTC products. Patients taking prescription ranitidine should speak with their health care professional about other treatment options before stopping the medicine, as there are multiple drugs approved for the same or similar uses as ranitidine that do not carry the same risks from NDMA. To date, the FDA's testing has not found NDMA in famotidine (Pepcid), cimetidine (Tagamet), esomeprazole (Nexium), lansoprazole (Prevacid) or omeprazole (Prilosec).

The FDA continues its ongoing review, surveillance, compliance and pharmaceutical quality efforts across every product area, and will continue to work with drug manufacturers to ensure safe, effective and high-quality drugs for the American public. The FDA encourages health care professionals and patients to report adverse reactions or quality problems with any human drugs to the agency's MedWatch Adverse Event Reporting program:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm; or
- Download and complete the form, then submit it via fax at 1-800-FDA-0178.

Current Drug Shortages Index (as of April 23, 2020):

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

Alogliptin Tablets	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Avycaz® (ceftazidime/avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Azithromycin Tablets	***Currently in Shortage***
Bacitracin Ophthalmic Ointment	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***

Calcium Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Carisoprodol Tablets, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Disulfiram Tablets	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***

Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxychloroquine Sulfate Tablets	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
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	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Nystatin Oral Suspension	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***

Promethazine (Phenergan) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Triamcinolone Acetonide (Triesence) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***