OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
April 8, 2020

No live meeting scheduled for April.
April 2020 will be a packet only meeting.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Wendi Chandler, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – April 8, 2020

DATE: March 29, 2020

NOTE: No live April meeting. April 2020 is a packet only meeting.

Enclosed are the following items related to the April packet.
Material is arranged in order of the agenda.

DUR Board Meeting Minutes – Appendix A

Update on Medication Coverage Authorization Unit/Prenatal Vitamin (PV) Utilization Update – Appendix B

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) – Appendix C

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

30-Day Notice to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat) – Appendix E

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

Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Dayvigo™ (Lemborexant) – Appendix G

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

Future Business

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Packet – April 8, 2020
No live April meeting. April 2020 is a packet only meeting.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. DUR Board Meeting Minutes – See Appendix A
A. March 11, 2020 DUR Minutes
B. March 11, 2020 DUR Recommendations Memorandum

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

2. Update on Medication Coverage Authorization Unit/Prenatal Vitamin (PV) Utilization Update – See Appendix B
A. Pharmacy Helpdesk Activity for March 2020
B. Medication Coverage Activity for March 2020
C. PV Utilization Update

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

3. 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 Suspension), Rybelsus® (Semaglutide Tablet), and Trijardy™ XR (Empagliflozin/ Linagliptin/Metformin ER Tablet) – See Appendix C
A. Current Prior Authorization Criteria
B. Utilization of Anti-Diabetic Medications
C. Prior Authorization of Anti-Diabetic Medications
D. Market News and Updates
E. Qternmet® XR (Dapagliflozin/Saxagliptin/Metformin ER Tablet) Product Summary
F. Riomet ER™ (Metformin ER Oral Suspension) Product Summary
G. Rybelsus® (Semaglutide Tablet) Product Summary
H. Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet) Product Summary
I. College of Pharmacy Recommendations
J. Utilization Details of Non-Insulin Anti-Diabetic Medications
K. Utilization Details of Insulin Medications

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

4. Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet) – See Appendix D
A. Current Prior Authorization Criteria
B. Utilization of Antihypertensive Medications
C. Prior Authorization of Antihypertensive Medications
D. Market News and Updates
E. Katerzia™ (Amlodipine Oral Suspension) Product Summary
F. Conjupri® (Levamlodipine Tablet) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Antihypertensive Medications

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

5. 30-Day Notice to Prior Authorize Ayvakit™ (Avapritinib), Bynfezia Pen™ (Octreotide), and Tazverik™ (Tazemetostat) – See Appendix E

A. Introduction
B. Market News and Updates
C. Product Summaries
D. Recommendations

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

6. Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™ (Bevacizumab-bvzr) – See Appendix F

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

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

7. Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Dayvigo™ (Lemborexant) – See Appendix G

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

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

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

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

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

A. Annual Review of the Pharmacy Benefit
B. Parkinson's Disease Medications
C. Granulocyte Colony-Stimulating Factors (G-CSFs)
D. Allergen Immunotherapies
E. Naglazyme® (Galsulfase) and Aldurazyme® (Laronidase)

**Future business subject to change.*

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, AMD 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.

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

The University of Oklahoma
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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

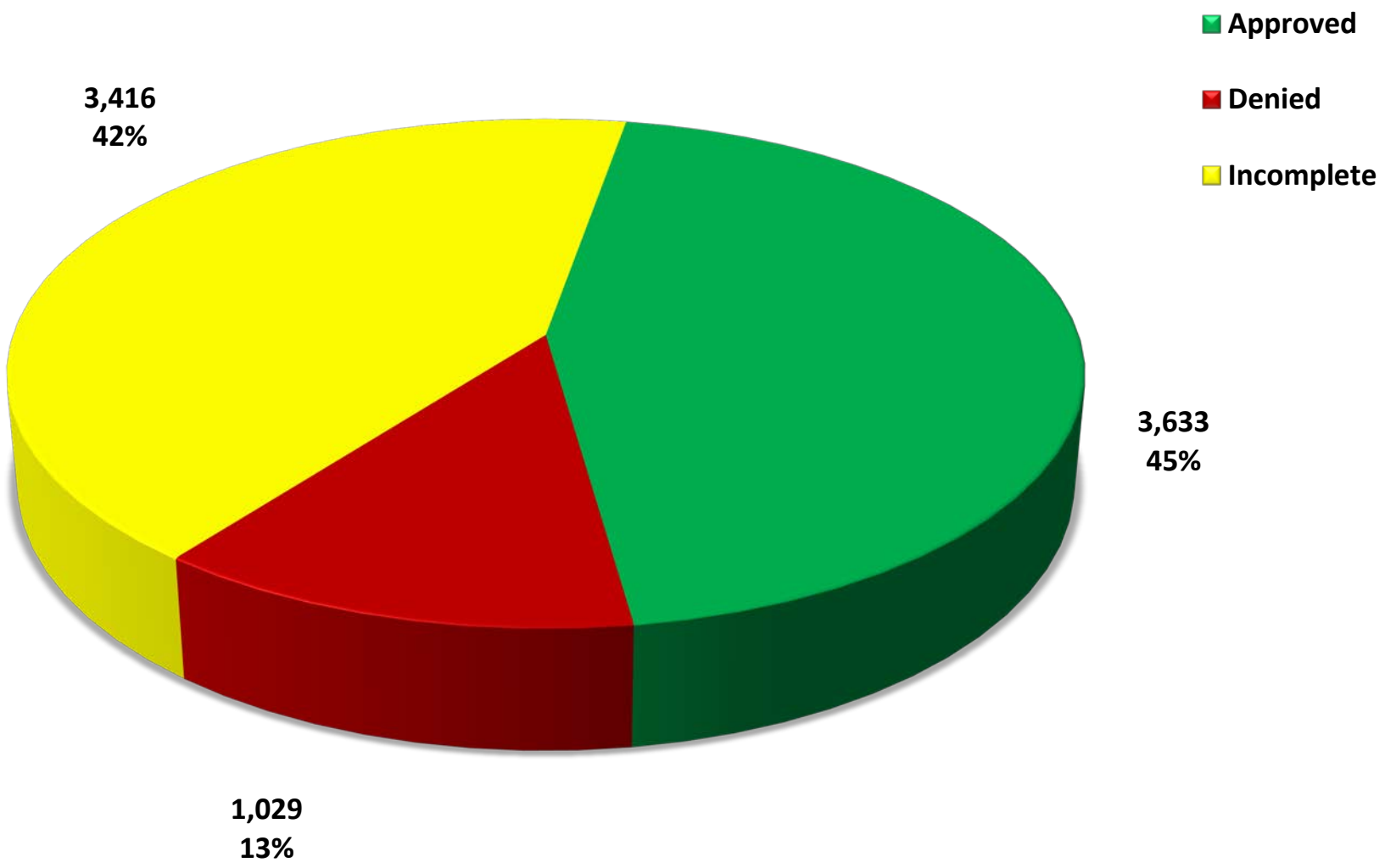
NO ACTION REQUIRED.

Recommendation 15: Future Business

NO ACTION REQUIRED.

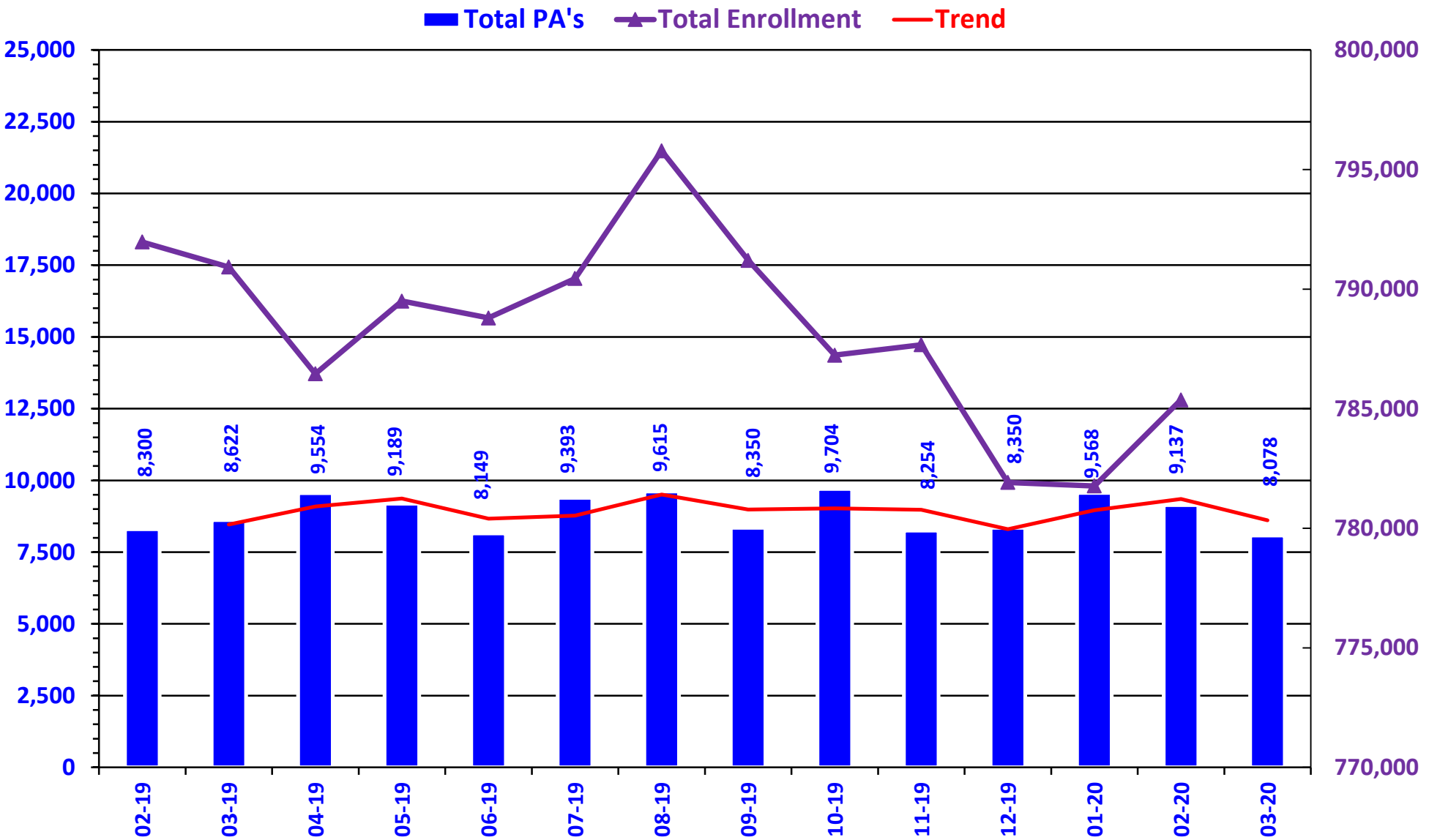
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH 2020*



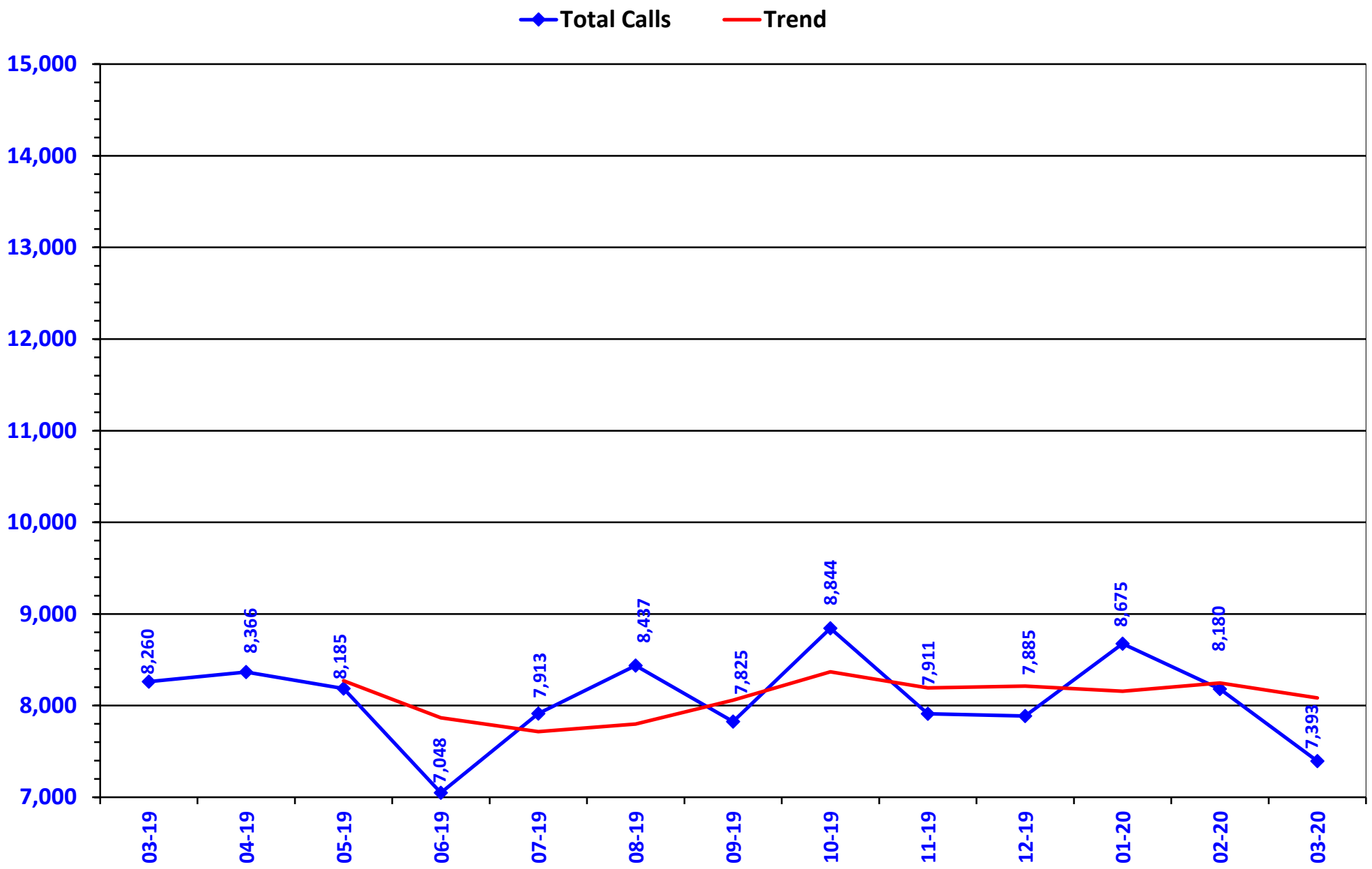
PA totals include approved/denied/incomplete/overrides
**Current as of March 29, 2020*

PRIOR AUTHORIZATION REPORT: MARCH 2019 – MARCH 2020*



PA totals include approved/denied/incomplete/overrides
**Current as of March 29, 2020*

CALL VOLUME MONTHLY REPORT:
MARCH 2019 – MARCH 2020



PA totals include approved/denied/incomplete/overrides
**Current as of March 29, 2020*

Prior Authorization Activity

3/1/2020 Through 3/29/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	92	8	13	71	360
Analgesic - NonNarcotic	22	0	2	20	0
Analgesic, Narcotic	311	95	31	185	169
Angiotensin Receptor Antagonist	14	0	3	11	0
Antiasthma	121	22	28	71	271
Antibiotic	32	18	2	12	234
Anticonvulsant	143	59	9	75	321
Antidepressant	187	45	31	111	337
Antidiabetic	241	86	38	117	354
Antihistamine	35	10	9	16	304
Antimigraine	153	26	69	58	177
Antineoplastic	90	61	9	20	177
Antiulcers	115	41	24	50	137
Anxiolytic	16	1	2	13	360
Atypical Antipsychotics	260	120	23	117	346
Biologics	166	78	24	64	290
Bladder Control	48	15	15	18	331
Blood Thinners	334	190	20	124	340
Botox	46	33	7	6	307
Buprenorphine Medications	69	9	4	56	85
Calcium Channel Blockers	16	4	3	9	257
Cardiovascular	82	31	12	39	317
Cephalosporins	11	4	0	7	7
Chronic Obstructive Pulmonary Disease	109	25	24	60	357
Constipation/Diarrhea Medications	133	29	40	64	247
Contraceptive	19	7	4	8	358
Dermatological	277	83	60	134	139
Diabetic Supplies	688	387	51	250	239
Endocrine & Metabolic Drugs	84	48	4	32	181
Erythropoietin Stimulating Agents	10	6	0	4	90
Fish Oils	19	1	11	7	360
Gastrointestinal Agents	94	27	20	47	200
Genitourinary Agents	11	2	1	8	10
Glaucoma	26	5	2	19	140
Growth Hormones	121	99	6	16	137
Hematopoietic Agents	24	11	1	12	107
Hepatitis C	129	72	14	43	8
HFA Rescue Inhalers	102	2	3	97	232
Insomnia	54	5	11	38	214
Insulin	194	62	22	110	352
Miscellaneous Antibiotics	14	1	1	12	7
Multiple Sclerosis	38	12	10	16	200
Muscle Relaxant	49	7	9	33	138
Nasal Allergy	74	10	21	43	194
Neurological Agents	103	31	24	48	206
Neuromuscular Agents	10	7	2	1	279
NSAIDs	30	3	6	21	251
Ocular Allergy	26	1	9	16	86
Ophthalmic Anti-infectives	14	1	4	9	117
Osteoporosis	23	10	5	8	324
Other*	262	72	48	142	269

* 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	16	1	2	13	7
Pediculicide	10	4	0	6	22
Respiratory Agents	41	27	2	12	143
Statins	10	3	2	5	296
Stimulant	630	305	58	267	350
Synagis	33	25	4	4	28
Testosterone	69	9	25	35	273
Thyroid	10	2	1	7	223
Topical Antifungal	21	2	7	12	17
Topical Corticosteroids	77	1	40	36	25
Vitamin	94	23	40	31	169
Pharmacotherapy	50	46	0	4	251
Emergency PAs	0	0	0	0	
Total	**6,402**	**2,430**	**972**	**3,000**	
Overrides					
Brand	38	23	1	14	261
Compound	7	7	0	0	60
Cumulative Early Refill	2	2	0	0	15
Diabetic Supplies	13	12	0	1	185
Dosage Change	275	258	0	17	18
High Dose	8	4	1	3	288
Ingredient Duplication	17	12	0	5	43
Lost/Broken Rx	76	66	2	8	16
MAT Override	177	132	4	41	68
NDC vs Age	313	207	24	82	256
NDC vs Sex	4	4	0	0	87
Nursing Home Issue	31	31	0	0	13
Opioid MME Limit	147	70	2	75	111
Opioid Quantity	35	26	3	6	159
Other*	48	36	3	9	11
Quantity vs. Days Supply	433	276	17	140	265
STBS/STBSM	9	7	0	2	123
Step Therapy Exception	2	0	0	2	0
Stolen	12	12	0	0	18
Third Brand Request	29	18	0	11	36
Overrides Total	**1,676**	**1,203**	**57**	**416**	
Total Regular PAs + Overrides	**8,078**	**3,633**	**1,029**	**3,416**	

Denial Reasons	
Unable to verify required trials.	2,707
Does not meet established criteria.	1,065
Lack required information to process request.	689
Other PA Activity	
Duplicate Requests	757
Letters	14,744
No Process	5
Changes to existing PAs	560
Helpdesk Initiated Prior Authorizations	651
PAs Missing Information	28

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

Prenatal Vitamin (PV) Utilization Update

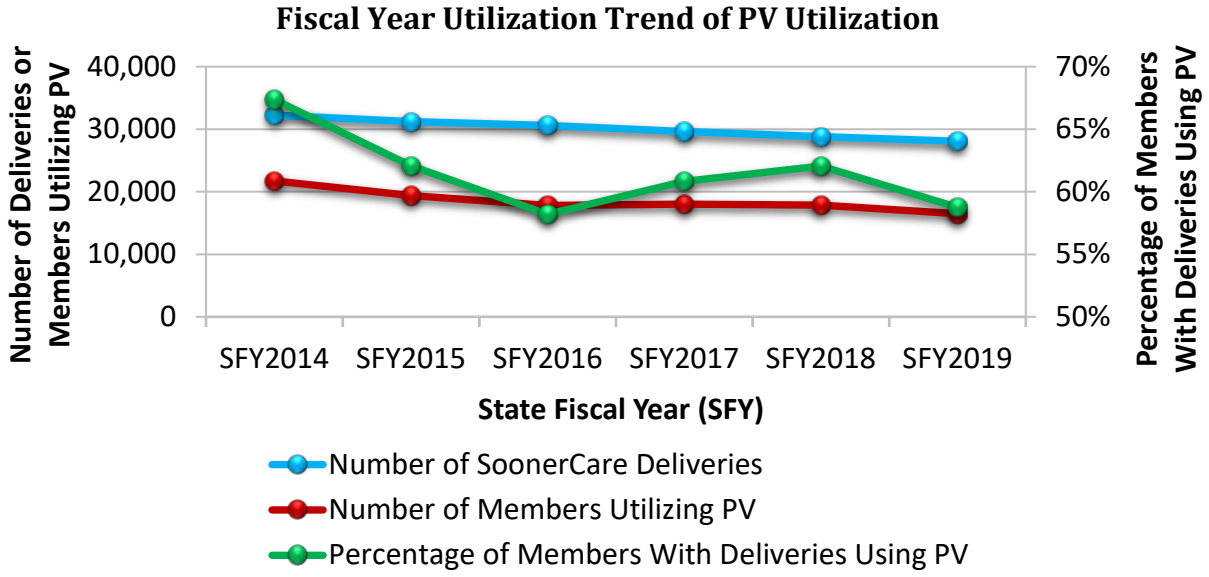
Oklahoma Health Care Authority
April 2020

Introduction

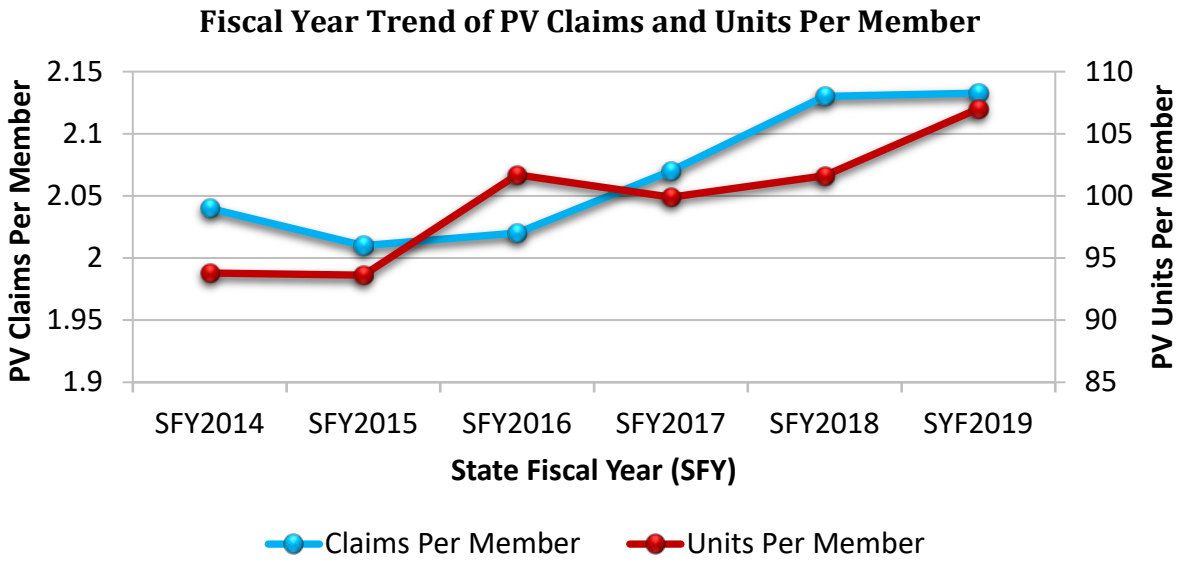
The College of Pharmacy and the Oklahoma Health Care Authority (OHCA) are engaged in an effort to increase utilization of PV among pregnant SoonerCare members. In 2014, SoonerCare added reminders regarding PV utilization to the SoonerCare "Text for Baby" program; however, this program ended June 2019. In November 2016, the College of Pharmacy began incorporating regular prenatal education, based on previous successful interventions, into its workflow to maintain increased utilization of PV. Ongoing interventions include reminders to prescribers of pregnant members if no paid claims for PV were found in the member's claims history and including a list of preferred PV available without prior authorization in response to each prior authorization received for a non-preferred PV. The preferred PV list is also available on the SoonerCare website. Additionally, in May 2018, educational outreach including prescriber letters, pharmacy fax blasts, and articles in the provider newsletter regarding declining utilization of PV among pregnant SoonerCare members were disseminated.

Utilization of PV: Fiscal Year Trends[1]

The following graph shows the fiscal year utilization of PV for the last 6 years, comparing the number of members utilizing PV to the number of SoonerCare deliveries. Prior to state fiscal year (SFY) 2016, a concerning decline was seen in the percentage of members utilizing PV compared to the number of deliveries. While the percentage improved in SFY 2017 and SFY 2018, PV utilization once again decreased in SFY 2019. Additionally, a large percentage of deliveries were not associated with a member utilizing PV. Please note, the right vertical axis starts at 50% of members in order to reflect small changes.



The following graph outlines the number of claims and units of PV each member received by SFY. While the claims per member has increased from SFY 2016, the number of claims per member still remains slightly >2. Since many PV formulations are packaged in 90- and 100-day supply bottles, the number of units per member was also assessed. In SFY 2019, members averaged 107.01 units equating to a little more than 3 months of therapy. Please note, the left vertical axis starts at 1.9 claims and the right vertical axis starts at 85 units in order to reflect small changes.



Discussion[2]

While deliveries have declined in the last several fiscal years, utilization of PV has also declined. The number of members utilizing PV compared to the number of SoonerCare deliveries shows <65% of members with deliveries utilize PV. After a slight increase in recent years, the percentage of members utilizing PV compared to the number of deliveries decreased in SFY 2019 (3.32% decrease from SFY 2018 to SFY 2019) which is concerning.

Another concern revealed by the claims analysis is the number of claims per member. Most members received only 2 paid claims for PV during a given fiscal year. This number has remained relatively steady over the last 5 fiscal years and was not accounted for by an increase in units implying a larger quantity per claim (e.g., 1 claim for a 3-month supply). The maximum benefit of PV requires continued use throughout pregnancy and ideally starts before the member becomes pregnant.

Utilization of PV is difficult to assess and may be falsely low due to the large number of over-the-counter (OTC) products available that members may be using. Data for use of OTC products for SoonerCare members are not obtainable and are therefore not included in this analysis. Another consideration is the potential use of PV samples supplied by the health care provider, which are also not included in this analysis.

Recommendations

Based on the decline in the percentage of members utilizing PV compared to the number of deliveries, further educational efforts are warranted. Efforts in this class appear to have an initial increase with a waning effect over time. Previous successful interventions included a letter sent to more than 3,000 SoonerCare prescribers emphasizing PV utilization. The mailing included a list of PV covered without prior authorization, as well as a sample prescription detailing how a physician could write for the desired ingredients in a PV and the pharmacist could select and dispense a SoonerCare-covered product based on the prescription. Similarly, a fax blast was sent to SoonerCare pharmacies which included a list of the PV that do not require prior authorization along with the National Drug Codes (NDCs) so the pharmacy could easily order a product from the list. The pharmacies and prescribers also received directions for accessing the SoonerCare website and locating the updated PV list of products covered by SoonerCare without prior authorization. Additionally, articles regarding the importance of PV have been included in the SoonerCare member and provider newsletters. Lastly, members enrolled in the former SoonerCare "Text for Baby" program received reminders regarding PV from 2014 until the program ended in June 2019.

The College of Pharmacy will continue incorporating regular prenatal education, based on previous successful interventions, into its workflow to maintain increased utilization of PV. Furthermore, an updated prescriber mailing and pharmacy fax blast, to include the current list of SoonerCare-covered PV, will be sent in regards to the declining utilization of PV among pregnant SoonerCare members with the goal of increasing appropriate PV use. Opportunities for new interventions will be sought wherever possible.

[1] Oklahoma Health Care Authority (OHCA). Annual Deliveries. Available online at: http://www.okhca.org/research.aspx?id=87. Last revised 11/05/2019. Last accessed 03/15/2020.

[2] March of Dimes. Fewer Than Half of U.S. Women Take Recommended Vitamins Prior to Pregnancy, According to March of Dimes New Prenatal Health & Nutrition Survey. Available online at: https://www.marchofdimes.org/news/fewer-than-half-of-u-s-women-take-recommended-vitamins-prior-to-pregnancy-according-to-march-of-dimes-new-prenatal-health-nutrition-survey.aspx. Issued 09/19/2017. Last accessed 03/15/2020.

Appendix C

Calendar Year 2019 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)

Oklahoma Health Care Authority
April 2020

Current Prior Authorization Criteria

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.

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.

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/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®**)	
	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®**)	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
	liraglutide (**Victoza®**)	lixisenatide (**Adlyxin®**)	
		semaglutide (**Ozempic®**)	
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™**)	
	empagliflozin/metformin (**Synjardy®**)	ertugliflozin/metformin (**Segluromet™**)	
	empagliflozin/metformin ER (**Synjardy® 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

Admelog® (Insulin Lispro) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Humalog® (insulin lispro) must be provided.

Afrezza® (Insulin Human Inhalation Powder) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus (DM); and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why other rapid-acting injectable insulins are not appropriate must be provided; and
4. For the diagnosis of type 1 DM, the member must use Afrezza® with a long-acting insulin; and
5. The member must not smoke or have chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD).

Basaglar® (Insulin Glargine) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir) must be provided.

Fiasp® (Insulin Aspart) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use NovoLog® (insulin aspart) must be provided.

Humalog® KwikPen® U-200 (Insulin Lispro 200 Units/mL) Approval Criteria:

1. Authorization of the 200 units/mL strength requires a patient-specific, clinically significant reason why the member cannot use the 100 units/mL strength.

Humulin® R (Insulin Human 500 Units/mL) U-500 Vials Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use the Humulin® R (insulin human) U-500 KwikPen®, which is available without prior authorization, must be provided.

Insulin Lispro (Generic Humalog® U-100) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use the brand formulation (Humalog®) must be provided.

Ryzodeg® (Insulin Degludec/Insulin Aspart) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir) with Novolog® (insulin aspart) must be provided.

Soliqua® 100/33 (Insulin Glargine/Lixisenatide) Approval Criteria:

1. An FDA approved diagnosis of type 2 diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with an alternative glucagon-like peptide 1 (GLP-1) receptor agonist must be provided; and
3. Current Tier-3 criteria will apply.

Toujeo® (Insulin Glargine) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) must be provided, and the member must be using a minimum of 100 units of Lantus® (insulin glargine) per day.

Tresiba® (Insulin Degludec) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir) must be provided.

Xultophy® 100/3.6 (Insulin Degludec/Liraglutide) Approval Criteria:

1. An FDA approved diagnosis of type 2 diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with Victoza® (liraglutide) must be provided; and
3. Current Tier-3 criteria will apply.

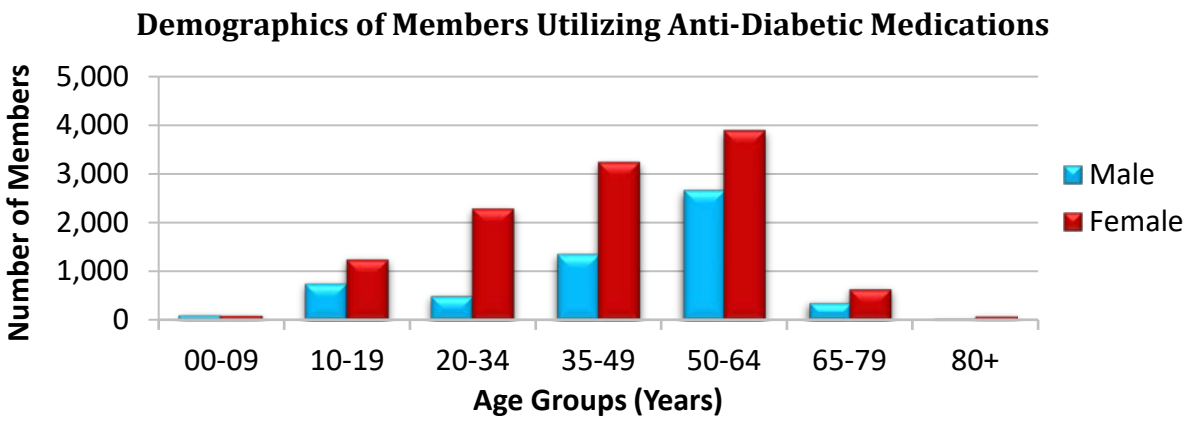
Utilization of Anti-Diabetic Medications: Calendar Year 2019

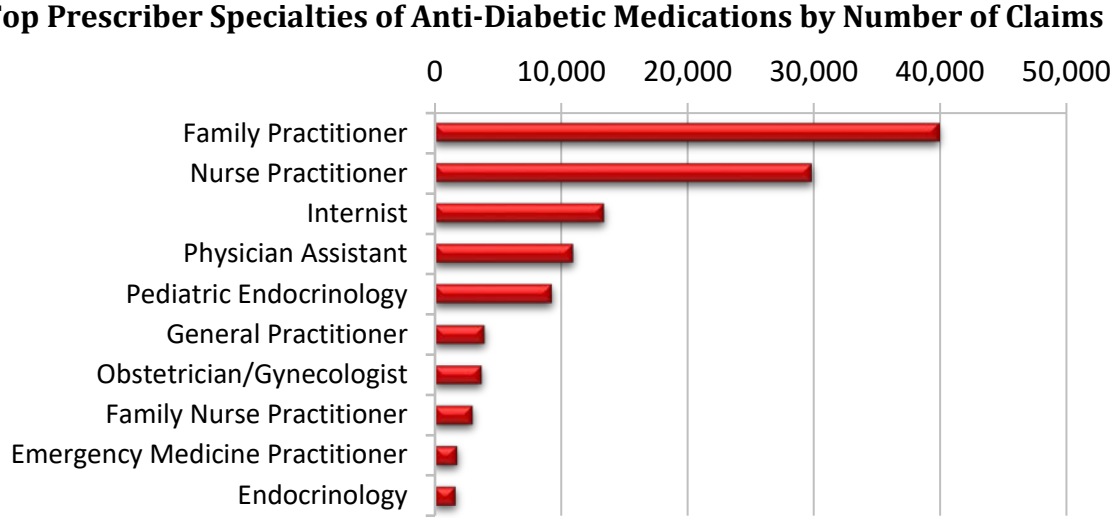
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	17,415	129,485	$40,970,194.70	$316.41	$8.30	5,944,463	4,937,249
2019	17,262	125,000	$43,342,987.84	$346.74	$8.67	6,015,194	5,001,302
% Change	**-0.90%**	**-3.50%**	**5.80%**	**9.60%**	**4.50%**	**1.20%**	**1.30%**
Change	**-153**	**-4,485**	**$2,372,793.14**	**$30.33**	**$0.37**	**70,731**	**64,053**

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

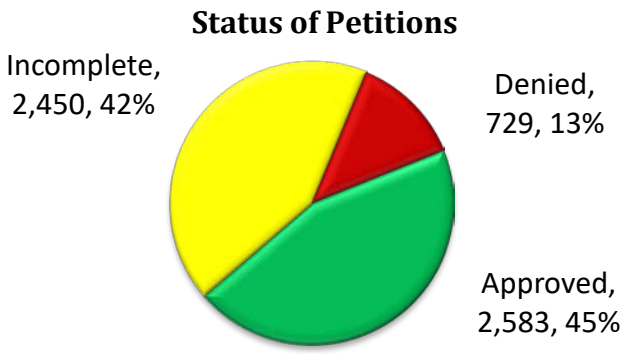
- The anti-diabetic medications are a supplementally rebated class of medications. Supplemental rebates are not reflected in the data in this report. Costs included in this report do not reflect net costs.





Prior Authorization of Anti-Diabetic Medications

There were 5,762 prior authorization requests submitted for anti-diabetic medications during calendar year 2019. Of the 5,762 total prior authorizations submitted, 3,163 were for non-insulin anti-diabetic medications and 2,599 were for insulin products. Computer edits are in place to detect lower tiered non-insulin medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for calendar year 2019.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27]

Anticipated Patent Expiration(s):

- Riomet® (metformin oral solution): August 2021
- Apidra® (insulin glulisine injection): January 2023
- Kombiglyze® XR (saxagliptin/metformin ER tablet): July 2025
- Actoplus Met XR® (pioglitazone/metformin ER tablet): July 2026; the manufacturer has discontinued marketing the brand formulation. No generic formulations are available.
- Januvia® (sitagliptin tablet): November 2026
- Janumet® XR (sitagliptin/metformin ER tablet): November 2026
- Synjardy® (empagliflozin/metformin tablet): April 2027
- Lantus® (insulin glargine injection): March 2028
- Bydureon® (exenatide ER injection): March 2028
- Janumet® (sitagliptin/metformin tablet): July 2028
- Onglyza® (saxagliptin tablet): November 2028
- Invokana® (canagliflozin tablet): February 2029
- Invokamet® (canagliflozin/metformin tablet): February 2029
- Invokamet® XR (canagliflozin/metformin ER tablet): February 2029
- Qtern® (dapagliflozin/saxagliptin tablet): December 2029
- Farxiga® (dapagliflozin tablet): May 2030
- Jentadueto® (linagliptin/metformin tablet): June 2030
- Steglatro™ (ertugliflozin tablet): July 2030
- Bydureon® BCise™ (exenatide ER auto-injector): October 2030
- Steglujan™ (ertugliflozin/sitagliptin tablet): October 2030
- Segluromet™ (ertugliflozin/metformin tablet): October 2030
- Xigduo® XR (dapagliflozin/metformin ER tablet): November 2030
- Qternmet® XR (dapagliflozin/saxagliptin/metformin ER tablet): November 2030
- Tradjenta® (linagliptin tablet): March 2031
- Tresiba® (insulin degludec injection): February 2032
- Xultophy® (insulin degludec/liraglutide injection): February 2032
- Cycloset® (bromocriptine tablet): April 2032
- Afrezza® (insulin human inhalation powder): July 2032
- Jentadueto XR® (linagliptin/metformin ER tablet): March 2033
- Apidra® SoloSTAR® (insulin glulisine injection pen): April 2033
- Lantus® SoloSTAR® (insulin glargine injection pen): April 2033
- Ryzodeg® 70/30 (insulin degludec/insulin aspart injection): May 2033; the manufacturer has discontinued marketing the brand formulation. No generic formulations are available.
- Ozempic® (semaglutide injection): June 2033
- Adlyxin® (lixisenatide injection): March 2034
- Rybelsus® (semaglutide tablet): May 2034
- Glyxambi® (empagliflozin/linagliptin tablet): June 2034
- Synjardy® XR (empagliflozin/metformin ER tablet): June 2034
- Trijardy™ XR (empagliflozin/linagliptin/metformin ER tablet): June 2034

- Jardiance® (empagliflozin tablet): June 2034
- Riomet ER™ (metformin ER oral suspension): May 2035
- Toujeo® SoloSTAR® (insulin glargine injection): September 2035
- Soliqua® (insulin glargine/lixisenatide injection): December 2035
- Victoza® (liraglutide injection): July 2037

Generic Formulation Update(s):

- **January 2019:** The U.S. Food and Drug Administration (FDA) granted the first tentative approval for an Abbreviated New Drug Application (ANDA) for dapagliflozin 5mg and 10mg tablets (Farxiga®). At this time multiple manufactures have been granted tentative approval for dapagliflozin 5mg and 10mg tablets. Patent issues must be resolved before the FDA can grant full approval. Dapagliflozin is a sodium-glucose cotransporter-2 (SGLT-2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM). Dapagliflozin is also indicated to reduce the risk of hospitalization for heart failure (HF) in adults with T2DM and established cardiovascular (CV) disease or multiple CV risk factors.

New FDA Drug Approval(s):

- **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 T2DM. Qternmet® XR initiation is intended only for patients currently taking metformin. Qternmet® XR is a once-daily, oral drug compromised of dapagliflozin (a 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 study arms in combination with metformin. AstraZeneca's launch plans for Qternmet® XR are pending.
- **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.
- **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 participants 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.

- **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 a serious condition called 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.

New FDA Approved Indication(s):

- **July 2019:** The FDA approved Victoza® (liraglutide injection) for treatment of pediatric patients 10 years of age or older with T2DM. Victoza® is the first non-insulin drug approved by the FDA to treat T2DM in pediatric patients since metformin was approved for pediatric use in 2000. Victoza® has been FDA approved to treat adult patients with T2DM since 2010. The efficacy and safety of Victoza® for reducing blood glucose in patients with T2DM was studied in several placebo-controlled trials in adults and 1 placebo-controlled trial with 134 pediatric patients 10 years of age and older for more than 26 weeks. Approximately 64% of patients in the pediatric study had a reduction in their HbA1c below 7% while on Victoza®, compared to only 37% who achieved these results with the placebo. The prescribing information for Victoza® includes a *Boxed Warning* to advise health care professionals and patients about the increased risk of thyroid C-cell tumors. For this reason, patients who have had medullary thyroid carcinoma (MTC) or have a family history of MTC should not use Victoza®, nor should patients who have an endocrine system condition called multiple endocrine neoplasia syndrome type 2 (MEN 2).
- **September 2019:** The FDA approved Invokana® (canagliflozin tablet) to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine (sCr), CV death, and hospitalization for 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, a randomized, double-blind study in 4,401 patients with T2DM, an estimated glomerular filtration rate (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.

- **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-TIMI 58 trial, the largest CV outcomes trial (CVOT) conducted in a broad patient population for an SGLT-2 inhibitor to date. This decision also follows the recent FDA Fast Track designations for the development of Farxiga®. In August 2019, the FDA granted Fast Track designation for the development of Farxiga® to delay the progression of renal failure and prevent CV and renal death in patients with chronic kidney disease (CKD). The designation was assigned to CKD patients with and without T2DM. The Phase 3 DAPA-CKD clinical trial is currently underway to evaluate the effect of Farxiga® on renal outcomes and CV mortality in patients with CKD with and without T2DM versus placebo, on top of standard of care. In September 2019, the FDA granted Fast Track designation for the development of Farxiga® to reduce the risk of CV death, HF with preserved ejection fraction (HFpEF), or the worsening of HF with reduced ejection fraction (HFrEF) based on data from the Phase 3 trials, DAPA-HF and DELIVER.
- **October 2019:** The FDA expanded the label for Fiasp® (insulin aspart 100 units/mL injection) to include use in insulin infusion pumps for the improvement of glycemic control in adults with type 1 (T1DM) or T2DM. Fiasp®, a rapid-acting insulin, was approved by the FDA in 2017 for use by intravenous (IV) infusion under the supervision of a health care professional or by subcutaneous (sub-Q) multiple daily injection (MDI) in adults with diabetes. The label change is based on the FDA's review of data from the ONSET 5 clinical trial, which confirmed the efficacy and safety of Fiasp® when used in insulin infusion pumps in adults with diabetes. Fiasp® has been shown to be well-tolerated and effective in pumps releasing steady doses throughout the day and mealtime doses during meals.
- **November 2019:** The FDA expanded the indication for Toujeo® (insulin glargine 300 units/mL injection) to include children as young as 6 years of age with T1DM and T2DM. The FDA first approved Toujeo® in 2015 for adults with T1DM and T2DM. The approval is based on results from the Phase 3 EDITION JUNIOR trial consisting of 463 children and adolescents (6 to 17 years of age) treated for T1DM for at least 1 year and with HbA1c between 7.5% and 11% at screening. Patients were randomized to Toujeo®

or insulin glargine 100 units/mL (Gla-100); patients continued to take their existing mealtime insulin. The primary endpoint was noninferior reduction in HbA1c after 26 weeks. The study met its primary endpoint, confirming a noninferior reduction in HbA1c with Toujeo® versus Gla-100 after 26 weeks (mean reduction: 0.4% vs. 0.4%; difference: 0.004%; 95% CI: –0.17 to 0.18; upper bound was below the prespecified noninferiority margin of 0.3%).

- **January 2020:** The FDA approved Fiasp® (insulin aspart 100 units/mL injection) for use as a new mealtime insulin option for children with diabetes. Fiasp® is the first and only fast-acting mealtime insulin injection that does not have a pre-meal dosing recommendation. Fiasp® is now available for use in children and adults in 3 different dosing options: MDI, continuous sub-Q insulin infusion pumps, and IV infusion under the supervision of a health care professional. The approval of Fiasp® for pediatric use was based on data from ONSET 7, a 26-week, Phase 3b, partially double-blind, basal-bolus, treat-to-target trial, which investigated the efficacy and safety of Fiasp® compared with conventional insulin aspart in 777 children with T1DM. The mean age of the patients at baseline was 11.7 years (range 2 to 17 years).
- **January 2020:** The FDA approved a label expansion based on a supplemental New Drug Application (sNDA) for Ozempic® (once-weekly semaglutide injection) for the indication of reducing the risk of major adverse CV events (MACE) including CV death, non-fatal MI, or non-fatal stroke in adults with T2DM and established CV disease. The approval is based on the SUSTAIN 6 CVOT, which demonstrated that Ozempic® statistically significantly reduced the risk of CV death, non-fatal MI, or non-fatal stroke by 26% versus placebo, when added to standard of care in patients with T2DM with increased CV risk. Ozempic® is an analogue of the naturally occurring hormone GLP-1. It is administered in a once-weekly injection of 0.5mg or 1mg and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM as well as to reduce the risk of major adverse CV events in adults with T2DM and established CV disease. Ozempic® was first approved by the FDA in 2017.
- **February 2020:** The FDA has approved Trulicity® (dulaglutide injection) for the reduction of MACE in adults with T2DM who have established CV disease or multiple CV risk factors. The new indication reflects the differentiated patient population of REWIND, the CVOT. While all participants had CV risk factors, the study consisted primarily of patients without established CV disease. REWIND showed a significant risk reduction in MACE, a composite endpoint of non-fatal MI, non-fatal stroke, or CV death. Results demonstrated consistent MACE risk reduction across major demographic and disease subgroups. The safety profile for Trulicity® was consistent with the GLP-1 receptor agonist class. The most common adverse events leading to medication discontinuation were gastrointestinal (GI) events.

Guideline Update(s):

- **April 2019:** The 2019 American Diabetes Association (ADA) consensus report on nutrition therapy for adults with diabetes or prediabetes was released and is an in-depth update to its 2014 nutrition therapy recommendations intended to provide clinical professionals with evidence-based guidance on how to individualize nutrition

therapy for adults with diabetes or prediabetes. There is strong evidence to support both the efficacy and cost-effectiveness of nutrition therapy as a key component of integrated management of patients with diabetes. This is increasingly relevant as it is evident that a "one-size-fits-all" eating plan is not suitable for prevention or management of diabetes, when also considering diverse cultural backgrounds, personal preferences, comorbidities, and socioeconomic settings. The ADA is now emphasizing that medical nutrition therapy (MNT) is fundamental for optimal diabetes management, and the new report also includes information on prediabetes. Key points, recommended for all adults with diabetes and prediabetes, include nutrition counseling that works toward improving or maintaining glycemic targets, achieving weight management goals, and improving CV risk factors within individualized treatment goals. It is important that all members of the health care team know and champion the benefits of nutrition therapy and key nutrition messages. One of the key recommendations is to refer adults living with T1DM or T2DM to individualized, diabetes-focused MNT at diagnosis and as needed throughout their life span, particularly during times of changing health status to achieve treatment goals. The MNT plan must also be coordinated and aligned with the overall management strategy, including use of medications and physical activity on an ongoing basis. In addition, patients with prediabetes who are overweight or obese should be referred to an intensive lifestyle intervention program that includes individualized goal-setting components, such as the Diabetes Prevention Program (DPP) and/or to individualized MNT. Another major recommendation is to refer adults with diabetes to comprehensive diabetes self-management education and support (DSMES) services according to national standards.

- **June 2019:** The ADA has updated its diabetes Standards of Care to incorporate results from the CREDENCE trial, published in the *New England Journal of Medicine.* In the placebo-controlled trial, the SGLT-2 inhibitor canagliflozin was associated with reduced risk for CV events and renal failure in patients with T2DM and CKD. The updates include: annual assessment of urinary albumin [e.g., spot urinary albumin-to-creatinine ratio (UACR)] and eGFR in all patients with T2DM; for patients with T2DM and diabetic kidney disease, clinicians should consider using an SGLT-2 inhibitor when the eGFR is ≥30 mL/min/1.73m^2, especially with UACR >300mg/g, to lower renal and CV risk; and for patients with CKD at elevated risk for CV events, a GLP-1 receptor agonist may lower risk for albuminuria progression and/or CV events.
- **January 2020:** The 2020 update to the ADA Standards of Medical Care in Diabetes was published in *Diabetes Care*. Major changes to the 2020 iteration involve recommendations for CV disease risk reduction, pharmacologic treatments, glycemic targets, and recommendations for individualized patient care. Accompanying the publication of the 2020 Standards of Care in *Diabetes Care* is an update to the consensus report by the ADA/European Association for the study of diabetes on management of hyperglycemia in T2DM. This consensus report and the 2020 Standards of Care now incorporate findings from major CV outcome trials published in 2019. These large-scale research projects that explored CV disease in diabetes have been central to building on the theme of patient-centered care, a major focus of the ADA's 2019 Standards of Care that is echoed in the 2020 update. For the second consecutive year,

the American College of Cardiology has endorsed the Cardiovascular Disease and Risk Management section of the ADA's Standards of Care. SGLT-2 inhibitors and GLP-1 receptor agonists have been recognized as recommended therapies for patients with T2DM and atherosclerotic CV disease (ASCVD). In the 2020 update, these recommendations have been individualized based on additional comorbidity burden. SGLT-2 inhibitors with demonstrated CV benefits are recommended for patients with T2DM plus ASCVD, ASCVD risk factors, or diabetic kidney disease to reduce the risk for CV events and HF hospitalization. GLP-1 receptor agonists with demonstrated CV benefits are recommended for patients with T2DM plus ASCVD or associated risk factors to reduce the risk for CV events. SGLT-2 inhibitors may be considered for patients with T2DM and established HF to reduce the risk for HF hospitalization. Recommendations for use of statin therapy to reduce ASCVD risk have also been revised to align with newer consensus guidelines. For primary prevention, it is recommended to use moderate-intensity statins in patients 40 to 75 years of age with diabetes who do not have established ASCVD. In cases of established ASCVD with comorbid diabetes, patients of all ages should receive high-intensity statins. For patients with ASCVD or other CVD risk factors whose LDL-C levels are controlled with statin therapy but for whom persistent hypertriglyceridemia (135 to 499mg/dL) is an issue, icosapent ethyl can be considered to reduce CV disease risk.

News:

- **August 2019:** Data from the Liraglutide Effect and Action in Diabetes: Evaluation of CV Outcome Results (LEADER) trial were published online in *Diabetes Care*. A post-hoc analysis found that patients taking Victoza® (liraglutide injection) were at increased risk for gallbladder and biliary tract-related events in the LEADER trial but the mechanisms are unclear. Primary results from LEADER, in which 9,340 patients with T2DM and high CV risk were randomized to liraglutide or placebo for a median 3.8 years, demonstrated a significantly decreased risk for MACE with liraglutide. The proportion of patients with acute gallstone disease was higher with liraglutide than placebo (3.1% vs. 1.9%; P<0.001), driven primarily by the rates of cholelithiasis (1.5% vs. 1.1%) and acute cholecystitis (0.8% vs. 0.4%). This post-hoc analysis is the first to explore the subtypes of gallstone disease observed and their implications. Overall, 275 events were reported in 235 patients, with 7 events subsequently excluded for non-relevance. Gallbladder or biliary tract-related events were higher with liraglutide versus placebo (141 vs. 88 patients; HR: 1.60; P<0.001). Baseline characteristics were similar between those experiencing events in the 2 groups. Among patients with events, those taking liraglutide were more likely than those in the placebo group to have uncomplicated gallbladder stones (16 vs. 5), complicated gallbladder stones (52 vs. 40), cholecystitis (51 vs. 33), and biliary obstruction (25 vs. 16). Cholecystectomy was more common in the liraglutide-treated patients than in the placebo group (1.74% vs. 1.11%, respectively; HR: 1.56; P=0.013). However, among those with gallbladder or biliary tract related events during the trial, the proportions undergoing cholecystectomy were similar (57% vs. 59%).

- **February 2020:** The FDA posted laboratory results showing N-Nitrosodimethylamine (NDMA) levels in some metformin products. The FDA has determined that the levels of NDMA in tested metformin products range from not detectable to low levels. To date, no sample of metformin that the FDA has tested exceeds the acceptable daily intake for NDMA. The FDA has not recommended metformin recalls in the United States. The FDA will continue to monitor NDMA in metformin, along with other drugs products, and will provide timely updates of new developments, including product recalls.

Pipeline:

- **March 2020:** The FDA granted Fast Track designation for the investigation of Jardiance® (empagliflozin tablet) to reduce the risk of kidney disease progression and CV death in adults with CKD. CKD is associated with an increased risk of premature death from CV causes and is the ninth leading cause of death in the United States. About two-thirds of cases are attributed to metabolic conditions such as diabetes (known as diabetic kidney disease), hypertension (HTN), and obesity. The ongoing EMPA-KIDNEY clinical study is evaluating the effect of Jardiance® on the progression of kidney disease and the occurrence of CV death in adults with established CKD with and without diabetes. The EMPA-KIDNEY study was initiated based on promising exploratory results from the landmark EMPA-REG OUTCOME® trial, which found that treatment with Jardiance® reduced the risk of new-onset and worsening kidney disease by 39% in adults with T2DM and established CV disease compared with placebo. Jardiance® is a once-daily tablet used along with diet and exercise to lower blood glucose in adults with T2DM and to reduce the risk of CV death in adults with T2DM and known CV disease. In June 2019, the FDA granted Fast Track designation to the clinical investigation of Jardiance® to reduce the risk of CV death and hospitalization for HF in patients with chronic HF.

Qternmet® XR (Dapagliflozin/Saxagliptin/Metformin ER Tablet) Product Summary[28,29]

Indication(s): Qternmet® XR (dapagliflozin/saxagliptin/metformin ER tablet) is an SGLT-2 inhibitor, a DPP-4 inhibitor, and a biguanide combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Limitation(s) of Use:

- Not indicated for use in patients with T1DM or treatment of diabetic ketoacidosis
- Intended only for patients currently taking metformin

Dosing:

- Qternmet® XR is supplied as an ER oral tablet in the following strengths:
  - 2.5mg dapagliflozin/2.5mg saxagliptin/1,000mg metformin ER tablet
  - 5mg dapagliflozin/2.5mg saxagliptin/1,000mg metformin ER tablet
  - 5mg dapagliflozin/5mg saxagliptin/1,000mg metformin ER tablet
  - 10mg dapagliflozin/5mg saxagliptin/1,000mg metformin ER tablet
- Renal function should be assessed before initiation of therapy and periodically thereafter.

- The starting total daily dose of Qternmet® XR should be individualized based on the patient's current regimen, effectiveness, and tolerability.
- 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 a 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 tablets should be swallowed whole, and should not be crushed, cut, or chewed.
- Qternmet® XR should be discontinued at the time of, or prior to, an iodinated contrast imaging procedure.

Boxed Warning: Lactic Acidosis

- There have been post-marketing cases of metformin-associated lactic acidosis, including fatal cases. These cases had a subtle onset and were accompanied by nonspecific symptoms such as malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence; however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. Metformin-associated lactic acidosis was characterized by elevated blood lactate concentrations (>5mmol/L), anion gap acidosis (without evidence of ketonuria or ketonemia), increased lactate/pyruvate ratio, and metformin plasma levels generally >5mcg/mL. Metformin decreases liver uptake of lactate increasing lactate blood levels which may increase the risk of lactic acidosis, especially in patients at risk. If metformin-associated lactic acidosis is suspected, general supportive measures should be instituted promptly in a hospital setting, along with immediate discontinuation of Qternmet® XR.

Efficacy: 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 HbA1c compared to the active comparator or placebo study arms in combination with metformin.

Cost Comparison: Qternmet® XR cost and launch date information is not available at this time.

Riomet ER™ (Metformin ER Oral Suspension) Product Summary[30]

Indication(s): Riomet ER™ (metformin ER oral suspension) is a biguanide indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with T2DM.

Dosing:

- 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.
- Patients receiving metformin IR treatment may be switched to Riomet ER™ once daily at the same total daily dose, up to 2,000mg (20mL) once daily.
- In patients with renal impairment, renal function with eGFR should be assessed prior to initiation.
- Riomet ER™ should not be used in patients with eGFR <30mL/min/1.73m^2 and initiation is not recommended in patients with eGFR between 30 and 45mL/min/1.73m^2. The risks and benefits of continuing Riomet ER™ if eGFR falls below 45mL/min/1.73m^2 should be assessed. Riomet ER™ should be discontinued if eGFR falls below 30mL/min/1.73m^2.
- Riomet ER™ may need to be discontinued at time of, or prior to, iodinated contrast imagine procedures.
- Riomet ER™ is supplied as a powder for oral suspension which must be reconstituted with the accompanying diluent prior to dispensing. Both the powder and diluent contain metformin.

Boxed Warning: Lactic Acidosis

- Postmarketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. Symptoms included malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Laboratory abnormalities included elevated blood lactate levels, anion gap acidosis, increased lactate/pyruvate ratio, and metformin plasma levels generally >5mcg/mL. Risk factors include renal impairment, concomitant use of certain drugs, 65 years of age or older, radiological studies with contrast, surgery and other procedures, hypoxic states, excessive alcohol intake, and hepatic impairment. Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high-risk groups are provided in the *Full Prescribing Information*. If lactic acidosis is suspected, Riomet ER™ should be discontinued and general supportive measures instituted in a hospital setting. Prompt hemodialysis is recommended.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Riomet ER™ (metformin ER oral suspension) 500mg/5mL	**$1.25**	**$750.00[+]**	**$9,000.00[+]**
Riomet® (metformin oral solution) 500mg/5mL	$1.40	$840.00[+]	$10,080.00[+]
metformin oral tablet 1,000mg	$0.02	$1.20[+]	$14.40[+]

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.
Units = milliliter (mL) or tablet; ER = extended-release
[+] Cost based on a maximum FDA recommended dose of 2,000mg daily.

Rybelsus® (Semaglutide Tablet) Product Summary[31,32]

Indication(s): Rybelsus® (semaglutide tablet) is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Limitation(s) of Use:

- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise
- Has not been studied in patients with a history of pancreatitis
- Not indicated for use in patients with T1DM or treatment of diabetic ketoacidosis

Dosing:

- 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®.
- Rybelsus® tablets should be swallowed whole. Tablets should not be cut, crushed, or chewed.
- 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 sub-Q 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.
- Patients treated with Rybelsus® 14mg daily can be transitioned to Ozempic® sub-Q injection 0.5mg once weekly. Patients can start Ozempic® the day after their last dose of Rybelsus®.

Boxed Warning: Risk of Thyroid C-Cell Tumors

- In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures. It is unknown whether Rybelsus® causes thyroid C-cell tumors, including MTC, in humans, as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans. Rybelsus® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of Rybelsus® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Efficacy:

- The efficacy of Rybelsus® was evaluated in several clinical studies as monotherapy and in combination with metformin, sulfonylureas, SGLT-2 inhibitors, insulins, and thiazolidinediones in patients with T2DM. The efficacy of Rybelsus® was compared with placebo, Jardiance® (empagliflozin), Januvia® (sitagliptin), and Victoza® (liraglutide). The primary endpoint in the clinical studies was a reduction in HbA1c.
  - Throughout the clinical studies, Rybelsus® provided a clinically significant reduction from baseline in HbA1c vs. placebo.
  - Treatment with Rybelsus® 14 mg resulted in a statistically significant reduction in HbA1c vs. empagliflozin 25mg (-1.3 vs. -0.9, respectively; P<0.001)
  - Treatment with Rybelsus® 7mg and 14mg resulted in a statistically significant reduction in HbA1c compared to empagliflozin 100mg (-1.0 and -1.3 vs. -0.8, respectively; P<0.001).
  - Treatment with Rybelsus® 14mg resulted in noninferior reductions in HbA1c vs. liraglutide 1.8mg (-1.2 vs. -1.1, respectively).
- In addition, Rybelsus® was evaluated in a double-blind, placebo-controlled, CV outcomes trial (PIONEER 6) in 3,183 patients with inadequately controlled T2DM and atherosclerotic CV disease. Patients were randomized to Rybelsus® or placebo, both in addition to standard of care, for a median observation time of 16 months. The primary endpoint was the time to first occurrence of a 3-part composite outcome of MACE which included CV death, non-fatal MI and non-fatal stroke.
  - The total number of primary component MACE endpoints was 137 [61 (3.8%) with Rybelsus® vs. 76 (4.8%) with placebo]. No increased risk for MACE was observed with Rybelsus®.
  - The FDA is still reviewing Novo Nordisk's application for Rybelsus® seeking an additional indication to reduce the risk of MACE in adults with T2DM and established CV disease. A decision is expected in the first quarter of 2020.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Rybelsus® (semaglutide tablet) 14mg	**$25.75**	**$772.50⁺**	**$9,270.00⁺**
Ozempic® (semaglutide injection) 2mg/1.5mL	$519.69	$1,559.07*	$18,708.84*
Victoza® (liraglutide injection) 18mg/3mL	$103.38	$930.42±	$11,165.04±

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = tablet or mL
⁺ Rybelsus® cost is based on a maximum FDA recommended dose of 14mg daily.
* Ozempic® cost is based on the maximum FDA recommended dose of 1mg injection per week.
± Victoza® cost is based on the maximum FDA recommended dose of 1.8mg daily.

Trijardy™ XR (Empagliflozin/Linagliptin/Metformin ER Tablet) Product Summary[33,34]

Indication(s): Trijardy™ XR (empagliflozin/linagliptin/metformin ER tablet) is an SGLT-2 inhibitor, a DPP-4 inhibitor, and a biguanide combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Limitation(s) of Use:

- Not recommended for patients with T1DM or for the treatment of diabetic ketoacidosis
- Has not been studied in patients with a history of pancreatitis

Dosing:

- Trijardy™ XR is supplied as an ER oral tablet in the following strengths:
  - 5mg empagliflozin/2.5mg linagliptin/1,000mg metformin ER tablet
  - 10mg empagliflozin/5mg linagliptin/1,000mg metformin ER tablet
  - 12.5mg empagliflozin/2.5mg linagliptin/1,000mg metformin ER tablet
  - 25mg empagliflozin/5mg linagliptin/1,000mg 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.
- Trijardy™ XR should be taken once daily with a meal in the morning.
- Trijardy™ XR tablets should be swallowed whole and should not be split, crushed, dissolved, or chewed.
- Trijardy™ XR should not be initiated or continued if the patient's eGFR is <45mL/min/1.73m^2.
- Trijardy™ XR is contraindicated in patients with an eGFR <30mL/min/1.73m^2.
- Trijardy™ XR may need to be discontinued at time of, or prior to, iodinated contrast imaging procedures.

Boxed Warning: Lactic Acidosis

- There have been postmarketing cases of metformin-associated lactic acidosis, including fatal cases. These cases had a subtle onset and were accompanied by nonspecific symptoms such as malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence; however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. Metformin-associated lactic acidosis was characterized by elevated blood lactate concentrations (>5mmol/L), anion gap acidosis (without evidence of ketonuria or ketonemia), increased lactate/pyruvate ratio, and metformin plasma levels generally >5mcg/mL. Metformin decreases liver uptake of lactate increasing lactate blood levels, which may increase the risk of lactic acidosis, especially in patients at risk. If lactic acidosis is suspected, Trijardy™ XR should be discontinued and general supportive measures instituted in a hospital setting. Prompt hemodialysis is recommended.

Efficacy: 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.

Cost Comparison:

Medication	Cost Per Tablet	Cost Per Month	Cost Per Year
Trijardy™ XR (empagliflozin/linagliptin/metformin ER tablet) 12.5mg/2.5mg/1,000mg	**$8.71**	**$522.60[+]**	**$6,271.20[+]**
metformin oral tablet 1,000mg	$0.02	$1.20[*]	$14.40[*]
Glyxambi® (empagliflozin/linagliptin tablet) 25mg/5mg	$17.25	$517.50[±]	$6,210.00[±]

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended-release
[+]Cost based on the maximum FDA recommended dose of Trijardy™ XR (25mg empagliflozin/5mg linagliptin/2,000mg metformin ER once daily).
[*]Cost based on the maximum FDA recommended dose of metformin (2,000mg daily).
[±] Cost based on the maximum FDA recommended dose of Glyxambi® (25mg empagliflozin/5mg linagliptin once daily).

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 heart failure (HF) hospitalization 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 heart failure (HF) hospitalization 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®**)

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
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®**)	
	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 (**Ozempic®**)	
		semaglutide (Rybelsus®)	
GLP-1 Agonists/Insulin			
		insulin degludec/ liraglutide (**Xultophy® 100/3.6**)+	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		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™**)	
	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®**)	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		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

Utilization Details of Non-Insulin Anti-Diabetic Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
ALPHA-GLUCOSIDASE INHIBITOR PRODUCTS						
ACARBOSE TAB 25MG	63	23	$1,632.60	3.01	2.74	$25.91
ACARBOSE TAB 100MG	21	5	$563.46	2.29	4.2	$26.83
ACARBOSE TAB 50MG	19	5	$567.96	3.57	3.8	$29.89
SUBTOTAL	**103**	**33**	**$2,764.02**	**2.96**	**3.12**	**$26.84**
BIGUANIDE PRODUCTS						
METFORMIN TAB 500MG	17,302	5,506	$166,532.36	2.03	3.14	$9.63
METFORMIN TAB 1000MG	12,352	3,804	$123,388.38	1.96	3.25	$9.99
METFORMIN TAB 500MG ER	5,113	1,805	$56,342.23	2.22	2.83	$11.02
METFORMIN TAB 850MG	768	249	$8,047.83	1.99	3.08	$10.48
METFORMIN TAB 750MG ER	670	244	$8,127.58	1.52	2.75	$12.13
RIOMET SOL 500MG/5ML	60	11	$31,730.77	14.94	5.45	$528.85
METFORMIN TAB 1000MG ER	11	1	$2,797.41	2	11	$254.31
RIOMET SOL 500MG/5ML	1	1	$854.91	20	1	$854.91
SUBTOTAL	**36,277**	**11,621**	**$397,821.47**	**2.03**	**3.12**	**$10.97**
DPP-4 INHIBITOR PRODUCTS						
JANUVIA TAB 100MG	3,163	781	$2,298,611.22	1	4.05	$726.72
TRADJENTA TAB 5MG	1,192	192	$501,912.24	1	6.21	$421.07
JANUVIA TAB 50MG	703	180	$493,491.68	1.12	3.91	$701.98
JANUVIA TAB 25MG	222	58	$137,567.91	1.02	3.83	$619.68
ONGLYZA TAB 5MG	177	38	$108,177.86	1.02	4.66	$611.17
ONGLYZA TAB 2.5MG	29	7	$13,349.42	1.18	4.14	$460.32
ALOGLIPTIN TAB 25MG	18	6	$5,176.44	0.94	3	$287.58
NESINA TAB 6.25MG	3	1	$1,177.26	1	3	$392.42
ALOGLIPTIN TAB 6.25MG	3	1	$494.39	1	3	$164.80
NESINA TAB 12.5MG	2	1	$785.92	1	2	$392.96
SUBTOTAL	**5,512**	**1,265**	**$3,560,744.34**	**1.02**	**4.36**	**$646.00**
DPP-4 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
JANUMET TAB 50-1000MG	1,159	194	$504,980.60	1.94	5.97	$435.70
JANUMET XR TAB 50-1000MG	348	60	$133,400.23	1.73	5.8	$383.33
JANUMET XR TAB 100-1000MG	299	53	$129,613.65	1	5.64	$433.49
JANUMET TAB 50-500MG	153	33	$68,603.67	1.98	4.64	$448.39

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
JANUMET XR TAB 50-500MG	39	6	$9,407.21	1.08	6.5	$241.21
JENTADUETO TAB 2.5-1000MG	33	8	$19,918.73	2	4.13	$603.60
KOMBIGLYZ XR TAB 5-1000MG	21	3	$12,316.20	1.43	7	$586.49
KOMBIGLYZ XR TAB 2.5-1000MG	10	5	$3,704.78	1.64	2	$370.48
JENTADUETO TAB 2.5-500MG	4	1	$5,065.43	2	4	$1,266.3
JENTADUETO TAB 2.5-850MG	4	1	$5,064.13	2	4	$1,266.0
KOMBIGLYZ XR TAB 5-500MG	2	1	$819.96	1	2	$409.98
SUBTOTAL	**2,072**	**365**	**$892,894.59**	**1.76**	**5.68**	**$430.93**
DPP-4 INHIBITOR/TZD COMBINATION PRODUCTS						
OSENI TAB 25-30MG	5	1	$4,837.51	1	5	$967.50
SUBTOTAL	**5**	**1**	**$4,837.51**	**1**	**5**	**$967.50**
GLINIDE PRODUCTS						
REPAGLINIDE TAB 1MG	40	10	$957.41	2.39	4	$23.94
NATEGLINIDE TAB 60MG	52	11	$2,212.15	2.75	4.73	$42.54
NATEGLINIDE TAB 120MG	47	10	$2,210.63	3	4.7	$47.03
REPAGLINIDE TAB 1MG	38	6	$873.51	2.16	6.33	$22.99
REPAGLINIDE TAB 2MG	14	4	$419.96	4.71	3.5	$30.00
REPAGLINIDE TAB 0.5MG	4	1	$85.72	3	4	$21.43
SUBTOTAL	**155**	**32**	**$5,801.97**	**2.83**	**4.84**	**$31.35**
GLP-1 AGONIST PRODUCTS						
VICTOZA INJ 18MG/3ML	3,888	847	$3,019,860.96	0.25	4.59	$776.71
TRULICITY INJ 1.5/0.5ML	1,001	162	$713,797.48	0.07	6.18	$713.08
BYDUREON PEN INJ 2MG	633	149	$429,337.36	0.14	4.25	$678.26
TRULICITY INJ 0.75/0.5ML	531	124	$381,367.16	0.07	4.28	$718.21
OZEMPIC INJ 2/1.5ML	92	34	$66,968.03	0.05	2.71	$727.91
OZEMPIC INJ 2/1.5ML	72	18	$53,733.63	0.1	4	$746.30
BYDUREON BC INJ 2/0.85ML	19	4	$12,890.27	0.12	4.75	$678.44
BYETTA INJ 5MCG	18	9	$12,770.27	0.04	2	$709.46
BYETTA INJ 10MCG	14	5	$15,547.28	0.08	2.8	$1,110.5
BYDUREON INJ 2MG	4	4	$2,557.60	0.14	1	$639.40
TANZEUM INJ 30MG	3	1	$1,532.33	0.14	3	$510.78
SUBTOTAL	**6,275**	**1,357**	**$4,710,362.37**	**0.19**	**4.62**	**$750.66**
GLP-1 AGONIST/INSULIN COMBINATION PRODUCTS						
SOLIQUA INJ U-100/ML-33MCG/ML	60	12	$37,609.87	0.38	5	$626.83
XULTOPHY INJ U-100/ML-3.6MG/ML	44	16	$42,796.01	0.33	2.75	$972.64
SUBTOTAL	**104**	**28**	**$80,405.88**	**0.36**	**3.71**	**$773.13**
SGLT-2 INHIBITOR PRODUCTS						
JARDIANCE TAB 25MG	1,583	326	$755,345.65	1	4.86	$477.16
JARDIANCE TAB 10MG	1,037	276	$487,768.01	1	3.76	$470.36
FARXIGA TAB 10MG	515	118	$245,548.16	1	4.36	$476.79
INVOKANA TAB 300MG	437	58	$210,172.64	1	7.53	$480.94
FARXIGA TAB 5MG	264	80	$125,715.80	1	3.3	$476.20
INVOKANA TAB 100MG	126	28	$60,403.00	1	4.5	$479.39

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
STEGLATRO TAB 5MG	4	2	$1,109.32	1	2	$277.33
STEGLATRO TAB 15MG	2	2	$546.48	1	1	$273.24
SUBTOTAL	**3,968**	**890**	**$1,886,609.06**	**1**	**4.46**	**$475.46**
SGLT-2 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
SYNJARDY TAB 12.5-1000MG	118	17	$54,639.09	1.95	6.94	$463.04
XIGDUO XR TAB 10-1000MG	77	14	$36,885.84	1	5.5	$479.04
SYNJARDY XR TAB 25-1000MG	65	14	$31,184.49	1	4.64	$479.76
XIGDUO XR TAB 5-1000MG	54	15	$22,185.98	1.72	3.6	$410.85
INVOKAMET TAB 150-1000MG	36	8	$17,104.40	2	4.5	$475.12
SYNJARDY XR TAB 12.5-1000MG	25	6	$7,766.41	1.28	4.17	$310.66
SYNJARDY TAB 5-1000MG	19	8	$7,958.43	1.74	2.38	$418.86
SYNJARDY XR TAB 5-1000MG	18	4	$4,380.46	1	4.5	$243.36
INVOKAMET TAB 50-1000MG	11	1	$5,285.89	2	11	$480.54
SYNJARDY TAB 5-500MG	9	3	$4,369.64	2	3	$485.52
XIGDUO XR TAB 10-500MG	9	2	$4,354.13	1	4.5	$483.79
INVOKAMET XR TAB 150-1000	7	1	$3,378.83	2	7	$482.69
INVOKAMET TAB 50-500MG	6	1	$2,859.97	2	6	$476.66
XIGDUO XR TAB 2.5-1000MG	6	1	$2,944.04	2	6	$490.67
SUBTOTAL	**463**	**98**	**$206,511.69**	**1.53**	**4.72**	**$446.03**
SULFONYLUREA PRODUCTS						
GLIPIZIDE TAB 5MG	2,338	693	$19,702.12	1.48	3.37	$8.43
GLIPIZIDE TAB 10MG	2,270	602	$20,044.95	1.78	3.77	$8.83
GLYBURIDE TAB 5MG	2,225	520	$34,268.92	2.03	4.28	$15.40
GLIMEPIRIDE TAB 4MG	1,302	320	$14,300.68	1.41	4.07	$10.98
GLIMEPIRIDE TAB 2MG	797	249	$8,351.03	1.28	3.2	$10.48
GLIPIZIDE ER TAB 10MG	641	193	$13,060.43	1.38	3.32	$20.38
GLYBURIDE TAB 2.5MG	485	217	$6,615.74	1.29	2.24	$13.64
GLIPIZIDE ER TAB 5MG	458	174	$7,482.55	1.25	2.63	$16.34
GLIMEPIRIDE TAB 1MG	413	134	$4,295.74	1.14	3.08	$10.40
GLIPIZIDE ER TAB 2.5MG	274	101	$4,445.85	1.14	2.71	$16.23
GLIPIZIDE XL TAB 10MG	209	69	$3,593.79	1.39	3.03	$17.20
GLIPIZIDE XL TAB 5MG	191	83	$2,904.15	1.35	2.3	$15.20
GLYBURIDE TAB 1.25MG	71	24	$1,005.11	1.28	2.96	$14.16
GLYBURID MCR TAB 3MG	56	11	$633.07	1.81	5.09	$11.30
GLYBURID MCR TAB 6MG	36	5	$394.72	1.7	7.2	$10.96
GLIPIZIDE XL TAB 2.5MG	14	12	$287.16	1	1.17	$20.51
GLYBURID MCR TAB 1.5MG	2	2	$27.71	3.5	1	$13.86
SUBTOTAL	**11,782**	**3,409**	**$141,413.72**	**1.55**	**3.46**	**$12.00**
SULFONYLUREA/BIGUANIDE COMBINATION PRODUCTS						
GLYB/METFORM TAB 5-500MG	316	51	$3,952.44	3.09	6.2	$12.51
GLIP/METFORM TAB 5-500MG	137	27	$3,431.55	2.28	5.07	$25.05
GLYB/METFORM TAB 2.5-500MG	98	20	$1,158.96	3.16	4.9	$11.83
GLIP/METFORM TAB 2.5-500MG	39	9	$1,329.39	3.28	4.33	$34.09

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
GLYB/METFORM TAB 1.25-250MG	6	2	$54.42	1.08	3	$9.07
GLIP/METFORM TAB 2.5-250MG	1	1	$38.06	1	1	$38.06
SUBTOTAL	**597**	**110**	**$9,964.82**	**2.88**	**5.43**	**$16.69**
SGLT-2 INHIBITOR/DPP-4 INHIBITOR COMBINATION PRODUCTS						
GLYXAMBI TAB 25-5MG	100	16	$52,570.21	1	6.25	$525.70
GLYXAMBI TAB 10-5MG	33	7	$15,617.67	1	4.71	$473.26
QTERN TAB 10MG/5MG	3	1	$1,443.99	1	3	$481.33
SUBTOTAL	**136**	**24**	**$69,631.87**	**1**	**5.67**	**$512.00**
TZD PRODUCTS						
PIOGLITAZONE TAB 30MG	881	276	$12,365.99	0.99	3.19	$14.04
PIOGLITAZONE TAB 15MG	742	219	$8,567.34	1.04	3.39	$11.55
PIOGLITAZONE TAB 45MG	475	137	$7,228.78	1	3.47	$15.22
AVANDIA TAB 4MG	13	2	$2,636.96	1.15	6.5	$202.84
SUBTOTAL	**2,111**	**634**	**$30,799.07**	**1.01**	**3.33**	**$14.59**
TZD/BIGUANIDE COMBINATION PRODUCTS						
PIOGLITA/MET TAB 15-850MG	27	6	$1,471.48	1.66	4.5	$54.50
PIOGLITA/MET TAB 15-500MG	2	2	$114.53	2	1	$57.27
SUBTOTAL	**29**	**8**	**$1,586.01**	**1.68**	**3.63**	**$54.69**
TOTAL	**69,589**	**13,038***	**$12,002,148.39**	**1.67**	**5.34**	**$172.47**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
ER, XL, XR = extended-release; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide 1; SGLT-2 = sodium-glucose cotransporter 2; TZD = thiazolidinedione

Utilization Details of Insulin Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	COST/ DAY	COST/ CLAIM
INSULIN ASPART PRODUCTS						
NOVOLOG INJ FLEXPEN U-100/ML	7,908	2,172	$5,296,987.63	0.53	$18.56	$669.83
NOVOLOG INJ U-100/ML	4,052	893	$2,185,848.30	0.68	$18.31	$539.45
NOVOLOG INJ PENFILL U-100/ML	571	121	$307,681.20	0.45	$14.21	$538.85
FIASP FLEX INJ TOUCH U-100/ML	77	16	$34,723.47	0.51	$12.87	$450.95
FIASP INJ U-100/ML	24	3	$21,557.52	1.09	$30.53	$898.23
SUBTOTAL	**12,632**	**3,205**	**$7,846,798.12**	**0.57**	**$18.25**	**$621.18**
INSULIN ASPART/NPH COMBINATION PRODUCTS						
NOVOLOG MIX INJ FLEX 70/30 U-100/ML	700	172	$620,286.14	0.73	$25.77	$886.12
NOVOLOG MIX INJ 70/30 U-100/ML	232	55	$185,834.87	1	$27.38	$801.01
SUBTOTAL	**932**	**227**	**$806,121.01**	**0.79**	**$26.12**	**$864.94**
INSULIN DEGLUDEC PRODUCTS						
TRESIBA FLEX INJ U-200/ML	863	193	$724,161.37	0.36	$23.15	$839.12
TRESIBA FLEX INJ U-100/ML	699	181	$346,213.63	0.38	$12.13	$495.30
TRESIBA INJ U-100/ML	1	1	$332.48	0.29	$9.78	$332.48
SUBTOTAL	**1,563**	**375**	**$1,070,707.48**	**0.37**	**$17.89**	**$685.03**
INSULIN DETEMIR PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	COST/ DAY	COST/ CLAIM
LEVEMIR INJ FLEXT U-100/ML	6,733	1,847	$3,829,569.01	0.47	$13.72	$568.78
LEVEMIR INJ U-100/ML	2,480	584	$1,275,642.66	0.53	$15.62	$514.37
SUBTOTAL	**9,213**	**2,431**	**$5,105,211.67**	**0.48**	**$14.15**	**$554.13**
INSULIN GLARGINE PRODUCTS						
LANTUS SOLOS INJ U-100/ML	12,949	3,282	$6,760,943.73	0.45	$12.26	$522.12
LANTUS INJ U-100/ML	4,796	1,106	$2,329,749.54	0.56	$15.25	$485.77
TOUJEO SOLO INJ U-300/ML	478	91	$417,242.50	0.33	$27.74	$872.89
TOUJEO MAX INJ U-300/ML	94	24	$118,395.14	0.48	$40.09	$1,259.52
BASAGLAR INJ U-100/ML	68	16	$17,487.50	0.44	$7.78	$257.17
SUBTOTAL	**18,385**	**4,519**	**$9,643,818.41**	**0.47**	**$13.32**	**$524.55**
INSULIN GLULISINE PRODUCTS						
APIDRA INJ SOLOSTAR U-100/ML	323	75	$245,585.04	0.54	$19.15	$760.33
APIDRA INJ U-100/ML	89	15	$40,258.80	0.62	$17.28	$452.35
SUBTOTAL	**412**	**90**	**$285,843.84**	**0.55**	**$18.87**	**$693.80**
INSULIN LISPRO PRODUCTS						
HUMALOG KWIK INJ U-100/ML	4,027	1,151	$2,765,104.94	0.55	$18.34	$686.64
HUMALOG INJ U-100/ML	2,998	688	$1,594,093.15	0.7	$18.15	$531.72
HUMALOG JR INJ U-100/ML	476	108	$250,624.18	0.43	$14.66	$526.52
HUMALOG INJ U-100/ML	304	53	$187,314.33	0.58	$19.29	$616.17
HUMALOG KWIK INJ U-200/ML	63	13	$106,565.42	0.81	$55.39	$1,691.51
INSULIN LISP INJ U-100/ML	2	1	$2,136.42	2	$35.61	$1,068.21
ADMELOG INJ U-100/ML	1	1	$142.17	0.33	$4.74	$142.17
SUBTOTAL	**7,871**	**2,015**	**$4,905,980.61**	**0.59**	**$18.35**	**$623.30**
INSULIN LISPRO/NPH COMBINATION PRODUCTS						
HUMALOG MIX INJ 75/25KWP U-100/ML	152	41	$135,037.84	0.74	$25.53	$888.41
HUMALOG MIX SUS 75/25 U-100/ML	60	13	$38,511.67	0.7	$19.17	$641.86
HUMALOG MIX INJ 50/50KWP U-100/ML	30	7	$26,575.89	0.83	$28.64	$885.86
HUMALOG MIX INJ 50/50 U-100/ML	13	2	$14,067.57	1.31	$36.16	$1,082.12
SUBTOTAL	**255**	**63**	**$214,192.97**	**0.77**	**$24.86**	**$839.97**
NPH (N) INSULIN PRODUCTS						
HUMULIN N INJ U-100/ML	418	145	$101,629.06	0.5	$7.38	$243.13
NOVOLIN N INJ U-100/ML	334	110	$73,532.74	0.48	$6.55	$220.16
HUMULIN N INJ U-100KWP	286	129	$141,163.95	0.4	$12.28	$493.58
NOVOLIN N INJ RELION U-100/ML	235	80	$10,794.92	0.52	$1.27	$45.94
SUBTOTAL	**1,273**	**464**	**$327,120.67**	**0.48**	**$7.27**	**$256.97**
REGULAR (R) INSULIN PRODUCTS						
HUMULIN R INJ U-100/ML	758	216	$192,062.90	0.55	$8.40	$253.38
NOVOLIN R INJ U-100/ML	446	137	$87,564.99	0.5	$6.67	$196.33
HUMULIN R INJ U-500/ML	330	67	$440,698.90	0.48	$44.02	$1,335.45
NOVOLIN R INJ RELION U-100/ML	265	75	$18,709.24	0.6	$2.04	$70.60
HUMULIN R INJ U-500/ML	14	4	$22,998.87	0.55	$39.38	$1,642.78
SUBTOTAL	**1,813**	**499**	**$762,034.90**	**0.53**	**$13.67**	**$420.32**
R/N INSULIN COMBINATION PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	COST/ DAY	COST/ CLAIM
HUMULIN INJ 70/30 U-100/ML	359	69	$131,259.02	0.83	$12.35	$365.62
NOVOLIN INJ 70/30 U-100/ML	274	80	$88,899.47	0.71	$9.57	$324.45
NOVOLIN 70/30 INJ RELION U-	205	53	$17,303.25	0.8	$2.55	$84.41
HUMULIN INJ 70/30KWP U-100/ML	175	45	$125,023.07	0.63	$19.19	$714.42
NOVOLIN INJ FLEXPEN U-100/ML	49	25	$10,524.96	0.68	$7.26	$214.80
SUBTOTAL	**1,062**	**272**	**$373,009.77**	**0.75**	**$10.76**	**$351.23**
TOTAL	**55,411**	**7,804***	**$31,340,839.45**	**0.52**	**$15.42**	**$565.61**

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

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Appendix D

Calendar Year 2019 Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Katerzia™ (Amlodipine Oral Suspension) and Conjupri® (Levamlodipine Tablet)

Oklahoma Health Care Authority
April 2020

Current Prior Authorization Criteria

There are 7 major subcategories of antihypertensive medications divided by drug class currently included in the Antihypertensive Product Based Prior Authorization (PBPA) category:

1. Angiotensin I Converting Enzyme Inhibitors (ACEIs)
2. Calcium Channel Blockers (CCBs)
3. ACEI/CCB Combination Products
4. ACEI/Hydrochlorothiazide (HCTZ) Combination Products
5. Angiotensin II Receptor Blockers (ARBs)
6. ARB Combination Products
7. Direct Renin Inhibitors (DRIs) and DRI Combination Products

Antihypertensive Medications Tier-2 Approval Criteria:
(or Tier-3 approval criteria when no Tier-2 medications exist)

1. A documented inadequate response to 2 Tier-1 medications (trials must include medication(s) from all available classes where applicable); or
2. An adverse drug reaction to all Tier-1 classes of medications; or
3. Previous stabilization on the Tier-2 medication; or
4. A unique indication for which the Tier-1 antihypertensive medications lack.

Antihypertensive Medications Tier-3 Approval Criteria:

1. A documented inadequate response to 2 Tier-1 medications and documented inadequate response to all available Tier-2 medication(s); or
2. An adverse drug reaction to all Tier-1 and Tier-2 classes of medications; or
3. Previous stabilization on the Tier-3 medication; or
4. A unique indication for which the lower tiered antihypertensive medications lack.

Tekturna® (Aliskiren Tablet) and Tekturna HCT® (Aliskiren/Hydrochlorothiazide Tablet) Approval Criteria:

1. An FDA approved indication; and
2. A recent trial, within the previous 6 months and at least 4 weeks in duration, of an angiotensin I converting enzyme inhibitor (ACEI) [or an angiotensin II receptor blocker (ARB) if previous trial of an ACEI] and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control; and
3. May be used as either monotherapy or combination therapy.

Tekturna® (Aliskiren Oral Pellet) Approval Criteria:

1. An FDA approved indication; and
2. A recent trial, within the previous 6 months and at least 4 weeks in duration, of an angiotensin I converting enzyme inhibitor (ACEI) [or an angiotensin II receptor blocker (ARB) if previous trial of an ACEI] and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control; and
3. Member must be 6 years of age or older; and
4. A patient-specific, clinically significant reason why the member cannot use Tekturna® tablets must be provided.

The following restrictions also apply for each individual product based on U.S. Food and Drug Administration (FDA) approval information, special formulations, or individualized Drug Utilization Review (DUR) Board recommended criteria:

Cardizem® CD (Diltiazem CD 360mg Capsule Only) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use (2) 180mg Cardizem® CD (diltiazem CD) capsules must be provided.

CaroSpir® (Spironolactone Oral Suspension) Approval Criteria:

1. An FDA approved indication; and
2. A patient-specific, clinically significant reason why the member cannot use spironolactone oral tablets must be provided.

Consensi® (Amlodipine/Celecoxib Tablet) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the individual components separately, which are available without prior authorization, must be provided; and
2. A quantity limit of 30 tablets per 30 days will apply.

Epaned® (Enalapril Oral Solution) Approval Criteria:

1. An age restriction for members age 7 years or older will apply with the following criteria:
    a. Consideration for approval requires a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation even when crushed.

Hemangeol® (Propranolol Hydrochloride Oral Solution) Approval Criteria:

1. An FDA approved indication for the treatment of proliferating infantile hemangioma requiring systemic therapy.

Kapspargo™ Sprinkle [Metoprolol Succinate Extended-Release (ER) Capsule] Approval Criteria:

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

Monopril-HCT® (Fosinopril/Hydrochlorothiazide Tablet) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the individual components must be provided.

Prestalia® (Perindopril/Amlodipine Tablet) Approval Criteria:

1. An FDA approved diagnosis; and
2. Documented trials of inadequate response to 2 Tier-1 angiotensin converting enzyme inhibitors (ACEIs) in combination with amlodipine; and
3. A patient-specific, clinically significant reason why the member cannot use the individual components separately must be provided; and
4. A quantity limit of 30 tablets per 30 days will apply.

Prexxartan® (Valsartan Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use valsartan oral tablets in place of the oral solution formulation even when the tablets are crushed must be provided.

Qbrelis® (Lisinopril Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use lisinopril oral tablets in place of the oral solution formulation even when the tablets are crushed must be provided.

Sotylize® (Sotalol Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of life-threatening ventricular arrhythmias or for the maintenance of normal sinus rhythm in members with highly symptomatic atrial fibrillation/flutter; and
2. A patient-specific, clinically significant reason why the member cannot use sotalol oral tablets in place of the oral solution formulation must be provided; and
3. A quantity limit of 64mL per day or 1,920mL per 30 days will apply.

Vecamyl® (Mecamylamine Tablet) Approval Criteria:

1. An FDA approved diagnosis of moderately severe-to-severe essential hypertension or uncomplicated malignant hypertension; and
2. Use of at least 6 classes of medications, in the past 12 months, that did not yield adequate blood pressure control. Treatment must have included combination therapy with a diuretic and therapy with at least a 4-drug regimen. Medications can be from, but not limited to, the following classes: angiotensin I converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), direct renin inhibitors (DRIs), beta-blockers, alpha-blockers, alpha-agonists, diuretics; and
3. Prescriber must verify member does not have any of the following contraindications:
    a. Coronary insufficiency; or
    b. Recent myocardial infarction; or
    c. Rising or elevated blood urea nitrogen (BUN), or known renal insufficiency; or
    d. Uremia; or
    e. Glaucoma; or
    f. Organic pyloric stenosis; or
    g. Currently receiving sulfonamides or antibiotics; or
    h. Known sensitivity to Vecamyl® (mecamylamine).

The following Tier charts contain the current Antihypertensive Medication Tier structures. Most classes are based on supplemental rebate participation. Tier-2 criteria applies for Tier-3 medications when there are no Tier-2 medications available. Special dosage formulation criteria applies where applicable.

Angiotensin Converting Enzyme Inhibitors (ACEIs)		
Tier-1	**Tier-2**	**Special PA**
benazepril (Lotensin®)	captopril (Capoten®)	enalapril oral solution (Epaned®)
enalapril (Vasotec®)		lisinopril oral solution (Qbrelis®)
enalaprilat (Vasotec® IV)		
fosinopril (Monopril®)		
lisinopril (Prinivil®, Zestril®)		
moexipril (Univasc®)		
perindopril erbumine (Aceon®)		
quinapril (Accupril®)		
ramipril (Altace®)		
trandolapril (Mavik®)		

IV = intravenous; PA = prior authorization

Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Hydrochlorothiazide (HCTZ) Combinations		
Tier-1	**Tier-2**	**Special PA**
benazepril/HCTZ (Lotensin® HCT)	captopril/HCTZ (Capozide®)	fosinopril/HCTZ (Monopril-HCT®)
enalapril/HCTZ (Vasoretic®)		
lisinopril/HCTZ (Prinzide®, Zestoretic®)		
moexipril/HCTZ (Uniretic®)		
quinapril/HCTZ (Accuretic®)		

HCTZ = hydrochlorothiazide; PA = prior authorization

Angiotensin Receptor Blockers (ARBs) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
amlodipine/valsartan (Exforge®)	amlodipine/valsartan/HCTZ (Exforge® HCT) - **generic**	azilsartan (Edarbi®)
amlodipine/valsartan/HCTZ (Exforge® HCT) - **brand only**	candesartan (Atacand®)	azilsartan/chlorthalidone (Edarbyclor®)
irbesartan (Avapro®)	olmesartan/amlodipine/HCTZ (Tribenzor®)	candesartan/HCTZ (Atacand® HCT)
irbesartan/HCTZ (Avalide®)	telmisartan/HCTZ (Micardis® HCT)	eprosartan (Teveten®)
losartan (Cozaar®)		eprosartan/HCTZ (Teveten® HCT)
losartan/HCTZ (Hyzaar®)		telmisartan/amlodipine (Twynsta®)
olmesartan (Benicar®)		
olmesartan/amlodipine (Azor®)		
olmesartan/HCTZ (Benicar HCT®)		
telmisartan (Micardis®)		
valsartan (Diovan®)		
valsartan/HCTZ (Diovan HCT®)		

HCTZ = hydrochlorothiazide

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)	diltiazem CD 360mg (Cardizem® CD)
diltiazem (Tiazac®, Taztia XT®)	diltiazem SR (Cardizem® SR)	
diltiazem CD (Cardizem® CD)*	isradipine (Dynacirc®, Dynacirc CR®)	
diltiazem ER (Cartia XT®, Diltia XT®)	nicardipine (Cardene® SR)	
diltiazem XR (Dilacor® XR)	nisoldipine (Sular®)	
felodipine (Plendil®)	verapamil (Covera-HS®)	
nicardipine (Cardene®)	verapamil ER (Verelan®, Verelan® PM)	
nifedipine (Adalat®, Procardia®)		
nifedipine ER (Adalat® CC)		
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.

Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Calcium Channel Blocker (CCB) Combinations		
Tier-1	**Tier-2**	**Special PA**
benazepril/amlodipine (Lotrel®)	trandolapril/verapamil (Tarka®)	perindopril/amlodipine (Prestalia®)

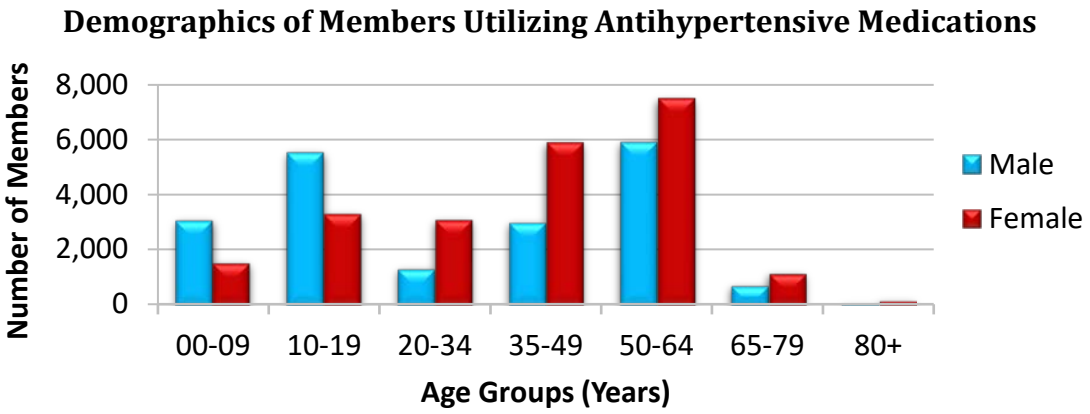
PA = prior authorization

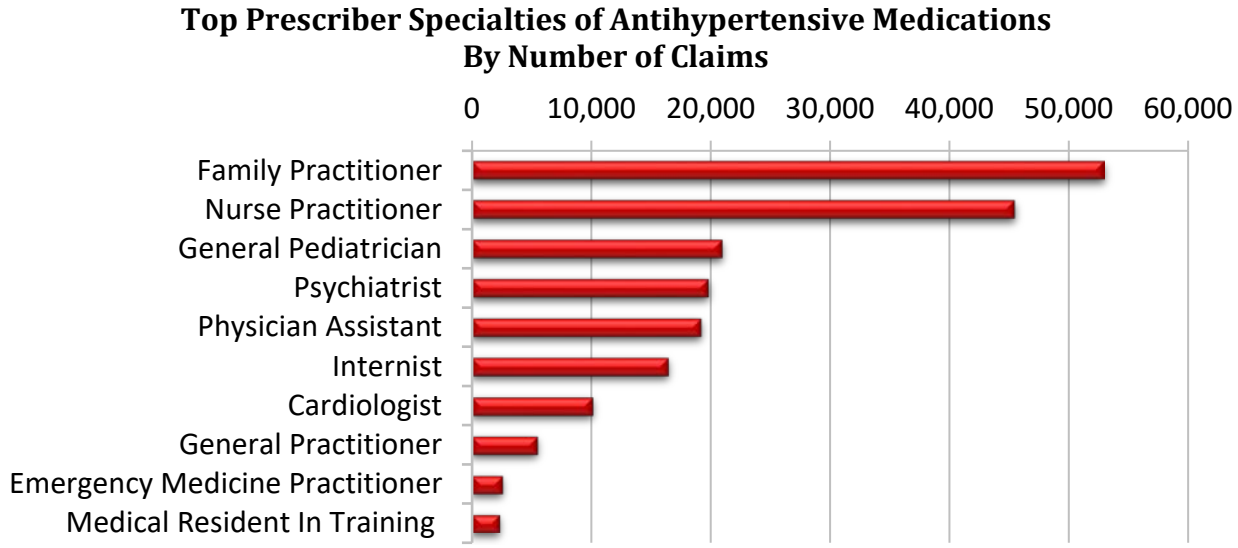
Utilization of Antihypertensive Medications: Calendar Year 2019

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	43,357	217,682	$2,941,667.00	$13.51	$0.33	11,079,517	9,008,289
2019	42,378	210,634	$3,010,569.07	$14.29	$0.34	11,022,535	8,984,778
% Change	**-2.3%**	**-3.2%**	**2.3%**	**5.8%**	**3.0%**	**-0.5%**	**-0.3%**
Change	**-979**	**-7,048**	**$68,902.07**	**$0.78**	**$0.01**	**-56,982**	**-23,511**

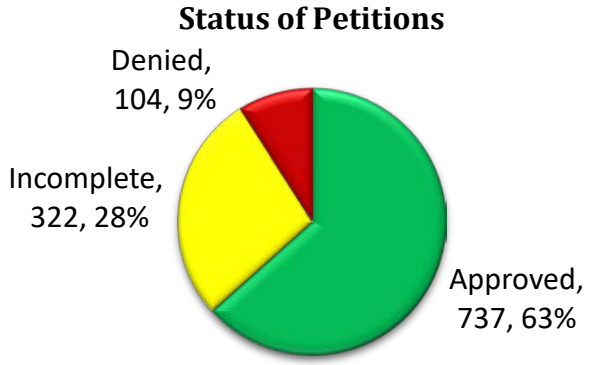
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Antihypertensive Medications

There were 1,163 prior authorization requests submitted for antihypertensive medications during calendar year 2019. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for calendar year 2019.



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

Anticipated Patent Expiration(s):

- Tekturna® (aliskiren tablet): August 2026
- Edarbi® (azilsartan tablet): March 2028
- Tekturna HCT® [aliskiren/hydrochlorothiazide (HCTZ) tablet]: July 2028
- Hemangeol® (propranolol hydrochloride oral solution): October 2028
- Prestalia® (perindopril arginine/amlodipine tablet): October 2029
- Consensi® (amlodipine/celecoxib tablet): February 2030
- Edarbyclor® (azilsartan/chlorthalidone tablet): February 2030
- Kapspargo™ Sprinkle [metoprolol succinate extended-release (ER) capsule]: July 2035
- Qbrelis® (lisinopril oral solution): November 2035
- Epaned® (enalapril oral solution): March 2036
- CaroSpir® (spironolactone oral suspension): October 2036

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

- **July 2019:** Azurity Pharmaceuticals announced the FDA approval of Katerzia™ (amlodipine) 1mg/mL oral suspension for the treatment of hypertension (HTN) in adults and pediatric patients 6 years of age and older and for the treatment of coronary artery disease (CAD) in adults.
- **December 2019:** CSPC Pharmaceutical Group Announced the FDA approval of Conjupri® (levamlodipine maleate) tablets for the treatment of HTN.

News:

- **September 2019:** A study that included 608,452 patients with HTN (18 to 100 years of age) during 9 consecutive influenza seasons (2007 to 2016) from Danish nationwide health care registers determined that influenza vaccination in patients with HTN is associated with a reduced risk of death during influenza season. After adjusting for patient differences, in a given influenza season, vaccination was associated with an 18% relative reduction in the risk of dying from all causes, a 16% relative reduction in the risk of dying from any cardiovascular (CV) cause, and a 10% relative reduction in the risk of dying from myocardial infarction (MI) or stroke. Regarding the relationship between influenza and CV disease, the author noted that influenza can trigger a strong immune reaction in the body that may increase the risk of MI or stroke.
- **October 2019:** A multinational, retrospective, comparative cohort study using data from 6 administrative claims and 3 electronic health record databases over 17 years to compare the effectiveness and safety endpoints of 5 commonly used antihypertensive drug classes [thiazide or thiazide-like diuretics, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), dihydropyridine calcium channel blockers (CCBs), or non-dihydropyridine CCBs] for monotherapy was published in *The Lancet*. The study, part of the Large-Scale Evidence Generation and Evaluation in a Network of Databases (LEGEND) Hypertension study, found that patients initiating treatment with a thiazide or thiazide-like diuretic had a significantly lower risk of acute MI [hazard ratio (HR): 0.84; 95% confidence interval (CI): 0.75 to 0.95], hospitalization for heart failure (HF) (HR: 0.83; 95% CI: 0.74 to 0.95), and stroke (HR: 0.83; 95% CI: 0.74 to 0.95), as

compared with patients initiating treatment with an ACEI. The author concluded that 1.3 CV events would be avoided for every 1,000 patients initiated with a thiazide or thiazide-like diuretic instead of an ACEI. Additionally, the thiazide or thiazide-like diuretic safety profile was also markedly better than the ACEIs. Patients who initiated treatment with a non-dihydropyridine CCB had a significantly higher risk of poor effectiveness outcomes compared with all other class choices, but less adequate cohort balance and equipoise in these comparisons might limit their generalizability. Finally, there were no significant effectiveness differences between the remaining classes.

- **February 2020:** A study based on data generated by the LEGEND Hypertension study found that chlorthalidone causes more serious side effects than hydrochlorothiazide (HCTZ). The 2 treatments were similarly effective in preventing MI, hospitalization for HF, and stroke. However, researchers found that chlorthalidone was associated with a significantly higher risk of hypokalemia (HR: 2.72; 95% CI: 2.38 to 3.12), hyponatremia (HR: 1.31; 95% CI: 1.16 to 1.47), acute renal failure (HR: 1.37; 95% CI: 1.15 to 1.63), chronic kidney disease (HR: 1.24; 95% CI: 1.09 to 1.42), and type 2 diabetes mellitus (HR: 1.21; 95% CI: 1.12 to 1.30). Researchers also found that chlorthalidone may lower the risk of abnormal weight gain (HR: 0.73; 95% CI: 0.61 to 0.86). The findings, published in *JAMA Internal Medicine*, contrast with American College of Cardiology and American Heart Association 2017 treatment guidelines recommending chlorthalidone over HCTZ, based on the drug's longer half-life and indirect evidence that it may be more effective in reducing CV risk.

Katerzia™ (Amlodipine Oral Suspension) Product Summary[7]

Indication(s): Katerzia™ is a CCB and may be used alone or in combination with other antihypertensive and antianginal agents for the treatment of the following:

- HTN in adults and children 6 years of age and older:
  - Lowering blood pressure (BP) reduces the risk of fatal and nonfatal CV events, primarily stroke and MI
- CAD in adults:
  - Chronic stable angina
  - Vasospastic angina (Prinzmetal's or variant angina)
  - Angiographically documented CAD in patients without HF or an ejection fraction (EF) <40%

Dosing:

- Katerzia™ oral suspension contains 1mg/mL of amlodipine (equivalent to 1.3mg of amlodipine benzoate) in an aqueous, white to off-white, liquid suspension.
- Katerzia™ is supplied as 150mL in a 185mL high-density polyethylene (HDPE) bottle with a child-resistant cap and tamper-evident seal.
- Katerzia™ oral suspension should be shaken before using and should be refrigerated at 2°C to 8°C (36°F to 46°F). It is recommended to avoid freezing Katerzia™ and to avoid excessive heat. Katerzia™ should be protected from light.

- Adult Dosing:
  - HTN: The recommended initial dose is 5mg once daily, with a maximum dose of 10mg once daily.
  - Angina: The recommended dose is 5 to 10mg once daily.
  - CAD: The recommended dose is 5 to 10mg once daily.
- For small, fragile, or elderly patients, or patients with hepatic insufficiency, the recommended initial dose is 2.5mg once daily, then titrated to response.
- Pediatric Dosing (6 to 17 Years of Age):
  - The recommended dose for HTN is 2.5 to 5mg once daily. Doses in excess of 5mg daily have not been studied in pediatric patients.

Contraindication(s):

- Known hypersensitivity to amlodipine or any inactive ingredients of Katerzia™

Safety:

- Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis; however, acute hypotension is unlikely.
- Worsening angina and acute MI can develop after starting or increasing the dose of amlodipine, particularly in patients with severe obstructive CAD.
- Dosing should be titrated slowly in patients with severe hepatic impairment.

Efficacy:

- HTN:
  - The antihypertensive efficacy of amlodipine has been demonstrated in a total of 15 double-blind, placebo-controlled, randomized trials involving 800 adult patients on amlodipine and 538 on placebo. Once daily administration produced statistically significant reductions in BP at 24 hours post dose, averaging about 12/6mmHg in the standing position and 13/7mmHg in the supine position.
  - A total of 268 hypertensive pediatric patients 6 to 17 years of age were randomized first to amlodipine 2.5mg or 5mg once daily for 4 weeks and then randomized again to the same dose or to placebo for another 4 weeks. Patients receiving 2.5mg or 5mg at the end of 8 weeks had significantly lower systolic BP than those secondarily randomized to placebo. Treatment effect was a 5mmHg reduction in systolic BP on the 5mg dose and a 3.3mmHg reduction on the 2.5mg dose.
- Chronic Stable Angina:
  - The effectiveness of 5 to 10mg per day of amlodipine in exercise-induced angina has been evaluated in 8 placebo-controlled, double-blind clinical trials of up to 6 weeks duration involving 1,038 patients with chronic stable angina. In 5 of the 8 studies, significantly increased exercise time, increased time to 1mm ST segment deviation, and decreased angina attack rate were seen with the 10mg dose. Increases in symptom-limited exercise time averaged 12.8% (63 seconds) for amlodipine 10mg, and averaged 7.9% (38 seconds) for amlodipine 5mg.

- Vasospastic Angina:
  - In a double-blind, placebo-controlled clinical trial of 4 weeks duration in 50 patients, amlodipine therapy decreased vasospastic angina attacks by approximately 4 per week compared with a placebo decrease of approximately 1 per week (P<0.01).
- CAD:
  - In the PREVENT trial, 825 patients with angiographically documented CAD were randomized to amlodipine (5 to 10mg once daily) or placebo and followed for 3 years. The data suggested a favorable outcome with respect to fewer hospitalizations for angina and revascularization procedures in patients with CAD.
  - In the CAMELOT trial, 1,318 patients with CAD recently documented by angiography, without left main coronary disease and without HF or an EF <40% were randomized to double-blind treatment with either amlodipine (5 to 10mg once daily) or placebo in addition to standard care. The mean duration of follow-up was 19 months. The primary endpoint was the time to first occurrence of 1 of the following events: hospitalization for angina pectoris, coronary revascularization, MI, CV death, resuscitated cardiac arrest, hospitalization for HF, stroke/transient ischemic attack, or peripheral vascular disease. A total of 110 (16.6%) and 151 (23.1%) first events occurred in the amlodipine and placebo groups, respectively (HR: 0.691; 95% CI: 0.540 to 0.884; P=0.003).

Cost Comparison:

Medication	Cost Per Unit[+]	Cost Per Month*	Cost Per Year*
Katerzia™ (amlodipine) 1mg/mL oral suspension	**$3.31**	**$993.00**	**$11,916.00**
amlodipine 10mg tablet	$0.02	$0.60	$7.20

[+]Unit = milliliter (mL) or tablet
*Costs based on a maximum FDA recommended dose of amlodipine (10mg daily).
Costs do not reflect rebated prices or net costs. National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Conjupri® (Levamlodipine Tablet) Product Summary[8]

Indication(s): Conjupri® (levamlodipine tablet) 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.

Dosing:
- Conjupri® is supplied as 1.25mg, 2.5mg (functionally scored), and 5mg (functionally scored) tablets.
- The recommended dosage is based on patient age and indication:
  - Adult HTN: The recommended starting dose is 2.5mg once daily, and titrated according to BP goals, with a maximum dose of 5mg once daily.

- For small, fragile, or elderly patients, or patients with hepatic insufficiency, the recommended starting dose is 1.25mg once daily.

- Pediatric HTN (6 Years of Age and Older): The recommended starting dose is 1.25mg to 2.5mg once daily and titrated to response; doses in excess of 2.5mg daily have not been studied in pediatric patients.

Contraindication(s):

- Known hypersensitivity to amlodipine or any inactive ingredients of Conjupri®

Safety:

- Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis; however, acute hypotension is unlikely.
- Worsening angina and acute MI can develop after starting or increasing the dose of amlodipine, particularly in patients with severe obstructive CAD.
- Dosing should be titrated slowly in patients with severe hepatic impairment.

Cost Comparison: Cost information for Conjupri® 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 based on 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 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 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)*

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
diltiazem CD (Cardizem® CD)*	isradipine (Dynacirc®, Dynacirc CR®)	**levamlodipine (Conjupri®)**
diltiazem ER (Cartia XT®, Diltia XT®)	**nicardipine (Cardene®)**	
diltiazem XR (Dilacor® XR)	nicardipine (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.

Utilization Details of Antihypertensive Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
CALCIUM CHANNEL BLOCKERS (CCB)						
CCB TIER-1 UTILIZATION						
AMLODIPINE TAB 10MG	14,478	787,056	4,510	$132,527.27	$0.17	$9.15
AMLODIPINE TAB 5MG	11,151	550,940	3,848	$100,104.31	$0.18	$8.98
AMLODIPINE TAB 2.5MG	1,672	75,270	559	$15,888.80	$0.21	$9.50
NIFEDIPINE TAB 30MG ER	1,095	40,317	620	$21,462.90	$0.53	$19.60
NIFEDIPINE TAB 60MG ER	566	24,917	253	$12,727.17	$0.51	$22.49
NIFEDIPINE TAB 30MG ER	489	21,062	264	$9,939.64	$0.47	$20.33
NIFEDIPINE CAP 10MG	453	8,889	377	$20,855.73	$2.35	$46.04
DILTIAZEM CAP 240MG ER	354	16,776	113	$7,989.01	$0.48	$22.57
DILTIAZEM CAP 180MG ER	322	14,345	107	$6,580.04	$0.46	$20.43
NIFEDIPINE TAB 60MG ER	320	14,132	136	$7,042.41	$0.50	$22.01
CARTIA XT CAP 180MG/24HR	271	14,023	104	$5,777.35	$0.41	$21.32
DILTIAZEM TAB 30MG	236	7,186	70	$3,741.26	$0.52	$15.85
CARTIA XT CAP 240MG/24HR	228	11,684	83	$5,207.84	$0.45	$22.84
NIFEDIPINE TAB 90MG ER	221	11,868	98	$7,318.18	$0.62	$33.11
DILTIAZEM TAB 60MG	210	6,871	62	$3,755.01	$0.55	$17.88
NIFEDIPINE TAB 90MG ER	205	11,295	75	$5,809.97	$0.51	$28.34
DILTIAZEM TAB 120MG	199	7,965	51	$4,607.81	$0.58	$23.15
VERAPAMIL TAB 80MG	186	6,750	63	$2,266.76	$0.34	$12.19
VERAPAMIL TAB 120MG	180	6,503	47	$2,467.02	$0.38	$13.71
VERAPAMIL TAB 40MG	129	4,043	38	$2,077.22	$0.51	$16.10

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
DILTIAZEM CAP 360MG ER	115	5,599	28	$3,814.72	$0.68	$33.17
DILT-XR CAP 180MG	107	4,753	26	$3,244.40	$0.68	$30.32
NIFEDIPINE CAP 20MG	96	2,660	61	$11,090.55	$4.17	$115.53
DILT-XR CAP 240MG	91	4,225	28	$3,036.13	$0.72	$33.36
DILTIAZEM TAB 90MG	86	3,056	19	$2,283.21	$0.75	$26.55
VERAPAMIL CAP 120MG SR	66	2,510	14	$3,892.96	$1.55	$58.98
DILT-XR CAP 120MG	65	2,286	21	$1,476.18	$0.65	$22.71
DILTIAZEM CAP 120MG/24	64	3,570	30	$1,526.76	$0.43	$23.86
DILTIAZEM CAP 240MG/24	60	2,756	20	$1,750.27	$0.64	$29.17
DILTIAZEM CAP 300MG ER	58	2,670	21	$1,845.09	$0.69	$31.81
DILTIAZEM CAP 180MG/24	43	3,040	17	$1,360.16	$0.45	$31.63
FELODIPINE TAB 5MG ER	39	1,590	7	$721.18	$0.45	$18.49
CARTIA XT CAP 300MG/24HR	38	1,860	15	$1,270.23	$0.68	$33.43
DILTIAZEM CAP 60MG ER	23	925	6	$3,385.11	$3.66	$147.18
DILTIAZEM CAP 420MG/24	17	1,170	7	$1,483.49	$1.27	$87.26
FELODIPINE TAB 10MG ER	14	600	4	$274.67	$0.46	$19.62
DILTIAZEM CAP 300MG ER	13	750	6	$584.99	$0.78	$45.00
DILTIAZEM CAP 120MG ER	9	365	5	$1,699.76	$4.66	$188.86
NICARDIPINE CAP 20MG	9	240	2	$2,097.73	$8.74	$233.08
VERAPAMIL CAP 360MG SR	8	480	3	$2,056.42	$4.28	$257.05
NORVASC TAB 10MG	7	300	1	$2,659.11	$8.86	$379.87
NIMODIPINE CAP 30MG	6	288	4	$3,242.54	$11.26	$540.42
FELODIPINE TAB 2.5MG ER	6	180	1	$93.77	$0.52	$15.63
DILTIAZEM CAP 240MG ER	3	150	2	$91.97	$0.61	$30.66
TAZTIA XT CAP 360MG/24	2	120	1	$76.13	$0.63	$38.07
VERAPAMIL CAP 120MG ER	1	30	1	$67.02	$2.23	$67.02
DILTIAZEM CAP 120MG ER	1	30	1	$21.55	$0.72	$21.55
CCB TIER-1 SUBTOTAL	**34,012**	**1,688,095**	**10,388**	**$433,291.80**	**$0.26**	**$12.74**
CCB TIER-2 UTILIZATION						
DILTIAZEM CAP 120MG ER	453	20,158	151	$9,447.48	$0.47	$20.86
VERAPAMIL TAB 240MG ER	354	17,482	92	$5,708.52	$0.33	$16.13
CARTIA XT CAP 120/24HR	330	15,572	123	$6,634.44	$0.43	$20.10
VERAPAMIL TAB 120MG ER	271	12,115	86	$5,210.31	$0.43	$19.23
VERAPAMIL TAB 180MG ER	200	9,590	65	$3,471.64	$0.36	$17.36
VERAPAMIL CAP 180MG SR	66	3,930	15	$5,880.72	$1.50	$89.10
VERAPAMIL CAP 240MG SR	65	4,355	22	$5,921.99	$1.36	$91.11
DILTIAZEM ER TAB 180MG	20	940	6	$2,394.90	$2.55	$119.75
MATZIM LA TAB 240MG/24	18	660	5	$1,720.35	$2.61	$95.58
AMLOD/ATORVA TAB 10-80MG	18	1,260	4	$5,716.71	$4.54	$317.60
AMLOD/ATORVA TAB 10-20MG	17	1,050	4	$3,445.14	$3.28	$202.66
DILTIAZEM ER TAB 240MG	14	1,080	5	$2,681.47	$2.48	$191.53
AMLOD/ATORVA TAB 10-40MG	13	870	4	$3,215.00	$3.70	$247.31
AMLOD/ATORVA TAB 5-20MG	12	620	3	$2,344.35	$3.78	$195.36

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
AMLOD/ATORVA TAB 5-10MG	11	690	4	$1,894.83	$2.75	$172.26
AMLOD/ATORVA TAB 5-40MG	11	990	3	$4,272.13	$4.32	$388.38
VERAPAMIL CAP 100MG ER	10	300	1	$1,336.95	$4.46	$133.70
DILTIAZEM ER TAB 360MG	9	750	3	$2,579.77	$3.44	$286.64
CARDIZEM LA TAB 120MG	8	120	1	$929.12	$7.74	$116.14
VERAPAMIL CAP 200MG ER	7	360	2	$525.48	$1.46	$75.07
AMLOD/ATORVA TAB 10-10MG	6	420	3	$1,304.54	$3.11	$217.42
MATZIM LA TAB 360MG/24	4	240	1	$844.74	$3.52	$211.19
VERAPAMIL CAP 240MG ER	3	210	2	$315.76	$1.50	$105.25
ISRADIPINE CAP 2.5MG	3	130	1	$271.25	$2.09	$90.42
VERAPAMIL CAP 180MG ER	3	150	2	$207.65	$1.38	$69.22
MATZIM LA TAB 180MG/24	3	90	2	$207.58	$2.31	$69.19
VERAPAMIL CAP 300MG ER	2	120	2	$250.76	$2.09	$125.38
DILTIAZEM CAP 90MG ER	2	60	1	$173.86	$2.90	$86.93
MATZIM LA TAB 420MG/24	2	60	1	$242.14	$4.04	$121.07
AMLOD/ATORVA TAB 2.5-10MG	1	90	1	$363.29	$4.04	$363.29
CCB TIER-2 SUBTOTAL	**1,936**	**94,462**	**531**	**$79,512.87**	**$0.84**	**$41.11**
CCB SPECIAL PRIOR AUTHORIZATION (PA) UTILIZATION						
KATERZIA SUS 1MG/ML	25	1,053	16	$11,583.71	$11.00	$463.35
DILTIAZEM CAP 360MG CD	8	540	3	$1,669.86	$3.09	$208.73
CCB SPECIAL PA SUBTOTAL	**33**	**3,950**	**19**	**$13,253.57**	**$8.32**	**$401.62**
CCB TOTAL	**35,981**	**1,784,150**	**10,791***	**$526,058.24**	**$0.29**	**$14.62**
ANGIOTENSIN RECEPTOR BLOCKERS (ARB) AND COMBINATION PRODUCTS						
ARB TIER-1 UTILIZATION						
LOSARTAN POT TAB 50MG	4,639	233,479	1,533	$48,427.51	$0.21	$10.44
LOSARTAN POT TAB 100MG	3,796	217,836	1,277	$41,608.97	$0.19	$10.96
LOSARTAN POT TAB 25MG	2,796	143,659	973	$27,881.33	$0.19	$9.97
LOSARTAN/HCT TAB 100-25MG	1,055	62,598	379	$14,016.33	$0.22	$13.29
LOSARTAN/HCT TAB 50-12.5MG	885	45,905	321	$10,596.62	$0.23	$11.97
LOSARTAN/HCT TAB 100-12.5MG	661	36,774	227	$8,906.23	$0.24	$13.47
IRBESARTAN TAB 150MG	222	11,180	78	$3,834.89	$0.34	$17.27
OLMESA MEDOX TAB 40MG	206	9,200	62	$2,876.59	$0.31	$13.96
OLMESA MEDOX TAB 20MG	167	10,172	78	$2,374.32	$0.23	$14.22
VALSARTAN TAB 160MG	166	7,410	57	$3,959.66	$0.53	$23.85
TELMISARTAN TAB 40MG	152	7,845	59	$4,600.60	$0.59	$30.27
VALSARTAN TAB 80MG	147	5,917	53	$2,802.80	$0.47	$19.07
TELMISARTAN TAB 80MG	130	6,952	44	$3,936.77	$0.57	$30.28
IRBESARTAN TAB 300MG	106	6,090	49	$2,240.67	$0.37	$21.14
OLM MED/HCTZ TAB 40-25MG	97	5,501	32	$1,708.30	$0.31	$17.61
VALSARTAN TAB 320MG	92	5,068	34	$2,866.39	$0.57	$31.16
IRBESAR/HCTZ TAB 150-12.5MG	91	4,481	29	$1,937.45	$0.43	$21.29
VALSART/HCTZ TAB 320-25MG	91	5,375	26	$2,229.47	$0.41	$24.50
OLM MED/HCTZ TAB 20-12.5	87	4,640	31	$1,324.62	$0.29	$15.23

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
VALSART/HCTZ TAB 160-25MG	84	4,000	24	$1,413.36	$0.35	$16.83
IRBESARTAN TAB 75MG	82	3,690	26	$1,424.31	$0.39	$17.37
VALSART/HCTZ TAB 160-12.5MG	78	3,699	24	$1,319.11	$0.36	$16.91
VALSART/HCTZ TAB 80-12.5MG	74	3,405	22	$1,132.92	$0.33	$15.31
VALSARTAN TAB 40MG	73	2,975	29	$1,373.66	$0.46	$18.82
TELMISARTAN TAB 20MG	71	3,302	29	$1,973.97	$0.60	$27.80
IRBESAR/HCTZ TAB 300-12.5MG	67	3,765	24	$1,605.80	$0.43	$23.97
OLM MED/HCTZ TAB 40-12.5MG	58	3,595	15	$1,066.54	$0.30	$18.39
VALSART/HCTZ TAB 320-12.5MG	23	1,110	9	$488.35	$0.44	$21.23
OLMESA MEDOX TAB 5MG	20	789	12	$242.92	$0.31	$12.15
BENICAR HCT TAB 40-25MG	6	157	1	$1,607.90	$10.24	$267.98
COZAAR TAB 50MG	6	300	1	$1,648.79	$5.50	$274.80
DIOVAN TAB 160MG	5	450	1	$3,627.81	$8.06	$725.56
BENICAR TAB 40MG	5	450	1	$4,383.99	$9.74	$876.80
DIOVAN TAB 320MG	3	263	1	$2,719.49	$10.34	$906.50
MICARDIS TAB 40MG	3	270	1	$1,898.27	$7.03	$632.76
BENICAR HCT TAB 20-12.5MG	1	90	1	$642.19	$7.14	$642.19
ARB TIER-1 SUBTOTAL	**16,245**	**862,392**	**4,562**	**$216,698.90**	**$0.25**	**$13.34**
ARB TIER-2 UTILIZATION						
CANDESARTAN TAB 8MG	54	2,332	15	$2,573.34	$1.10	$47.65
TELMISA/HCTZ TAB 80-12.5MG	46	1,920	9	$2,809.17	$1.46	$61.07
CANDESARTAN TAB 16MG	42	1,590	12	$1,465.23	$0.92	$34.89
TELMISA/HCTZ TAB 80-25MG	39	1,860	9	$2,379.96	$1.28	$61.02
TELMISA/HCTZ TAB 40-12.5MG	22	840	7	$921.57	$1.10	$41.89
CANDESARTAN TAB 32MG	20	1,260	6	$1,833.40	$1.46	$91.67
OLM MED/AMLO TAB/HCTZ 20-5-12.5MG	15	690	2	$1,151.55	$1.67	$76.77
CANDESARTAN TAB 4MG	13	447	8	$322.35	$0.72	$24.80
OLM MED/AMLO TAB/HCTZ 40-10-25MG	13	690	3	$1,338.45	$1.94	$102.96
EXFORGEH/5-TAB 160-12.5MG	13	390	2	$3,417.24	$8.76	$262.86
AMLOD/VALSAR TAB/HCTZ 10-320-25MG	12	360	1	$583.61	$1.62	$48.63
OLM MED/AMLO TAB/HCTZ 40-5-25MG	6	480	2	$941.33	$1.96	$156.89
AMLOD/VALSAR TAB/HCTZ 10-160-25MG	6	180	1	$275.21	$1.53	$45.87
EXFORGEH/10-TAB 160-25MG	6	180	2	$1,784.00	$9.91	$297.33
EXFORGEH/5-TAB 160-25MG	6	180	1	$1,562.94	$8.68	$260.49
EXFORGEH/10-TAB 320-25MG	5	150	2	$1,879.82	$12.53	$375.96
OLM MED/AMLO TAB/HCTZ 40-10-12.5MG	2	60	1	$130.05	$2.17	$65.03
AMLOD/VALSAR TAB/HCTZ 5-160-25MG	1	30	1	$49.25	$1.64	$49.25
OLM MED/AMLO TAB/HCTZ 40-5-12.5MG	1	90	1	$194.39	$2.16	$194.39
ARB TIER-2 SUBTOTAL	**322**	**13,729**	**78**	**$25,612.86**	**$1.87**	**$79.54**
ARB TIER-3 UTILIZATION						
EDARBYCLOR TAB 40-12.5MG	7	450	3	$2,820.40	$6.27	$402.91
EDARBI TAB 80MG	6	540	2	$3,562.32	$6.60	$593.72
EDARBI TAB 40MG	5	210	2	$950.04	$4.52	$190.01

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
EDARBYCLOR TAB 40-25MG	4	120	2	$769.26	$6.41	$192.32
ARB TIER-3 SUBTOTAL	**22**	**1,320**	**9**	**$8,102.02**	**$6.14**	**$368.27**
ARB TOTAL	**16,589**	**877,441**	**4,617***	**$250,413.78**	**$0.29**	**$15.10**
ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEI) AND COMBINATION PRODUCTS						
ACEI TIER-1 UTILIZATION						
LISINOPRIL TAB 20MG	15,360	770,981	4,956	$140,081.90	$0.18	$9.12
LISINOPRIL TAB 10MG	14,631	725,048	4,987	$133,307.95	$0.18	$9.11
LISINOPRIL TAB 40MG	7,553	421,535	2,248	$83,726.19	$0.20	$11.09
LISINOPRIL TAB 5MG	6,668	327,990	2,173	$61,589.55	$0.19	$9.24
LISINOP/HCTZ TAB 20-12.5MG	4,197	209,712	1,292	$43,143.91	$0.21	$10.28
LISINOP/HCTZ TAB 20-25MG	3,980	235,738	1,318	$38,013.82	$0.16	$9.55
LISINOPRIL TAB 2.5MG	3,025	138,113	959	$28,800.35	$0.21	$9.52
LISINOP/HCTZ TAB 10-12.5MG	2,393	127,217	824	$23,725.54	$0.19	$9.91
ENALAPRIL TAB 20MG	855	37,091	188	$16,933.47	$0.46	$19.81
LISINOPRIL TAB 30MG	852	44,993	288	$9,198.81	$0.20	$10.80
ENALAPRIL TAB 5MG	798	31,331	179	$15,949.02	$0.51	$19.99
ENALAPRIL TAB 2.5MG	714	25,548	140	$12,999.49	$0.51	$18.21
ENALAPRIL TAB 10MG	712	32,220	184	$12,728.58	$0.40	$17.88
BENAZEPRIL TAB 20MG	268	14,142	75	$2,803.12	$0.20	$10.46
BENAZEPRIL TAB 10MG	223	9,587	54	$2,426.20	$0.25	$10.88
BENAZEPRIL TAB 40MG	178	10,100	49	$1,898.52	$0.19	$10.67
RAMIPRIL CAP 10MG	114	5,504	34	$1,042.60	$0.19	$9.15
QUINAPRIL TAB 40MG	100	5,355	25	$1,476.52	$0.28	$14.77
ENALAPR/HCTZ TAB 10-25MG	92	4,942	29	$1,763.54	$0.36	$19.17
QUINAPRIL TAB 20MG	81	3,510	16	$1,191.03	$0.34	$14.70
BENAZEP/HCTZ TAB 10-12.5MG	76	3,996	21	$2,956.66	$0.74	$38.90
BENAZEP/HCTZ TAB 20-12.5MG	73	3,233	19	$3,257.82	$1.01	$44.63
RAMIPRIL CAP 5MG	69	3,250	17	$608.21	$0.19	$8.81
BENAZEP/HCTZ TAB 20-25MG	61	2,997	15	$2,859.46	$0.95	$46.88
ENALAPR/HCTZ TAB 5-12.5MG	61	1,890	10	$1,023.21	$0.54	$16.77
RAMIPRIL CAP 2.5MG	52	3,120	22	$518.69	$0.17	$9.97
FOSINOPRIL TAB 10MG	43	1,998	9	$696.66	$0.35	$16.20
RAMIPRIL CAP 1.25MG	43	1,830	15	$606.90	$0.33	$14.11
FOSINOPRIL TAB 40MG	28	1,380	11	$571.51	$0.41	$20.41
BENAZEPRIL TAB 5MG	28	1,330	10	$305.06	$0.23	$10.90
FOSINOPRIL TAB 20MG	22	1,140	5	$382.34	$0.34	$17.38
QUINAPRIL TAB 10MG	20	1,344	5	$289.67	$0.22	$14.48
QUINAPRIL TAB 5MG	16	780	3	$235.29	$0.30	$14.71
QNAPRIL/HCTZ TAB 20-12.5MG	11	330	1	$339.73	$1.03	$30.88
QNAPRIL/HCTZ TAB 20-25MG	10	360	1	$196.05	$0.54	$19.61
BENAZEP/HCTZ TAB 5-6.25MG	5	390	2	$486.68	$1.25	$97.34
MOEXIPRIL TAB 15MG	3	270	1	$36.30	$0.13	$12.10
TRANDOLAPRIL TAB 4MG	3	150	1	$79.47	$0.53	$26.49

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
QNAPRIL/HCTZ TAB 10-12.5MG	3	270	1	$141.51	$0.52	$47.17
PERINDOPRIL TAB 8MG	2	60	1	$60.70	$1.01	$30.35
ACEI TIER-1 SUBTOTAL	**63,423**	**3,210,775**	**17,534**	**$648,452.03**	**$0.20**	**$10.22**
ACEI TIER-2 UTILIZATION						
CAPTOPRIL TAB 25MG	124	4,091	21	$6,868.86	$1.68	$55.39
CAPTOPRIL TAB 50MG	92	2,738	13	$8,604.76	$3.14	$93.53
CAPTOPRIL TAB 12.5MG	18	780	4	$974.72	$1.25	$54.15
CAPTOPR/HCTZ TAB 50-25MG	10	300	1	$1,074.27	$3.58	$107.43
CAPTOPR/HCTZ TAB 25-15MG	8	420	2	$518.65	$1.23	$64.83
ACEI TIER-2 SUBTOTAL	**252**	**8,329**	39	**$18,041.26**	**$2.17**	**$71.59**
ACEI SPECIAL PA UTILIZATION						
EPANED SOL 1MG/ML	1,133	43,924	227	$345,366.35	$7.86	$304.82
QBRELIS SOL 1MG/ML	53	1,952	14	$19,949.50	$10.22	$376.41
EPANED SOL 1MG/ML	4	150	3	$975.19	$6.50	$243.80
ACEI SPECIAL PA SUBTOTAL	**1,190**	**46,026**	**243**	**$366,291.04**	**$7.96**	**$307.81**
ACEI TOTAL	**64,865**	**3,265,130**	**17,796***	**$1,032,784.33**	**$0.32**	**$15.92**
ACEI AND CCB COMBINATION PRODUCTS						
ACEI/CCB TIER-1 UTILIZATION						
AMLOD/BENAZP CAP 10-20MG	183	11,058	60	$2,787.33	$0.25	$15.23
AMLOD/BENAZP CAP 10-40MG	138	9,259	51	$3,144.95	$0.34	$22.79
AMLOD/BENAZP CAP 5-20MG	123	6,525	37	$1,854.78	$0.28	$15.08
AMLOD/BENAZP CAP 5-10MG	66	3,905	26	$993.63	$0.25	$15.06
AMLOD/BENAZP CAP 5-40MG	23	1,885	6	$457.06	$0.24	$19.87
AMLOD/BENAZP CAP 2.5-10MG	18	750	5	$258.65	$0.34	$14.37
ACEI/CCB TIER-1 SUBTOTAL	**551**	**33,382**	**162**	**$9,496.40**	**$0.28**	**$17.23**
ACEI/CCB TOTAL	**551**	**33,382**	**162***	**$9,496.40**	**$0.28**	**$17.23**
DIRECT RENIN INHIBITORS (DRI)						
TEKTURNA TAB 300MG	2	180	1	$1,512.21	$8.40	$756.11
DRI TOTAL	**2**	**180**	**1***	**$1,512.21**	**$8.40**	**$756.11**
CLONIDINE PRODUCTS						
CLONIDINE UTILIZATION (NO PA REQUIRED)						
CLONIDINE TAB 0.1MG	55,158	1,724,574	11,698	$588,201.31	$0.34	$10.66
CLONIDINE TAB 0.2MG	21,114	680,620	3,726	$233,526.17	$0.34	$11.06
CLONIDINE TAB 0.3MG	5,265	170,792	832	$62,378.38	$0.37	$11.85
CLONIDINE DIS 0.1/24HR	307	8,616	93	$14,978.29	$1.74	$48.79
CLONIDINE DIS 0.2/24HR	255	7,168	70	$17,381.42	$2.42	$68.16
CLONIDINE DIS 0.3/24HR	194	5,480	54	$17,842.71	$3.26	$91.97
CLONIDINE TOTAL	**82,293**	**2,597,250**	**14,681***	**$934,308.28**	**$0.36**	**$11.35**
SOTALOL PRODUCTS						
SOTALOL UTILIZATION (NO PA REQUIRED)						
SOTALOL HCL TAB 80MG	203	6,791	50	$2,964.28	$0.44	$14.60
SOTALOL HCL TAB 120MG	113	3,400	17	$1,965.04	$0.58	$17.39
SOTALOL AF TAB 80MG	33	983	7	$525.80	$0.53	$15.93

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
SOTALOL HCL TAB 160MG	18	620	4	$365.91	$0.59	$20.33
SOTALOL AF TAB 120MG	3	90	1	$47.22	$0.52	$15.74
SOTALOL SUBTOTAL	**370**	**11,884**	**75**	**$5,868.25**	**$0.49**	**$15.86**
SOTALOL SPECIAL PA UTILIZATION						
SOTYLIZE SOL 5MG/ML	44	1,418	8	$24,869.36	$17.54	$565.21
SOTALOL SPECIAL PA SUBTOTAL	**44**	**1,418**	**8**	**$24,869.36**	**$17.54**	**$565.21**
SOTALOL TOTAL	**414**	**13,302**	**68***	**$30,737.61**	**$2.31**	**$74.25**
PROPRANOLOL SOLUTION PRODUCTS						
PROPRANOLOL UTILIZATION (NO PA REQUIRED)						
PROPRANOLOL SOL 20MG/5ML	849	24,577	219	$21,674.73	$0.88	$25.53
PROPRANOLOL SOL 40MG/5ML	15	426	8	$378.90	$0.89	$25.26
PROPRANOLOL SUBTOTAL	**864**	**25,003**	**223**	**$22,053.63**	**$0.88**	**$25.53**
PROPRANOLOL SPECIAL PA UTILIZATION						
HEMANGEOL SOL 4.28MG/ML	17	518	8	$10,398.82	$20.07	$611.70
PROPRANOLOL SPECIAL PA SUBTOTAL	**17**	**518**	**8**	**$10,398.82**	**$20.07**	**$611.70**
PROPRANOLOL TOTAL	**881**	**25,521**	**226***	**$32,452.45**	**$1.27**	**$36.84**
SPIRONOLACTONE PRODUCTS						
SPIRONOLACTONE UTILIZATION (NO PA REQUIRED)						
SPIRONOLACT TAB 25MG	4,736	206,956	1,484	$54,886.09	$0.27	$11.59
SPIRONOLACT TAB 50MG	2,012	80,012	703	$32,986.40	$0.41	$16.39
SPIRONOLACT TAB 100MG	1,329	55,136	435	$26,510.36	$0.48	$19.95
SPIRONOLACTONE SUBTOTAL	**8,077**	**342,104**	**2,408**	**$114,382.85**	**$0.33**	**$14.16**
SPIRONOLACTONE SPECIAL PA UTILIZATION						
CAROSPIR SUS 25MG/5ML	168	4,903	46	$48,170.78	$9.82	$286.73
SPIRONOLACTONE SPECIAL PA SUBTOTAL	**168**	**4,903**	**46**	**$48,170.78**	**$9.82**	**$286.73**
SPIRONOLACTONE TOTAL	**8,245**	**347,007**	**2,450***	**$162,553.63**	**$0.47**	**$19.72**
MISCELLANEOUS (MISC) COMBINATION PRODUCTS						
MISC UTILIZATION (NO PA REQUIRED)						
BISOPRL/HCTZ TAB 5-6.25MG	177	8,870	51	$3,831.65	$0.43	$21.65
BISOPRL/HCTZ TAB 10/6.25MG	143	6,807	33	$4,044.78	$0.59	$28.29
ATENOL/CHLOR TAB 50-25MG	133	7,580	42	$3,844.61	$0.51	$28.91
ATENOL/CHLOR TAB 100-25MG	115	5,130	27	$3,748.49	$0.73	$32.60
METOPRL/HCTZ TAB 50-25MG	96	4,286	25	$5,651.85	$1.32	$58.87
BISOPRL/HCTZ TAB 2.5/6.25MG	82	5,450	22	$3,004.63	$0.55	$36.64
METOPRL/HCTZ TAB 100-25MG	45	2,275	13	$3,835.18	$1.69	$85.23
PROPRAN/HCTZ TAB 80/25MG	11	330	1	$705.12	$2.14	$64.10
METOPRL/HCTZ TAB 100-50MG	8	597	2	$1,014.30	$1.70	$126.79
PROPRAN/HCTZ TAB 40/25MG	3	90	3	$138.97	$1.54	$46.32
DUTOPROL TAB 50-12.5MG	1	30	1	$444.59	$14.82	$444.59
MISC TOTAL	**814**	**41,445**	**216***	**$30,264.17**	**$0.73**	**$37.18**
TOTAL	**210,634**	**8,984,778**	**42,378***	**$3,010,569.07**	**$0.34**	**$14.29**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

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Appendix E

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

Oklahoma Health Care Authority
April 2020

Introduction[1]

Sarcomas are a heterogeneous class of rare solid tumors derived from mesenchymal cells. Sarcomas have distinct clinical and pathologic features and are largely divided into 2 categories: soft-tissue and bone. These malignancies account for approximately 1% of all adult malignancies and 15% of pediatric malignancies.

Gastrointestinal stromal tumors (GIST) are the most common type of soft-tissue sarcoma of the gastrointestinal (GI) tract. Surgery and targeted therapies are the cornerstones of treatment of GIST as traditional chemotherapy has been largely ineffective. *KIT* and *PDGFRA* are common activating mutations involved in the pathogenesis of GIST. Approximately 80% of all GIST are positive for *KIT* mutation and another 5 to 10% possess *PDGFRA* mutation, making these mutations rational therapeutic targets. Tyrosine kinase inhibitors specific for these mutations have improved 2-year overall survival to approximately 80%.[1]

Epithelioid sarcomas are extremely rare soft-tissue sarcomas accounting for <1% of all subtypes diagnosed. The associated tissue is undifferentiated often resulting in a delay to diagnosis. Median overall survival of advanced disease is approximately 8 to 12 months. Tazverik™ (tazemetostat) is the first treatment option specifically for epithelioid sarcomas.

Market News and Updates[2,3,4]

Anticipated Patent Expiration(s):

- Ayvakit™ (avapritinib): October 2034
- Tazverik™ (tazemetostat): October 2035
- Bynfezia Pen™ (octreotide): May 2038

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

- **January 2020:** The FDA approved Ayvakit™ (avapritinib) for the treatment of adults with unresectable or metastatic 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, 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[5,6,7]

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 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 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 [Epitheloid 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.]

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Appendix F

Calendar Year 2019 Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Pemfexy™ (Pemetrexed), Rozlytrek® (Entrectinib), and Zirabev™ (Bevacizumab-bvzr)

Oklahoma Health Care Authority
April 2020

Introduction[1,2,3]

The American Cancer Society estimates that approximately 228,200 new lung cancer cases will be diagnosed in 2020, 84% of which are estimated to be non-small cell lung cancer (NSCLC). Lung cancer is the leading cause of cancer death accounting for approximately 25% of all cancer-related deaths among both males and females. Lung cancer is most commonly diagnosed in older people with the average age at diagnosis being 70 years. Over 95% of all lung cancer cases are classified as either small cell lung cancer (SCLC) or NSCLC. Defining the cell type is essential as the prognosis and treatment of the 2 types differs substantially. NSCLC is more common than SCLC, with NSCLC accounting for approximately 84% of all lung cancer diagnoses. There are many subtypes of NSCLC including adenocarcinomas, squamous cell carcinomas, and large cell carcinomas. Each subtype falls under the broad term of NSCLC, as the approach to initial treatment of localized disease is similar among the subtypes.

In advanced stages, treatment decisions are guided by the stage of the disease, histology, and molecular features of the tumor. Patient-specific factors such as performance status and comorbid conditions are also considered when determining treatment plans. Surgical resection provides the best chance for cure in patients with Stage I to II NSCLC and can be used in combination with cisplatin-based systemic chemotherapy and radiation. Chemotherapy or immunotherapy are the treatments of choice for Stage III to IV NSCLC. The role of molecularly targeted-therapy and immunotherapy has become part of standard-of-care treatment plans in select patients with NSCLC. SCLC differs in that there is no role for surgery in the treatment of this histology. Chemotherapy and radiation are the treatments of choice for SCLC, and immunotherapy is now an option for SCLC extended-stage disease.

Current Prior Authorization Criteria

Criteria for Keytruda® (pembrolizumab), Mekinist® (trametinib), Opdivo® (nivolumab), Tafinlar® (dabrafenib), Yervoy® (ipilimumab), and Zelboraf® (vemurafenib) for indications other than lung cancer diagnoses can be found in the November 2019 Drug Utilization Review (DUR) Board packet. These medications and criteria are reviewed annually with the skin cancer medications.

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

1. A diagnosis of recurrent or metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. First-line or recurrent setting; and
4. As a single-agent only.

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

1. A diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Progressed on or intolerant to crizotinib; and
4. As a single-agent only.

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

1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease after progression; and
3. In combination with docetaxel.

Cyramza® (Ramucirumab) Approval Criteria [Colorectal Cancer Diagnosis]:

1. A diagnosis of colorectal cancer; and
2. Subsequent therapy for metastatic disease after progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine; and
3. In combination with an irinotecan-based regimen.

Cyramza® (Ramucirumab) Approval Criteria [Esophageal Cancer Diagnosis]:

1. A diagnosis of unresectable, locally advanced, recurrent, or metastatic esophageal or esophagogastric junction adenocarcinoma; and
2. Karnofsky performance score ≥60%; and
3. As a single-agent or in combination with paclitaxel.

Cyramza® (Ramucirumab) Approval Criteria [Gastric Cancer Diagnosis]:

1. A diagnosis of gastric cancer; and
2. Member is not a surgical candidate or has unresectable, locally advanced, recurrent, or metastatic disease; and
3. Karnofsky performance score ≥60%; and
4. As a single-agent or in combination with paclitaxel.

Cyramza® (Ramucirumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. A diagnosis of HCC; and
2. Second-line or greater therapy; and
3. Previously failed sorafenib; and
4. Alpha-fetoprotein concentration ≥400ng/mL; and
5. As a single-agent.

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

The following criteria must be met when used in the <u>first-line setting:</u>

1. A diagnosis of metastatic NSCLC; and
2. Epidermal growth factor receptor (EGFR) mutation detected; and
3. As a single-agent only.

The following criteria must be met when used in the <u>second-line setting:</u>

1. A diagnosis of metastatic NSCLC; and
2. Progressed following platinum-based chemotherapy; and

3. As a single-agent or in combination with cetuximab in patients with a known sensitizing EGFR mutation who are T790M negative.

Gilotrif® (Afatinib) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. A diagnosis of head and neck cancer; and
2. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
3. Non-nasopharyngeal cancer must be 1 of the following:
    a. Newly diagnosed T4b, any N, M0 disease, unresectable nodal disease with no metastases, or for members who are unfit for surgery and have a performance status (PS) of 3; or
    b. Metastatic (M1) disease at initial presentation, recurrent/persistent disease with distant metastases, or unresectable locoregional recurrence or second primary with prior radiation therapy (RT) and PS of 0 to 2; or
    c. Unresectable locoregional recurrence without prior RT and PS of 3; and
4. As a single-agent only.

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

1. A diagnosis of Stage III NSCLC; and
2. Disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Imfinzi® (Durvalumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Progressed on or following platinum-containing chemotherapy.

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

1. A diagnosis of metastatic NSCLC; and
2. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for PD-L1 expression as follows:
    a. As a single-agent, first-line: ≥50%; or
    b. First-line in combination: no expression required; or
    c. As a single-agent, second-line: ≥1%; and
4. Member meets 1 of the following:
    a. Previously untreated, metastatic squamous NSCLC in combination with carboplatin and either paclitaxel or nab-paclitaxel; or
    b. Previously untreated, metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    c. New diagnosis as first-line therapy (member has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; or
    d. As a single-agent for disease progression on or after platinum-containing chemotherapy (e.g., cisplatin or carboplatin):

i. Members with EGFR-mutation-positive should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
    1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*
ii. Members with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
    1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*.

Keytruda® (Pembrolizumab) Approval Criteria [Nonmetastatic Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of Stage III nonmetastatic NSCLC; and
2. Ineligible for surgery or definitive chemoradiation; and
3. Tumor proportion scores for PD-L1 expression ≥1%; and
4. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

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

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

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

1. A diagnosis of metastatic NSCLC; and
2. Tumor expresses anaplastic lymphoma kinase (ALK) translocation; and
3. As a single-agent as second-line therapy following disease progression on either alectinib or ceritinib; or
4. As a single-agent as third-line or greater therapy following disease progression on crizotinib and 1 other ALK inhibitor (i.e., ceritinib or alectinib).

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

1. BRAF V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type BRAF NSCLC; and
2. In combination with Tafinlar® (dabrafenib); and
3. A diagnosis of refractory or metastatic disease.

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

1. A diagnosis of metastatic NSCLC; and
2. Tumor histology is 1 of the following:
    a. Adenocarcinoma; or
    b. Squamous cell; or
    c. Large cell; and

3. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
4. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. As a single-agent; and
6. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

Opdivo® (Nivolumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. A diagnosis of SCLC; and
2. Member meets 1 of the following:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease progression on initial chemotherapy; and
3. As a single-agent or in combination with Yervoy® (ipilimumab); and
4. Member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)].

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

1. BRAF V600E or V600K mutation; and
    a. Not indicated for wild-type BRAF NSCLC; and
2. As a single-agent or in combination with Mekinist® (trametinib); and
3. Refractory or metastatic disease.

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

1. A diagnosis of metastatic NSCLC; and
2. Epidermal growth factor receptor (EGFR) T790M mutation-positive disease and following progression on erlotinib, afatinib, or gefitinib for asymptomatic disease, symptomatic brain lesions, or multiple symptomatic systemic lesions; or
3. First-line treatment of members with EGFR exon 19 deletions or exon 21 L858R mutations.

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

1. A diagnosis of NSCLC; and
2. Recurrent or metastatic disease; and
3. Epidermal growth factor receptor (EGFR) mutation detected; and
4. As a single-agent.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Cancer Diagnosis]:

1. A diagnosis of pancreatic cancer; and
2. Locally advanced unresectable or metastatic disease; and
3. First-line agent only; and
4. In combination with gemcitabine.

Tarceva® (Erlotinib) Approval Criteria [Kidney Cancer Diagnosis]:

1. A diagnosis of kidney cancer; and
2. Non-clear cell type; and
3. Relapsed disease or surgically unresectable Stage IV disease; and

4. As a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Bone Cancer – Chordoma Diagnosis]:

1. A diagnosis of bone cancer – chordoma; and
2. Recurrent disease; and
3. As a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Adenocarcinoma Diagnosis]:

1. A diagnosis of pancreatic adenocarcinoma; and
2. Locally advanced, unresectable disease or metastatic disease; and
3. In combination with gemcitabine.

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

1. A diagnosis of non-squamous NSCLC; and
    a. First-line therapy; 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); and
    d. Atezolizumab and bevacizumab may be continued after the above combination in members without disease progression; or
2. A diagnosis of NSCLC; and
    a. Subsequent therapy for metastatic disease; and
    b. As a single-agent only.

Tecentriq® (Atezolizumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. A diagnosis of SCLC; and
2. First-line therapy; and
3. Extensive stage disease; and
4. In combination with carboplatin and etoposide.

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

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

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

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Progressed on or following platinum-containing chemotherapy or cisplatin ineligible members.

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

1. A diagnosis of metastatic NSCLC; and
2. Member has not received prior epidermal growth factor receptor (EGFR) therapy for metastatic disease; and

3. Members must meet 1 of the following:
    a. EGFR exon 19 deletion; or
    b. Exon 21 L858R substitution mutation.

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

1. A diagnosis of metastatic NSCLC; and
2. First-line or subsequent therapy; and
3. Anaplastic lymphoma kinase (ALK) or *ROS1*-positive; or
4. MET amplification; and
5. As a single-agent only.

Xalkori® (Crizotinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:

1. A diagnosis of soft tissue sarcoma – IMT; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. As a single-agent only.

Yervoy® (Ipilimumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. A diagnosis of SCLC; and
2. Member meets 1 of the following:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
3. In combination with nivolumab.

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

1. BRAF V600E or V600K mutation; and
    a. Not indicated for wild-type BRAF NSCLC; and
2. As a single-agent; and
3. Refractory or metastatic disease.

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

1. A diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. As a single-agent only.

Zykadia® (Ceritinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:

1. A diagnosis of soft tissue sarcoma – IMT; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. As a single-agent only.

Utilization of Lung Cancer Medications: Calendar Year 2019

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

Lung Cancer Medications Calendar Year Comparison: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	15	105	$935,038.80	$8,905.13	$298.93	11,104	3,128
2019	12	75	$774,416.37	$10,325.55	$344.19	8,430	2,250
% Change	**-20.00%**	**-28.60%**	**-17.20%**	**16.00%**	**15.10%**	**-24.10%**	**-28.10%**
Change	**-3**	**-30**	**-$160,622.43**	**$1,420.42**	**$45.26**	**-2,674**	**-878**

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

Lung Cancer Medications Calendar Year Comparison: Medical Claims

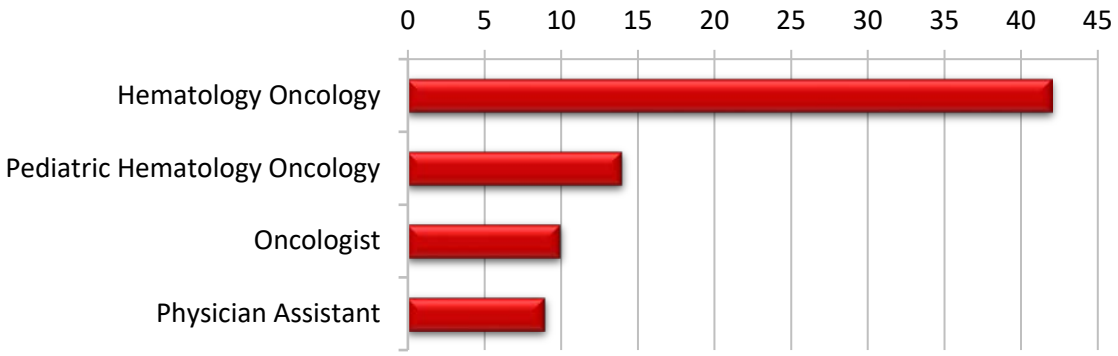
Calendar Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim
2018	494	1,774	$9,389,203.93	$5,292.67
2019	607	2,099	$11,694,791.98	$5,571.60
% Change	**22.87%**	**18.32%**	**24.56%**	**5.27%**
Change	**113**	**325**	**$2,305,588.05**	**$278.93**

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

Demographics of Members Utilizing Lung Cancer Medications: Pharmacy Claims

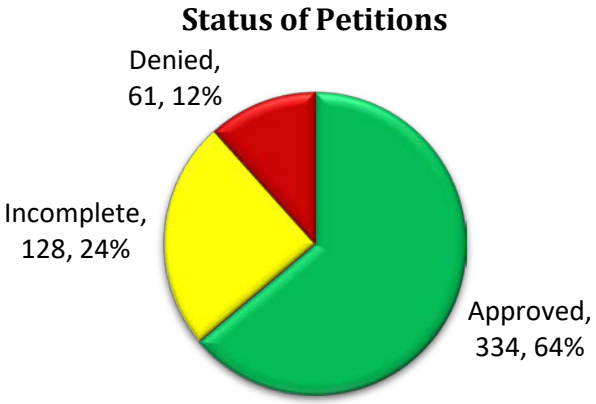
- Due to the small number of members utilizing lung cancer medications during calendar year 2019, detailed demographic information could not be provided.

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



Prior Authorization of Lung Cancer Medications

There were a total of 523 prior authorization requests submitted for lung cancer medications during calendar year 2019. The following chart shows the status of submitted petitions for calendar year 2019.



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

Anticipated Patent Expiration(s):

- Tarceva® (erlotinib): May 2021
- Alimta® (pemetrexed): May 2022
- Pemfexy™ (pemetrexed): May 2022
- Vizimpro® (dacomitinib): August 2028
- Xalkori® (crizotinib): November 2029
- Gilotrif® (afatinib): July 2030
- Tafinlar® (dabrafenib): October 2030
- Mekinist® (trametinib): January 2032
- Zykadia® (ceritinib): February 2032
- Alecensa® (alectinib): March 2032
- Zelboraf® (vemurafenib): June 2032
- Tagrisso® (osimertinib): January 2035
- Alunbrig® (brigatinib): November 2035
- Lorbrena® (lorlatinib): July 2036
- Rozlytrek® (entrectinib): July 2038

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

- **March 2019+:** The FDA approved Tecentriq® (atezolizumab) in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive SCLC.
- **March 2019:** The FDA approved Zykadia® (ceritinib) tablet formulation for the treatment of adults with metastatic 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.
- **April 2019+:** The FDA approved Keytruda® (pembrolizumab) for the first-line treatment of patients with Stage III NSCLC who are not candidates for surgical resection or

definitive chemoradiation or have metastatic NSCLC. Patients' tumors must have no epidermal growth factor receptor (EGFR) or ALK genomic aberrations and must express programmed death ligand-1 (PD-L1) [Tumor Proportion Score (TPS) ≥1%].

- **June 2019[+]:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) for the treatment of patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy and at least 1 other prior line of therapy.
- **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 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.

[+] These new FDA approved indications were previously reviewed with the lung cancer and skin cancer medications at the June 2019 and November 2019 Drug Utilization Review (DUR) Board meetings, respectively, and the current criteria are available in the Current Prior Authorization Criteria section of this report. They are included in the Market News and Updates section of this report to reflect updates that occurred during calendar year 2019.

Product Summaries[10,11,12]

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 Tecentriq® (atezolizumab) to reflect new FDA approved indications; changes and new criteria noted in red

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.

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.

Utilization Details of Lung Cancer Medications: Calendar Year 2019

Pharmacy Claims: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	20	3	$116,641.58	6.67	$5,832.08
MEKINIST TAB 2MG	13	5	$146,217.35	2.6	$11,247.49
SUBTOTAL	**33**	**8**	**$262,858.93**	**4.13**	**$7,965.42**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	12	1	$130,299.23	12	$10,858.27
SUBTOTAL	**12**	**1**	**$130,299.23**	**12**	**$10,858.27**
ALECTINIB PRODUCTS					
ALECENSA CAP 150MG	11	1	$161,884.61	11	$14,716.78
SUBTOTAL	**11**	**1**	**$161,884.61**	**11**	**$14,716.78**
DABRAFENIB PRODUCTS					
TAFINLAR CAP 75MG	10	3	$103,861.46	3.33	$10,386.15
SUBTOTAL	**10**	**3**	**$103,861.46**	**3.33**	**$10,386.15**
OSIMERTINIB PRODUCTS					
TAGRISSO TAB 80MG	6	1	$89,069.54	6	$14,844.92
SUBTOTAL	**6**	**1**	**$89,069.54**	**6**	**$14,844.92**
AFATINIB PRODUCTS					
GILOTRIF TAB 40MG	3	1	$26,442.60	3	$8,814.20
SUBTOTAL	**3**	**1**	**$26,442.60**	**3**	**$8,814.20**
TOTAL	**75**	**12***	**$774,416.37**	**6.25**	**$10,325.55**

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

Medical Claims: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9035 BEVACIZUMAB INJECTION	1,095	381	$2,090,513.26	$1,909.14
J9271 PEMBROLIZUMAB INJECTION	337	79	$3,628,649.00	$10,767.50
J9299 NIVOLUMAB INJECTION	309	62	$3,281,977.21	$10,621.29
J9305 PEMETREXED INJECTION	115	31	$706,531.01	$6,143.75
J9173 DURVALUMAB INJECTION	97	14	$617,582.84	$6,366.83
J9022 ATEZOLIZUMAB INJECTION	96	28	$919,424.28	$9,577.34

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9308 RAMUCIRUMAB INJECTION	38	6	$194,369.08	$5,114.98
J9228 IPILIMUMAB INJECTION	12	6	$255,745.30	$21,312.11
TOTAL	**2,099[+]**	**607***	**$11,694,791.98**	**$5,571.60**

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

[1] National Comprehensive Cancer Network. Non-small cell lung cancer (Version 3.2020). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Last revised 02/11/2020. Last accessed 03/23/2020.
[2] Small cell lung cancer (Version 3.2020). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Last revised 02/05/2020. Last accessed 03/23/2020.
[3] American Cancer Society. Cancer Facts & Figures 2020. Available online at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf. Last accessed 03/24/2020.
[4] 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 03/2020. Last accessed 03/18/2020.
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Appendix G

Calendar Year 2019 Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Dayvigo™ (Lemborexant)

Oklahoma Health Care Authority
April 2020

Current Prior Authorization Criteria

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)	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.

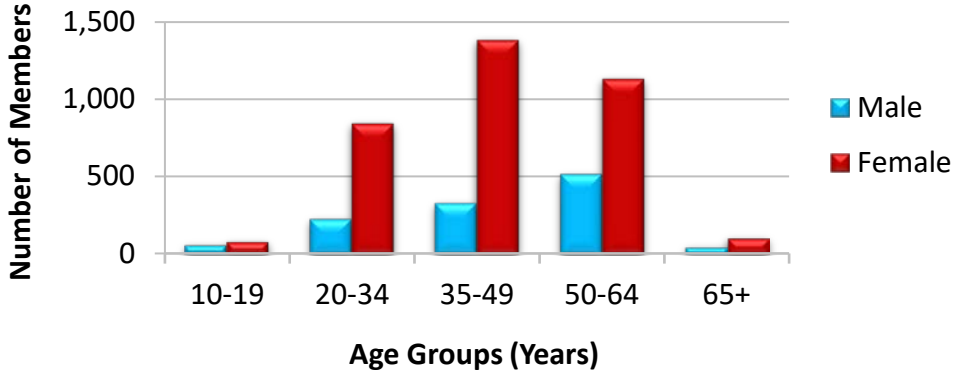
Utilization of Insomnia Medications: Calendar Year 2019

Comparison of Calendar Years: Insomnia Medications

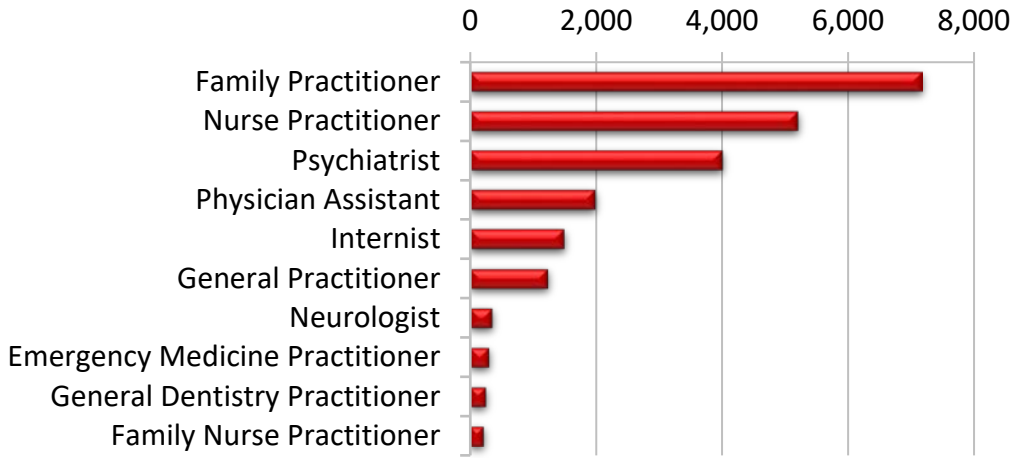
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	5,978	28,799	$892,807.19	$31.00	$1.06	842,214	839,003
2019	4,710	23,429	$837,299.88	$35.74	$1.23	681,347	679,583
% Change	**-21.20%**	**-18.60%**	**-6.20%**	**15.30%**	**16.00%**	**-19.10%**	**-19.00%**
Change	**-1,268**	**-5,370**	**-$55,507.31**	**$4.74**	**$0.17**	**-160,867**	**-159,420**

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

Demographics of Members Utilizing Insomnia Medications



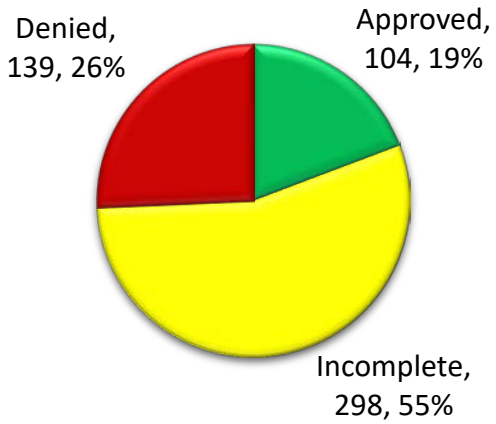
Top Prescriber Specialties of Insomnia Medications by Number of Claims



Prior Authorization of Insomnia Medications

There were 541 prior authorization requests submitted for insomnia 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]

Anticipated Patent Expiration(s):

- Silenor® (doxepin tablet): September 2030
- Edluar® [zolpidem sublingual (SL) tablet]: February 2031
- Zolpimist® (zolpidem oral spray): August 2032
- Belsomra® (suvorexant tablet): May 2033
- Hetlioz® (tasimelteon capsule): July 2035

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

- **December 2019:** The FDA approved Dayvigo™ (lemborexant), an orexin receptor antagonist, for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. The FDA has recommended that

lemborexant be classified as a controlled substance, and this recommendation has been submitted to the U.S. Drug Enforcement Administration (DEA). Dayvigo™ will be commercially available following scheduling by the DEA.

News:

- **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.

Pipeline:

- **Lemborexant:** Lemborexant (Dayvigo™) is also being investigated in patients with irregular sleep-wake rhythm disorder (ISWRD) and mild-to-moderate Alzheimer's dementia. Patients with ISWRD tend to have irregular bouts of involuntary sleep throughout the day and interrupted sleep at night; ISWRD is a common problem for patients with Alzheimer's dementia. A Phase 2 proof-of-concept clinical trial showed that patients with ISWRD and Alzheimer's dementia who were treated with lemborexant had a larger decrease in average duration of daytime sleep bouts, a larger decrease in average activity during the least active 5 hours of the day, and an earlier onset of the least active 5 hours of the day (but still during the night) compared to placebo-treated patients.
- **Tasimelteon:** Vanda Pharmaceuticals received a Complete Response Letter (CRL) from the FDA in August 2019 as part of its ongoing review of Vanda's supplemental New Drug Application (sNDA) for tasimelteon (Hetlioz®) for the treatment of Jet Lag Disorder (JLD). Vanda performed jet lag simulation studies and previously reported in May 2018 that JLD patients reported sleeping nearly 3 hours longer over the 3 nights following their transatlantic trip when treated with tasimelteon than they did over the 3 nights following their untreated transatlantic trip. In the CRL, the FDA asserted that these measures demonstrating improved sleep are of unclear clinical significance. Vanda will work with the FDA to address this conclusion regarding clinical significance and other FDA observations in the CRL. Vanda remains committed to obtaining FDA marketing approval for tasimelteon for the treatment of JLD in order to address this unmet medical need.

Dayvigo™ (Lemborexant) Product Summary[7]

Indication(s): Dayvigo™ (lemborexant) is an orexin receptor antagonist indicated for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

Dosing:

- Dayvigo™ is supplied as 5mg and 10mg oral tablets.
- The recommended dosage of lemborexant 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.
- Time to sleep onset may be delayed if taken with or soon after a meal.
- The maximum recommended dosage of lemborexant in patients with moderate (Child-Pugh class B) hepatic impairment is 5mg taken no more than once per night. Lemborexant is not recommended in patients with severe hepatic impairment.
- No dose adjustment is required in patients with mild, moderate, or severe renal impairment.
- The maximum recommended dosage of lemborexant when co-administered with weak CYP3A inhibitors is 5mg taken no more than once per night. Concomitant use of lemborexant with strong or moderate CYP3A inhibitors or with strong or moderate CYP3A inducers should be avoided (*refer to Dayvigo™ Prescribing Information for specific recommendations regarding drug interactions*).

Mechanism of Action: Lemborexant is an orexin receptor antagonist; the mechanism of action of lemborexant in the treatment of insomnia is presumed to be through antagonism of orexin receptors. The orexin neuropeptide signaling system plays a role in wakefulness. Lemborexant binds to orexin receptors OX1R and OX2R and acts as a competitive antagonist, and blocking the binding of wake-promoting neuropeptides orexin A and orexin B to receptors OX1R and OX2R is thought to suppress wake drive.

Contraindication(s): Lemborexant is contraindicated in patients with narcolepsy.

Safety:

- **Central Nervous System (CNS) Depressant Effects and Daytime Impairment:** Lemborexant is a CNS depressant that can impair daytime wakefulness even when used as prescribed. CNS depressant effects may persist in some patients for up to several days after discontinuing lemborexant. Prescribers should advise patients about the potential for next-day somnolence. Driving ability was impaired in some patients taking lemborexant 10mg. The risk of daytime impairment is increased if lemborexant is taken with less than a full night of sleep remaining or if a higher than recommended dose is taken. Co-administration with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) increases the risk of CNS depression, which can cause daytime impairment. Dosage adjustments of lemborexant and of concomitant CNS depressants may be necessary when administered together because of potentially

additive effects. The use of lemborexant with other drugs to treat insomnia is not recommended. Patients should be advised not to consume alcohol in combination with lemborexant because of additive effects.

- **Sleep Paralysis, Hypnagogic/Hypnopompic Hallucinations, and Cataplexy-Like Symptoms:** Sleep paralysis, an inability to move or speak for up to several minutes during sleep-wake transitions, and hypnagogic/hypnopompic hallucinations, including vivid and disturbing perceptions, can occur with the use of lemborexant. Prescribers should explain the nature of these events to patients when prescribing lemborexant. Symptoms similar to mild cataplexy can occur with lemborexant. Such symptoms can include periods of leg weakness lasting from seconds to a few minutes, can occur either at night or during the day, and may not be associated with an identified triggering event (e.g., laughter, surprise).
- **Complex Sleep Behaviors:** Complex sleep behaviors, including sleep-walking, sleep-driving, and engaging in other activities while not fully awake (e.g., preparing and eating food, making phone calls, having sex), have been reported to occur with the use of hypnotics such as lemborexant. These events can occur in hypnotic-naïve as well as in hypnotic-experienced patients. Patients usually do not remember these events. Complex sleep behaviors may occur following the first or any subsequent use of lemborexant, with or without the concomitant use of alcohol and other CNS depressants. Lemborexant should be discontinued immediately if a patient experiences a complex sleep behavior.
- **Patients with Compromised Respiratory Function:** The effect of lemborexant on respiratory function should be considered if prescribed to patients with compromised respiratory function. Lemborexant has not been studied in patients with moderate to severe obstructive sleep apnea (OSA) or in patients with chronic obstructive pulmonary disease (COPD).
- **Worsening of Depression/Suicidal Ideation:** In lemborexant clinical studies in patients with insomnia, the incidence of suicidal ideation or any suicidal behavior, as assessed by questionnaire, was higher in patients receiving lemborexant than in those receiving placebo (lemborexant 10mg: 0.3%; lemborexant 5mg: 0.4%; placebo: 0.2%). In primarily depressed patients treated with hypnotics, worsening of depression and suicidal thoughts and actions (including completed suicides) have been reported. Suicidal tendencies may be present in such patients and protective measures may be required. Intentional overdose is more common in this group of patients; therefore, the lowest number of tablets that is feasible should be prescribed at any 1 time. The emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.
- **Need to Evaluate for Co-Morbid Diagnoses:** Because sleep disturbances may be the presenting manifestation of a medical and/or psychiatric disorder, treatment of insomnia should be initiated only after careful evaluation of the patient. The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated. Worsening of insomnia or the emergence of new cognitive or behavioral abnormalities may be the

result of an unrecognized underlying psychiatric or medical disorder and can emerge during the course of treatment with sleep-promoting drugs such as lemborexant.

- **Pregnancy:** There are not available data on lemborexant use in pregnant women to evaluate for drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to lemborexant during pregnancy (*refer to Dayvigo™ Prescribing Information for additional details regarding the lemborexant pregnancy registry*).
- **Lactation:** There are no data on the presence of lemborexant in human milk, the effects on the breastfed infant, or the effects on milk production. Lemborexant and its metabolites are present in the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for lemborexant and any potential adverse effects on the breastfed infant from lemborexant or from the underlying maternal condition.
- **Pediatric Use:** The safety and effectiveness of lemborexant have not been established in pediatric patients.
- **Geriatric Use:** Of the 1,418 total patients treated with lemborexant in controlled Phase 3 studies, 491 patients were 65 years of age and older and 87 patients were 75 years of age and older. Overall, efficacy results for patients younger than 65 years of age were similar compared to patients 65 years of age and older. In a pooled analysis of Study 1 (the first 30 days) and Study 2, the incidence of somnolence in patients 65 years of age and older with lemborexant 10mg was higher (9.8%) compared to 7.7% in patients younger than 65 years of age. The incidence of somnolence with lemborexant 5mg was similar in patients 65 years of age and older (4.9%) and younger than 65 years of age (5.1%). Because lemborexant can increase somnolence and drowsiness, patients, particularly the elderly, are at a higher risk of falls. Caution should be exercised when using doses higher than 5mg in patients 65 years of age and older.

Adverse Reactions: 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.

Efficacy: The efficacy of lemborexant was evaluated in 2 clinical studies in patients with insomnia characterized by difficulties with sleep onset and/or sleep maintenance (Study 1 and Study 2).

- Study 1 was a 6-month, randomized, double-blind, placebo-controlled, multi-center study in adult patients 18 years of age and older who met DSM-5 criteria for insomnia disorder. Patients were randomized to placebo, lemborexant 5mg, or lemborexant 10mg once nightly. The primary efficacy endpoint was the mean change from baseline to the end of treatment (6 months) for log-transformed patient-reported (subjective) sleep onset latency (sSOL), defined as the estimated minutes from the time that the patient attempted to sleep until sleep onset. In Study 1, lemborexant 5mg and 10mg demonstrated statistically significant superiority in sSOL compared to placebo (*see efficacy results in the following table, Table 1*).

- Study 2 was a 1-month, randomized, double-blind, placebo- and active-controlled, multi-center, parallel-group clinical study in adult female patients at least 55 years of age and adult male patients at least 65 years of age who met DSM-5 criteria for insomnia disorder. Patients were randomized to placebo, lemborexant 5mg, lemborexant 10mg, or active comparator [zolpidem extended-release (ER) 6.25mg] once nightly. The primary efficacy endpoint was the mean change in log-transformed latency to persistent sleep (LPS) from baseline to the end of treatment (nights 29 and 30), as measured by overnight polysomnography (PSG) monitoring. LPS was defined as the number of minutes from lights off to the first 10 consecutive minutes of non-wakefulness. In Study 2, lemborexant 5mg and 10mg demonstrated statistically significant superiority in LPS compared to placebo (*see efficacy results in the following table, Table 1*).

Table 1. Lemborexant Efficacy Results in Patients with Insomnia (Study 1 and Study 2)

Study 1 Results						
Primary Endpoint	**Treatment Group**	**Number of ITT Patients**	**Baseline Mean[α] (SD)**	**Month 6 LS Mean[α] (SE)**	**Treatment Effect (95% CI)***	
Sleep Onset sSOL (minutes)	lemborexant 5mg	316	43.0 (31.5)	20.0 (1.1)	0.7 (0.6, 0.8)	
	lemborexant 10mg	315	45.0 (33.4)	19.2 (1.1)	0.7 (0.6, 0.8)	
	placebo	318	45.0 (31.8)	27.3 (1.4)	n/a	
Study 2 Results[8]						
Primary Endpoint	**Treatment Group**	**Number of ITT Patients**	**Baseline Mean[α] (SD)**	**Nights 29 and 30 LS Mean[α] (SE)**	**Treatment Effect (95% CI)***	**Treatment Effect (95% CI)[¥]**
Sleep Onset LPS (minutes)	lemborexant 5mg	266	44.9 (36.5)	25.8 (24.3)	0.77 (0.67, 0.89)	0.63 (0.56, 0.72)
	lemborexant 10mg	269	44.6 (33.0)	22.8 (17.5)	0.72 (0.63, 0.83)	0.59 (0.52, 0.68)
	placebo	208	43.9 (33.6)	36.0 (32.1)	n/a	n/a
	zolpidem ER 6.25mg	263	44.5 (38.3)	37.1 (28.4)	1.22 (1.06, 1.40)	n/a

ITT = intent to treat; SD = standard deviation; LS = least squares; SE = standard error; CI = confidence interval; sSOL = subjective sleep onset latency; LPS = latency to persistent sleep; ER = extended-release; n/a = not applicable

[α]Mean refers to geometric mean, which was used with log-transformed values to test for statistical significant treatment differences due to the nonnormal distribution of sSOL and LPS.

*Treatment effect (95% CI) refers to treatment difference compared to placebo.

[¥]Treatment effect (95% CI) refers to treatment difference compared to zolpidem ER.

Cost: Cost information for Dayvigo™ (lemborexant) is not yet available. Dayvigo™ is currently pending controlled substance scheduling by the DEA.

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.

Utilization Details of Insomnia Medications: Calendar Year 2019

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TIER-1 PRODUCTS					
ZOLPIDEM TAB 10MG	11,588	2,226	$113,407.09	$9.79	5.2
ZOLPIDEM TAB 5MG	2,694	895	$26,621.18	$9.88	3.0
TEMAZEPAM CAP 30MG	2,244	464	$24,737.03	$11.02	4.8
ESZOPICLONE TAB 3MG	1,703	360	$22,836.98	$13.41	4.7
TEMAZEPAM CAP 15MG	1,416	436	$15,595.32	$11.01	3.3
ESZOPICLONE TAB 2MG	558	209	$7,539.33	$13.51	2.7
ROZEREM TAB 8MG	549	135	$199,039.45	$362.55	4.1
TRIAZOLAM TAB 0.25MG	508	298	$15,974.43	$31.45	1.7
ZALEPLON CAP 10MG	434	136	$6,895.41	$15.89	3.2
ESZOPICLONE TAB 1MG	250	113	$4,020.90	$16.08	2.2
ZALEPLON CAP 5MG	109	42	$1,602.40	$14.70	2.6
FLURAZEPAM CAP 30MG	18	8	$397.42	$22.08	2.3
FLURAZEPAM CAP 15MG	10	5	$177.06	$17.71	2.0
ESTAZOLAM TAB 2MG	8	1	$200.28	$25.04	8.0
RAMELTEON TAB 8MG	8	8	$1,202.03	$150.25	1.0
ESTAZOLAM TAB 1MG	5	2	$125.68	$25.14	2.5
TRIAZOLAM TAB 0.125MG	4	4	$152.47	$38.12	1.0
SUBTOTAL	**22,106**	**4,603***	**$440,524.46**	**$19.93**	**4.8**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
TIER-2 PRODUCTS					
ZOLPIDEM ER TAB 12.5MG	1,104	172	$23,009.88	$20.84	6.4
ZOLPIDEM ER TAB 6.25MG	86	21	$1,663.14	$19.34	4.1
AMBIEN CR TAB 12.5MG	12	1	$6,112.30	$509.36	12.0
SUBTOTAL	**1,202**	**190***	**$30,785.32**	**$25.61**	**6.3**
TIER-3 PRODUCTS					
BELSOMRA TAB 20MG	25	4	$8,614.96	$344.60	6.3
BELSOMRA TAB 10MG	23	4	$7,838.17	$340.79	5.8
BELSOMRA TAB 15MG	2	2	$685.04	$342.52	1.0
SUBTOTAL	**50**	**10***	**$17,138.17**	**$342.76**	**5.0**
SPECIAL PRIOR AUTHORIZATION (PA) PRODUCTS					
TEMAZEPAM CAP 7.5MG	46	6	$2,903.02	$63.11	7.7
HETLIOZ CAP 20MG	22	2	$345,588.08	$15,708.55	11.0
TEMAZEPAM CAP 22.5MG	2	1	$178.86	$89.43	2.0
EDLUAR SUB 5MG	1	1	$181.97	$181.97	1.0
SUBTOTAL	**71**	**10***	**$348,851.93**	**$4,913.41**	**7.1**
TOTAL	**23,429**	**4,710***	**$837,299.88**	**$35.74**	**5.0**

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

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Appendix H

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: March 2nd, 2020

FDA Approves New Therapy for Patients with Previously Treated Multiple Myeloma

The FDA approved Sarclisa (isatuximab-irfc), in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor. Sarclisa, administered through intravenous (IV) infusion, is a CD38-directed cytolytic antibody that works by helping certain cells in the immune system attack multiple myeloma cancer cells. Sarclisa received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems. The National Cancer Institute estimates there will be 32,270 new cases of multiple myeloma and 12,830 related deaths in the United States in 2020.

The FDA approved Sarclisa based on the results of a clinical trial involving 307 patients with relapsed and refractory multiple myeloma who had received at least 2 prior therapies, including lenalidomide and a proteasome inhibitor. Half of the patients received Sarclisa in combination with pomalidomide and low-dose dexamethasone and the other half received only pomalidomide and low-dose dexamethasone. The efficacy of Sarclisa was based on progression-free survival (PFS), the amount of time a patient stays alive without the cancer growing. Patients who received Sarclisa in combination with pomalidomide and low-dose dexamethasone showed improvement in PFS with a 40% reduction in the risk of disease progression or death compared to patients who received pomalidomide and dexamethasone. These patients also had an overall response rate of 60.4%. In comparison, the patients who only received pomalidomide and low-dose dexamethasone had an overall response rate of 35.3%.

Common side effects for patients taking Sarclisa were neutropenia, infusion-related reactions, pneumonia, upper respiratory tract infection, diarrhea, anemia, lymphopenia, and thrombocytopenia. Sarclisa can cause serious side effects. Sarclisa can cause IV infusion-related reactions. In a grade 3 or higher (severe) reaction, the Sarclisa infusion should be permanently discontinued and health care professionals should institute appropriate medical management. Sarclisa can also cause neutropenia and health care professionals should monitor a patient's complete blood cell count periodically during treatment, as well as monitor patients with neutropenia for signs of infection. Higher incidences of second primary malignancies were observed in a controlled clinical trial of patients with multiple myeloma receiving Sarclisa. Therefore, health care professionals should monitor patients for the development of a second primary malignancy when taking Sarclisa.

Laboratory test interference may be experienced with Sarclisa. Blood banks should be informed that patients are receiving Sarclisa because the drug may interfere with certain tests that are done by blood banks for patients who need a blood transfusion. Health care professionals should type and screen patients prior to starting treatment with Sarclisa. Sarclisa may interfere with the assays used to monitor M-protein, which may impact the determination of complete response.

Health care professionals should advise pregnant women that Sarclisa may cause harm to a developing fetus. Women who are pregnant should not use Sarclisa. Women planning to become pregnant should use effective contraceptives during and for at least 5 months after treatment.

FDA NEWS RELEASE

For Immediate Release: March 4th, 2020

FDA Requires Stronger Warning about Risk of Neuropsychiatric Events Associated with Asthma and Allergy Medication Singulair and Generic Montelukast

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.

The FDA updated the product labeling in 2008 to include information about neuropsychiatric events reported with use of montelukast. In response to continued reports of suicide and other adverse events, the FDA evaluated available data regarding the risk of neuropsychiatric events, including reports submitted through the FDA Adverse Event Reporting System (FAERS) and observational studies in the published literature. The FDA also conducted an observational study using data in the Sentinel Distributed Database and presented the findings at an FDA advisory committee meeting in 2019.

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.

In addition to the *Boxed Warning*, the FDA is also requiring a new Medication Guide to be given to patients with each montelukast prescription. Additionally, health care professionals and patients should report side effects from montelukast to the FDA's MedWatch program.

FDA NEWS RELEASE

For Immediate Release: March 6th, 2020

FDA Approves New Treatment for Adults with Cushing's Disease

The FDA approved Isturisa (osilodrostat) oral tablet for adults with Cushing's disease who either cannot undergo pituitary gland surgery or have undergone the surgery but still have the disease. Cushing's disease is a rare disease in which the adrenal glands make too much cortisol. Isturisa is the first FDA-approved drug to directly address this cortisol overproduction by blocking the enzyme known as 11-beta-hydroxylase and preventing cortisol synthesis.

Cushing's disease is caused by a pituitary tumor that releases too much of a hormone called adrenocorticotropin, which stimulates the adrenal gland to produce an excessive amount of cortisol. The disease is most common among adults between the ages of 30 to 50 years, and it affects women 3 times more often than men. Cushing's disease can cause significant health issues, such as high blood pressure, obesity, type 2 diabetes, blood clots in the legs and lungs, bone loss and fractures, a weakened immune system, and depression. Patients may have thin arms and legs, a round red full face, increased fat around the neck, easy bruising, striae, and weak muscles.

Isturisa's safety and effectiveness for treating Cushing's disease among adults was evaluated in a study of 137 adult patients (about three-quarters women) with a mean age of 41 years. The majority of patients either had undergone pituitary surgery that did not cure Cushing's disease or were not surgical candidates. In the 24-week, single-arm, open-label period, all patients received a starting dose of 2mg of Isturisa twice a day that could be increased every 2 weeks up to 30mg twice a day. At the end of this 24-week period, about half of patients had cortisol levels within normal limits. After this point, 71 patients who did not need further dose increases and tolerated the drug for the last 12 weeks were entered an 8-week, double-blind, randomized

withdrawal study where they either received Isturisa or a placebo. At the end of this withdrawal period, 86% of patients receiving Isturisa maintained cortisol levels within normal limits compared to 30% of patients taking the placebo.

The most common side effects reported in the clinical trial for Isturisa were adrenal insufficiency, headache, vomiting, nausea, fatigue, and edema. Hypocortisolism, QTc prolongation, and elevations in adrenal hormone precursors and androgens may also occur in people taking Isturisa.

Isturisa is taken by mouth twice a day, in the morning and evening, as directed by a health care provider. After treatment has started, a provider may re-evaluate dosage, depending upon the patient's response. Isturisa was granted Orphan Drug designation by the FDA, which is a special status granted to a drug intended to treat a rare disease or condition.

FDA NEWS RELEASE

For Immediate Release: March 9th, 2020

FDA Approves First Treatment for Group of Progressive Interstitial Lung Diseases

The FDA approved Ofev (nintedanib) oral capsule to treat patients with chronic fibrosing interstitial lung diseases (ILD) with a progressive phenotype. It is the first FDA-approved treatment for this group of fibrosing lung diseases that worsen over time.

Chronic fibrosing ILD with a progressive phenotype encompasses a group of fibrotic lung diseases caused by different underlying diseases or conditions, including autoimmune ILD, hypersensitivity pneumonitis, and idiopathic nonspecific interstitial pneumonia. Characteristics of chronic fibrosing ILD include lung scarring and rapid disease progression, as assessed through worsening lung function tests, symptoms and/or imaging. Progressive lung scarring leads to breathlessness and respiratory failure. Lung function declines over time among these patients and can be debilitating and life-threatening.

Ofev's safety and effectiveness to treat chronic fibrosing ILD with a progressive phenotype in adults was evaluated in a randomized, double-blind, placebo-controlled study of 663 adults. The mean age of patients was 66 years and more patients were male (54%) than female. The primary test for effectiveness was the forced vital capacity, which is a measure of lung function. In the 52-week period, patients received either 150mg of Ofev twice a day or a placebo. After 52 weeks, people who received Ofev had less lung function decline compared to those on the placebo.

The most common side effects reported in the Ofev clinical trial were diarrhea, nausea, stomach pain, vomiting, liver problems, decreased appetite, headache, and weight loss. Ofev is not recommended for patients with moderate or severe hepatic impairment. Elevated liver enzymes, drug-induced liver injury, and gastrointestinal (GI) disorders have occurred among people taking Ofev. It may also cause embryo-fetal toxicity that can result in fetal harm, arterial thromboembolic events, bleeding, and GI perforation. P-glycoprotein and CYP3A4 inhibitor drugs, including ketoconazole and erythromycin, may increase nintedanib exposure; patients taking these inhibitors with Ofev should be closely monitored.

Ofev received Priority Review and Breakthrough Therapy designations from the FDA. Ofev was previously approved by the FDA to treat idiopathic pulmonary fibrosis and to slow the rate of decline in pulmonary function among patients with ILD associated with systemic sclerosis or scleroderma.

FDA NEWS RELEASE

For Immediate Release: March 19th, 2020

FDA Approves New Treatment for Pediatric Patients with Any Strain of Hepatitis C

The FDA approved a supplemental application for Epclusa (sofosbuvir/velpatasvir) to treat hepatitis C virus (HCV) in children 6 years of age and older or weighing at least 37 pounds (17 kilograms) with any of the 6 HCV genotypes without cirrhosis or with mild cirrhosis. Epclusa in combination with ribavirin is indicated for the treatment of pediatric patients 6 years of age and older or weighing at least 37 pounds with severe cirrhosis. The FDA previously approved Epclusa to treat HCV in adults.

HCV is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. According to the Centers for Disease Control and Prevention (CDC), in 2016 there were an estimated 2.4 million people in the United States with chronic HCV, and children born to HCV-positive mothers are at risk for HCV infection.

The pharmacokinetics, safety, and efficacy of Epclusa, taken orally for 12 weeks, for the treatment of HCV genotypes 1, 2, 3, 4, or 6 infection was established in an open-label, multicenter clinical trial that included a total of 173 treatment-naïve and treatment-experienced pediatric patients 6 years of age and older without cirrhosis or with mild cirrhosis. No meaningful differences in pharmacokinetics were seen in pediatric patients compared to adults. The safety and efficacy results were comparable to those observed in adults. In 102 patients ages 12 through 17, 93% of patients with genotype 1 and 100% of patients with genotypes 2, 3, 4 and 6 had no detectable virus in the blood 12 weeks after finishing treatment, suggesting the patients' infection was cured. Among the 71 patients 6 to 11 years of age with HCV genotypes 1, 2, 3, or 4, 93% with genotype 1, 91% with genotype 3, and 100% with genotypes 2 and genotype 4 had no virus detected in the blood 12 weeks after finishing treatment. The safety and efficacy of Epclusa for treatment of HCV genotype 5 in pediatric patients 6 years of age and older or weighing at least 37 pounds without cirrhosis or with mild cirrhosis are supported by sofosbuvir and velpatasvir exposures in adults and pediatric patients with HCV genotype 1, 2, 3, 4, or 6 infection. Similar data were used to support dosing recommendations for pediatric patients with HCV genotype 1, 2, 3, 4, 5, or 6 infection who have severe cirrhosis. The safety and effectiveness of Epclusa have not been established in pediatric patients younger than 6 years of age.

The most common adverse reactions observed with treatment with Epclusa in pediatric patients were fatigue and headache. The adverse reactions observed were consistent with those observed in clinical trials of Epclusa in adults. Epclusa includes a *Boxed Warning* that hepatitis B virus (HBV) reactivation has been reported in patients infected with both HCV and HBV who were taking or had completed treatment with HCV antivirals and were not taking HBV antivirals. HBV reactivation has resulted in fulminant hepatitis, hepatic failure, and death. Health care providers should test all patients for evidence of current or prior HBV infection before initiation of Epclusa and continue to monitor patients throughout the treatment.

FDA NEWS RELEASE

For Immediate Release: March 19th, 2020

Coronavirus (COVID-19) Update: FDA Continues to Facilitate Development of Treatments

The FDA continues to play a critical role in the multifaceted all-of-government response to the COVID-19 pandemic, which includes, among other things, facilitating medical countermeasures to treat and prevent the disease, and surveilling the medical product and food supply chains for potential shortages or disruptions and helping to mitigate such impacts, as necessary. As part of those efforts, President Trump has directed the FDA to continue its work with the public and private sector to ensure the availability of potentially safe and effective life-saving drugs to patients who are in desperate need, including those infected with COVID-19.

The FDA has been working closely with other government agencies and academic centers that are investigating the use of the drug chloroquine, which is already approved for treating malaria, lupus, and rheumatoid arthritis, to determine whether it can be used to treat patients with mild-to-moderate COVID-19 to potentially reduce the duration of symptoms, as well as viral shedding, which can help prevent the spread of disease. Studies are underway to determine the efficacy in using chloroquine to treat COVID-19.

The FDA wants to assure the American public that the agency continues to work with partners across the United States government and regulated industry to expedite the development and availability of critical medical products to prevent and treat this novel virus, including repurposing existing therapies that may help treat patients with COVID-19. While there are no FDA-approved therapeutics or drugs to treat, cure, or prevent COVID-19, there are several FDA-approved treatments that may help ease the symptoms from a supportive care perspective.

The FDA is working closely with innovators to expedite these efforts, including leveraging scientific information about the virus and trials currently being conducted in other countries such as China, Japan, South

Korea, and Italy as well as in the United States. Quickly after the emergence of this virus, the FDA began working directly with partners and innovators to foster the development of medical countermeasures against COVID-19, and are continuing to provide regulatory flexibility, advice, guidance, and technical assistance. The FDA continues to work with interested sponsors to help expedite any additional clinical trials for COVID-19 medical countermeasures that may be appropriate. The FDA is able to, and has been, turning around requests very quickly to assist in initiating clinical trials. For example, last month, the National Institutes of Health (NIH) began a randomized controlled trial for the treatment of COVID-19 patients with the investigational antiviral drug remdesivir. The FDA has been working with the drug sponsor, to find multiple pathways to both study the drug under the FDA's investigational new drug requirements, and thus collect helpful data about the efficacy of the drug, as well as provide the drug to patients under emergency use. The FDA is committed to continuing to make use of its expanded access program to allow the emergency use of this product for those patients, when appropriate. To date, the agency has already granted about 250 patients access to this product. The data collected from the expanded access program may contribute to the agency's understanding of the drug, but controlled clinical trials are needed to determine if it safe and effective for the treatment of COVID-19 infection.

Innovators are looking at products in a variety of areas, including the assessment of antiviral drugs that might treat the specific virus, as well as host targets, such as interleukin-6 (IL-6) receptor inhibitors that may be helpful in reducing lung inflammation and improving lung function in COVID-19 patients, thereby potentially slowing the progression of severe respiratory symptoms. Regeneron Pharmaceuticals Inc. has announced the initiation of a randomized controlled clinical trial of sarilumab, an antibody to the IL-6 receptor, to assess whether the modification of the inflammatory response by this treatment provides benefit to COVID-19 patients. There's also interest in evaluating whether therapies, such as convalescent plasma and hyperimmune globulin, antibody-rich blood products that are taken from blood donated by people who have recovered from the virus, could shorten the length or lessen the severity of the illness. The FDA is taking the lead on an urgent cross-government approach to facilitate the development of all of these products. Facilitating the ultimate widespread use and availability of safe and effective medical countermeasures is critical for a number of reasons, including that reducing the severity and duration of respiratory or other symptoms through medical treatments could help lessen the burden on medical personnel, equipment, and facilities. At the same time, the FDA will continue work to facilitate the development of treatment options in the near-term. The agency is also working with interagency partners, product developers, and international public health organizations to expedite the development of vaccines to the greatest extent possible. Recently NIH announced the start of a Phase 1 clinical trial in Seattle in 45 healthy adult volunteers to test the safety of an investigational vaccine designed to protect against COVID-19 infection. The FDA intends to use all of the regulatory flexibility granted to it by Congress to ensure the most efficient and timely development of vaccines to fight COVID-19.

FDA NEWS RELEASE

For Immediate Release: March 22nd, 2020

Coronavirus (COVID-19) Update: FDA Provides Update on Patient Access to Certain REMS Drugs during COVID-19 Public Health Emergency (PHE)

In the FDA's ongoing efforts to address the COVID-19 pandemic, the agency issued a new guidance to sponsors and health care providers regarding certain Risk Evaluation and Mitigation Strategy (REMS)-required testing during this time. For drugs subject to REMS with laboratory testing or imaging requirements, health care providers prescribing and/or dispensing these drugs should consider whether there are compelling reasons not to complete these tests or studies during this PHE and use their best medical judgment in weighing the benefits and risks of continuing treatment in the absence of laboratory testing and imaging studies. They should also communicate with their patients regarding these judgments including their benefits and risks.

The FDA does not intend to take action against sponsors and others for the duration of PHE for failing to adhere to REMS requirements for certain laboratory testing or imaging studies. The FDA may require REMS for certain drugs if the agency determines that it is necessary to ensure that the benefits of the drug outweigh its risks. Generally, REMS may include a medication guide, a patient package insert, a communication plan, and certain packaging and safe disposal technologies for drugs that pose a serious risk of abuse or overdose. The FDA also may require certain elements to assure safe use (ETASU) as part of REMS for a drug. ETASU are medical interventions or other actions health care professionals need to execute prior to prescribing or dispensing the drug to the patient such as a requirement to undergo monthly laboratory testing. Some actions may also be required in order for the patient to continue on treatment. The policy outlined in the guidance will be in effect for the duration of the PHE.

Current Drug Shortages Index (as of March 23rd, 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 Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Avycaz® (ceftazidime and avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
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***
Dexamethasone Sodium Phosphate 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 Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Latanoprost Ophthalmic Solution 0.005%	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***

Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***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***
Ranitidine Injection, USP	***Currently in Shortage***
Ranitidine Tablets/Capsules	***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***
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***