Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
April 10, 2019
4:00pm

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – April 10, 2019

DATE: March 29, 2019

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

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

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/Long-Acting Beta$_2$-Agonist Utilization: Pediatric Members – Appendix B

Action Item – Vote to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide) – Appendix C

Action Item – Vote to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat) – Appendix D

Action Item – Vote to Prior Authorize Copiktra™ (Duvelisib) – Appendix E

Action Item – Vote to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – Appendix F

Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Lorbrena® (Lorlatinib), Mvasi® (Bevacizumab-awwb), and Vizimpro® (Dacomitinib) – Appendix G

Annual Review of the SoonerCare Pharmacy Benefit – Appendix H

Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Fulphila® (Pegfilgrastim-jmdb), Nivestym™ (Filgrastim-aafi), and Udenyca™ (Pegfilgrastim-cbqv) – Appendix I

Annual Review of Anti-Diabetic Medications – Appendix J

30-Day Notice to Prior Authorize Cablivi® (Caplacizumab-yhdp) – Appendix K

30-Day Notice to Prior Authorize Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase) – Appendix L

Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Consensi® (Amlodipine/Celecoxib) and Kapspargo™ Sprinkle [Metoprolol Succinate Extended-Release (ER)] – Appendix M

Industry News and Updates – Appendix N

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – April 10, 2019 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. March 13, 2019 DUR Minutes – Vote
B. March 13, 2019 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/Long-Acting Beta$_2$-Agonist Utilization: Pediatric Members – See Appendix B

A. Medication Coverage Activity for March 2019
B. Pharmacy Helpdesk Activity for March 2019
C. Long-Acting Beta$_2$-Agonist Utilization: Pediatric Members

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

5. Action Item – Vote to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat) – See Appendix D

A. Introduction
B. Market News and Updates
C. Recommendations

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

7. Action Item – Vote to Prior Authorize Copiktra™ (Duvelisib) – See Appendix E

A. Introduction
B. Recommendations

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

8. Action Item – Vote to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib) – See Appendix F

A. Introduction
B. Recommendations

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

9. Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Lorbrena® (Lorlatinib), Mvasi® (Bevacizumab-awwb), and Vizimpro® (Dacomitinib) – See Appendix G

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. Holderread, Dr. Muchmore, Chairman:

10. Annual Review of the SoonerCare Pharmacy Benefit – See Appendix H

A. Summary
B. Medicaid Drug Rebate Program
C. Alternative Payment Models
D. Drug Approval Trends
E. Traditional Versus Specialty Pharmacy Products
F. Top 10 Therapeutic Classes by Reimbursement
G. Top 10 Medications by Reimbursement
H. Cost Per Claim
I. Conclusion
J. Top 100 Reimbursed Drugs by Fiscal Year
K. Top 50 Medications by Total Number of Claims
L. Top 10 Traditional and Specialty Therapeutic Categories by Fiscal Year

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

11. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Fulphila® (Pegfilgrastim-jmdb), Nivestym™ (Filgrastim-aafi), and Udenyca™ (Pegfilgrastim-cbqv) – See Appendix I

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

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

12. Annual Review of Anti-Diabetic Medications – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Anti-Diabetic Medications
C. Prior Authorization of Anti-Diabetic Medications
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Non-Insulin Anti-Diabetic Medications
G. Utilization Details of Insulin Medications

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

13. 30-Day Notice to Prior Authorize Cablivi® (Caplacizumab-yhdp) – See Appendix K

A. Introduction
B. Cablivi® (Caplacizumab-yhdp) Product Summary
C. College of Pharmacy Recommendations

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

14. 30-Day Notice to Prior Authorize Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase) – See Appendix L

A. Introduction
B. Aldurazyme® (Laronidase) Product Summary
C. Naglazyme® (Galsulfase) Product Summary
D. College of Pharmacy Recommendations

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

15. Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Consensi® (Amlodipine/Celecoxib) and Kapspargo™ Sprinkle [Metoprolol Succinate Extended-Release (ER)] – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Antihypertensive Medications
C. Prior Authorization of Antihypertensive Medications
D. Market News and Updates
E. Consensi® (Amlodipine/Celecoxib Tablets) Product Summary
F. Kapspargo™ Sprinkle (Metoprolol Succinate ER Capsules) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Antihypertensive Medications

Non-Presentation; Questions Only:

16. Industry News and Updates – See Appendix N

A. Introduction
B. News and Updates

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

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

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

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

No live meeting scheduled in May 2019. May 2019 will be a packet only meeting.

A. Bowel Preparation Medications
B. H.P. Acthar® Gel (Repository Corticotropin Injection)
C. Ophthalmic Anti-Inflammatories
D. Testosterone Medications

**Future business subject to change.*

19. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MARCH 13, 2019

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Sarai Connell, Pharm.D.; MBA; Resident	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Thomas Ha, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist		x
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Philip Looper, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Corby Thompson, Pharm.D.		x
Reagan Williams, Pharm.D.		x
Visiting Pharmacy Student(s): Shelby Teel, Justin Wilson, Charles Whitman, Beatrice Atoyebi, Jessica Rhotenberry, Jeramias Hoy		

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

OTHERS PRESENT:		
Tony Salicos, Greenwich	Tami Sova, Biogen	Vesta Valuckaite, Bayer
Kristi Kemp, Allergan	Karthik Rajasekaran, Greenwich	Ron Schnare, Takeda
Patrick Harvey, Walgreens	Frances Bauman, Novo Nordisk	Dave Poskey, UCB
Marc Parker, Sunovion	Rochelle Gerstner, Genentech	Garth Wright, Genentech
Jim Dunlap, PhRMA	Heidi Memmott, Takeda	Lori Howarth, Bayer
Cris Valladares, Celgene	Gia McLean, Celgene	Rachel Gragg, Teva
Brian Maves, Pfizer	Evie Knisely, Novartis	

PRESENT FOR PUBLIC COMMENT:	
Karthik Rajasekaran	Greenwich
Vesta Valuckaite	Bayer
Heidi Memmott	Takeda
Tami Sova	Biogen

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA ITEM NO. 7 KARTHIK RAJASEKARAN
2B: AGENDA ITEM NO. 13 VESTA VALUCKAITE
2C: AGENDA ITEM NO. 15 HEIDI MEMMOTT
2D: AGENDA ITEM NO. 16 TAMI SOVA

ACTION: NONE REQUIRED

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

3A: FEBRUARY 13, 2019 DUR MINUTES – VOTE
3B: FEBRUARY 13, 2019 DUR RECOMMENDATIONS MEMORANDUM
3C: CORRESPONDENCE

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/UPDATE: DRUG UTILIZATION REVIEW OF PRENATAL VITAMINS (PV)

4A: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2019
4B: PHARMACY HELPDESK ACTIVITY FOR FEBRUARY 2019
4C: UPDATE: DRUG UTILIZATION REVIEW OF PV

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE INBRIJA™ (LEVODOPA INHALATION) AND OSMOLEX ER™ [AMANTADINE EXTENDED-RELEASE (ER)]

5A: INTRODUCTION
5B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE AIMOVIG™ (ERENUMAB-AOOE), AJOVY™ (FREMANEZUMAB-VFRM), AND EMGALITY® (GALCANEZUMAB-GNLM)

6A: INTRODUCTION
6B: COST COMPARISON

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

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE EPIDIOLEX® (CANNABIDIOL), DIACOMIT® (STIRIPENTOL), AND SYMPAZAN™ (CLOBAZAM ORAL FILM)
7A: INTRODUCTION
7B: MARKET NEWS AND UPDATES
7C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Dr. Broyles moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE GAMIFANT® (EMAPALUMAB-LZSG)
8A: INTRODUCTION
8B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Broyles moved to approve; seconded by Dr. Duniphin
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE FIRDAPSE® (AMIFAMPRIDINE)
9A: INTRODUCTION
9B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Connell
Dr. Anderson moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE RETACRIT™ (EPOETIN ALFA-EPBX)
10A: INTRODUCTION
10B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread for Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE COPIKTRA™ (DUVELISIB)
11A: INTRODUCTION
11B: CURRENT PRIOR AUTHORIZATION CRITERIA
11C: UTILIZATION OF CLL MEDICATIONS
11D: PRIOR AUTHORIZATION OF CLL MEDICATIONS
11E: MARKET NEWS AND UPDATES
11F: COPIKTRA™ (DUVELISIB) PRODUCT SUMMARY
11G: RECOMMENDATIONS
11H: UTILIZATION DETAILS OF CLL MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF LYMPHOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ADCETRIS® (BRENTUXIMAB VEDOTIN), BELEODAQ® (BELINOSTAT), CALQUENCE® (ACALABRUTINIB), FOLOTYN® (PRALATREXATE), ISTODAX® (ROMIDEPSIN), POTELIGEO® (MOGAMULIZUMAB-KPKC), TRUXIMA® (RITUXIMAB-ABBS), ZEVALIN® (IBRITUMOMAB TIUXETAN), AND ZOLINZA® (VORINOSTAT)
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: 30-DAY NOTICE TO PRIOR AUTHORIZE LUTATHERA® (LUTETIUM LU 177 DOTATATE) AND VITRAKVI® (LAROTRECTINIB)
13A: INTRODUCTION
13B: MARKET NEWS AND UPDATES
13C: PRODUCT SUMMARIES
13D: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
14C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF ANTICOAGULANTS
14G: UTILIZATION DETAILS OF PLATELET AGGREGATION INHIBITORS
Materials included in agenda packet; presented by Dr. Holderread for Dr. Nawaz
Dr. Anderson moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF HEREDITARY ANGIOEDEMA (HAE) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TAKHZYRO™ (LANADELUMAB-FLYO) AND TO UPDATE THE PRIOR AUTHORIZATION CRITERIA FOR CINRYZE® (C1 ESTERASE INHIBITOR), HAEGARDA® (C1 ESTERASE INHIBITOR), AND KALBITOR® (ECALLANTIDE)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF HAE MEDICATIONS
15C: PRIOR AUTHORIZATION OF HAE MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: TAKHZYRO™ (LANADELUMAB-FLYO) PRODUCT SUMMARY
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF ANTICONVULSANTS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)**

17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)
17D: PRIOR AUTHORIZATION OF LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)
17E: MARKET NEWS AND UPDATES
17F: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: **ANNUAL REVIEW OF OSTEOPOROSIS MEDICATIONS**

18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF OSTEOPOROSIS MEDICATIONS
18C: PRIOR AUTHORIZATION OF OSTEOPOROSIS MEDICATIONS
18D: MARKET NEWS AND UPDATES
18E: COLLEGE OF PHARMACY RECOMMENDATIONS
18F: UTILIZATION DETAILS OF OSTEOPOROSIS MEDICATIONS

Materials included in agenda packet; presented by Dr. Connell

ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: **INDUSTRY NEWS AND UPDATES**

19A: INTRODUCTION
19B: NEWS AND UPDATES

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

21A: ANNUAL REVIEW OF PHARMACY BENEFIT
21B: ANTI-DIABETIC MEDICATIONS
21C: ANTIHYPERTENSIVE MEDICATIONS
21D: LUNG CANCER MEDICATIONS
21E: GRANULOCYTE COLONY-STIMULATING FACTORS (G-CSFs)

**Future business subject to change.*

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 22: **ADJOURNMENT**

The meeting was adjourned at 5:05pm.

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

Memorandum

Date: March 14, 2019

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

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

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of March 13, 2019

Recommendation 1: Update: Drug Utilization Review of Prenatal Vitamins (PV)

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Inbrija™ (Levodopa Inhalation) and Osmolex ER™ [Amantadine Extended-Release (ER)]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Inbrija™ (levodopa inhalation) and Osmolex ER™ (amantadine ER) with the following criteria:

Inbrija™ (Levodopa Inhalation) Approval Criteria:

1. An FDA approved indication for the treatment of "off" episodes in patients with Parkinson's disease (PD) treated with carbidopa/levodopa; and

2. Member must be taking levodopa/carbidopa in combination with Inbrija™. Inbrija™ has been shown to be effective only in combination with carbidopa/levodopa; and
3. The member must be experiencing motor fluctuations with a minimum of 2 hours of "off" time and demonstrate levodopa responsiveness; and
4. Member must not be taking nonselective monoamine oxidase inhibitors (MAOIs) concomitantly with Inbrija™ or within 2 weeks prior to initiating Inbrija™; and
5. A previous failed trial of immediate-release (IR) carbidopa/levodopa formulations alone or in combination with long-acting carbidopa/levodopa formulations or a reason why supplementation with IR carbidopa/levodopa formulations is not appropriate for the member must be provided; and
6. A quantity limit of 10 capsules for inhalation per day will apply.

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

1. An FDA approved indication for the treatment of Parkinson's disease (PD) or drug-induced extrapyramidal reactions in adults patients; and
2. Member must not have end-stage renal disease (ESRD) [creatinine clearance (CrCl) <15mL/min/1.73m^2]; and
3. A minimum of a 6-month trial of amantadine immediate-release (IR) that resulted in inadequate effects or intolerable adverse effects that are not expected to occur with amantadine ER; and
4. A patient-specific, clinically significant reason why amantadine IR products cannot be used must be provided; and
5. A quantity limit will apply based on FDA approved dosing regimen(s).

Additionally, the College of Pharmacy recommends updating the Nuplazid® (pimavanserin) prior authorization criteria based on recent U.S. Food and Drug Administration (FDA) safety warnings regarding concomitant therapy. The following criteria would apply (changes noted in red):

Nuplazid® (Pimavanserin) Approval Criteria:

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

6. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication; and
7. A quantity limit of 1 tablet or capsule daily will apply.

Lastly, the College of Pharmacy recommends updating the Gocovri™ (amantadine ER) criteria based on net cost compared to other amantadine ER products. The following criteria would apply (changes noted in red):

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

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

Recommendation 3: Vote to Prior Authorize Aimovig™ (Erenumab-aooe), Ajovy™ (Fremanezumab-vfrm), and Emgality® (Galcanezumab-gnlm)

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. Moving Treximet® (sumatriptan/naproxen) from the Special Prior Authorization (PA) Tier to Tier-1 based on net cost.
2. Updating the Onzetra® Xsail® (sumatriptan nasal powder) PA criteria as shown in red in the following criteria.
3. Removing Sumavel® DosePro® (sumatriptan 6mg/0.5mL injection) from the Tier Chart based on product discontinuation.
4. The prior authorization of Aimovig™ (erenumab-aooe), Ajovy™ (fremanezumab-vfrm), and Emgality® (galcanezumab-gnlm) with the following criteria. Please note, criteria may change based on supplemental rebate participation.

Proposed changes are shown in red in the following Anti-Migraine Medications Tier Chart:

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®)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
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®)			sumatriptan injection (Imitrex®)
			~~**sumatriptan injection (Sumavel® DosePro®)**~~
			sumatriptan injection (Zembrace™ SymTouch™)
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)

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 ~~Onzetra® Xsail® or~~ Zembrace™ SymTouch™ 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 Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual components separately or lower-tiered triptan medications.~~

4. 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.
5. 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®).
6. 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.
7. 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).

Aimovig™ (Erenumab-aooe) and Ajovy™ (Fremanezumab-vfrm) Approval Criteria:

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:
    a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
    b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months; and
        i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and
4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 3 agents with different mechanisms of action. This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. 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

8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Aimovig™, Ajovy™) recommended as treatment (not necessarily prescribed by a neurologist); and
10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. ~~Members who smoke or use tobacco products will not be approved~~ Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. A patient-specific, clinically significant reason why the member cannot use Emgality® (galcanezumab-gnlm) must be provided; and*
14. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
15. Quantity limits will apply based on FDA-approved dosing:
    a. For Aimovig™, a quantity limit of 1 syringe or autoinjectors per 30 days will apply; and
    b. For Ajovy™, a quantity limit of 1 syringe per 30 days will apply. Requests for quarterly dosing (675mg every 3 months) will be approved for a quantity limit override upon meeting Ajovy™ approval criteria.
    [*The manufacturer of Emgality® has currently provided a supplemental rebate to be the preferred CGRP inhibitor; however, Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.]

Emgality® (Galcanezumab-gnlm) Approval Criteria:*

1. An FDA approved indication for the preventive treatment of migraine in adults; and
2. Member must be 18 years of age or older; and
3. Member has documented chronic migraine or episodic migraine headaches:

a. Chronic migraine: 15 or more headache days per month with 8 or more migraine days per month; or
b. Episodic migraine: 4 to 14 migraine days per month on average for the past 3 months; and
    i. For episodic migraine, member must have had a history of migraines for a duration of 12 months or longer; and

4. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes, but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, central venous thrombosis); or
    b. Decreased intracranial pressure (e.g., post-lumbar puncture headache, dural tear after trauma); and
5. Migraine headache exacerbation secondary to other medication therapies or conditions have been ruled out and/or treated. This includes, but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
6. The member has failed medical migraine preventive therapy with at least 2* agents with different mechanisms of action. (*The manufacturer of Emgality® has currently provided a supplemental rebate to require a trial with 2 other migraine preventive therapies; however, Emgality® will follow the original criteria and require trials with 3 other migraine preventive therapies if the manufacturer chooses not to participate in supplemental rebates.) This includes, but is not limited to:
    a. Select antihypertensive therapy (e.g., beta-blocker therapy); or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy [e.g., tricyclic antidepressants (TCA), serotonin and norepinephrine reuptake inhibitors (SNRI)]; and
7. 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
8. Member is not taking any medications that are likely to be the cause of the headaches; and
9. Member must have been evaluated within the last 6 months by a neurologist for migraine headaches and the requested medication (e.g., Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and

10. Member will not use requested medication concurrently with botulinum toxin for the prevention of migraine or with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
11. ~~Members who smoke or use tobacco products will not be approved~~ Other aggravating factors that are contributing to the development of episodic/chronic migraine headaches are being treated when applicable (e.g., smoking); and
12. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
13. Initial approvals will be for the duration of 3 months. Compliance and information regarding efficacy, such as a reduction in monthly migraine days, will be required for continued approval. Continuation approvals will be granted for the duration of 1 year; and
14. A quantity limit of 1 syringe or pen per 30 days will apply. Requests for an initial loading dose (240mg administered as 2 consecutive 120mg injections) will be approved for a quantity limit override upon meeting Emgality® approval criteria.
    [*The manufacturer of Emgality® has currently provided a supplemental rebate to be the preferred CGRP inhibitor; however, Emgality® will follow the original criteria similar to the other CGRP inhibitors if the manufacturer chooses not to participate in supplemental rebates.]

Recommendation 4: Vote to Prior Authorize Epidiolex® (Cannabidiol), Diacomit® (Stiripentol), and Sympazan™ (Clobazam Oral Film)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Epidiolex® (cannabidiol oral solution), Diacomit® (stiripentol), and Sympazan™ (clobazam oral film) with the following criteria:

Epidiolex® (Cannabidiol Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Lennox-Gastaut syndrome (LGS); or
    b. Dravet syndrome; and
2. Member must be 2 years of age or older; and
3. Initial prescription must be written by, or in consultation with, a neurologist; and
4. For a diagnosis of Dravet syndrome, the member must have failed or be inadequately controlled with at least 1 anticonvulsant; or
5. For a diagnosis of LGS, the member must have failed therapy with at least 3 other anticonvulsants; and
6. Members currently stable on Epidiolex® and who have a seizure diagnosis will be grandfathered; and
7. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and

8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Diacomit® (Stiripentol) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Dravet syndrome in members 2 years of age and older; and
2. Initial prescription must be written by, or in consultation with, a neurologist; and
3. Member must have failed or be inadequately controlled with clobazam and valproate; and
4. Member must take clobazam and valproate concomitantly with Diacomit® or a reason why concomitant clobazam and valproate are not appropriate for the member must be provided; and
5. Members currently stable on Diacomit® and who have a seizure diagnosis will be grandfathered; and
6. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
7. For Diacomit® powder for oral suspension, an age restriction of 12 years and younger will apply. Members older than 12 years of age will require a patient-specific, clinically significant reason why the member cannot take the oral capsule formulation; and
8. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Sympazan™ (Clobazam Oral Film) Approval Criteria:

1. An FDA approved indication of adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in members 2 years of age and older; and
2. Previous failure of at least 2 non-benzodiazepine anticonvulsants; and
3. Previous failure of clonazepam; and
4. A patient-specific, clinically significant reason why the member cannot use clobazam oral tablets or clobazam oral suspension must be provided; and
5. Initial approvals will be for the duration of 3 months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Additionally, the College of Pharmacy recommends updating the approval criteria for Trokendi XR® [topiramate extended-release (ER)] to require a reason why the member cannot use Qudexy® XR (topiramate ER) based on net cost (changes noted in red):

Trokendi XR® [Topiramate Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. Partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
    b. Adjunctive therapy in seizures associated with Lennox-Gastaut syndrome (LGS); or
    c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate), must be provided; and

3. A patient-specific, clinically significant reason why the member cannot use Qudexy® XR (topiramate ER) must be provided; and
4. Members currently stable on Trokendi XR® (topiramate ER) and who have a seizure diagnosis will be grandfathered; and
5. A quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (200mg).

Lastly, the College of Pharmacy recommends updating the approval criteria for Briviact® (brivaracetam) to add an age restriction on the oral solution to be consistent with other anticonvulsants with special formulations (changes noted in red):

Briviact® (Brivaracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be prescribed by, or in consultation with, a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants; and
4. Members currently stable on Briviact® and who have a seizure diagnosis will be grandfathered; and
5. For Briviact® oral solution, an age restriction of 12 years and younger will apply. Members older than 12 years of age will require a patient-specific, clinically significant reason why the member cannot take the oral tablet formulation; and
6. Approval length for Briviact® intravenous (IV) will be for a maximum of 7 days of therapy. Further approval may be granted if the prescriber documents an ongoing need for Briviact® IV therapy over Briviact® oral formulations.

Recommendation 5: Vote to Prior Authorize Gamifant® (Emapalumab-lzsg)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Gamifant® (emapalumab-lzsg) with the following criteria:

Gamifant® (Emapalumab-lzsg) Approval Criteria:

1. An FDA approved indication for the treatment of adult and pediatric patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or who are intolerant to conventional HLH therapy; and
2. Diagnosis of primary HLH must be confirmed by 1 of the following:
    a. Genetic testing confirming mutation of a gene known to cause primary HLH (e.g., *PRF*, *UNC13D*, *STX11*); or
    b. Family history consistent with primary HLH; or
    c. Member meets at least 5 of the following 8 diagnostic criteria:
        i. Fever; or
        ii. Splenomegaly; or
        iii. Cytopenias affecting at least 2 of 3 lineages in the peripheral blood (hemoglobin <9, platelets <100 x 10^9/L, neutrophils <1 x 10^9/L); or
        iv. Hypertriglyceridemia (fasting triglycerides >3mmol/L or ≥265mg/dL) and/or hypofibrinogenemia (≤1.5g/L); or

v. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy; or
vi. Low or absent natural killer (NK)-cell activity; or
vii. Hyperferritinemia (ferritin ≥500mcg/L); or
viii. High levels of soluble interleukin-2 receptor (soluble CD25 ≥2,400U/mL); and

3. Gamifant® must be prescribed by, or in consultation with, a physician who specializes in the treatment of immune deficiency disorders; and
4. Member must have at least 1 of the following:
   a. Failure of at least 1 conventional HLH treatment (e.g., etoposide, dexamethasone, cyclosporine); or
   b. Documentation of progressive disease despite conventional HLH treatment; or
   c. A patient-specific, clinically significant reason why conventional HLH treatment is not appropriate for the member must be provided; and
5. Prescriber must verify dexamethasone dosed at least 5mg/m^2/day will be used concomitantly with Gamifant®; and
6. Prescriber must verify member has received or will receive prophylaxis for herpes zoster, *Pneumocystis jirovecii,* and fungal infection(s); and
7. Prescriber must verify member will be monitored for tuberculosis (TB), adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated; and
8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
9. Approvals will be for the duration of 6 months with reauthorization granted if the prescriber documents the member is responding well to treatment, no unacceptable toxicity has occurred, and the member has not received hematopoietic stem cell transplantation (HSCT).

Recommendation 6: Vote to Prior Authorize Firdapse® (Amifampridine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Firdapse® (amifampridine) with the following criteria:

Firdapse® (Amifampridine) Approval Criteria:

1. A diagnosis of Lambert-Eaton myasthenic syndrome (LEMS); and
2. Diagnosis must be confirmed by 1 of the following:
   a. A high titer anti-P/Q-type voltage-gated calcium channel (VGCC) antibody assay; or
   b. A confirmatory electrodiagnostic study [e.g., repetitive nerve stimulation (RNS), needle electromyography (EMG), single-fiber electromyography (SFEMG)]; and
3. Firdapse® must be prescribed by, or in consultation with, a neurologist or oncologist; and
4. Member must not have a history of seizures or be taking medications that lower the seizure threshold (e.g., bupropion, tramadol, amphetamines, theophylline); and
5. A quantity limit of 240 tablets per 30 days will apply; and

6. Initial approvals will be for 6 months. Continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with Firdapse®.

Recommendation 7: Vote to Prior Authorize Retacrit™ (Epoetin Alfa-epbx)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Retacrit™ (epoetin alfa-epbx). The following criteria would apply (changes noted in red):

Epogen® (Epoetin Alfa), Procrit® (Epoetin Alfa), and Retacrit™ (Epoetin Alfa-epbx) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Anemia due to chemotherapy in patients with non-myeloid malignancies; or
    b. Anemia in zidovudine-treated Human Immunodeficiency Virus (HIV)-infected patients; or
    c. The reduction of allogeneic blood transfusion(s) in surgery patients; or
    d. Anemia associated with chronic renal failure; and
        i. For the diagnosis of anemia associated with chronic renal failure: member must not be receiving dialysis [erythropoietin stimulating agents (ESAs) are included in the bundled dialysis payment if member is on any form of dialysis and cannot be billed separately]; and
2. Authorization of Retacrit™ requires a patient-specific, clinically significant reason why the member cannot use Procrit® or Epogen®; and
3. Recent hemoglobin levels must be provided; and
4. Approvals will be for the duration of 16 weeks of therapy. Recent hemoglobin levels must be provided with continuation requests, and further approval may be granted if the member's recent hemoglobin level is <11g/dL.

Recommendation 8: Annual Review of Chronic Lymphocytic Leukemia (CLL) Medications and 30-Day Notice to Prior Authorize Copiktra™ (Duvelisib)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the Xarelto® (rivaroxaban) prior authorization approval criteria based on the FDA approved expanded indication. The following criteria would apply (changes noted in red):

Xarelto® (Rivaroxaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; or
    c. Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery; ~~and~~ or
    d. In combination with aspirin, to reduce the risk of major cardiovascular events [cardiovascular (CV) death, myocardial infarction (MI), and stroke] in members with chronic coronary artery disease (CAD) or peripheral artery disease (PAD); and
2. Xarelto® (rivaroxaban) 15mg and 20mg:
    a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. Xarelto® (rivaroxaban) 10mg:
    a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use in patients following hip or knee replacement surgery; or
4. Xarelto® (rivaroxaban) 2.5mg:
    a. Must be used in combination with aspirin 75 to 100mg to reduce the risk of major CV events in members with chronic CAD or PAD.

Recommendation 12: Annual Review of Hereditary Angioedema (HAE) Medications and 30-Day Notice to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Multiple Sclerosis (MS) Medications

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Luxturna™ (Voretigene Neparvovec-rzyl)

NO ACTION REQUIRED.

Recommendation 15: Annual Review of Osteoporosis Medications

NO ACTION REQUIRED.

Recommendation 16: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 17: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

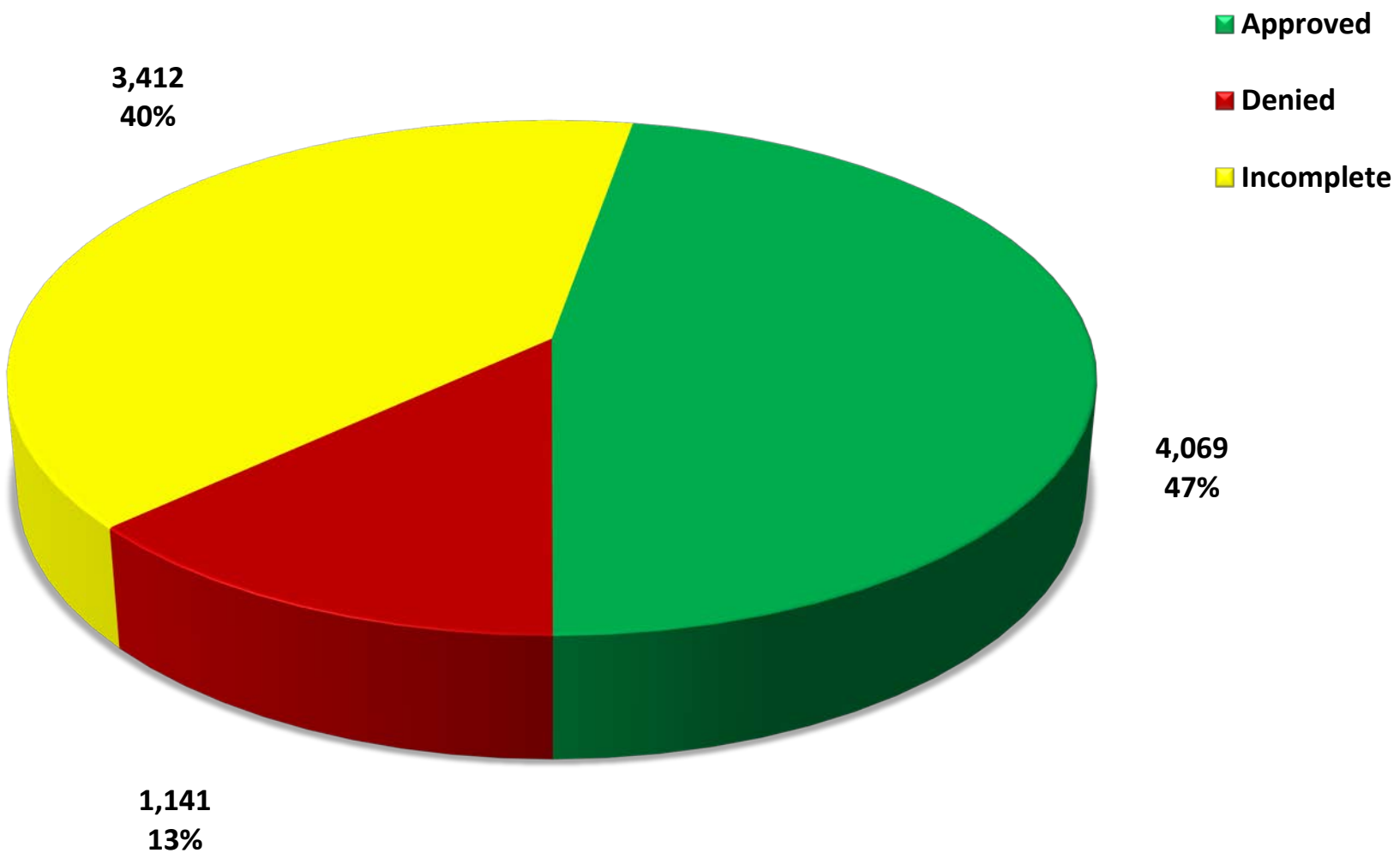
NO ACTION REQUIRED.

Recommendation 18: Future Business

NO ACTION REQUIRED.

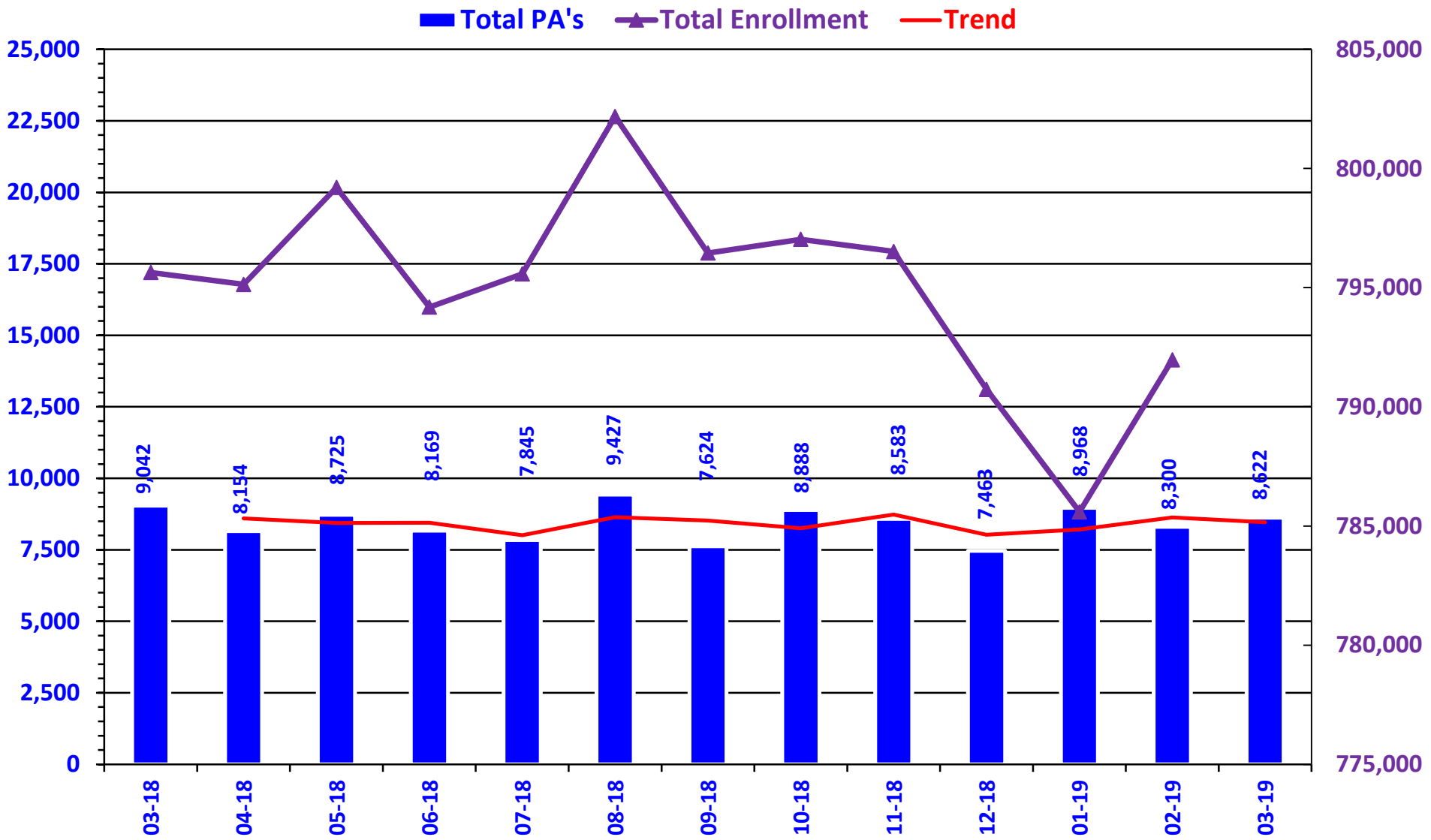
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH 2019



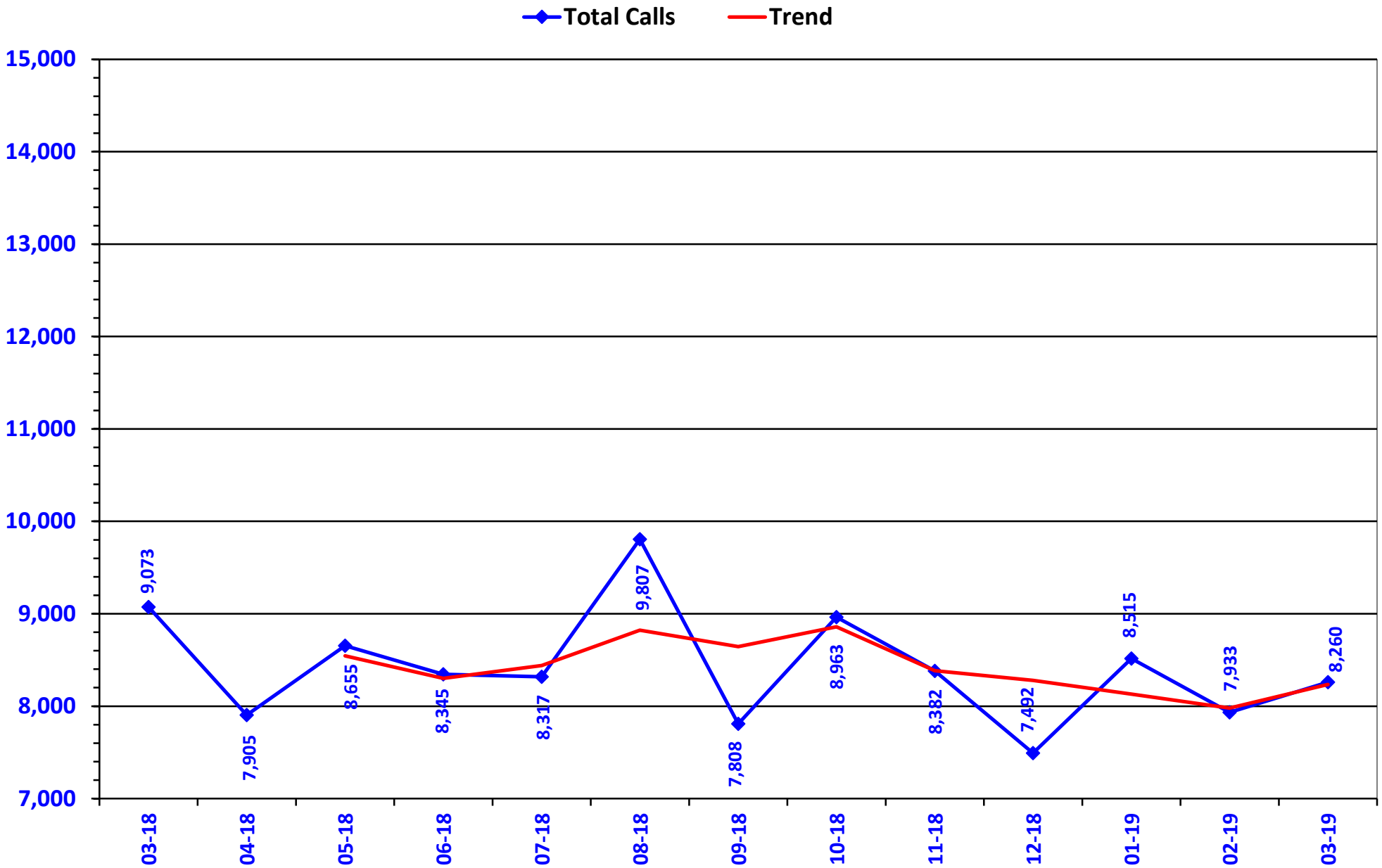
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MARCH 2018 – MARCH 2019



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MARCH 2018 – MARCH 2019



Prior Authorization Activity

3/1/2019 Through 3/31/2019

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	107	7	35	65	334
Analgesic - NonNarcotic	18	0	4	14	0
Analgesic - Narcotic	357	167	34	156	153
Angiotensin Receptor Antagonist	38	2	10	26	358
Antiasthma	92	17	23	52	247
Antibiotic	29	14	3	12	250
Anticonvulsant	179	73	19	87	260
Antidepressant	194	48	39	107	339
Antidiabetic	230	66	38	126	349
Antigout	11	6	2	3	359
Antihistamine	25	2	10	13	357
Antimigraine	142	16	27	99	144
Antineoplastic	92	65	7	20	167
Antiparasitic	27	4	2	21	12
Antiulcers	197	49	63	85	141
Anxiolytic	15	1	1	13	73
Atypical Antipsychotics	228	123	15	90	355
Biologics	171	85	24	62	278
Bladder Control	63	12	15	36	309
Blood Thinners	288	161	20	107	336
Botox	26	20	5	1	324
Buprenorphine Medications	450	285	15	150	74
Cardiovascular	65	22	8	35	305
Chronic Obstructive Pulmonary Disease	134	20	38	76	310
Constipation/Diarrhea Medications	158	30	51	77	203
Contraceptive	21	10	3	8	357
Dermatological	289	79	81	129	116
Diabetic Supplies	478	268	22	188	195
Endocrine & Metabolic Drugs	141	86	11	44	127
Erythropoietin Stimulating Agents	21	12	0	9	106
Fibromyalgia	2	1	1	0	359
Gastrointestinal Agents	110	36	16	58	201
Glaucoma	16	9	0	7	230
Growth Hormones	124	89	8	27	151
Hematopoietic Agents	12	2	5	5	267
Hepatitis C	144	94	21	29	8
HFA Rescue Inhalers	109	7	25	77	121
Insomnia	31	7	7	17	165
Insulin	137	53	18	66	329
Miscellaneous Antibiotics	19	3	2	14	8
Multiple Sclerosis	40	16	9	15	241
Muscle Relaxant	45	2	13	30	27
Nasal Allergy	77	11	27	39	142
Neurological Agents	61	16	14	31	215
NSAID's	24	0	7	17	0
Ocular Allergy	31	4	9	18	150
Osteoporosis	16	9	0	7	357

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Other*	343	58	83	202	229
Otic Antibiotic	10	1	2	7	17
Pediculicide	25	0	8	17	0
Respiratory Agents	36	20	3	13	244
Statins	16	2	6	8	223
Stimulant	714	347	62	305	345
Synagis	60	33	10	17	40
Testosterone	58	17	14	27	291
Topical Antifungal	31	4	6	21	101
Topical Corticosteroids	77	3	45	29	49
Vitamin	88	26	33	29	195
Pharmacotherapy	90	80	0	10	223
Emergency PAs	0	0	0	0	
Total	**6,832**	**2,700**	**1,079**	**3,053**	
Overrides					
Brand	39	30	2	7	259
Compound	19	14	0	5	42
Diabetic Supplies	7	6	0	1	130
Dosage Change	424	391	4	29	13
High Dose	5	3	0	2	295
Ingredient Duplication	13	8	1	4	12
Lost/Broken Rx	109	102	0	7	13
NDC vs Age	304	193	24	87	268
Nursing Home Issue	53	50	0	3	11
Opioid MME Limit	51	32	3	16	79
Opioid Quantity	31	26	1	4	138
Other*	60	43	4	13	12
Prescriber Temp Unlock	1	0	0	1	0
Quantity vs. Days Supply	596	421	20	155	255
STBS/STBSM	38	22	2	14	94
Stolen	7	5	0	2	14
Third Brand Request	33	23	1	9	16
Overrides Total	**1,790**	**1,369**	**62**	**359**	
Total Regular PAs + Overrides	**8,622**	**4,069**	**1,141**	**3,412**	

Denial Reasons	
Unable to verify required trials.	2,786
Does not meet established criteria.	1,167
Lack required information to process request.	592

Other PA Activity	
Duplicate Requests	544
Letters	12,027
No Process	6
Changes to existing PAs	650
Helpdesk Initiated Prior Authorizations	635
PAs Missing Information	20

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

Long-Acting Beta$_2$-Agonist Utilization: Pediatric Members

Oklahoma Health Care Authority
April 2019

Introduction[1]

The Drug Utilization Review (DUR) Board requested a review of claims for pediatric SoonerCare members utilizing single component long-acting beta$_2$-agonists (LABA) in late 2014. The claims analysis was conducted and presented to the DUR Board in February 2015, again in October 2016, and again in January 2018. The following report is an update to ensure appropriate utilization is still in effect.

Current clinical guidelines do not recommend use of LABA medications alone in pediatric patients with asthma. Guidelines suggest using a concomitant inhaled corticosteroid (ICS) with a LABA medication or using an ICS alone. The purpose of this claims analysis was to evaluate potential inappropriate use of single-component LABA medications in the pediatric SoonerCare population.

Claims Analysis

The claims analysis included members 18 years of age and younger with a paid claim for a single-component LABA. The review period was for 1 year (March 1, 2018 to February 28, 2019) and members with a single-component LABA medication claim were further evaluated for a single-component ICS medication during the same month.

Results

10 Members had a paid claim for a single-component LABA medication. This is a decline of 66% from 2016 and 9% from 2018.

3 Members (of the 10) did not have a paid claim for an ICS during the same month as the LABA medication. This is a decline of 75% from 2016 and 25% from 2018. Two of the 3 members had only 1 paid claim for a LABA medication.

1 Member (of the 3) had more than 1 paid claim for a LABA medication. This is a decline of 83% from 2016 and 50% from 2018.

1 Member (of the 3) had a paid claim for a LABA medication within the last 90 days. This is equivalent to the 2016 and 2018 analyses.

Recommendations

The SoonerCare claims analysis of pediatric utilization of single-component LABA medications did not reveal a pressing need for intervention. Results of this analysis revealed reduced single-component LABA utilization in the pediatric population when compared to the number of members found in October 2016 and January 2018. Most pediatric members utilizing single-component LABA medications had only 1 paid claim for a single-component LABA or were being followed by a pulmonary specialist. Based on these findings, the College of Pharmacy does not recommend any changes to the current LABA criteria at this time.

[1] U.S. Department of Health and Human Services and National Heart Lung and Blood Institute. Guidelines from the National Asthma Education and Prevention Program: Diagnosing and Managing Asthma. Available online at: https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf. Last revised 09/2012. Last accessed 03/21/2019.

Appendix C

Vote to Prior Authorize Takhzyro™ (Lanadelumab-flyo) and to Update the Prior Authorization Criteria for Cinryze® (C1 Esterase Inhibitor), Haegarda® (C1 Esterase Inhibitor), and Kalbitor® (Ecallantide)

Oklahoma Health Care Authority
April 2019

Introduction[1,2,3]

Takhzyro™ (lanadelumab-flyo) is a plasma kallikrein inhibitor indicated for prophylaxis of hereditary angioedema (HAE) attacks in patients 12 years of age and older. It is supplied as a 300mg/2mL ready-to-use solution in a single-dose glass vial. The vials should be refrigerated at 36 to 46°F (2 to 8°C) until 15 minutes before use. Takhzyro™ is intended for self-administration or administration by a caregiver. The patient or caregiver should be trained by a health care professional prior to use. The recommended starting dose is 300mg given subcutaneously (sub-Q) every 2 weeks. A dosing interval of 300mg every 4 weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months.

Cost Comparison:

Medication	Cost Per Vial	Cost Per 28 Days*
Takhzyro™ (lanadelumab-flyo)	**$22,070.00**	**$44,140.00**
Cinryze® [C1 esterase inhibitor (human)]	$2,758.79	$44,140.64
Haegarda® [C1 esterase inhibitor (human)]	$1,880.00 – $2,820.00	$37,600.00[Δ]

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.
*Cost per 28 days based on U.S. Food and Drug Administration (FDA) recommended dosing.
[Δ]Cost based on FDA recommended dosing of 60 IU/kg twice weekly for a 75kg patient.

Guideline Update(s):

- **Global Guidelines for the Diagnosis and Management of HAE:** In February 2018, the first revision and update of the global guideline for the diagnosis and management of HAE was published in the *World Allergy Organization Journal*. While several of the recommendations have remained the same, first-line and second-line treatment for long-term prophylaxis have changed. For first-line treatment, the guidelines recommend the use of plasma-derived C1 inhibitor (C1-INH) for long-term prophylaxis of HAE attacks in adults. Consistent with the previous guideline, C1-INH continues to be the first-line recommendation for long-term prophylaxis in children and, if needed, in pregnant or breastfeeding women. Additionally, due to the adverse androgenic and anabolic effects, drug interactions, and contraindications, the current guidelines now recommend the use of androgens as second-line for long-term prophylaxis in adults rather than first-line. The current guidelines do not recommend antifibrinolytics for long-term prophylaxis as data for their efficacy are largely lacking.

Recommendations

The College of Pharmacy recommends the prior authorization of Takhzyro™ (lanadelumab-flyo) with criteria similar to Cinryze® and Haegarda® (C1 esterase inhibitors) and to update the current Cinryze® and Haegarda® criteria to be consistent with current guideline recommendations (changes shown in red):

Cinryze® (C1 Esterase Inhibitor), ~~and~~ Haegarda® (C1 Esterase Inhibitor), and Takhzyro™ (Lanadelumab-flyo) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Must be used for *prophylaxis* of HAE; and
3. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy; and
4. History of at least 1 or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or 3 or more emergency medical treatments per year; or
5. ~~Member meets the following:~~ Approval consideration will be given if the member has a recent hospitalization for a severe episode of angioedema; and
   a. ~~Documented intolerance, insufficient response, or contraindication to attenuated androgens (e.g., danazol, stanozolol, oxandrolone, methyltestosterone); and~~
   b. ~~Documented intolerance, insufficient response, or contraindication to antifibrinolytic agents (e.g., ε – aminocaproic acid, tranexamic acid); or~~
   c. ~~Recent hospitalization for severe episode of angioedema; and~~
6. Authorization of Takhzyro™ (lanadelumab-flyo) will also require a patient-specific, clinically significant reason why the member cannot use Cinryze® or Haegarda® (C1 esterase inhibitor); and
7. Cinryze® Dosing:
   a. The recommended dose of Cinryze® is 1,000 units intravenously (IV) every 3 to 4 days, approximately 2 times per week, to be infused at a rate of 1mL/min; and
   b. Initial doses should be administered in an outpatient setting by a health care provider; members can be taught by their health care provider to self-administer Cinryze® IV; and
   c. A quantity limit of 8,000 units per month will apply (i.e., 2 treatments per week or 8 treatments per 28 days); or
8. Haegarda® Dosing:
   a. The recommended dose of Haegarda® is 60 IU/kg subcutaneously (sub-Q) twice weekly; and
   b. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
   c. A quantity limit of 2 treatments per week or 8 treatments 28 days will apply; or
9. Takhzyro™ Dosing:
   a. The recommended dose of Takhzyro™ is 300mg sub-Q every 2 weeks (dosing every 4 weeks may be considered in some members); and
   b. Prescriber must verify member or caregiver has been trained by a health care professional on proper storage and sub-Q administration of Takhzyro™; and

c. A quantity limit of (2) 300mg/2mL vials per 28 days will apply.

Additionally, the College of Pharmacy recommends updating the current Kalbitor® (ecallantide) criteria based on net cost (changes shown in red):

Ruconest® (C1 Esterase Inhibitor) and Kalbitor® (Ecallantide) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema (HAE); and
2. Ruconest® and Kalbitor® must be used for *treatment* of acute attacks of HAE; and
3. A patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor) and Firazyr® (icatibant) must be provided.

[1] Takhzyro™ (lanadelumab-flyo) Prescribing Information. Shire Plc. Available online at: https://www.shirecontent.com/PI/PDFs/TAKHZYRO_USA_ENG.pdf. Last revised 08/2018. Last accessed 03/20/2019.

[2] Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema– the 2017 revision and update. *World Allergy Organ J* 2018; 11:5.

[3] Craig T, Pursun EA, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. *World Allergy Organ J* 2012; 5(12):182-199.

Appendix D

Vote to Prior Authorize Adcetris® (Brentuximab Vedotin), Beleodaq® (Belinostat), Calquence® (Acalabrutinib), Folotyn® (Pralatrexate), Istodax® (Romidepsin), Poteligeo® (Mogamulizumab-kpkc), Truxima® (Rituximab-abbs), Zevalin® (Ibritumomab Tiuxetan), and Zolinza® (Vorinostat)

Oklahoma Health Care Authority
April 2019

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

Adcetris® (Brentuximab Vedotin):

- **Therapeutic Class:** CD30-directed antibody-drug conjugate
- **Indication(s):** For the treatment of adult patients with:
  - Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
  - cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
  - cHL after failure of auto-HSCT or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
  - Previously untreated, systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphoma (PTCL), including angioimmunoblastic T-cell lymphoma (AITL) and PTCL, not otherwise specified (NOS), in combination with cyclophosphamide, doxorubicin, and prednisone
  - sALCL after failure of at least 1 prior multi-agent chemotherapy regimen
  - Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy
- **How Supplied:** 50mg lyophilized powder in a single-dose vial (SDV)
- **Dose:**
  - Recommended dose as monotherapy is 1.8mg/kg via intravenous (IV) infusion up to a maximum of 180mg every 3 weeks
  - Recommended dose in combination with chemotherapy for previously untreated Stage III or IV cHL is 1.2mg/kg via IV infusion up to a maximum of 120mg every 2 weeks for a maximum of 12 doses

Beleodaq® (Belinostat):

- **Therapeutic Class:** Histone deacetylase (HDAC) inhibitor
- **Indication(s):** For the treatment of patients with relapsed or refractory PTCL
  - This indication is approved under accelerated approval based on tumor response rate and duration of response; an improvement in survival or disease-related symptoms has not been established (continued approval for this indication may be

contingent upon verification and description of clinical benefit in the confirmatory trial)

- **How Supplied:** 500mg lyophilized powder in SDV for reconstitution
- **Dose:** Recommended dose is 1,000mg/m^2 administered over 30 minutes by IV infusion once daily on days 1 to 5 of a 21-day cycle
  - Cycles can be repeated until disease progression or unacceptable toxicity
  - Treatment discontinuation or interruption with or without dosage reductions by 25% may be needed to manage adverse reactions

Calquence® (Acalabrutinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least 1 prior therapy
  - This indication is approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 100mg capsule
- **Dose:** 100mg orally approximately every 12 hours

Folotyn® (Pralatrexate):

- **Therapeutic Class:** Folate analog metabolic inhibitor
- **Indication(s):** For the treatment of patients with relapsed or refractory PTCL
  - This indication is based on ORR; clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated
- **How Supplied:** 20mg/mL and 40mg/2mL SDVs
- **Dose:** Recommended dose is 30mg/m^2 administered as an IV push over 3 to 5 minutes once weekly for 6 weeks in 7-week cycles; dose omissions and/or dose reductions may be needed to manage adverse drug reactions

Istodax® (Romidepsin):

- **Therapeutic Class:** HDAC inhibitor
- **Indication(s):**
  - Treatment of cutaneous T-cell lymphoma (CTCL) in adult patients who have received at least 1 prior systemic therapy
  - Treatment of PTCL in adult patients who have received at least 1 prior therapy
    - This indication is approved under accelerated approval based on response rate; continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 10mg SDV for reconstitution
- **Dose:**
  - 14mg/m^2 administered via IV infusion over a 4-hour period on days 1, 8, and 15 of a 28-day cycle
  - Cycles should be repeated every 28 days provided that the patient continues to benefit from and tolerates the drug

- Discontinuation or interruption of treatment (with or without dose reduction to 10mg/m^2) may be needed to manage drug toxicity

Poteligeo® (Mogamulizumab-kpkc):

- **Therapeutic Class:** CC chemokine receptor type 4 (CCR4)-directed monoclonal antibody
- **Indication(s):** For the treatment of adult patients with relapsed or refractory MF or Sézary syndrome (SS) after at least 1 prior systemic therapy
- **How Supplied:** 20mg/5mL (4mg/mL) solution in a SDV
- **Dose:** 1mg/kg as an IV infusion over at least 60 minutes on days 1, 8, 15, and 22 of the first 28-day cycle and on days 1 and 15 of each subsequent cycle

Truxima® (Rituximab-abbs):

- **Therapeutic Class:** CD20-directed cytolytic antibody; Truxima® is biosimilar to Rituxan® for the following indications listed
- **Indication(s):** For the treatment of adult patients with:
  - Non-Hodgkin's lymphoma (NHL):
    - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single-agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single-agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
- **How Supplied:** 100mg/10mL (10mg/mL) and 500mg/50mL (10mg/mL) solution in SDVs
- **Dose:** 375mg/m^2 as an IV infusion

Zevalin® (Ibritumomab Tiuxetan):

- **Therapeutic Class:** CD20-directed radiotherapeutic antibody
- **Indication(s):** For the treatment of patients with:
  - Relapsed or refractory, low-grade or follicular B-cell NHL
  - Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy
- **How Supplied:** A kit is used for preparing Y-90 radiolabeled Zevalin®; kit includes:
  - 1 Zevalin® vial containing 3.2mg ibritumomab tiuxetan in 2mL 0.9% sodium chloride
  - (1) 50mM sodium acetate vial
  - 1 formulation buffer vial
  - 1 empty reaction vial
- **Dose:**
  - Day 1: Administer rituximab 250mg/m^2 IV
  - Day 7, 8, or 9: Administer rituximab 250mg/m^2 IV

- If platelets ≥150,000/mm^3: Within 4 hours after rituximab infusion, administer 0.4mCi/kg Y-90 Zevalin® IV
- If platelets ≥100,000 but ≤149,000/mm^3 in relapsed or refractory patients: Within 4 hours after rituximab infusion, administer 0.3mCi/kg Y-90 Zevalin® IV

Zolinza® (Vorinostat):

- **Therapeutic Class:** HDAC inhibitor
- **Indication(s):** For the treatment of cutaneous manifestations in patients with CTCL who have progressive, persistent, or recurrent disease on or following 2 systemic therapies
- **How Supplied:** 100mg capsule
- **Dose:** 400mg orally once daily with food; dosage reduction may be required for patients intolerant to therapy and in patients with mild or moderate hepatic impairment

Market News and Updates[10,11,12]

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

- **Keytruda® (Pembrolizumab):** In October 2018, the U.S. Food and Drug Administration (FDA) approved Keytruda® (pembrolizumab) in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC). In November 2018, the FDA approved Keytruda® for the treatment of patients with hepatocellular carcinoma (HCC) who have previously been treated with sorafenib. In December 2018, the FDA granted accelerated approval to Keytruda® for adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC). In February 2019, the FDA approved Keytruda® for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.

Recommendations

- 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 Adcetris® (brentuximab vedotin), Beleodaq® (belinostat), Calquence® (acalabrutinib), Folotyn® (pralatrexate), Istodax® (romidepsin), Poteligeo® (mogamulizumab-kpkc), Truxima® (rituximab-abbs), Zevalin® (ibritumomab tiuxetan), and Zolinza® (vorinostat) with the following criteria listed in red

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. Single-agent for disease progression on or after platinum-containing chemotherapy (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 [Melanoma Diagnosis]:

1. Member meets 1 of the following:
    a. Adjuvant treatment of members with melanoma with involvement of lymph node(s) following complete resection; or
    b. A diagnosis of unresectable or metastatic melanoma; and
2. Pembrolizumab must be used as a single-agent; and
3. Member meets 1 of the following:
    a. Pembrolizumab is being used as first-line therapy; or
    b. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used; and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
5. For adjuvant treatment of melanoma, dose as follows:
    a. 200mg every 3 weeks; and
    b. Maximum duration of 1 year.

Keytruda® (Pembrolizumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Relapsed or progressive disease; and
2. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Member must have been previously treated with sorafenib.

Keytruda® (Pembrolizumab) Approval Criteria [Merkel Cell Carcinoma (MCC) Diagnosis]:

1. A diagnosis of recurrent, locally advanced or metastatic MCC; and
2. No history of prior systemic chemotherapy; and
3. Pembrolizumab must be used as a single-agent; and
4. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease; or
2. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) for primary treatment or in relapsed/refractory disease with regional nodes.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Systemic Diagnosis]:

1. In previously untreated disease in combination with cyclophosphamide, doxorubicin, and prednisone (CHP); or
2. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Classical Hodgkin Lymphoma Diagnosis]:

1. In previously untreated Stage III or IV disease in combination with doxorubicin, vinblastine, and dacarbazine; or
2. In relapsed/refractory disease after failure of ≥2 multi-agent chemotherapy regimens in non-autologous stem cell transplant (SCT) candidates or after failure of autologous SCT as a single-agent; or
3. In relapsed/refractory disease if not previously used in combination with multi-agent chemotherapy; or
4. Consolidation following autologous SCT in members at high risk of relapse or progression.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade Lymphoma Diagnosis]:

1. As a single-agent; and
2. CD30+ disease; and
3. For DLBCL relapsed/refractory disease in non-autologous stem cell transplant (SCT) candidates; or
4. For members who have transformed to DLBCL from follicular lymphoma or marginal zone lymphoma and received ≥2 lines of therapy for indolent or transformed disease.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. Treatment of previously untreated CD30+ disease in combination with cyclophosphamide, doxorubicin, and prednisone (CHP); or
2. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. CD30+ disease; and
2. Member meets 1 of the following:
    a. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) in nonresponders to first-line therapy for chronic/smoldering subtype; or
    b. In combination with CHP for first-line therapy for acute or lymphoma subtype; or
    c. In combination with CHP for continued treatment in responders to first-line therapy for acute or lymphoma subtype; or
    d. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. CD30+ disease; and
2. As a single-agent; and
3. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Beleodaq® (Belinostat) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent for primary treatment or relapsed refractory with multifocal lesions, or cutaneous ALCL with regional nodes.

Beleodaq® (Belinostat) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. Primary treatment in Stage IV non Sézary or visceral disease (solid organ) with or without radiation therapy for local control; or
2. Primary treatment for large cell transformation with generalized cutaneous or extracutaneous lesions with or without skin-directed therapy; or
3. As a single-agent (with or without skin-directed therapy) in relapsed/refractory disease.

Beleodaq® (Belinostat) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

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

Beleodaq® (Belinostat) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

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

Beleodaq® (Belinostat) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and

2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

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.

Folotyn® (Pralatrexate) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease.

Folotyn® (Pralatrexate) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

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

Folotyn® (Pralatrexate) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Folotyn® (Pralatrexate) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

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

Istodax® (Romidepsin) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and

2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

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

Truxima® (Rituximab-abbs) Approval Criteria:

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

Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) (Grade 1-2) Diagnosis]:

1. As a single-agent in relapsed or refractory disease.

Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) or Marginal Zone Lymphoma (MZL) Transformed to Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. As a single-agent; and
2. Member meets 1 of the following:
    a. Minimal or no chemotherapy prior to histologic transformation to DLBCL (FISH for MYC and BCL2 and/or BCL6 must show no translocation) and have partial response, no response, or progressive disease after chemoimmunotherapy; or
    b. ≥2 prior therapies of chemoimmunotherapy for indolent or transformed disease.

Zolinza® (Vorinostat) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

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[2] Beleodaq® Prescribing Information. Spectrum Pharmaceuticals, Inc. Available online at: http://www.beleodaq.com/downloads/Beleodaq_PI.pdf. Last revised 04/2017. Last accessed 03/21/2019.
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[4] Folotyn® Prescribing Information. Allos Therapeutics. Available online at: http://www.folotyn.com/HCP/downloads/folotyn-pi_Nov2016.pdf. Last revised 11/2016. Last accessed 03/21/2019.
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[6] Poteligeo® Prescribing Information. Kyowa Kirin, Inc. Available online at: https://www.poteligeohcp.com/assets/files/full-prescribing-information.pdf. Last revised 08/2018. Last accessed 03/21/2019.
[7] Truxima® Prescribing Information. Celltrion, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761088s000lbl.pdf. Last revised 11/2018. Last accessed 03/21/2019.
[8] Zevalin® Prescribing Information. Spectrum Pharmaceuticals, Inc. Available online at: http://www.zevalin.com/downloads/Zevalin_Package_Insert.pdf. Last revised 08/2013. Last accessed 03/20/2019.
[9] Zolinza® Prescribing Information. Merck & Co., Inc. Available online at: https://www.merck.com/product/usa/pi_circulars/z/zolinza/zolinza_pi.pdf. Last revised 12/2018. Last accessed 03/21/2019.
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[11] Merck. FDA Approves Merck's Keytruda® (pembrolizumab) for the Treatment of Patients with Hepatocellular Carcinoma (HCC) Who Have Been Previously Treated with Sorafenib. *Business Wire*. Available online at: https://www.mrknewsroom.com/news-release/research-and-development-news/fda-approves-mercks-keytruda-pembrolizumab-treatment-pati. Issued 11/09/2018. Last accessed 03/21/2019.
[12] DiGrande S. Pembrolizumab Plus Chemotherapy Approved to Treat Metastatic Squamous NSCLC. *AJMC*. Available online at: https://www.ajmc.com/newsroom/pembrolizumab-plus-chemotherapy-approved-to-treat-metastatic-squamous-nsclc. Issued 11/01/2018. Last accessed 03/21/2019.

Appendix E

Vote to Prior Authorize Copiktra™ (Duvelisib)

Oklahoma Health Care Authority
April 2019

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

- **Copiktra™ (duvelisib):** In September 2018, the U.S. Food and Drug Administration (FDA) approved Copiktra™ (duvelisib) for the treatment of adults with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least 2 prior therapies. The FDA also granted accelerated approval to duvelisib for patients with follicular lymphoma (FL) after at least 2 systemic therapies.
- **Venclexta® (venetoclax):** In June 2018, the FDA approved Venclexta® (venetoclax) for the treatment of patients with CLL or SLL, with or without 17p deletion, who have received at least 1 prior therapy. The FDA granted venetoclax in combination with rituximab Breakthrough Therapy designation and granted the application priority review. In November 2018, the FDA granted accelerated approval to Venclexta® (venetoclax) in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC) for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are 75 years of age or older, or who have comorbidities that preclude use of intensive induction chemotherapy. This indication was approved under accelerated approval based on response rates and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- **Imbruvica® (ibrutinib):** In August 2018, the FDA approved Imbruvica® (ibrutinib) in combination with rituximab for the treatment of Waldenström's macroglobulinemia (WM). The approval expanded the label for ibrutinib in WM beyond its previously approved use as monotherapy to include combination use with rituximab. This approval is the first approved non-chemotherapy combination option for the treatment of WM.
- **Gazyva® (obinutuzumab):** In January 2019, the FDA approved Imbruvica® (ibrutinib) in combination with Gazyva® (obinutuzumab) for use in untreated patients with CLL/SLL. This is the first approval for a non-chemotherapy combination regimen for treatment-naïve patients with CLL/SLL.

Recommendations

- 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 Copiktra™ (duvelisib) with the following criteria listed in red

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

1. In combination with chlorambucil, bendamustine, or ibrutinib for first-line therapy; or
2. As a single-agent for relapsed or refractory disease.

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

1. As first-line or subsequent therapy for CLL/SLL; and
2. As a single-agent or in combination with bendamustine, rituximab, or obinutuzumab.

Imbruvica® (Ibrutinib) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. As first-line or subsequent therapy; and
2. As a single-agent or in combination with rituximab.

Venclexta® (Venetoclax) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Member meets 1 of the following:
    a. Member must be 75 years of age or older; or
    b. If the member is younger than 75 years of age, they must be unable to tolerate intensive induction chemotherapy; and
2. Must be used as first-line therapy; and
3. Must be used in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC).

Copiktra™ (Duvelisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of relapsed or refractory FL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. Must be used as a single-agent.

Copiktra™ (Duvelisib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. A diagnosis of relapsed or refractory CLL or SLL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. Must be used as a single-agent.

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[1] FDA News. FDA approves Copiktra for leukemia, lymphoma subtypes. *Healio*. Available online at: https://www.healio.com/hematology-oncology/leukemia/news/online/%7B46b7b1cf-8180-4811-965b-a3667938799a%7D/fda-approves-copiktra-for-leukemia-lymphoma-subtypes. Issued 09/25/2018. Last accessed 03/20/2019.

[2] U.S. Food and Drug Administration (FDA). FDA approves venetoclax for CLL or SLL, with or without 17p deletion, after one prior therapy. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm610308. Issued 06/08/2018. Last accessed 03/20/2019.

[3] FDA Approves Second-Line Venetoclax for CLL or SLL With or Without 17p Deletion. *The ASCO Post*. Available online at: http://www.ascopost.com/News/58930. Issued 06/08/2018. Last accessed 03/20/2019.

[4] Janssen Pharmaceuticals, Inc. U.S. FDA Approves Imbruvica (ibrutinib) Plus Rituximab as First Non-Chemotherapy Combination Regimen for Patients with Waldenström's Macroglobulinemia, a Rare Blood Cancer. Available online at: https://www.janssen.com/us-fda-approves-imbruvica-ibrutinib-plus-rituximab-first-non-chemotherapy-combination-regimen. Issued 08/27/2018. Last accessed 03/20/2019.

[5] AbbVie. Venclexta® (venetoclax) for Treatment of Newly-Diagnosed Acute Myeloid Leukemia Patients Ineligible for Intensive Chemotherapy. *PR Newswire*. Available online at: https://news.abbvie.com/news/abbvie-receives-us-fda-accelerated-approval-for-venclexta-venetoclax-for-treatment-newly-diagnosed-acute-myeloid-leukemia-patients-ineligible-for-intensive-chemotherapy.htm. Issued 11/21/2018. Last accessed 03/20/2019.

[6] Mulcahy N. FDA Approves First Nonchemo Regimen for CLL/SLL. *Medscape*. Available online at: https://www.medscape.com/viewarticle/908324?nlid=127747_4822&src=WNL_mdplsfeat_190205_mscpedit_phar&uac=255225HG&spon=30&impID=1877202&faf=1. Issued 01/28/2019. Last accessed 03/20/2019.

Appendix F

Vote to Prior Authorize Lutathera® (Lutetium Lu 177 Dotatate) and Vitrakvi® (Larotrectinib)

Oklahoma Health Care Authority
April 2019

Introduction[1,2,3,4]

Lutathera® (Lutetium Lu 177 Dotatate):

- **Therapeutic Class:** Radiolabeled somatostatin analog
- **Indication(s):** For the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults
- **How Supplied:** 370MBq/mL (10mCi/mL) in single-dose vials (SDVs)
- **Dose:** 7.4GBq (200mCi) via intravenous (IV) infusion every 8 weeks for a total of 4 doses; please refer to prescribing information for further details regarding appropriate administration of premedication and concomitant medications with lutetium Lu 177 dotatate

Vitrakvi® (Larotrectinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For the treatment of adult and pediatric patients with solid tumors that:
  - Have an neurotrophic receptor tyrosine kinase *(NTRK)* gene fusion without a known acquired resistance mutation; and
  - Are metastatic or where surgical resection is likely to result in severe morbidity; and
  - Have no satisfactory alternative treatments or that have progressed following treatment
    - This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response; continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- **How Supplied:** 25mg and 100mg capsules; 20mg/mL oral solution
- **Dose:**
  - Recommended dose in adult and pediatric patients with body surface area (BSA) $\geq 1.0 m^2$ is 100mg orally twice daily
  - Recommended dose in pediatric patients with BSA $<1.0 m^2$ is $100 mg/m^2$ orally twice daily

Recommendations

Lutathera® (Lutetium Lu 177 Dotatate) Approval Criteria [Gastroenteropancreatic Neuroendocrine Tumor (GEP-NET) Diagnosis]:

1. Diagnosis of progressive locoregional advanced disease or metastatic disease; and
2. Positive imaging of somatostatin receptor; and
3. Must be used as second-line or subsequent therapy following progression on octreotide or lanreotide; or
4. May be used first-line for treatment of pheochromocytoma/paraganglioma.

Vitrakvi® (Larotrectinib) Approval Criteria [Solid Tumors With Neurotrophic Receptor Tyrosine Kinase (*NTRK*) Gene Fusion Diagnosis]:

1. Diagnosis of a solid tumor with a *NTRK* gene fusion without a known acquired resistance mutation; and
2. Disease is metastatic or surgical resection (or radioactive iodine refractory if thyroid carcinoma) is contraindicated; and
3. Documentation of no satisfactory alternative treatments or progression following acceptable alternative treatments.

[1] U.S. Food and Drug Administration (FDA). FDA News Release: FDA approves new treatment for certain digestive tract cancers. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm594043.htm. Issued 01/26/2018. Last accessed 03/11/2019.

[2] Lutathera® Prescribing Information. Advanced Accelerator Applications. Available online at: https://s3-eu-west-1.amazonaws.com/s3-lutathera/wp-content/uploads/sites/4/2018/07/12102858/LUTATHERA_lutetium_Lu_177_dotatate_FDA_Prescribing_Information.pdf. Last revised 07/2018. Last accessed 03/11/2019.

[3] FDA News Release: FDA approves an oncology drug that targets a key genetic driver of cancer, rather than a specific type of tumor. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm626710.htm. Issued 11/26/2018. Last accessed 03/11/2019.

[4] Vitrakvi® Prescribing Information. Loxo Oncology, Inc. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/vitrakvi_PI.pdf. Last revised 11/2018. Last accessed 03/11/2019.

Appendix G

Calendar Year 2018 Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Lorbrena® (Lorlatinib), Mvasi® (Bevacizumab-awwb), and Vizimpro® (Dacomitinib)

Oklahoma Health Care Authority
April 2019

Introduction[1,2]

The American Cancer Society estimates that approximately 228,150 new lung cancer cases will be diagnosed in 2019, 84% of which are estimated to be non-small cell lung cancer (NSCLC).[2] 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. 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 October 2018 Drug Utilization Review (DUR) Board packet. These medications and criteria are reviewed annually with the skin cancer medications. Criteria for Keytruda® (pembrolizumab) for NSCLC has changes noted in red that are anticipated to be voted on by the DUR Board in the April 2019 DUR meeting.

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. Alectinib may be used in first-line or recurrent setting; and
4. Alectinib must be used 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. Brigatinib must be used 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. Ramucirumab must be used 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. Ramucirumab must be used 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. Member must have a Karnofsky performance score ≥60%; and
3. Ramucirumab must be used 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. Member must have a Karnofsky performance score ≥60%; and
4. Ramucirumab must be used as a single-agent or in combination with paclitaxel.

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. Afatinib when used in the first-line setting must be used 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. Afatinib when used in the second-line setting may be used 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. Afatinib must be used 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. 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*

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

1. BRAF V600E or V600K mutation detected by an FDA-approved test; and
   a. Trametinib is not indicated for wild-type BRAF NSCLC; and
2. Trametinib must be used 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. Nivolumab must be used 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. One of the following criteria is met:
   a. Disease relapsed within 6 months of initial chemotherapy; or
   b. Disease progression on initial chemotherapy; and
3. Nivolumab must be used 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 detected by an FDA-approved test; and
   a. Dabrafenib is not indicated for wild-type BRAF NSCLC; and
2. Dabrafenib must be used as a single-agent or in combination with Mekinist® (trametinib); and

3. Diagnosis of 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; ot
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. Erlotinib must be used as a single-agent only.

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

1. A diagnosis of pancreatic cancer; and
2. Locally advanced unresectable or metastatic disease; and
3. Erlotinib must be used as a first-line agent only; and
4. Erlotinib must be used 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 for surgically unresectable Stage IV disease; and
4. Erlotinib must be used 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. Erlotinib must be used 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. Erlotinib must be used in combination with gemcitabine.

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

1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease; and
3. Atezolizumab must be used as a single-agent only.

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

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and

2. Progressed on or following platinum-containing chemotherapy or cisplatin ineligible members.

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

1. A diagnosis of metastatic NSCLC (first-line or subsequent therapy); and
2. Anaplastic lymphoma kinase (ALK) or ROS1 positivity; or
3. MET amplification; and
4. Crizotinib must be used 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. ALK positivity; and
3. Crizotinib must be used 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. Used in combination with nivolumab.

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

1. BRAF V600E or V600K mutation; and
    a. Vemurafenib is not indicated for wild-type BRAF NSCLC
2. Vemurafenib must be used as a single-agent; and
3. A diagnosis of 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. Ceritinib must be used 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. ALK positivity; and
3. Ceritinib must be used as a single-agent only.

Utilization of Lung Cancer Medications: Calendar Year 2018

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
2017	17	113	$915,312.43	$8,100.11	$305.51	8,208	2,996
2018	15	105	$935,038.80	$8,905.13	$298.93	11,104	3,128
% Change	**-11.80%**	**-7.10%**	**2.20%**	**9.90%**	**-2.20%**	**35.30%**	**4.40%**
Change	**-2**	**-8**	**$19,726.37**	**$805.02**	**-$6.58**	**2,896**	**132**

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

Lung Cancer Medications Calendar Year Comparison: Medical Claims

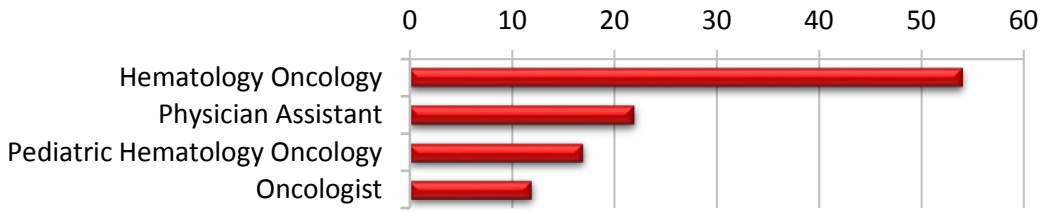
Calendar Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim
2017	456	1,722	$7,377,241.04	$4,284.11
2018	494	1,774	$9,389,203.93	$5,292.67
% Change	**8.33%**	**3.02%**	**27.27%**	**23.54%**
Change	**38**	**52**	**$2,011,962.89**	**$1,008.56**

*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

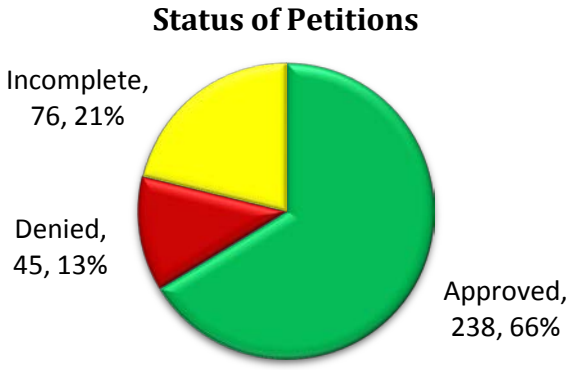
- Due to the small number of members utilizing lung cancer medications during calendar year 2018, detailed demographic information could not be provided.

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



Prior Authorization of Lung Cancer Medications

There were a total of 359 prior authorization requests submitted for 185 unique members for lung cancer medications during calendar year 2018. The following chart shows the status of submitted petitions for calendar year 2018.



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

Anticipated Patent Expiration(s):

- Tarceva® (erlotinib): May 2021
- Alimta® (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
- Lorbrena® (lorlatinib): March 2033
- Alunbrig® (brigatinib): April 2034
- Tagrisso® (osimertinib): January 2035

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

- **August 2018:** The FDA approved Opdivo® (nivolumab) for patients with metastatic SCLC with progression after platinum-based chemotherapy and at least 1 other line of therapy. This indication is accounted for in the current nivolumab prior authorization criteria.
- **August 2018:** The FDA updated the prescribing information for Keytruda® (pembrolizumab) and Tecentriq® (atezolizumab) to require the use of an FDA-approved companion diagnostic test to determine programmed death-ligand 1 (PD-L1) levels in tumor tissue from patients with locally advanced or metastatic urothelial cancer who are cisplatin-ineligible.
- **August 2018:** The FDA approved Keytruda® (pembrolizumab) for use in combination with Alimta® (pemetrexed) and platinum as first-line treatment of patients with metastatic, non-squamous (NSq) NSCLC, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations. Criteria for pembrolizumab for this indication was presented to the DUR Board in October 2017.
- **September 2018:** The FDA approved Mvasi® (bevacizumab-awwb) as a biosimilar to Avastin® (bevacizumab) for the treatment of multiple types of cancer including

metastatic colorectal cancer, NSq NSCLC, glioblastoma, metastatic renal cell carcinoma (mRCC), and cervical cancer.

- **September 2018:** The FDA approved Vizimpro® (dacomitinib) for the first-line treatment of patients with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations.
- **October 2018:** The FDA approved Keytruda® (pembrolizumab) for use in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic, squamous NSCLC. Criteria for pembrolizumab for this indication was presented to the DUR Board in March 2019.
- **November 2018:** The FDA approved Lorbrena® (lorlatinib) for patients with ALK-positive metastatic NSCLC whose disease has progressed on crizotinib and at least 1 other ALK inhibitor for metastatic disease or whose disease has progressed on alectinib or ceritinib as the first ALK inhibitor therapy for metastatic disease.
- **November 2018:** The FDA approved Keytruda® (pembrolizumab) for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with Nexavar® (sorafenib). Criteria for pembrolizumab for this indication was presented to the DUR Board in March 2019.
- **December 2018:** The FDA approved Tecentriq® (atezolizumab) in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of patients with metastatic NSq NSCLC with no EGFR or ALK genomic tumor aberrations.
- **December 2018:** The FDA approved Keytruda® (pembrolizumab) for the treatment of recurrent, locally advanced or metastatic Merkel cell carcinoma (MCC) in adult and pediatric patients. Criteria for pembrolizumab for this indication was presented to the DUR Board in March 2019.
- **February 2019:** The FDA approved Keytruda® (pembrolizumab) for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection. Criteria for pembrolizumab for this indication was presented to the DUR Board in March 2019.
- **March 2019:** The FDA approved Tecentriq® (atezolizumab) for PD-L1 positive, unresectable, locally advanced or metastatic triple-negative breast cancer.
- **March 2019:** The FDA approved Tecentriq® (atezolizumab) in combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage SCLC.

Safety Update(s):

- **March 2019:** The FDA issued a warning regarding the risks associated with the investigational use of Venclexta® (venetoclax) for the treatment of patients with multiple myeloma. Venetoclax is not approved for the treatment of multiple myeloma. The FDA reviewed data from the BELLINI clinical trial evaluating the use of venetoclax with Velcade® (bortezomib) and dexamethasone in patients with multiple myeloma, and the interim trial results demonstrated an increased risk of death for patients receiving venetoclax as compared to the control group. The FDA is requiring that no new patients be enrolled in the BELLINI trial. Patients taking venetoclax for an approved indication should continue to take their medication as directed by their health care professional.

Product Summaries[7,8,9]

Lorbrena® (Lorlatinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Patients with ALK-positive, metastatic NSCLC whose disease has progressed on:
    - Crizotinib and at least 1 other ALK inhibitor for metastatic disease; or
    - Alectinib as the first ALK inhibitor therapy for metastatic disease; or
    - Ceritinib as the first ALK inhibitor therapy for metastatic disease
  - This indication was approved under accelerated approval based on tumor response rate and duration of response; continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial
- **How Supplied:** 25mg or 100mg oral tablets
- **Dose:** 100mg by mouth once daily
- **Cost:** Wholesale Acquisition Cost (WAC) of $535.19 per 100mg tablet, resulting in a monthly cost of $16,055.70

Mvasi® (Bevacizumab-awwb):

- **Therapeutic Class:** Vascular endothelial growth factor (VEGF)-specific angiogenesis inhibitor
- **Indication(s):**
  - Metastatic colorectal cancer, with intravenous (IV) 5-fluorouracil (5FU)-based chemotherapy for first- or second-line treatment
  - Metastatic colorectal cancer, with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab-containing regimen
  - NSq NSCLC, with carboplatin and paclitaxel for first-line treatment of unresectable, locally advanced, recurrent or metastatic disease
  - Glioblastoma, as a single-agent for adult patients with progressive disease following prior therapy
  - mRCC with interferon alfa
  - Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan
- **How Supplied:** 100mg/4mL and 400mg/16mL single-dose vials for IV infusion
- **Dose:**
  - Metastatic Colorectal Cancer:
    - 5mg/kg IV every 2 weeks with bolus irinotecan/leucovorin/5FU; or
    - 1 mg/kg IV every 2 weeks with leucovorin/5FU/oxaliplatin; or
    - 5mg/kg IV every 2 weeks or 7.5mg/kg IV every 3 weeks with fluoropyrimidine/irinotecan- or fluoropyrimidine/oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab-containing regimen
  - NSq NSCLC: 15mg/kg IV every 3 weeks

- Glioblastoma: 10mg/kg IV every 2 weeks
- mRCC: 10mg/kg IV every 2 weeks
- Cervical Cancer: 15mg/kg IV every 3 weeks

- **Cost:** Not yet available

Vizimpro® (Dacomitinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** First-line treatment of patients with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations
- **How Supplied:** 15mg, 30mg, or 45mg oral tablets
- **Dose:** 45mg by mouth once daily
- **Cost:** WAC of $413.33 per 45mg oral tablet, resulting in a monthly cost of $12,399.90

Recommendations

- The prior authorization of Lorbrena® (lorlatinib), Mvasi® (bevacizumab-awwb), and Vizimpro® (dacomitinib) 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

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. Used as a single-agent as second-line therapy following disease progression on either alectinib or ceritinib; or
4. Used 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).

Mvasi® (Bevacizumab-awwb) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Avastin® (bevacizumab) which is available without prior authorization.

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. Atezolizumab must be used 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. Atezolizumab must be used 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. Atezolizumab must be used 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).

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.

Utilization Details of Lung Cancer Medications: Calendar Year 2018

Pharmacy Claims: Calendar Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	29	5	$149,553.93	5.8	$5,157.03
MEKINIST TAB 2MG	21	3	$226,647.25	7	$10,792.73
SUBTOTAL	**50**	**8**	**$376,201.18**	**6.25**	**$7,524.02**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	25	3	$233,643.54	8.33	$9,345.74
SUBTOTAL	**25**	**3**	**$233,643.54**	**8.33**	**$9,345.74**
DABRAFENIB PRODUCTS					
TAFINLAR CAP 75MG	12	1	$119,297.04	12	$9,941.42
SUBTOTAL	**12**	**1**	**$119,297.04**	**12**	**$9,941.42**
ALECTINIB PRODUCTS					
ALECENSA CAP 150MG	9	1	$130,670.38	9	$14,518.93
SUBTOTAL	**9**	**1**	**$130,670.38**	**9**	**$14,518.93**
ERLOTINIB PRODUCTS					
TARCEVA TAB 150MG	6	1	$50,750.70	6	$8,458.45
SUBTOTAL	**6**	**1**	**$50,750.70**	**6**	**$8,458.45**
AFATINIB PRODUCTS					
GILOTRIF TAB 20MG	2	1	$16,314.64	2	$8,157.32
GILOTRIF TAB 30MG	1	1	$8,161.32	1	$8,161.32
SUBTOTAL	**3**	**2**	**$24,475.96**	**1.5**	**$8,158.65**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	29	5	$149,553.93	5.8	$5,157.03
MEKINIST TAB 2MG	21	3	$226,647.25	7	$10,792.73
SUBTOTAL	**50**	**8**	**$376,201.18**	**6.25**	**$7,524.02**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	25	3	$233,643.54	8.33	$9,345.74
SUBTOTAL	**25**	**3**	**$233,643.54**	**8.33**	**$9,345.74**
TOTAL	**105**	**15***	**$935,038.80**	**7**	**$8,905.13**

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

Medical Claims: Calendar Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9035 BEVACIZUMAB INJECTION	1,078	347	$2,281,160.64	$2,116.10
J9299 NIVOLUMAB INJECTION	381	75	$3,223,007.04	$8,459.33
J9271 PEMBROLIZUMAB INJECTION	190	46	$1,983,600.42	$10,440.00
J9305 PEMETREXED INJECTION	133	31	$829,148.36	$6,234.20
J9228 IPILIMUMAB INJECTION	32	17	$758,192.04	$23,693.50
J9308 RAMUCIRUMAB INJECTION	16	6	$157,849.43	$9,865.59
J9022 ATEZOLIZUMAB INJECTION	15	6	$156,246.00	$10,416.40
TOTAL	**1,774[+]**	**494***	**$9,389,203.93**	**$5,292.67**

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

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[1] National Comprehensive Cancer Network. Non-small cell lung cancer (Version 43.2019). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Last revised 01/18/2019. Small cell lung cancer (Version 1.2019). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Last revised 10/10/2018. Last accessed 03/25/2019.

[2] American Cancer Society. Cancer Facts & Figures 2019. Available online at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf. Last accessed 03/19/2019.

[3] 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 02/2019. Last accessed 03/19/2019.

[4] FDA. Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Last revised 03/19/2019. Last accessed 03/19/2019.

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[6] FDA. FDA Warns about the risks associated with the investigational use of Venclexta in Multiple Myeloma. Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm634120.htm?utm_campaign=FDA%20warns%20about%20the%20risks%20associated%20with%20the%20investigational%20use%20of%20Venclexta&utm_medium=email&utm_source=Eloqua. Issued 03/21/2019. Last accessed 03/26/2019.

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[8] Mvasi® Prescribing Information. Amgen, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761028s000lbl.pdf. Last revised 09/2017. Last accessed 03/20/2019.

[9] Vizimpro® Prescribing Information. Pfizer, Inc. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=11019. Last revised 09/2018. Last accessed 03/20/2019.

Appendix H

Fiscal Year 2018 Annual Review of the SoonerCare Pharmacy Benefit

Oklahoma Health Care Authority
April 2019

Summary[1,2,3,4]

During State Fiscal Year (SFY) 2018, prescription drugs accounted for $543 million of the approximate $5.3 billion in total SoonerCare funding. According to the Centers for Medicare and Medicaid Services (CMS), national health spending is projected to grow at an average rate of 5.5% annually and Medicaid expenditures are expected to grow at a rate of 5.8% annually. Comparing SoonerCare pharmacy data from SFY 2017, the total reimbursement increased by 5.7% from SFY 2017 to 2018, less than the CMS-estimated Medicaid expenditure increases. The pharmacy cost per member per year (PMPY; total pharmacy cost per total members) increased from $506.47 in SFY 2017 to $532.62 in 2018, a 4.9% increase. Reimbursement increases per member can largely be attributed to the increase in cost per claim for specialty medications as well as an increase in the number of claims for specialty medications. Recently, the specialty pharmaceutical products total pharmacy reimbursement has been on the incline as a result of orphan drug approvals for rare diseases and the high costs associated with these therapies. During SFY 2017, SoonerCare spent 37.7% of total pharmacy expenditures on 0.84% of claims for medications costing greater than $1,000 per claim and in SFY 2018, spent 42.6% of total pharmacy expenditures on 0.92% of claims for medications costing greater than $1,000 per claim. Claims costing greater than $1,000 per claim are largely specialty medications but may include some traditional medications.

Due to new federal regulations, SoonerCare implemented a new pricing methodology for pharmacy claims reimbursement on January 3, 2017. Ingredient reimbursement changed from an estimated acquisition cost (EAC) to an actual acquisition cost (AAC). In addition, the professional dispensing fee increased from $3.60 in 2016 to $10.55 starting in January 2017; professional dispensing fees are included in the reimbursement totals in the following report. The impact of the pricing methodology and dispensing fee change are estimated to be budget neutral. This change in reimbursement should be considered when evaluating reimbursement changes from year to year. Medications with a very low cost per claim and large volume of claims will appear to increase in price due to the increase in dispensing fee; however, these increases will be neutralized by changes in ingredient reimbursement for higher cost medications. Further, Indian Health Service (IHS) reimbursement was updated to the Federal Office of Management and Budget (OMB) encounter rate. In order to more accurately compare SFY 2018 with previous fiscal years, IHS data was excluded from the analysis.

Costs in this report do not reflect the federal and state supplemental rebates that are provided by medication manufacturers. Many products, particularly the Hepatitis C antiviral medications, attention-deficit/hyperactivity disorder (ADHD) medications, antipsychotic medications, endocrine medications, and pain medications are heavily influenced by supplemental rebates

and net costs are substantially lower than the total reimbursement to pharmacies shown in this analysis.

Total Pharmacy State Fiscal Year (SFY) Comparison							
SFY	**Claims**	**Members**	**Utilizers***	**Reimbursement**	**Cost/Claim**	**Cost/Member**	**Cost/Day**
2016	5,891,156	1,052,826	542,290	$495,171,030	$84.05	$470.33	$3.32
2017	5,897,218	1,014,983	541,021	$514,062,768	$87.17	$506.47	$3.40
2018	5,802,025	1,020,726	535,823	$543,569,067	$93.70	$532.62	$3.61

*Total number of unduplicated utilizers.
Reimbursement does not reflect rebated costs or net costs.

The per member per year (PMPY) value reflects the total pharmacy cost divided by the unduplicated number of members (total enrollees) for each time period. In order to reflect an accurate PMPY value, average monthly enrollment is used in place of annual enrollment, and dual eligible and IHS members are excluded. The PMPY value is used across benefit plans with similar populations to accurately assess healthcare spending. The following table contains the adjusted PMPY values for the last 3 years.

Calendar Year	CY 2016	CY 2017	CY 2018
Adjusted PMPY	$715	$735	$803

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

To measure the success of the SoonerCare pharmacy benefit management, Oklahoma's Medicaid statistics were compared to the Medicaid statistics of the largest PBM in the United States, Express Scripts (ESI). For CY 2017, ESI's Medicaid PMPY was $1,241 – 69% higher than OHCA's $735. If OHCA had experienced the same PMPY as ESI for CY 2017, it would have cost over $359 million more than the $521 million spent. Similarly, for CY 2018, ESI's Medicaid PMPY was $1,342 – 67% higher than OHCA's $803. At the ESI PMPY rate, it would have cost over $371 million more than the $554 million spent during CY 2018 for pharmacy reimbursement.

Calendar Year	ESI	OHCA	Percent Difference
2016	$1,196	$715	67%
2017	$1,241	$735	69%
2018	$1,342	$803	67%

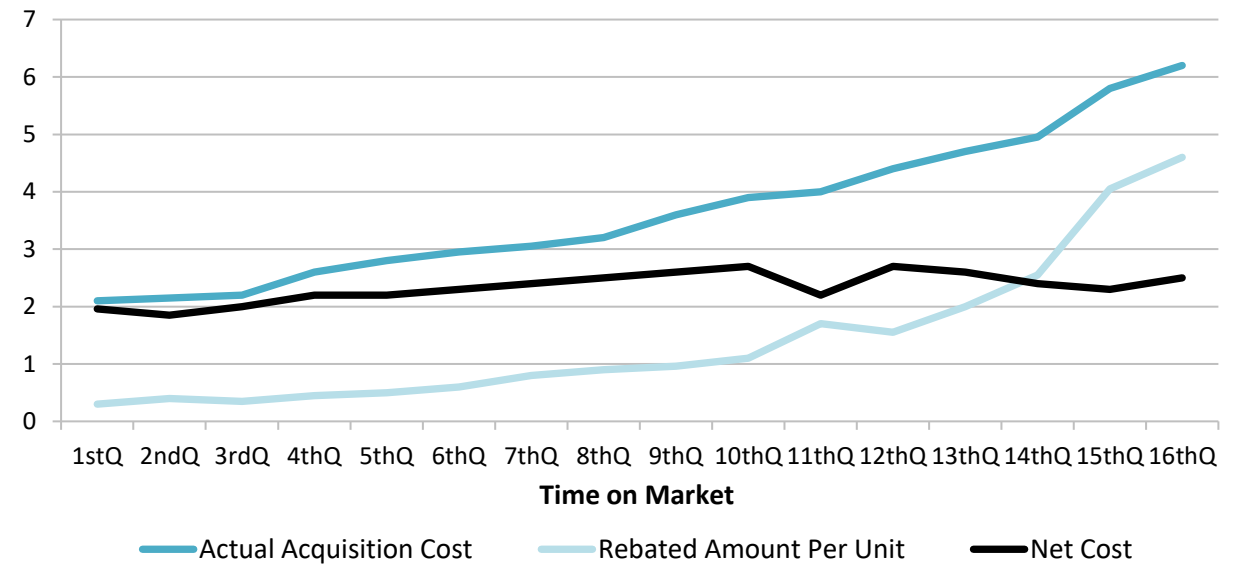
SoonerCare prior authorization policies, coupled with quantity limits and monthly prescription limits, yield better than average results while still providing a comprehensive pharmacy benefit for approximately 800,000 SoonerCare members. Looking at the cost to manage the pharmacy benefit, the OHCA pharmacy department has a cost of about $1 million. OHCA's partner, PMC,

spent about $4 million of their $4.4 million contract in recent years. As a return on investment (ROI), using the overage generated by the ESI PMPY rate, for CY 2017 the ROI is $72 to $1 and for 2018 it is $74 to $1.

Medicaid Drug Rebate Program[5,6,7]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Participation in the federal drug rebate program requires Medicaid coverage with limited exceptions (e.g., cosmetic medications, fertility medications). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any commercial payer. Best prices are reported to CMS by the manufacturer, but are not publicly available.

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



Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. In SFY 2018, OHCA collected $331 million in federal rebates and $20 million in state supplemental rebates, resulting in a total increase in rebate collection from SFY 2017 ($283 million federal; $22 million state). These rebates are collected after reimbursement for the medication and are not reflected in this report.

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

The introduction of a greater number of costly specialty medications, finite Medicaid budgets, and Medicaid policy and access requirements has resulted in alternative payment arrangements as particularly compelling opportunities. Medicaid programs must provide comprehensive care to vulnerable individuals while operating under limited budgets and regulatory requirements. An alternative payment model (APM) is an agreement between a payer and manufacturer that is intended to provide improved patient care or increased access to evidence-based therapies while lowering costs or improving health outcomes. In general, there are 2 types of APMs:

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

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

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

IV = intravenous

Drug Approval Trends[14,15,16]

During SFY 2018, the U.S. Food and Drug Administration (FDA) approved the first generic product of several key medications that may have a significant effect on SoonerCare reimbursement. The first generic for Strattera® (atomoxetine) was FDA approved in May 2017. Based on supplemental rebates, brand Strattera® was preferred during all of SFY 2017; however, in August 2017 (SFY 2018) SoonerCare updated to prefer generic atomoxetine. This will most likely have a significant effect on reimbursement, as Strattera® has been one of the top 10 drugs by reimbursement for the past 3 years. Other key first time generic approvals during SFY 2018 include Effient® (prasugrel tablets) in July 2017, Tamiflu® (oseltamivir oral suspension) in September 2017, Suboxone® (buprenorphine/naloxone films) in June 2018, Makena® (hydroxyprogesterone caproate injection) in June 2018, and Aubagio® (teriflunomide tablets) in July 2018.

A total of 59 novel drugs were approved by the FDA during calendar year 2018. The active ingredient or ingredients in a novel drug have never before been approved in the United States. Of the novel drugs approved, 19 were considered first in class and 34 were approved to treat rare or "orphan" diseases.

Select Novel Drugs Approved During Calendar Year 2018

Drug Name	Date Approved	FDA-Approved Indication	Estimated Annual Cost*
Firdapse® (amifampridine)	11/28/2018	Treatment for adults with Lambert-Eaton myasthenic syndrome (LEMS)	$184,928
Vitrakvi® (larotrectinib)	11/26/2018	Treatment for patients with cancers that have a specific genetic biomarker	$393,602
Yupelri™ (revefenacin)	11/09/2018	Treatment for adults with chronic obstructive pulmonary disease (COPD)	$12,355
Onpattro® (patisiran)	08/10/2018	Treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults	$484,500
Orilissa® (elagolix)	07/23/2018	Management of moderate-to-severe pain associated with endometriosis	$10,137
Epidiolex® (cannabidiol)	06/25/2018	Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years and older	$22,230
Palynziq™ (pegvaliase-pqpz)	05/24/2018	Treatment for adults with phenylketonuria (PKU)	$177,632-$355,264
Aimovig™ (erenumab-aooe)	05/17/2018	Preventative treatment for adults with migraines	$6,687
Crysvita® (burosumab-twza)	04/17/2018	Treatment for adults and children with x-linked hypophosphatemia (XLH)	$88,400 - $795,600
Symdeko® (tezacaftor/ivacaftor)	02/12/2018	Treatment of cystic fibrosis (CF) in patients 12 years and older	$291,200

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

Traditional Versus Specialty Pharmacy Products

Traditional pharmaceuticals include products that are typically non-injectable and do not require special transportation, storage, administration, and are not typically indicated for rare diseases requiring unique management. These products treat many common chronic diseases such as diabetes, hypertension (HTN), and chronic obstructive pulmonary disease (COPD). Traditional pharmaceuticals carry the bulk of the reimbursement costs accounting for 83.2% of the total pharmacy reimbursement and more than 99% of utilizers in SFY 2018. Specialty products, in contrast, are typically injectable and require special handling such as refrigerated transport and special administration techniques or are indicated for rare diseases requiring unique management. These products include treatments for cystic fibrosis (CF), hemophilia, rheumatoid arthritis (RA), and genetic deficiencies, for example. Specialty pharmaceuticals have become a larger part of reimbursement over the last 5 years, now comprising close to 17% of the total expenditures. Newly FDA approved therapies for RA and dermatological conditions have led to an increase in specialty pharmaceutical expenditures this past year.

Top 10 Therapeutic Classes by Reimbursement: Fiscal Year 2018[17,18,19,20,21]

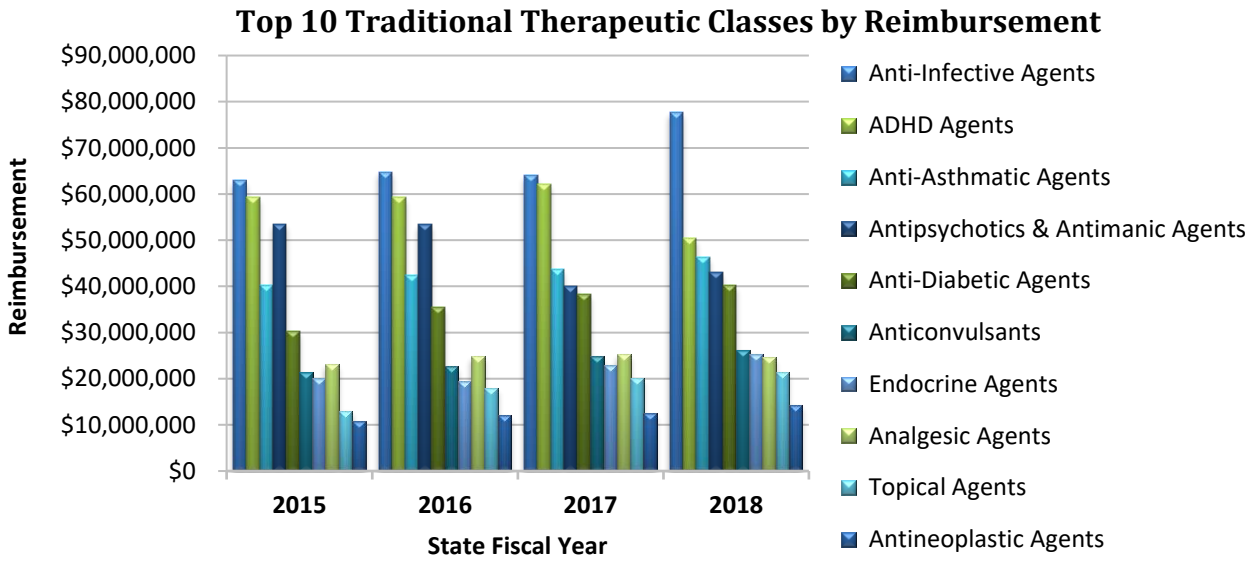
Traditional Top 10 Classes by Reimbursement				
2015	2016	2017	2018	Therapeutic Class
$62,972,086	$64,753,193	$63,996,676	**$77,754,042**	**Anti-Infective Agents**
$59,222,643	$59,210,124	$62,118,533	**$50,326,685**	**ADHD Agents**
$40,250,424	$42,407,875	$43,565,926	**$46,258,925**	**Anti-Asthmatic Agents**
$53,508,208	$53,434,190	$39,977,374	**$43,111,772**	**Antipsychotics/Antimanic Agents**
$30,259,419	$35,416,629	$38,298,122	**$40,247,671**	**Anti-Diabetic Agents**
$21,264,626	$22,587,039	$24,851,122	**$26,190,057**	**Anticonvulsants**
$20,090,703	$19,378,355	$22,954,966	**$25,402,170**	**Endocrine Agents**
$23,157,175	$24,729,391	$25,210,044	**$24,633,644**	**Analgesic Agents**
$12,977,166	$17,927,089	$20,067,381	**$21,345,644**	**Topical Agents**
$10,780,515	$12,125,906	$12,518,084	**$14,310,913**	**Antineoplastic Agents**

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

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

- The anti-infective agent reimbursement increased by $13 million; $3 million of which is from an increase in utilization of anti-influenza treatments alone. According to the Centers for Disease Control and Prevention (CDC), the 2017 to 2018 influenza season was considered “high severity”. The other $10 million comes from the newer hepatitis C treatments, and the removal of the minimum fibrosis score requirement resulting in substantial increases in utilization and subsequently reimbursement.
- Reimbursement declined by more than $11.7 million in the ADHD agents category. Cost reductions in the ADHD class are due to reassessment of tier structure based on net costs as well as multiple manufacturers of generic atomoxetine getting FDA approval for marketing in May 2017, along with increased availability of other generic stimulant medications.

- Antipsychotic reimbursement increases can be accounted for by increased utilization of long-acting injectable antipsychotics as well as utilization of brand formulation oral medications. Many medications in this class do have supplemental rebates in place with Oklahoma Medicaid and net cost increases are not reflected in this analysis.
- The anti-diabetic medications saw a $1.9 million spending increase from SFY 2017. These products have significant federal rebates designed to keep the Medicaid net cost relatively flat; however, rebates are not accounted for in this analysis.
- Analgesic agents saw more than a $575,000 decline in reimbursement from SFY 2017 to 2018 as a result of numerous opioid anlagesic initiatives intended to encourage guideline-recommended prescribing and utilization of opioid analgesics.
- Reimbursement for topical medications increased by $1.2 million this past SFY, a result of FDA approval of new medications for the treatment of atopic dermatitis. The FDA approved Eucrisa® (crisaborole) in December 2016 for the treatment of mild-to-moderate eczema (atopic dermatitis) in patients 2 years of age and older. Crisaborole is an appropriate treatment option particularly for patients who have eczema on the face or groin where topical corticosteroids are not appropriate. Utilization of crisaborole in SFY 2018 accounted for more than $1 million of the $1.2 million reimbursement increase from SFY 2017. Crisaborole is a supplementally rebated medication and net cost increases are not reflected in this analysis.
- Lung cancer medications increased by $2 million since 2017, accounting for the increase in antineoplastic agents. Medications in this category can be used for several different types of cancer of which the data does not differentiate.
- Costs in this report do not reflect the federal and state supplemental rebates that are provided by medication manufacturers. Many branded products, particularly the anti-infective agents, ADHD agents, antipsychotic agents, endocrine agents, and analgesic agents are heavily influenced by supplemental rebates and net costs are substantially lower than the total reimbursement paid to pharmacies shown in this analysis.

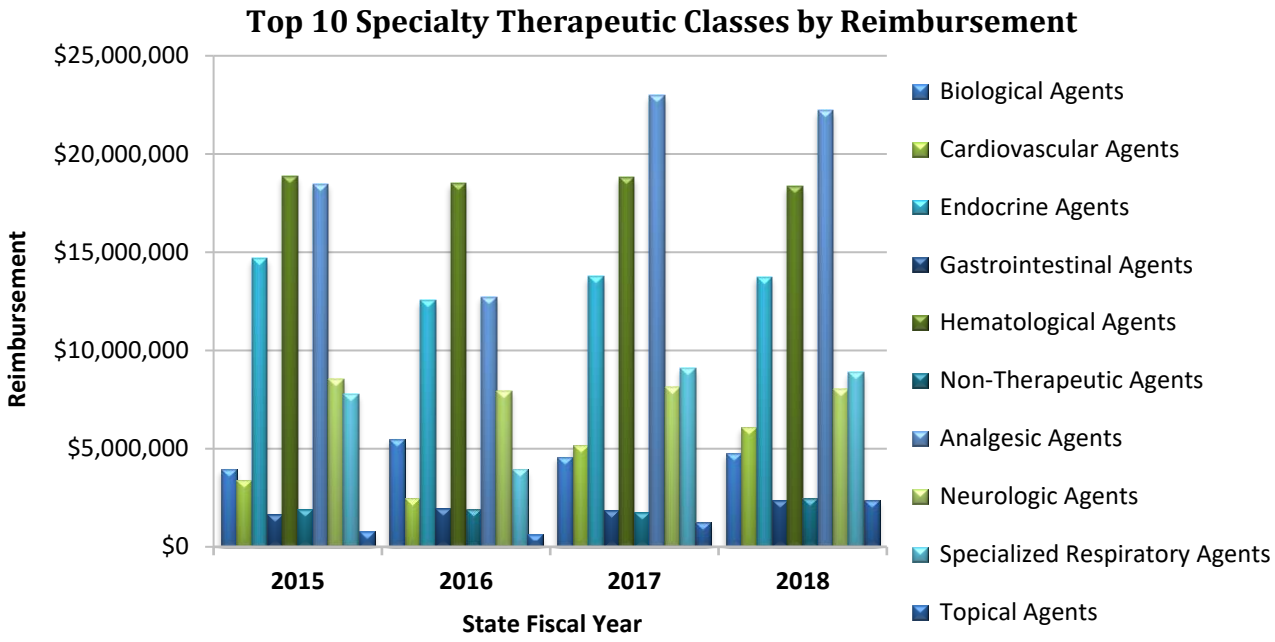


Specialty Top 10 Classes by Reimbursement				
2015	2016	2017	2018	Therapeutic Class
$12,732,939	$18,481,116	$22,988,676	**$22,236,627**	**Analgesic Agents**
$18,497,494	$18,852,788	$18,813,132	**$18,339,418**	**Hematological Agents**
$12,528,464	$14,684,343	$13,782,182	**$13,738,382**	**Endocrine Agents**
$3,959,014	$7,754,987	$9,093,408	**$8,860,036**	**Specialized Respiratory Agents**
$7,930,952	$8,540,617	$8,139,124	**$8,035,140**	**Neurologic Agents**
$2,441,564	$3,387,174	$5,143,843	**$6,071,976**	**Cardiovascular Agents**
$5,459,825	$3,935,198	$4,581,237	**$4,745,569**	**Biological Agents**
$1,930,027	$1,928,230	$1,780,090	**$2,473,095**	**Non-Therapeutic Agents**
$638,208	$793,104	$1,253,685	**$2,380,074**	**Topical Agents**
$1,962,601	$1,642,701	$1,856,032	**$2,360,853**	**Gastrointestinal Agents**

Costs do not reflect rebated prices or net costs.

Specialty therapeutic products costs are high largely in part due to biologic therapies and the therapies focused on rare diseases including CF, hemophilia, and pulmonary arterial hypertension (PAH). Continuous review and management of biological agents and gastrointestinal agents has promoted minimal reimbursement increases other than expected yearly price increases by product manufacturers and declines in reimbursement for analgesic agents, hematological agents, endocrine agents, specialized respiratory agents, and neurologic agents.

- The cost of specialty analgesic agents declined for the first time in several fiscal years. Reimbursement in this class is largely attributed to targeted immunomodulatory agents such as Humira® (adalimumab), Enbrel® (etanercept), Ilaris® (canakinumab), Orencia® (abatacept), Simponi® (golimumab), Xeljanz® (tofacitinib), Otezla® (apremilast), and Kineret® (anakinra). The majority of utilization was seen in Tier-2 medications, which are supplementally rebated medications. The supplementally rebated prices and net costs are not reflected in this analysis.
- Cardiovascular agents saw a significant increase in reimbursement from SFY 2017 to 2018. Reimbursement for the specialty cardiovascular agents is largely comprised of medications indicated to treat PAH. Both the number of members utilizing PAH medications as well as the number of claims increased in SFY 2018 compared to SFY 2017 accounting for virtually all of the $928,133 increase.
- Topical agents saw the largest increase in reimbursement from SFY 2017 to 2018. This class includes medications indicated for psoriasis and atopic dermatitis. Dupixent® (dupilumab) was FDA approved in March 2017 and was the first biologic medication to treat atopic dermatitis in patients whose eczema was not adequately controlled by topical therapies. Utilization of dupilumab in SFY 2018 accounted for $460,883 of the $1.1 million reimbursement increase from SFY 2017. Other increases can be accounted for by increased utilization of Cosentyx® (secukinumab) following FDA approval of several new indications including for the treatment of moderate-to-severe scalp psoriasis in February 2018.



Top 10 Medications by Reimbursement: Fiscal Year 2018

Most of the top 10 medications by reimbursement are still branded at this time and not available in a generic formulation. Oseltamivir jumped from the 9th spot to the 6th ranking in SFY 2018 due to the influenza epidemic as mentioned earlier in this report. Insulin glargine has decreased in ranking due to market competition. Aripiprazole and atomoxetine have fallen out of the top 10 due to generic availability and subsequent lower costs. The top products typically come from highly utilized classes such as atypical antipsychotics, ADHD therapies, respiratory medications, including rescue and maintenance therapies, and the anti-infective class, including antiviral medications for hepatitis C. Top drug reimbursement rankings change from year to year only slightly for several reasons: high use, broad use between age demographics, and high costs of new therapies such as those indicated for hepatitis C.

Top 10 Medications by Reimbursement*				
Rank	**2015**	**2016**	**2017**	**2018**
1	aripiprazole	lisdexamfetamine	lisdexamfetamine	**lisdexamfetamine**
2	lisdexamfetamine	aripiprazole	ledipasavir/sofosbuvir	**paliperidone inj**
3	albuterol	ledipasavir/sofosbuvir	paliperidone inj	**ledipasavir/sofosbuvir**
4	methylphenidate	methylphenidate	methylphenidate	**albuterol**
5	sofosbuvir	albuterol	albuterol	**adalimumab**
6	oseltamivir	paliperidone inj	adalimumab	**oseltamivir**
7	ledipasavir/sofosbuvir	atomoxetine	atomoxetine	**methylphenidate**
8	insulin glargine	adalimumab	insulin glargine	**lurasidone**
9	guanfacine ER	insulin glargine	oseltamivir	**sofosbuvir/velpatasvir**
10	atomoxetine	sofosbuvir	somatropin inj	**insulin glargine**

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

Cost Per Claim

Claims for generic medications made up 83.6% of the volume while only accounting for 27.1% of the reimbursement amount in SFY 2018. The SoonerCare cost per claim of traditional medications rose by 8.4% in SFY 2018 in comparison to SFY 2017, and the cost per specialty claim increased by 3.1%. As mentioned previously, specialty costs are largely driven by the significant cost associated with medications for rare diseases.

Cost per Claim			
Drug Class	**SFY 2016**	**SFY 2017**	**SFY 2018**
Traditional	$70.31	$72.13	$78.16
Specialty	$4,984.75	$5,321.87	$5,485.05

Reimbursement does not reflected rebated costs or net costs.

Conclusion

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

Top 100 Reimbursed Drugs by Fiscal Year

Top 100 Reimbursed Drugs by Fiscal Year		SFY 2018		SFY 2017	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
lisdexamfetamine	Vyvanse	**1**	**$25,086,619.83**	1	$23,954,004.55
paliperidone injection	Invega Trinz/Sust	**2**	**$17,612,374.59**	3	$14,324,277.92
ledipasvir/sofosbuvir	Harvoni	**3**	**$15,933,872.05**	2	$14,625,414.97
albuterol	Multiple Products	**4**	**$14,897,379.33**	5	$13,946,946.82
adalimumab	Humira	**5**	**$14,163,188.51**	6	$13,348,634.96
oseltamivir	Tamiflu*	**6**	**$11,642,564.82**	9	$8,731,566.07
methylphenidate	Multiple Products	**7**	**$10,302,880.07**	4	$14,211,904.52
lurasidone	Latuda	**8**	**$9,754,545.62**	12	$8,025,256.20
sofosbuvir/velpatasvir	Epclusa	**9**	**$9,545,422.66**	14	$7,069,087.91
insulin glargine	Lantus/Toujeo	**10**	**$8,989,940.75**	8	$9,175,011.68
somatropin	Multiple Products	**11**	**$8,860,134.27**	10	$8,304,384.02
fluticasone inhalation	Flovent	**12**	**$8,713,522.09**	11	$8,251,000.69
fluticasone/salmeterol	Advair	**13**	**$7,724,395.78**	19	$5,405,558.38
insulin aspart	Novolog	**14**	**$7,691,280.39**	13	$7,618,874.60
lumacaftor/ivacaftor	Orkambi	**15**	**$6,824,219.89**	16	$6,580,338.71
hydroxyprogesterone caproate	Makena	**16**	**$6,658,862.97**	18	$5,962,535.57
etanercept	Enbrel	**17**	**$6,493,382.51**	17	$6,348,980.27
ciprofloxacin/dexamethasone otic	Ciprodex	**18**	**$5,814,720.61**	21	$5,187,832.67
antiinhibitor coagulant complex	Feiba	**19**	**$5,780,915.33**	40	$2,497,213.00
oxycodone	Multiple Products	**20**	**$5,500,196.87**	15	$6,964,663.98
elbasvir/grazoprevir	Zepatier	**21**	**$5,244,710.30**	68	$1,543,340.25
dexmethylphenidate	Focalin*	**22**	**$4,940,696.71**	26	$4,419,315.74
insulin lispro	Humalog	**23**	**$4,884,230.20**	24	$4,591,398.21
insulin detemir	Levemir	**24**	**$4,859,296.17**	22	$4,906,607.94
buprenorphine/naloxone	Multiple Products	**25**	**$4,712,276.44**	28	$4,140,795.80
Blood glucose test strips	Multiple Products	**26**	**$4,453,999.93**	27	$4,395,990.24
aripiprazole	Abilify*	**27**	**$4,301,167.33**	23	$4,635,410.47
glecaprevir/pibrentasvir	Mavyret	**28**	**$4,173,662.90**	NA	****
clobazam	Onfi*	**29**	**$4,113,164.13**	33	$3,311,213.10
atomoxetine	Strattera*	**30**	**$4,073,782.53**	7	$13,135,839.23
amphetamine/ dextroamphetamine	Multiple Products	**31**	**$4,070,259.95**	25	$4,548,721.03
pregabalin	Lyrica	**32**	**$4,037,343.89**	30	$4,098,391.34
lacosamide	Vimpat	**33**	**$3,974,274.79**	31	$3,642,713.25
antihemophilic factor (recombinant)	Multiple Products	**34**	**$3,628,231.20**	29	$4,112,292.00
nusinersen	Spinraza	**35**	**$3,571,541.65**	NA	****
epinephrine	Multiple Products	**36**	**$3,236,337.27**	20	$5,380,707.65
tiotropium	Spiriva	**37**	**$3,155,794.85**	35	$3,000,855.71

Top 100 Reimbursed Drugs by Fiscal Year		SFY 2018		SFY 2017	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
dornase alfa	Pulmozyme	**38**	**$3,054,487.66**	34	$3,037,127.57
sildenafil	Revatio*	**39**	**$2,911,996.07**	59	$1,787,647.45
ivermectin	Sklice	**40**	**$2,894,794.20**	38	$2,693,631.58
hydrocodone/acetaminophen	Multiple Products	**41**	**$2,869,336.68**	32	$3,334,546.79
palivizumab	Synagis	**42**	**$2,734,231.87**	37	$2,785,035.85
sitagliptin	Januvia	**43**	**$2,667,189.78**	44	$2,412,513.31
pancrelipase	Multiple Products	**44**	**$2,594,038.12**	42	$2,469,781.19
amoxicillin	Amoxil*	**45**	**$2,532,282.58**	46	$2,215,229.54
liraglutide	Victoza	**46**	**$2,419,030.61**	54	$1,901,436.32
cetirizine	Multiple Products	**47**	**$2,387,645.36**	53	$1,922,062.15
montelukast	Singulair*	**48**	**$2,309,465.98**	48	$2,110,167.33
deferasirox	Jadenu/Exjade	**49**	**$2,300,173.66**	64	$1,642,546.27
ivacaftor	Kalydeco	**50**	**$2,271,323.67**	73	$1,403,634.25
glatiramer acetate	Copaxone*	**51**	**$2,258,264.98**	43	$2,427,922.48
canakinumab	Ilaris	**52**	**$2,208,083.66**	49	$2,062,531.33
rifaximin	Xifaxan	**53**	**$2,150,664.84**	52	$1,979,593.11
antihemophilic factor (recombinant)	Advate	**54**	**$2,140,059.36**	36	$2,823,984.84
azithromycin	Zithromax*	**55**	**$1,991,242.90**	51	$1,993,930.96
infliximab	Remicade	**56**	**$1,991,061.52**	85	$1,231,500.38
sapropterin	Kuvan	**57**	**$1,981,912.60**	56	$1,872,591.33
vigabatrin	Sabril*	**58**	**$1,910,975.75**	47	$2,133,072.37
eculizumab	Soliris	**59**	**$1,888,266.53**	61	$1,711,063.67
palbociclib	Ibrance	**60**	**$1,786,146.82**	78	$1,335,746.00
budesonide inhalation	Pulmicort*	**61**	**$1,763,013.83**	39	$2,515,672.74
amoxicillin/clavulanate	Augmentin*	**62**	**$1,760,726.66**	62	$1,679,394.38
varenicline	Chantix	**63**	**$1,739,126.43**	71	$1,439,536.89
beclomethasone inhalation	Qvar	**64**	**$1,721,341.51**	45	$2,228,840.71
cefdinir	Omnicef*	**65**	**$1,689,398.62**	50	$2,040,795.76
corticotropin injection	H.P. Acthar	**66**	**$1,663,736.36**	60	$1,721,095.62
rufinamide	Banzel	**67**	**$1,585,518.23**	69	$1,502,656.87
ipratropium/albuterol	Combivent*	**68**	**$1,582,628.75**	63	$1,658,156.47
dasatinib	Sprycel	**69**	**$1,556,481.47**	57	$1,848,594.31
glycerol phenylbutyrate	Ravicti	**70**	**$1,547,010.90**	114	$865,562.10
antihemophilic factor (recombinant)	Eloctate	**71**	**$1,518,777.95**	74	$1,392,066.37
gabapentin	Neurontin*	**72**	**$1,515,567.73**	76	$1,377,086.69
elvitegravir/cobicistat/ emtricitabine/tenofovir	Genvoya	**73**	**$1,454,546.10**	119	$832,179.41
oxycodone/acetaminophen	Multiple Products	**74**	**$1,447,175.15**	55	$1,899,686.19

Top 100 Reimbursed Drugs by Fiscal Year		SFY 2018		SFY 2017	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
everolimus	Afinitor	**75**	**$1,436,839.01**	139	$703,164.10
apixaban	Eliquis	**76**	**$1,426,924.45**	105	$944,106.38
abacavir/dolutegravir/lamivudine	Triumeq	**77**	**$1,411,343.52**	77	$1,352,124.88
dimethyl fumarate	Tecfidera	**78**	**$1,410,744.35**	65	$1,627,492.10
fluticasone propionate nasal	Flonase*	**79**	**$1,375,701.66**	89	$1,190,151.53
guanfacine	Intuniv*	**80**	**$1,350,679.00**	82	$1,266,682.55
oxcarbazepine	Multiple Products	**81**	**$1,341,810.03**	72	$1,431,674.73
fingolimod	Gilenya	**82**	**$1,330,831.81**	110	$859,686.22
chlorpromazine	Thorazine*	**83**	**$1,288,941.63**	92	$1,130,711.94
levothyroxine	Multiple Products	**84**	**$1,282,317.12**	90	$1,172,147.51
ustekinumab	Stelara	**85**	**$1,276,244.50**	109	$900,016.15
asfotase alfa	Strensiq	**86**	**$1,272,955.80**	81	$1,268,376.77
paliperidone tablet	Invega*	**87**	**$1,255,599.58**	58	$1,788,805.07
budesonide/formoterol fumarate	Symbicort	**88**	**$1,193,990.50**	66	$1,590,711.89
secukinumab	Cosentyx	**89**	**$1,183,105.47**	213	$404,893.36
antihemophilic factor (recombinant)	Nuwiq	**90**	**$1,178,575.78**	174	$547,543.27
rivaroxaban	Xarelto	**91**	**$1,170,132.47**	98	$1,029,488.19
tobramycin inhalation	Multiple Products	**92**	**$1,141,262.14**	75	$1,383,885.46
prenatal vitamin	Multiple Products	**93**	**$1,131,592.97**	177	$536,894.21
antihemophilic factor - pegylated	Adynovate	**94**	**$1,083,086.30**	287	$266,532.38
leuprolide acetate injection	Lupron Depot-Ped	**95**	**$1,081,169.68**	80	$1,285,342.68
etonogestrel/ethinyl estradiol VA	Nuvaring	**96**	**$1,079,860.43**	96	$1,063,093.80
eltrombopag	Promacta	**97**	**$1,074,325.86**	201	$436,954.82
emtricitabine/tenofovir DF	Truvada	**98**	**$1,068,728.55**	86	$1,205,663.93
antihemophilic factor/VWF	Wilate/Humate	**99**	**$1,065,168.93**	172	$548,935.03
mometasone/formoterol fumarate	Dulera	**100**	**$1,060,031.21**	163	$593,785.77

*Includes brand and generic where applicable.

SFY = state fiscal year; NA = not applicable; Trinz = Trinza; Sust = Sustenna; DF = disoproxil fumarate; VA = vaginal; VWF = von Willebrand factor

Reimbursement does not reflect rebated costs or net costs.

Top 50 Medications by Total Number of Claims: Fiscal Year 2018

Top 50 Medications by Total Number of Claims									
Rank	**Generic Name**	**Brand Name**	**Claims**	**Members**	**Cost**	**Units/ Day**	**Cost/ Claim**	**Claims/ Member**	**% Cost+**
1	albuterol	Multiple	226,589	95,615	$14,897,379.33	2.22	$65.75	2.37	11.71%
2	cetirizine	Multiple	212,477	91,191	$2,387,645.36	2.99	$11.24	2.33	1.88%
3	amoxicillin	Amoxil*	211,856	155,154	$2,532,282.58	11.93	$11.95	1.37	1.99%
4	hydrocodone/acetaminophen	Multiple	156,997	60,411	$2,869,336.68	4.02	$18.28	2.60	2.26%
5	montelukast	Singulair*	141,493	40,189	$2,309,465.98	1	$16.32	3.52	1.82%
6	azithromycin	Zithromax*	108,749	83,128	$1,991,242.90	3	$18.31	1.31	1.57%
7	fluticasone propionate nasal	Flonase*	97,249	51,450	$1,375,701.66	0.43	$14.15	1.89	1.08%
8	lisdexamfetamine	Vyvanse	95,164	16,635	$25,086,619.83	1	$263.61	5.72	19.72%
9	gabapentin	Neurontin*	94,860	19,763	$1,515,567.73	3.15	$15.98	4.80	1.19%
10	clonidine	Catapres*	84,040	15,150	$896,498.56	1.46	$10.67	5.55	0.70%
11	methylphenidate	Multiple	80,057	12,484	$10,302,880.07	1.34	$128.69	6.41	8.10%
12	oseltamivir	Tamiflu*	78,077	73,704	$11,642,564.82	10.46	$149.12	1.06	9.15%
13	sertraline hcl	Zoloft*	74,520	18,649	$902,816.12	1.16	$12.12	4.00	0.71%
14	ondansetron	Zofran*	74,110	58,005	$1,038,398.15	2.27	$14.01	1.28	0.82%
15	omeprazole	Prilosec*	65,996	20,328	$791,489.42	1.17	$11.99	3.25	0.62%
16	fluoxetine	Prozac*	64,412	15,301	$801,294.43	1.23	$12.44	4.21	0.63%
17	trazodone	Desyrel*	63,944	15,388	$780,502.20	1.2	$12.21	4.16	0.61%
18	cefdinir	Omnicef*	63,939	49,626	$1,689,398.62	6.66	$26.42	1.29	1.33%
19	amoxicillin/clavulanate	Augmentin*	62,349	52,238	$1,760,726.66	8.22	$28.24	1.19	1.38%
20	ibuprofen	Motrin*	61,746	42,332	$681,756.02	3.05	$11.04	1.46	0.54%
21	prednisone	Multiple	61,097	44,878	$657,893.28	1.88	$10.77	1.36	0.52%
22	loratadine	Multiple	54,589	24,493	$663,209.38	2.72	$12.15	2.23	0.52%
23	cephalexin	Keflex*	53,901	46,617	$1,006,654.39	9.59	$18.68	1.16	0.79%
24	alprazolam	Xanax*	53,672	8,935	$551,751.07	2.3	$10.28	6.01	0.43%
25	lisinopril	Multiple	52,115	14,481	$478,811.72	1.09	$9.19	3.60	0.38%
26	amphetamine/dextroamphetamine	Multiple	51,753	8,276	$4,070,259.95	1.45	$78.65	6.25	3.20%
27	levothyroxine	Multiple	51,058	10,661	$1,282,317.12	1	$25.11	4.79	1.01%
28	oxycodone/acetaminophen	Multiple	50,565	21,508	$1,447,175.15	3.73	$28.62	2.35	1.14%
29	quetiapine	Seroquel*	49,400	8,945	$944,658.87	1.43	$19.12	5.52	0.74%
30	guanfacine extended-release	Intuniv*	49,201	8,284	$1,350,679.00	1	$27.45	5.94	1.06%
31	triamcinolone topical	Multiple	48,841	34,844	$715,047.53	4.43	$14.64	1.40	0.56%

Top 50 Medications by Total Number of Claims									
Rank	**Generic Name**	**Brand Name**	**Claims**	**Members**	**Cost**	**Units/ Day**	**Cost/ Claim**	**Claims/ Member**	**% Cost+**
32	sulfamethoxazole/trimethoprim	Bactrim*	48,121	38,880	$1,022,146.61	7.48	$21.24	1.24	0.80%
33	metformin	Multiple	43,928	10,796	$405,106.39	2.03	$9.22	4.07	0.32%
34	mupirocin	Bactroban*	42,840	36,354	$663,201.10	2.21	$15.48	1.18	0.52%
35	risperidone	Risperdal*	42,724	7,213	$638,152.73	1.53	$14.94	5.92	0.50%
36	prednisolone sodium phosphate	Multiple	41,707	31,615	$833,461.61	6.68	$19.98	1.32	0.66%
37	fluticasone propionate inhalation	Flovent	40,360	16,501	$8,713,522.09	0.33	$215.89	2.45	6.85%
38	prednisolone syrup	Prelone*	38,938	30,239	$458,365.88	6.55	$11.77	1.29	0.36%
39	tramadol	Ultram*	38,549	14,734	$384,457.88	3.84	$9.97	2.62	0.30%
40	escitalopram	Lexapro*	38,448	10,012	$507,595.10	1.05	$13.20	3.84	0.40%
41	aripiprazole	Abilify*	37,804	8,138	$4,301,167.33	0.97	$113.78	4.65	3.38%
42	cyclobenzaprine	Flexeril*	37,025	17,466	$340,073.64	2.41	$9.18	2.12	0.27%
43	citalopram	Celexa*	35,686	9,973	$355,657.99	1.01	$9.97	3.58	0.28%
44	atorvastatin	Lipitor*	35,639	9,891	$476,124.17	1	$13.36	3.60	0.37%
45	ranitidine	Zantac*	35,511	15,451	$459,711.15	3.46	$12.95	2.30	0.36%
46	clonazepam	Klonopin*	34,565	7,035	$419,097.72	2.1	$12.12	4.91	0.33%
47	oxycodone	Multiple	34,496	5,847	$5,500,196.87	3.13	$159.44	5.90	4.32%
48	hydroxyzine hcl	Atarax*	33,698	15,427	$484,572.93	4.17	$14.38	2.18	0.38%
49	levetiracetam	Keppra*	32,783	5,121	$1,010,361.31	5.33	$30.82	6.40	0.79%
50	topiramate	Multiple	32,610	7,368	$807,247.36	1.95	$24.75	4.43	0.63%

HCl = hydrochloride

*Includes brand and generic where applicable.

+Percent cost of top 50 medications by total number of claims.

Reimbursement does not reflect rebated costs or net costs.

Top 10 Traditional and Specialty Therapeutic Categories by Fiscal Year

Top 10 Traditional Therapeutic Categories by Fiscal Year*				
Anti-Infective Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antiviral Agents	100,474	$59,136,192.28	69,572	$44,631,903.14
Anti-Infectives	88,938	$5,029,214.67	95,866	$5,490,445.37
Penicillins	284,190	$4,569,834.92	288,169	$4,171,933.42
Cephalosporins	126,462	$3,274,251.15	125,004	$3,582,716.89
Macrolide Antibiotics	111,772	$2,749,642.19	116,690	$2,728,658.25
Antifungal Agents	25,920	$1,053,527.94	27,158	$1,111,119.39
Anthelmintic Agents	2,889	$972,299.48	3,417	$1,011,430.31
Tetracyclines	23,306	$546,309.64	23,941	$673,627.88
Fluoroquinolones	17,324	$216,922.07	19,568	$197,724.97
Antimalarial Agents	4,130	$156,611.96	4,045	$314,267.14
Antimycobacterial Agents	416	$27,162.22	357	$45,386.84
Aminoglycosides	395	$25,180.90	423	$44,791.15
Sulfonamides	30	$1,837.58	5	$1,345.57
Amebicides	0	$0.00	0	$0.00
Total:	**786,246**	**$77,758,987.00**	**774,215**	**$64,005,350.32**
Attention Deficit Hyperactivity Disorder (ADHD) Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
ADHD/Anti-Narcolepsy Agents	340,569	$50,329,755.71	344,401	$62,132,427.83
Total:	**340,569**	**$50,329,755.71**	**344,401**	**$62,132,427.83**
Anti-Asthmatic and Bronchodilator Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anti-Asthmatic and Bronchodilator Agents	487,711	$46,261,773.92	481,564	$43,568,035.58
Total:	**487,711**	**$46,261,773.92**	**481,564**	**$43,568,035.58**
Antipsychotics	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antipsychotics	214,470	$43,096,795.40	206,360	$39,972,739.77
Total:	**214,470**	**$43,096,795.40**	**206,360**	**$39,972,739.77**

Anti-Diabetic Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Anti-Diabetic Agents	134,314	$40,256,493.78	133,204	$38,319,076.05
Total:	**134,314**	**$40,256,493.78**	**133,204**	**$38,319,076.05**
Anticonvulsant Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticonvulsant Agents	326,296	$26,191,398.13	328,840	$24,852,925.84
Total:	**326,296**	**$26,191,398.13**	**328,840**	**$24,852,925.84**
Analgesic Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Analgesics - Narcotic	352,626	$19,293,549.14	409,441	$22,110,845.96
Analgesics - Anti-Inflammatory	137,473	$4,556,705.95	141,766	$2,222,717.23
Analgesics - Non-Narcotic	8,538	$306,574.68	10,235	$429,634.56
Migraine Agents	11,660	$291,222.22	11,522	$270,934.70
Gout Agents	5,818	$185,631.43	5,991	$171,089.80
Local Anesthetics - Parenteral	143	$2,171.04	258	$3,343.56
General Anesthetics	0	$0.00	76	$1,832.42
Total:	**516,258**	**$24,635,854.46**	**579,289**	**$25,210,398.23**
Endocrine Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Endocrine Agents	19,087	$8,819,161.83	19,547	$8,307,546.84
Contraceptives	99,149	$5,822,948.03	103,948	$5,899,104.90
Progestins	7,002	$5,580,617.55	6,302	$3,961,174.13
Corticosteroids	177,175	$2,716,326.32	176,884	$2,417,274.88
Thyroid Agents	55,022	$1,428,278.36	55,511	$1,288,533.40
Estrogens	8,993	$868,834.23	9,757	$947,661.75
Androgen - Anabolic Agents	613	$134,507.97	560	$127,409.73
Oxytocics	198	$46,590.01	207	$27,085.02
Total:	**367,239**	**$25,417,264.30**	**372,716**	**$22,975,790.65**

Topical Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Dermatological Agents	200,455	$12,562,767.61	208,817	$11,976,857.00
Otic Agents	29,868	$6,047,061.24	28,050	$5,460,709.99
Ophthalmic Agents	62,047	$2,233,534.15	63,029	$2,168,109.15
Mouth/Throat/Dental Agents	25,067	$398,418.03	23,991	$340,969.93
Anorectal Agents	1,304	$105,604.66	1,397	$121,576.06
Total:	**318,741**	**$21,347,385.69**	**325,284**	**$20,068,222.13**
Cardiovascular Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Vasopressors	8,974	$3,293,253.15	10,084	$5,425,404.58
Antihypertensives	219,079	$3,027,787.38	221,942	$2,637,733.31
Beta Blockers	83,005	$2,230,851.15	81,666	$2,042,411.24
Antihyperlipidemics	74,479	$1,409,447.61	73,670	$1,627,721.00
Other Cardiovascular Agents	1,271	$1,030,935.38	899	$711,190.51
Diuretics	52,941	$801,064.17	52,767	$693,869.79
Antianginal Agents	7,335	$744,332.47	7,697	$774,829.43
Calcium Channel Blockers	38,264	$572,412.41	37,385	$486,137.84
Cardiotonics	3,051	$178,456.39	3,316	$148,650.37
Antiarrhythmic Agents	2,440	$123,756.75	2,422	$121,014.14
Total:	**490,839**	**$13,412,296.86**	**491,848**	**$14,668,962.21**

Top 10 Specialty Therapeutic Categories by Fiscal Year*

Pain Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Analgesics - Anti-Inflammatory	4,533	$22,239,054.04	4,634	$22,987,790.64
Local Anesthetics - Parenteral	96	$2,330.96	45	$889.21
Total:	**4,629**	**$22,241,385.00**	**4,679**	**$22,988,679.85**

Hematological Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Other Hematological Agents	575	$16,526,194.27	709	$16,422,436.53
Hematopoietic Agents	528	$1,813,224.53	670	$2,390,696.13
Total:	**1,103**	**$18,339,418.80**	**1,379**	**$18,813,132.66**
Endocrine Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Endocrine Agents	3,256	$12,453,730.05	3,158	$11,561,298.40
Progestins	330	$1,284,652.36	597	$2,224,730.78
Total:	**3,586**	**$13,738,382.41**	**3,755**	**$13,786,029.18**
Specialized Respiratory Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Specialized Respiratory Agents	1,193	$8,860,036.53	1,233	$9,093,408.80
Total:	**1,193**	**$8,860,036.53**	**1,233**	**$9,093,408.80**
Psychotherapeutic/Neurologic Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Psychotherapeutic & Neurological Agents	1,336	$8,035,140.56	1,378	$8,139,124.40
Total:	**1,336**	**$8,035,140.56**	**1,378**	**$8,139,124.40**
Cardiovascular Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Cardiovascular Agents	1,154	$6,051,156.21	1,059	$5,158,254.29
Total:	**1,154**	**$6,051,156.21**	**1,059**	**$5,158,254.29**
Biological Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Passive Immunizing Agents	2,173	$4,209,552.00	2,155	$4,032,225.25
Other Biological Agents	13	$534,809.15	14	$547,781.49
Total:	**2,186**	**$4,744,361.15**	**2,169**	**$4,580,006.74**
Non-Therapeutic Agents	**2018**		**2017**	
	Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidotes	262	$2,473,095.89	257	$1,780,090.76
Total:	**262**	**$2,473,095.89**	**257**	**$1,780,090.76**

Gastrointestinal Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Gastrointestinal Agents	430	$2,360,853.20	348	$1,856,032.89
Total:	**430**	**$2,360,853.20**	**348**	**$1,856,032.89**

Anti-Infective Agents	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Aminoglycosides	369	$1,137,647.59	340	$1,383,885.46
Other Anti-Infective Agents	90	$746,122.78	86	$666,053.61
Antivirals	0	$0.00	3	$10,820.50
Total:	**459**	**$1,883,770.37**	**429**	**$2,060,759.57**

Total	2018		2017	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Top 10 Traditional and Specialty Therapeutic Categories	**3,999,021**	**$457,435,605.37**	**4,054,407**	**$444,029,447.75**

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

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Appendix I

Calendar Year 2018 Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Fulphila® (Pegfilgrastim-jmdb), Nivestym™ (Filgrastim-aafi), and Udenyca™ (Pegfilgrastim-cbqv)

Oklahoma Health Care Authority
April 2019

Current Prior Authorization Criteria

Granix® (Tbo-filgrastim) and Zarxio® (Filgrastim-sndz) Approval Criteria:

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

Utilization of G-CSFs: Calendar Year 2018

Comparison of Calendar Years for G-CSFs: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	63	222	$1,168,702.97	$5,264.43	$256.07	1,786	4,564
2018	57	241	$1,185,495.01	$4,919.07	$258.28	1,626	4,590
% Change	**-9.50%**	**8.60%**	**1.40%**	**-6.60%**	**0.90%**	**-9.00%**	**0.60%**
Change	**-6**	**19**	**$16,792.04**	**-$345.36**	**$2.21**	**-160**	**26**

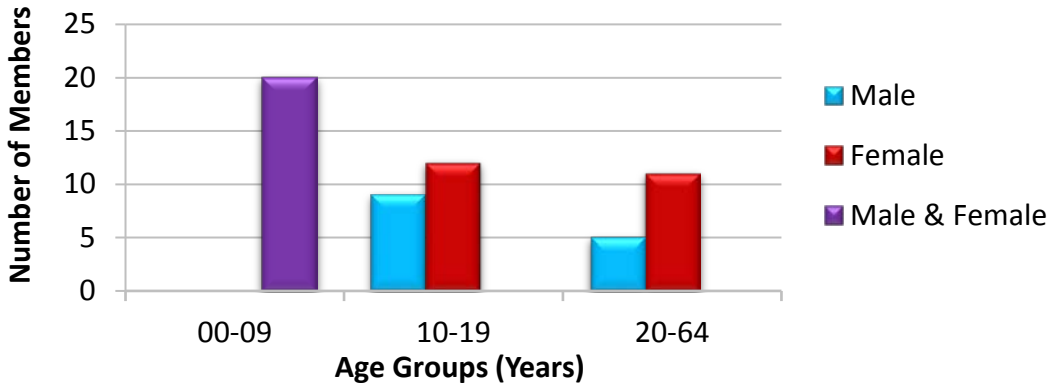
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Calendar Years for G-CSFs: Medical Claims

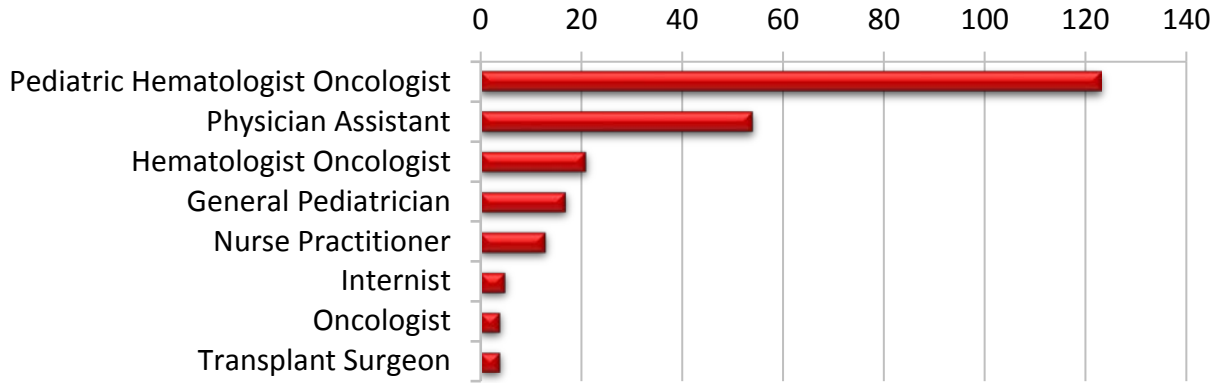
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2017	233	796	$2,632,356.34	$3,306.98	3.4
2018	234	750	$3,039,174.61	$4,052.23	3.2
% Change	**0.43%**	**-5.78%**	**15.45%**	**22.54%**	**-5.73%**
Change	**1**	**-46**	**$406,818.27**	**$745.25**	**-0.2**

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

Demographics of Members Utilizing G-CSFs: Pharmacy Claims



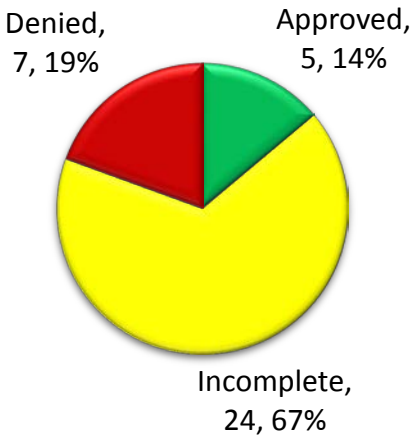
Top Prescriber Specialties of G-CSFs by Number of Claims: Pharmacy Claims



Prior Authorization of G-CSFs

There were 36 prior authorization requests submitted for G-CSFs during calendar year 2018. Currently, Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are available without prior authorization. The following chart shows the status of the submitted petitions for calendar year 2018.

Status of Petitions



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

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

- **June 2018:** The FDA approved Fulphila® (pegfilgrastim-jmdb) as the first biosimilar to Neulasta® (pegfilgrastim). Fulphila® is indicated for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy. Neulasta® was first FDA approved in 2002 and is also indicated for hematopoietic subsyndrome of acute radiation syndrome, in addition to the above listed indication for prophylaxis of febrile neutropenia. Pegfilgrastim is a pegylated derivative of filgrastim and has a longer elimination half-life compared to filgrastim.
- **July 2018:** The FDA approved Nivestym™ (filgrastim-aafi) as a biosimilar to Neupogen® (filgrastim). Filgrastim-aafi is indicated for prophylaxis of febrile neutropenia in patients with acute myeloid leukemia receiving induction or consolidation chemotherapy and in patients with non-myeloid malignancies who receive myeloablative chemotherapy followed by bone marrow transplantation or who receive myelosuppressive chemotherapy for harvesting of peripheral blood stem cells and for symptomatic chronic (severe) neutropenic disorder. Neupogen® was first FDA approved in 1991 and has all of the above listed indications, as well as an additional indication for hematopoietic subsyndrome of acute radiation syndrome.
- **August 2018:** The FDA expanded the indication of Granix® (tbo-filgrastim) to include use in pediatric patients 1 month of age and older. The label expansion also included approval of a new vial presentation of the product, available as 300mcg/mL and 480mcg/1.6mL single-dose vials, to add to the currently available prefilled syringe formulations. Granix® was first FDA approved in 2012 for use in adult patients, as the safety and effectiveness had not yet been established in pediatric patients. Granix® is indicated for prophylaxis of severe neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy. Granix® is not technically considered a biosimilar to Neupogen® (filgrastim) because it was approved under the Biologics License Application (BLA) pathway prior to the FDA establishing an abbreviated licensure pathway for biosimilar products.
- **November 2018:** The FDA approved Udenyca™ (pegfilgrastim-cbqv) as a biosimilar to Neulasta® (pegfilgrastim). Udenyca™ is the first pegfilgrastim biosimilar approved by both the FDA and the European Commission (EC). Udenyca™ is indicated for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy.

Pipeline:

- **Pegfilgrastim Biosimilar:** Sandoz, a Novartis division in biosimilars, received EC approval in November 2018 for Ziextenzo®, a biosimilar to pegfilgrastim. Sandoz previously received a Complete Response Letter (CRL) from the FDA in 2016 regarding the proposed pegfilgrastim biosimilar product, after which Sandoz worked with the FDA to address its concerns. Sandoz agreed with the FDA to undertake an additional study, with the goal of a 2019 resubmission of its BLA for its proposed pegfilgrastim biosimilar.
- **Pegfilgrastim Biosimilar:** Pfizer is currently developing PF-06881894 as a proposed biosimilar to pegfilgrastim. PF-06881894 is currently in Phase 1 clinical trials.

Recommendations

The College of Pharmacy recommends the prior authorization of Fulphila® (pegfilgrastim-jmdb), Nivestym™ (filgrastim-aafi), and Udenyca™ (pegfilgrastim-cbqv) with the following criteria (changes shown in red):

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

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

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

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

Utilization Details of G-CSFs: Calendar Year 2018

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PEGFILGRASTIM PRODUCTS						
NEULASTA 6MG/0.6ML	126	30	$565,852.47	$4,490.89	4.2	47.73%
SUBTOTAL	**126**	**30**	**$565,852.47**	**$4,490.89**	**4.2**	**47.73%**
FILGRASTIM PRODUCTS						
NEUPOGEN 300MCG/ML	63	13	$305,488.35	$4,849.02	4.8	25.77%
NEUPOGEN 300MCG/0.5ML	24	6	$204,013.27	$8,500.55	4.0	17.21%
NEUPOGEN 480MCG/0.8ML	20	14	$77,216.84	$3,860.84	1.4	6.51%
NEUPOGEN 480MCG/1.6ML	7	3	$30,782.33	$4,397.48	2.3	2.60%
GRANIX 300MCG/0.5ML	1	1	$2,141.75	$2,141.75	1.0	0.18%
SUBTOTAL	**115**	**37**	**$619,642.54**	**$5,388.20**	**3.1**	**52.27%**
TOTAL	**241**	**57***	**$1,185,495.01**	**$4,919.07**	**4.2**	**100%**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PEGFILGRASTIM INJ J2505	664	223	$3,000,143.41	$4,518.29	3.0	98.72%
FILGRASTIM INJ J1442	86	19	$39,031.20	$453.85	4.5	1.28%
TOTAL	**750**	**234***	**$3,039,174.61**	**$4,052.23**	**3.2**	**100%**

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

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Appendix J

Calendar Year 2018 Annual Review of Anti-Diabetic Medications

Oklahoma Health Care Authority
April 2019

Current Prior Authorization Criteria

Diabetes 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; or
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; or
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 (T2D) and CV disease for patients with the diagnosis of T2D at high risk for CV events. Tier structure rules for this indication will apply.

Diabetes 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); or
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 (T2D) and CV disease for patients with the diagnosis of T2D at high risk for CV events. Tier structure rules for this indication will apply.

Diabetes 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.

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:

- An FDA approved diagnosis of diabetes mellitus; and
- 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 unit/mL strength requires a patient-specific, clinically significant reason why the member cannot use the 100 unit/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.

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.

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			
		dapagliflozin/saxagliptin (**Qtern®**)	
		empagliflozin/linagliptin (**Glyxambi®**)	
		ertugliflozin/sitagliptin	

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		(**Steglujan™**)	
Dopamine Agonists			
		bromocriptine (**Cycloset®**)	
Glinides			
repaglinide (**Prandin®**)	nateglinide (**Starlix®**)		
	repaglinide/metformin (**Prandimet®**)		
GLP-1 Agonists			
	exenatide (**Byetta®**)	dulaglutide (**Trulicity®**)	exenatide ER autoinjector (**Bydureon® BCise™**)
	exenatide ER (**Bydureon®**)	lixisenatide (**Adlyxin™**)	
	liraglutide (**Victoza®**)	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®**)			

Anti-Diabetic Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Thiazolidinediones			
pioglitazone (**Actos®**)		pioglitazone/glimepiride (**Duetact®**)	
		pioglitazone/metformin (**Actoplus Met®**, **Actoplus Met XR®**)	
		rosiglitazone (**Avandia®**)	

*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 of Anti-Diabetic Medications: Calendar Year 2018

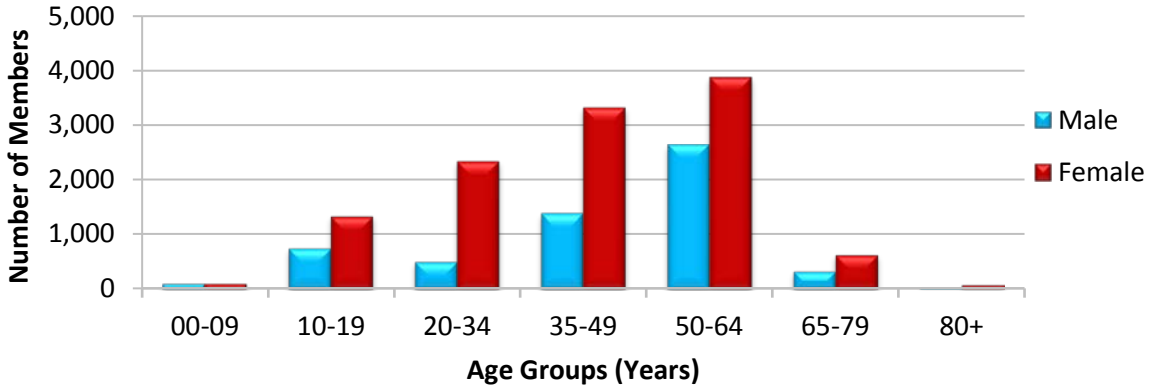
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	17,581	132,846	$37,849,332.40	$284.91	$8.07	5,612,978	4,690,882
2018	17,402	129,449	$40,966,879.12	$316.47	$8.30	5,943,599	4,937,039
% Change	**-1.00%**	**-2.60%**	**8.20%**	**11.10%**	**2.90%**	**5.90%**	**5.20%**
Change	**-179**	**-3,397**	**$3,117,546.72**	**$31.56**	**$0.23**	**330,621**	**246,157**

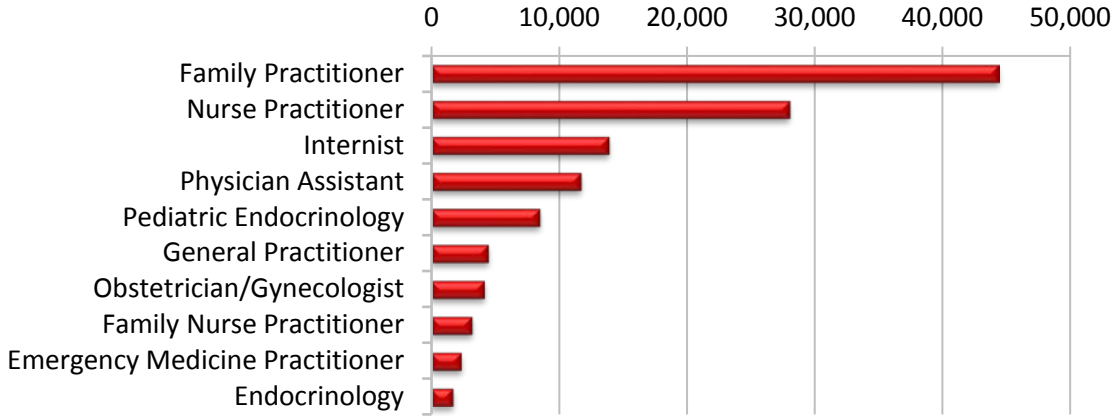
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- The diabetes 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.

Demographics of Members Utilizing Anti-Diabetic Medications



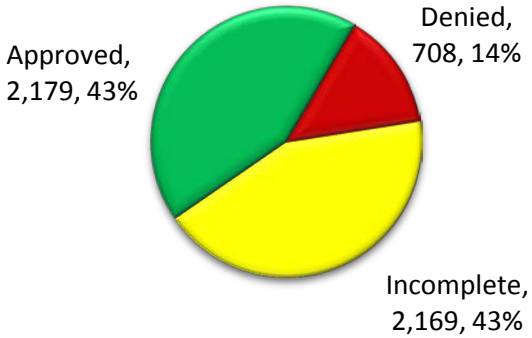
Top Prescriber Specialties of Anti-Diabetic Medications by Number of Claims



Prior Authorization of Anti-Diabetic Medications

There were 5,056 prior authorization requests submitted for anti-diabetic medications during calendar year 2018. Of the 5,056 total prior authorizations submitted, 2,776 were for non-insulin anti-diabetic medications and 2,280 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 2018.

Status of Petitions



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]

Anticipated Patent Expiration(s):

- Byetta® [exenatide extended-release (ER) injection]: January 2020
- Riomet® (metformin oral solution): August 2021
- Apidra® (insulin glulisine injection): January 2023
- Kombiglyze® XR (saxagliptin/metformin ER tablets): July 2025
- Actoplus Met XR® (pioglitazone/metformin ER tablets): July 2026
- Januvia® (sitagliptin tablets): November 2026
- Janumet XR® (sitagliptin/metformin ER tablets): November 2026
- Synjardy® (empagliflozin/metformin tablets): April 2027
- Synjardy XR® (empagliflozin/metformin ER tablets): April 2027

- Lantus® (insulin glargine injection): March 2028
- Janumet® (sitagliptin/metformin tablets): July 2028
- Onglyza® (saxagliptin tablets): November 2028
- Invokana® (canagliflozin tablets): February 2029
- Invokamet® (canagliflozin/metformin tablets): February 2029
- Invokamet XR® (canagliflozin/metformin ER tablets): February 2029
- Qtern® (dapagliflozin/saxagliptin tablets): December 2029
- Bydureon® (exenatide ER injection): May 2030
- Farxiga® (dapagliflozin tablets): May 2030
- Jentadueto® (linagliptin/metformin tablets): June 2030
- Steglatro™ (ertugliflozin tablets): July 2030
- Bydureon® BCise™ (exenatide ER auto-injector): October 2030
- Steglujan™ (ertugliflozin/sitagliptin tablets): October 2030
- Segluromet™ (ertugliflozin/metformin tablets): October 2030
- Xigduo® XR (dapagliflozin/metformin ER tablets): November 2030
- Tradjenta® (linagliptin tablets): March 2031
- Toujeo® (insulin glargine injection): May 2031
- Ozempic® (semaglutide injection): February 2032
- Tresiba® (insulin degludec injection): February 2032
- Xultophy® (insulin degludec/liraglutide injection): February 2032
- Cycloset® (bromocriptine tablets): April 2032
- Afrezza® (insulin human inhalation powder): July 2032
- Adlyxin™ (lixisenatide injection): August 2032
- Jentadueto XR® (linagliptin/metformin ER tablets): March 2033
- Ryzodeg® 70/30 (insulin degludec/insulin aspart injection): May 2033
- Glyxambi® (empagliflozin/linagliptin tablets): June 2034
- Jardiance® (empagliflozin tablets): June 2034
- Soliqua® (insulin glargine/lixisenatide injection): December 2035
- Victoza® (liraglutide injection): January 2037

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

- **February 2019:** The FDA approved a label update for Farxiga® (dapagliflozin) and Xigduo® XR (dapagliflozin/metformin ER) expanding use in patients with type 2 diabetes mellitus (T2D) and moderate renal impairment [chronic kidney disease (CKD) with an estimated glomerular filtration rate (eGFR) of 45 to 59mL/min/1.73m^2]. Dapagliflozin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D. Dapagliflozin/metformin ER is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D when treatment with both dapagliflozin and metformin is appropriate. The updated labels lower the eGFR threshold to 45mL/min/1.73m^2 from 60mL/min/1.73m^2, expanding the potential population of patients with T2D and impaired renal function who may benefit from the medicine. Dapagliflozin and dapagliflozin/metformin ER are not recommended when the eGFR is <45mL/min/1.73m^2 and remain contraindicated in patients with severe renal impairment (eGFR <30mL/min/1.73m^2), end-stage renal disease (ESRD), or in patients

on dialysis. The updates were based on the results of DERIVE, a Phase 3 study of patients with inadequately controlled T2D [hemoglobin A1C (HbA_{1c}) 7.0 to 11.0%] and an eGFR of 45 to 59mL/min/1.73m^2 who received either dapagliflozin 10mg or placebo over 24 weeks. At week 24, dapagliflozin 10mg provided statistically significant reductions in HbA_{1c} compared with placebo. The safety profile following a treatment duration of 24 weeks was similar to that seen in the overall dapagliflozin clinical trial program.

Pipeline:

- **Lusduna™ Nexvue™ (Insulin Glargine Injection):** The FDA granted tentative approval to Merck for Lusduna™ Nexvue™ (insulin glargine injection) 100 units/mL, a follow-on biologic basal insulin in a pre-filled dosing device in July 2017. With the tentative approval, Lusduna™ Nexvue™ had met all required regulatory standards for follow-on biologics of clinical and nonclinical safety, efficacy, and quality, but is subject to an automatic stay due to a lawsuit from Sanofi claiming patent infringement. Under the Hatch-Waxman Act, the initiation of Sanofi's lawsuit in September 2016 automatically invoked a stay on final FDA approval of Lusduna™ Nexvue™ for a period of up to 30 months, or in the event a court finds in favor of Merck, whichever comes sooner. In a filing in Korea in October 2018, Samsung Bioepis disclosed that Merck had canceled the development and commercialization partnership for Lusduna™ Nexvue™ in the United States. Merck paid Samsung Bioepis $155 million to cover the investment made so far in the product, plus interest. A Merck spokesperson said the company assessed the market outlook, including the anticipated pricing and cost of production before discontinuing the development of Lusduna™ Nexvue™. Eli Lilly and Boehringer Ingelheim's Lantus® biosimilar, Basaglar® (insulin glargine injection), launched in December 2016 under a settlement with Sanofi.
- **Semaglutide:** In March 2019, Novo Nordisk announced the submission of 2 new drug applications (NDA) for oral semaglutide and a supplemental New Drug Application (sNDA) for once-weekly Ozempic® (semaglutide). An NDA was submitted for oral semaglutide seeking approval for the treatment of adults with T2D. A priority review voucher (PRV) has been applied to the NDA, leading to an anticipated review time of 6 months from the submission date, according to standard FDA review timelines. The submission for oral semaglutide for the treatment of glycemic control in adults with T2D is based on the results from 10 PIONEER clinical trials, which included 9,543 adults with T2D. In the PIONEER program, patients treated with oral semaglutide achieved greater blood glucose reductions compared to sitagliptin, empagliflozin, liraglutide, and placebo. In addition, oral semaglutide demonstrated greater reductions in mean body weight versus most comparators. Across the PIONEER trials, oral semaglutide had a safe and well-tolerated profile, with the most common adverse event being nausea. A second NDA was submitted for oral semaglutide seeking approval for a cardiovascular (CV) risk reduction indication in adults with T2D. The NDA for an oral semaglutide CV risk reduction indication has an anticipated 10-month review time from the submission date, according to standard FDA review timelines. Finally, an sNDA was submitted for Ozempic® for a CV risk reduction indication in adults with T2D. The sNDA for an

Ozempic® CV risk reduction indication has an anticipated 10-month review time from the submission date. The applications for the oral semaglutide and Ozempic® CV risk reduction indications are based on the results of 2 CV outcomes trials evaluating the effects of adding semaglutide or placebo to standard of care on the risk of CV events.

- **Zynquista™ (Sotagliflozin):** In March 2019, the FDA issued a Complete Response Letter (CRL) regarding the NDA for sotagliflozin, a novel, first-in-class, dual, oral sodium-glucose cotransporter type 1 and 2 (SGLT-1/2) inhibitor for the treatment of adults with type 1 diabetes (T1D) in combination with insulin. Sanofi announced an NDA submission in May 2018 with results from the inTandem clinical trials. In the clinical trial inTandem1, sotagliflozin met the primary endpoint of change in HbA_{1c} levels from baseline to 24 weeks. Changes in HbA_{1c} levels were 0.43% for the 200mg dose, 0.49% for the 400mg dose, and 0.08% for placebo. The clinical trial inTandem2 produced similar results. The third inTandem trial included 1,405 patients with T1D and baseline HbA_{1c} levels between 7 and 11%. The randomized, double-blind study showed that 400mg sotagliflozin reduced HbA_{1c} 0.79% from baseline compared with 0.33% for placebo after 24 weeks of treatment ($P<0.001$). Sanofi and Lexicon will work closely with the FDA to determine the appropriate next steps.
- **TTP399:** TTP399 is an oral, liver-selective glucokinase activator (GKA). Because it exhibits an insulin-independent mechanism of action, it may be suitable as an adjunctive treatment for T1D. In clinical trials for T2D, TTP399 has shown significant reductions in postprandial glucose, increased percentage time in range, and decreased percentage time in hypo- or hyperglycemia. Moreover, TTP399 significantly reduced HbA_{1c} without significant hypoglycemia, dyslipidemia, or ketoacidosis. The Simplici-T1 trial is an adaptive 3-part (sentinel, learning phase, and confirming phase) Phase 1b/2 proof-of-concept study designed to explore the effect of TTP399 as adjunctive therapy for the treatment of T1D. The aims of the study are to evaluate the safety of TTP399 and evaluate whether TTP399 can replace or reduce mealtime insulin bolus and improve HbA_{1c} in patients with T1D. The sentinel phase, an open-label, dose escalation study in 5 adults with T1D on insulin pump therapy and continuous glucose monitoring (CGM), showed that TTP399 was well tolerated. No incidents of severe hypoglycemia or diabetic ketoacidosis (DKA) were observed. When compared to baseline, trends toward improved glycemic control while reducing insulin dose were observed with TTP399 treatment, supporting continuing to the randomized, placebo-controlled phase of the study.
- **RT-200 (Urocortin 2 Gene Transfer):** RT-200 is a novel, intravenous (IV), single-dose, investigational paracrine gene therapy designed to provide substantially improved, sustained outcomes in T2D patients by normalizing blood glucose. RT-200 delivers the human gene encoding urocortin 2 via an adeno-associated virus (AAV) that is able to enter cells, primarily in the liver, but cannot reproduce itself. The technology has been shown to safely and efficiently deliver the urocortin 2 gene therapy in mice. Preclinical data indicate that gene transfer, via a one-time IV injection of a viral vector encoding urocortin 2, increases insulin sensitivity and glucose disposal, provides long-lasting resolution of abnormal glucose homeostasis, and reduces fatty infiltration of the liver in 2 mouse models of insulin resistance. These findings indicate a promising strategy for

treating clinical T2D and unlock the potential for the treatment of other CV and metabolic diseases, including nonalcoholic fatty liver disease (nonalcoholic steatohepatitis – NASH). In similar protocols in which mice were dosed initially prior to being fed a high-fat diet, treated mice did not develop T2D in their lifetime, signaling a potential for a preventative therapy. Once all preclinical studies with urocortin 2 gene transfer are completed, Renova Therapeutics plans to submit an Investigational New Drug (IND) Application to the FDA in which patients with T2D are enrolled to receive RT-200 in well-controlled and safely conducted clinical trials.

- **Generic Liraglutide:** Novo Nordisk filed a lawsuit in March 2017 after Teva Pharmaceuticals submitted an abbreviated new drug application (ANDA) to the FDA seeking approval for a generic version of liraglutide (Victoza®) in which Novo Nordisk alleged that Teva was engaging in patent infringement. In March 2019, Teva agreed to a settlement with Novo Nordisk which is subject to review by the Federal Trade Commission and the Department of Justice that awards Teva a license to launch a generic version of liraglutide starting in December 2023. Teva could launch the generic sooner than the December date under certain circumstances, but it would be no earlier than March 2023, unless the Victoza® patents are no longer in effect or another generic version of the treatment is launched.

News:

- **April 2018:** A systematic review and meta-analysis of 236 clinical trials, that included more than 176,000 patients, was published in the *Journal of the American Medical Association* (*JAMA*), and evaluated the association between the use of sodium-glucose cotransporter 2 (SGLT-2) inhibitors, glucagon-like pepetide-1 (GLP-1) agonists, and dipeptidyl peptidase 4 (DPP-4) inhibitors with all-cause mortality. Important CV outcomes trials such as OUTCOME, LEADER, and TECOS were included. Secondary outcomes included CV mortality, heart failure (HF) events, myocardial infarction (MI), and safety endpoints such as adverse events and hypoglycemia. The study only analyzed outcomes by drug class, not individual drugs. SGLT-2 inhibitors came out on top compared to GLP-1 agonists and DDP-4 inhibitors in terms of mortality, CV, and safety endpoints. Compared with control groups, SGLT-2 inhibitors were associated with reduced all-cause mortality [hazard ratio (HR) 0.80, 95% confidence interval (CI) 0.71 to 0.89], as were GLP-1 agonists (HR 0.88, 95% CI 0.81 to 0.94). However, DPP-4 inhibitors were not associated with reduced all-cause mortality (HR 1.02, 95% CI 0.94 to 1.11). Compared with DPP-4 inhibitors, both SGLT-2 inhibitors and GLP-1 agonists were associated with reduced all-cause mortality (SGLT-2 inhibitors HR: 0.78, 95% CI 0.68 to 0.90; GLP-1 agonists HR: 0.86, 95% CI 0.77 to 0.96). There was no significant difference when SGLT-2 inhibitors and GLP-1 agonists were compared with each other. SGLT-2 inhibitors were associated with reduced HF events when compared with controls (HR 0.62, 95% CI 0.54 to 0.72), with DPP-4 inhibitors (HR 0.55, 95% CI 0.46 to 0.67), and with GLP-1 agonists (HR 0.67, 95% CI 0.57 to 0.80). Risk for HF was not significantly different when GLP-1 agonists and DPP-4 inhibitors were compared with controls, but the risk was lower for GLP-1 agonists compared with DPP-4 inhibitors (HR 0.82, 95% CI 0.70 to 0.95). Only SGLT-2 inhibitors were associated with reduced MI risk compared with

controls (HR 0.86, 95% CI 0.77 to 0.97). All 3 drug classes were linked with increased hypoglycemia risk compared with controls. Finally, SGLT-2 inhibitors were associated with reductions in serious adverse events compared with controls (HR 0.90, 95% CI 0.85 to 0.96), with DPP-4 inhibitors (HR 0.91, 95% CI 0.84 to 0.98), and with GLP-1 agonists (HR 0.92, 95% CI 0.85 to 0.99). For GLP-1 agonists, there was a higher risk for adverse events leading to trial withdrawal compared with controls (HR 2.00, 95% CI 1.70 to 2.37), with SGLT-2 inhibitors (HR 1.80, 95% CI 1.44 to 2.25), and with DPP-4 inhibitors (HR 1.93, 95% CI 1.59 to 2.35).

- **April 2018:** A renal-outcome analysis of the Canagliflozin Cardiovascular Assessment Study (CANVAS) trial program was presented at the National Kidney Foundation's Spring Clinical Meeting. The analysis excluded stage 4 and higher kidney disease (eGFR <30mL/min/1.73m^2). Patients with both preserved and reduced kidney function were less likely to have the prespecified outcome of a 40% decline in eGFR, end-stage kidney disease (ESKD), or renal death on Invokana® (canagliflozin) compared to placebo (HR 0.53, 95% CI 0.39 to 0.73 and HR 0.76, 95% CI 0.49 to 1.17, P=0.28 for heterogeneity). Additionally, both groups also saw similar outcomes in a composite endpoint of doubling of serum creatinine, ESKD, or renal death (HR 0.42, 95% CI 0.23 to 0.75 and HR 0.81, 95% CI 0.37 to 1.77, P=0.21 for heterogeneity). Results of the first renal outcome trial with a specific primary composite endpoint evaluating an SGLT-2 inhibitor in patients with diabetic kidney disease, CREDENCE trial (Canagliflozin and Renal Events in Diabetes with Established Neuropathy Clinical Evaluation), are expected in 2019.
- **June 2018:** Results of the OBSERVE-4D study (Canagliflozin vs Other Antihyperglycemic Agents on the Risk of Below-Knee Amputation for Patients with T2DM, a Real-World Analysis of >700,000 US Patients) were presented as a late-breaking poster at the American Diabetes Association (ADA) 2018 Scientific Sessions. The study found no increased risk of below-knee lower extremity (BKLE) amputation with Invokana® (canagliflozin) compared to other SGLT-2 inhibitors or non-SGLT-2 anti-hyperglycemic medicines. In addition to the general T2D population, similar results were also seen in a subset of patients with T2D and established CV disease (CVD). OBSERVE-4D is the largest, real-world observational study to evaluate the risk of BKLE amputation and hospitalization for HF across anti-hyperglycemic therapies. Concern about amputations with the use of canagliflozin was solidified with the final results of the CANVAS, in which there was a 2-fold excess risk for BKLE amputations among patients taking canagliflozin, although the absolute risk was low (6.3 vs. 3.4 cases/1,000 patient-years). These findings were presented at last year's ADA meeting, but prior to that the FDA had already placed a *Boxed Warning* regarding amputations in the canagliflozin label based on CANVAS interim data. No such signal has been seen for other SGLT-2 inhibitors at this time.
- **August 2018:** Findings from a retrospective case-control study published in *JAMA Dermatology* found a greater risk of bullous pemphigoid, a chronic blistering skin condition, in T2D patients taking certain DPP-4 inhibitors. New data join emerging literature linking the increased incidence of bullous pemphigoid in recent years with certain medications, and specifically, DPP-4 inhibitors. Another study, published online in July 2018 in *Diabetes Care*, also found an association between DPP-4 inhibitors and

bullous pemphigoid in adverse event reporting data from Japan. Both studies point specifically to a greater risk of bullous pemphigoid for patients with T2D taking vildagliptin (not approved in the United States) and linagliptin, but not sitagliptin.

- **August 2018:** The FDA issued a Drug Safety Communication warning that cases of a rare but serious infections of the genitals and area around the genitals called necrotizing fasciitis of the perineum (also known as Fournier's gangrene), have been reported with SGLT-2 inhibitors. A new warning about this risk is required to be added to the prescribing information and to the patient medication guide of all SGLT-2 inhibitors. SGLT-2 inhibitors lower blood sugar by causing the kidneys to remove sugar from the body through the urine. First approved in 2013, medicines in the SGLT-2 inhibitor class include canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin. In the 5 years from March 2013 to May 2018, the FDA has identified 12 cases of Fournier's gangrene in patients taking an SGLT-2 inhibitor. This number includes only reports submitted to FDA and found in the medical literature, so there may be additional cases about which the FDA is unaware. Fournier's gangrene developed within several months of the patients starting an SGLT-2 inhibitor and the drug was stopped in most cases. All 12 patients were hospitalized and required surgery. Some patients required multiple disfiguring surgeries, some developed complications, and 1 patient died. In comparison, only 6 cases of Fournier's gangrene (all in men) were identified in review of other anti-diabetic drug classes over a period of more than 30 years.
- **September 2018:** AstraZeneca announced positive results from the Phase 3 DECLARE-TIMI 58 CV outcomes trial (CVOT) for Farxiga® (dapagliflozin). The trial evaluated the CV outcomes of dapagliflozin versus placebo over a period of up to 5 years, across 33 countries, and in more than 17,000 adults with T2D who have multiple CV risk factors or established CVD. In the DECLARE (Dapagliflozin Effect on Cardiovascular Events)-TIMI 58 trial, dapagliflozin met its primary safety endpoint of non-inferiority for major adverse cardiovascular events (MACE). Dapagliflozin achieved a statistically significant reduction in the composite endpoint of hospitalization for HF or CV death, 1 of the 2 primary efficacy endpoints.
- **October 2018:** Findings from the Empagliflozin as Adjunctive to Insulin Therapy (EASE) trials in type-1 diabetes (T1D) was published in *Diabetes Care*. The new data come from 2 double-blind, placebo-controlled Phase 3 trials: EASE-2 and EASE-3. In EASE-2, a total of 730 patients with T1D and HbA_{1c} 7.5 to 10.0% were randomized to 10mg or 25mg of empagliflozin daily or placebo for 52 weeks. In EASE-3, 734 similar patients were randomized to 2.5mg, 10mg, or 25mg of empagliflozin or placebo daily for 26 weeks. Overall, empagliflozin significantly improved glycemic control and decreased weight without increasing hypoglycemia. The 10mg and 25mg doses, the 2 currently approved for treating T2D, were associated with a 3- to 4-fold increased risk for DKA as well as genital infections.
- **October 2018:** Results from the double-blind, randomized placebo-controlled Harmony Outcomes trial published in *The Lancet* indicate that adding the GLP-1 receptor agonist Tanzeum® (albiglutide) to standard care may reduce CV risk among patients with T2D and existing CVD. The composite CV outcome of MI, stroke, or death from CV causes occurred over a median follow-up of 1.6 years in 7% of the 4,731 participants who were

randomly assigned to receive subcutaneous (sub-Q) albiglutide 30mg once weekly (with intensification to 50mg once weekly if additional glucose lowering was needed) in addition to standard diabetes and CVD treatment. By comparison, 428 patients (9%) given add-on placebo experienced the composite outcome, translating into corresponding event rates of 4.57 versus 5.87 per 100 person-years and a significant 22% risk reduction for those in the albiglutide group. When the components of the composite outcome were analyzed separately, albiglutide reduced the risk for MI by a nominally significant 25% relative to placebo, but the HR for death from CV causes and stroke were not statistically significant between the 2 groups.

- **November 2018:** Eli Lilly announced that Trulicity® (dulaglutide) significantly reduced MACE, a composite endpoint of CV death, non-fatal MI, or non-fatal stroke, meeting the primary efficacy objective in the REWIND trial. Dulaglutide is the first T2D medicine to demonstrate superiority in the reduction of MACE events in a clinical trial that included a majority of participants who did not have established CVD. The study included a majority of patients without established CVD at baseline, a first for the GLP-1 receptor agonist class. REWIND assessed the risk of MACE in adults with T2D with a wide range of CV risk. The study compared the effect of once weekly dulaglutide 1.5mg to placebo when added to standard of care. REWIND had a median follow-up period of more than 5 years, the longest for a CV outcome trial in the GLP-1 receptor agonist class. Of the 9,901 REWIND participants, the mean baseline HbA_{1C} was 7.3%, and only 31% had established CVD. The safety profile of dulaglutide in REWIND was generally consistent with the GLP-1 receptor agonist class. Lilly plans to submit these data to regulatory authorities next year and to share detailed results at the ADA Scientific Sessions in June 2019.
- **December 2018:** A cohort study of 132,737 adults with T2D published in *JAMA Network Open* found basal insulin and sulfonylureas were associated with significantly increased CV risk when given as second-line therapy for patients with T2D. Basal insulin was associated with a 36% increase in risk for CV events (HR 1.36, 95% CI 1.23 to 1.49), which included a composite of congestive HF, stroke, ischemic heart disease, and peripheral artery disease (PAD). SGLT-2 inhibitors were not linked with any change in CV risk (HR 0.81, 95% CI 0.57 to 1.53), nor were thiazolidinediones (TZDs) (HR 0.92, 95% CI 0.76 to 1.11). GLP-1 receptor agonists, however, were associated with a lower incidence of CV events (HR 0.78, 95% CI 0.6 to -0.96) and a significant reduction in stroke risk (HR 0.65, 95% CI 0.44 to 0.97), although these effects were not significant in all sensitivity analyses. The study concluded clinicians may consider prescribing newer anti-diabetic medication classes more routinely after metformin rather than sulfonylureas or basal insulin.

Guideline Update(s):

- **October 2018:** The ADA and the European Association for the Study of Diabetes (EASD) have issued an updated consensus statement outlining the management of hyperglycemia in T2D. The report includes updated guidelines based on new literature published since 2014 and was co-published in *Diabetologia* and *Diabetes Care* during the 2018 EASD Annual Meeting in Berlin, Germany. The guidelines were informed by an

expert panel of members from both societies. Recommendations in the report highlight the importance of patient-centered decision making for glycemic management and improvement of diet and exercise for patients with T2D through diabetes self-management education and support. Metformin is the preferred first-line glucose-lowering medication for most patients with T2D. Stepwise addition to initial medications (i.e., adding glucose-lowering medications to metformin treatment) is generally preferred over initial combination therapy. Patient preferences are a major factor in medication adherence and should be considered specifically when selecting glucose-lowering medications. Clinical characteristics such as the presence of comorbid CVD, or renal conditions should also inform medication choices. In addition, access, cost, and insurance coverage for glucose-lowering medications are important considerations when choosing a therapy.

- **November 2018:** The American College of Cardiology (ACC) released new guidance on the use of therapies for CV risk reduction in patients with T2D and atherosclerotic CVD. In response to the introduction of certain SGLT-2 inhibitors and GLP-1 agonists that reduce the risk of MACE, the authors of the guidance sought to summarize key evidence from recent studies and provide practical guidance on the use of specific glucose-lowering agents for the reduction of CV risk in patients with T2D. They recommend that, following discussion with the patient, clinicians should consider adding SGLT-2 inhibitors and GLP-1 agonists to the treatment regimen of patients with T2D and atherosclerotic CVD to lower CV risk.

Recommendations

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

Utilization Details of Non-Insulin Anti-Diabetic Medications: Calendar Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
ALPHA-GLUCOSIDASE INHIBITOR PRODUCTS						
ACARBOSE TAB 25MG	102	24	$2,334.64	2.69	4.25	$22.89
ACARBOSE TAB 50MG	30	6	$813.83	2.99	5	$27.13
ACARBOSE TAB 100MG	14	3	$409.22	2.93	4.67	$29.23
SUBTOTAL	**146**	**33**	**$3,557.69**	**2.78**	**4.42**	**$24.37**
AMYLINOMIMETIC PRODUCTS						
SYMLINPEN 60 INJ 1000MCG	1	1	$861.30	0.1	1	$861.30
SUBTOTAL	**1**	**1**	**$861.30**	**0.1**	**1**	**$861.30**
BIGUANIDE PRODUCTS						
METFORMIN TAB 500MG	19,440	5,670	$177,007.11	2.05	3.43	$9.11
METFORMIN TAB 1000MG	14,786	3,916	$133,932.71	1.96	3.78	$9.06
METFORMIN TAB 500MG ER	4,847	1,633	$48,692.53	2.18	2.97	$10.05
METFORMIN TAB 850MG	985	286	$9,059.74	2	3.44	$9.20
METFORMIN TAB 750MG ER	658	200	$8,539.02	1.6	3.29	$12.98
RIOMET SOL 500MG/5ML	34	9	$15,865.30	14.87	3.78	$466.63

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
METFORMIN TAB 1000MG ER	11	2	$4,155.86	2	5.5	$377.81
SUBTOTAL	**40,761**	**11,716**	**$397,252.27**	**2.03**	**3.48**	**$9.75**
DPP-4 INHIBITOR PRODUCTS						
JANUVIA TAB 100MG	3,237	808	$2,159,505.75	1.01	4.01	$667.13
TRADJENTA TAB 5MG	1,151	164	$454,814.95	1	7.02	$395.15
JANUVIA TAB 50MG	781	196	$500,767.67	1.12	3.98	$641.19
JANUVIA TAB 25MG	224	57	$126,327.82	1.03	3.93	$563.96
ONGLYZA TAB 5MG	188	39	$105,494.70	1.02	4.82	$561.14
ONGLYZA TAB 2.5MG	20	8	$14,981.11	1.19	2.5	$749.06
ALOGLIPTIN TAB 25MG	12	3	$3,309.01	1	4	$275.75
NESINA TAB 25MG	10	2	$4,388.51	1	5	$438.85
SUBTOTAL	**5,623**	**1,277**	**$3,369,589.52**	**1.02**	**4.40**	**$599.25**
DPP-4 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
JANUMET TAB 50-1000MG	1,162	210	$489,210.53	1.94	5.53	$421.01
JANUMET XR TAB 100-1000MG	373	59	$155,372.00	0.99	6.32	$416.55
JANUMET XR TAB 50-1000MG	358	55	$131,361.53	1.77	6.51	$366.93
JANUMET TAB 50-500MG	153	39	$63,358.21	1.92	3.92	$414.11
JENTADUETO TAB 2.5-1000MG	56	9	$25,268.00	2	6.22	$451.21
KOMBIGLYZ XR TAB 2.5-1000MG	52	10	$20,514.66	1.87	5.2	$394.51
JANUMET XR TAB 50-500MG	34	5	$7,675.96	1.06	6.8	$225.76
KOMBIGLYZ XR TAB 5-1000MG	21	4	$8,135.57	1.1	5.25	$387.41
JENTADUETO TAB 2.5-500MG	5	2	$5,168.93	2	2.5	$1,033.7
JENTADUETO TAB 2.5-850MG	4	1	$4,777.84	2	4	$1,194.4
JENTADUETO TAB XR 5-1000MG	2	1	$809.50	1	2	$404.75
SUBTOTAL	**2,220**	**395**	**$911,652.73**	**1.74**	**5.62**	**$410.65**
DPP-4 INHIBITOR/TZD COMBINATION PRODUCTS						
OSENI TAB 25-30MG	5	1	$4,004.93	1	5	$800.99
ALOG/PIOGLIT TAB 25-30MG	2	1	$1,053.52	1	2	$526.76
SUBTOTAL	**7**	**2**	**$5,058.45**	**1**	**3.5**	**$722.64**
GLINIDE PRODUCTS						
REPAGLINIDE TAB 1MG	40	10	$957.41	2.39	4	$23.94
NATEGLINIDE TAB 60MG	40	10	$2,117.88	3.1	4	$52.95
NATEGLINIDE TAB 120MG	32	10	$1,730.44	2.49	3.2	$54.08
REPAGLINIDE TAB 2MG	28	6	$1,063.92	4.78	4.67	$38.00
REPAGLINIDE TAB 0.5MG	5	2	$124.48	2.71	2.5	$24.90
SUBTOTAL	**145**	**38**	**$5,994.13**	**3.07**	**3.82**	**$41.34**
GLP-1 AGONIST PRODUCTS						
VICTOZA INJ 18MG/3ML	3,637	762	$2,643,398.57	0.26	4.77	$726.81
TRULICITY INJ 1.5/0.5ML	644	105	$436,983.30	0.07	6.13	$678.55
BYDUREON PEN INJ 2MG	462	115	$291,437.53	0.14	4.02	$630.82
TRULICITY INJ 0.75/0.5ML	247	63	$173,318.24	0.07	3.92	$701.69
BYDUREON INJ 2MG	63	18	$40,345.48	0.14	3.5	$640.40
BYDUREON BC INJ 2/0.85ML	24	6	$15,474.70	0.12	4	$644.78

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
BYETTA INJ 10MCG	20	9	$21,736.08	0.07	2.22	$1,086.8
BYETTA INJ 5MCG	18	10	$12,274.72	0.02	1.8	$681.93
TANZEUM INJ 50MG	13	2	$6,614.28	0.14	6.5	$508.79
TANZEUM INJ 30MG	12	4	$6,100.76	0.14	3	$508.40
OZEMPIC INJ 2/1.5ML	11	6	$7,452.59	0.11	1.83	$677.51
OZEMPIC INJ 2/1.5ML	10	5	$7,092.10	0.05	2	$709.21
SUBTOTAL	**5,161**	**1,105**	**$3,662,228.35**	**0.21**	**4.67**	**$709.60**
GLP-1 AGONIST/INSULIN COMBINATION PRODUCTS						
SOLIQUA INJ U-100/ML-33MCG/ML	46	11	$29,975.48	0.36	4.18	$651.64
XULTOPHY INJ U-100/ML-3.6MG/ML	32	7	$30,858.40	0.45	4.57	$964.33
SUBTOTAL	**78**	**18**	**$60,833.88**	**0.39**	**4.33**	**$779.92**
SGLT-2 INHIBITOR PRODUCTS						
JARDIANCE TAB 25MG	982	207	$434,887.65	1	4.74	$442.86
JARDIANCE TAB 10MG	730	191	$330,662.87	1	3.82	$452.96
INVOKANA TAB 300MG	553	88	$248,808.56	1	6.28	$449.93
FARXIGA TAB 10MG	336	78	$150,153.13	1	4.31	$446.88
INVOKANA TAB 100MG	276	50	$123,400.74	0.99	5.52	$447.10
FARXIGA TAB 5MG	128	41	$56,882.29	1	3.12	$444.39
STEGLATRO TAB 5MG	7	1	$1,887.29	1	7	$269.61
STEGLATRO TAB 15MG	1	1	$264.72	1	1	$264.72
SUBTOTAL	**3,013**	**657**	**$1,346,947.25**	**1.0**	**4.59**	**$447.05**
SGLT-2 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
SYNJARDY TAB 12.5-1000MG	98	15	$42,884.77	1.93	6.53	$437.60
INVOKAMET TAB 150-1000MG	69	12	$29,507.44	1.94	5.75	$427.64
XIGDUO XR TAB 10-1000MG	50	10	$22,520.51	1	5	$450.41
XIGDUO XR TAB 5-1000MG	41	10	$18,109.56	1.95	4.1	$441.70
INVOKAMET TAB 50-1000MG	32	5	$14,111.91	2	6.4	$441.00
SYNJARDY TAB 5-500MG	18	5	$7,536.50	1.83	3.6	$418.69
INVOKAMET XR TAB 150-1000MG	17	3	$7,498.72	1.94	5.67	$441.10
SYNJARDY TAB 5-1000MG	17	5	$7,649.52	2	3.4	$449.97
SYNJARDY XR TAB 12.5-1000MG	12	2	$3,428.59	1.25	6	$285.72
INVOKAMET TAB 50-500MG	10	1	$4,533.83	2	10	$453.38
SYNJARDY XR TAB 25-1000MG	9	3	$4,081.80	1	3	$453.53
SYNJARDY XR TAB 5-1000MG	9	2	$2,072.79	1	4.5	$230.31
XIGDUO XR TAB 5-500MG	6	4	$2,735.31	1	1.5	$455.89
SYNJARDY XR TAB 10-1000MG	6	1	$5,535.90	2	6	$922.65
XIGDUO XR TAB 2.5-1000MG	1	1	$471.41	2	1	$471.41
SUBTOTAL	**395**	**79**	**$172,678.56**	**1.75**	**5**	**$437.16**
SULFONYLUREA PRODUCTS						
GLIPIZIDE TAB 5MG	2,430	720	$21,521.28	1.49	3.38	$8.86
GLYBURIDE TAB 5MG	2,394	623	$33,856.89	2.09	3.84	$14.14
GLIPIZIDE TAB 10MG	2,376	634	$20,188.64	1.82	3.75	$8.50
GLIMEPIRIDE TAB 4MG	1,357	345	$14,670.10	1.42	3.93	$10.81

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
GLIMEPIRIDE TAB 2MG	885	278	$9,663.95	1.25	3.18	$10.92
GLYBURIDE TAB 2.5MG	609	301	$7,640.69	1.41	2.02	$12.55
GLIPIZIDE ER TAB 10MG	516	151	$12,128.84	1.33	3.42	$23.51
GLIMEPIRIDE TAB 1MG	474	129	$4,429.64	1.18	3.67	$9.35
GLIPIZIDE ER TAB 5MG	385	141	$6,177.11	1.15	2.73	$16.04
GLIPIZIDE ER TAB 2.5MG	334	101	$5,483.76	1.1	3.31	$16.42
GLIPIZIDE XL TAB 5MG	246	89	$3,878.26	1.42	2.76	$15.77
GLIPIZIDE XL TAB 10MG	245	83	$4,930.28	1.29	2.95	$20.12
GLYBURIDE TAB 1.25MG	122	52	$1,666.29	1.34	2.35	$13.66
GLYBURID MCR TAB 3MG	41	9	$464.54	1.89	4.56	$11.33
GLYBURID MCR TAB 6MG	35	8	$542.85	1.98	4.38	$15.51
GLIPIZIDE XL TAB 2.5MG	20	9	$338.33	1.03	2.22	$16.92
GLYBURID MCR TAB 1.5MG	12	2	$140.44	1.5	6	$11.70
CHLORPROPAM TAB 100MG	1	1	$31.93	1	1	$31.93
SUBTOTAL	**12,482**	**3,676**	**$147,753.82**	**1.57**	**3.40**	**$11.84**
SULFONYLUREA/BIGUANIDE COMBINATION PRODUCTS						
GLYB/METFORM TAB 5-500MG	360	52	$4,598.78	3.13	6.92	$12.77
GLIP/METFORM TAB 5-500MG	134	24	$3,869.55	2.32	5.58	$28.88
GLYB/METFORM TAB 2.5-500MG	65	18	$831.73	2.9	3.61	$12.80
GLIP/METFORM TAB 2.5-500MG	56	15	$2,217.85	2.92	3.73	$39.60
GLIP/METFORM TAB 2.5-250MG	12	2	$435.77	2.08	6	$36.31
GLYB/METFORM TAB 1.25-250MG	7	2	$84.64	1.2	3.5	$12.09
SUBTOTAL	**634**	**113**	**$12,038.32**	**2.85**	**5.61**	**$18.99**
SGLT-2 INHIBITOR/DPP-4 INHIBITOR COMBINATION PRODUCTS						
GLYXAMBI TAB 25-5MG	83	14	$42,307.57	1	5.93	$509.73
GLYXAMBI TAB 10-5MG	20	5	$10,166.42	1	4	$508.32
QTERN TAB 10MG/5MG	8	1	$3,718.57	1	8	$464.82
SUBTOTAL	**111**	**20**	**$56,192.56**	**1**	**5.55**	**$506.24**
TZD PRODUCTS						
PIOGLITAZONE TAB 30MG	925	246	$13,160.56	0.99	3.76	$14.23
PIOGLITAZONE TAB 15MG	676	208	$8,766.73	1.04	3.25	$12.97
PIOGLITAZONE TAB 45MG	460	125	$6,867.31	1	3.68	$14.93
AVANDIA TAB 4MG	15	2	$3,897.23	1.1	7.5	$259.82
SUBTOTAL	**2,076**	**581**	**$32,691.83**	**1.01**	**3.57**	**$15.75**
TZD/BIGUANIDE COMBINATION PRODUCTS						
PIOGLITA/MET TAB 15-850MG	44	6	$2,893.72	1.77	7.33	$65.77
PIOGLITA/MET TAB 15-500MG	21	3	$1,400.80	2	7	$66.70
ACTOPLUS MET TAB XR 15-1000MG	2	1	$1,873.37	1	2	$936.69
SUBTOTAL	**67**	**10**	**$6,167.89**	**1.77**	**6.7**	**$92.06**
TOTAL	**72,920**	**13,151***	**$10,191,498.55**	**1.69**	**5.54**	**$139.76**

*Total number of unduplicated members.
Costs not take into account 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 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	COST/ DAY	COST/ CLAIM
INSULIN ASPART PRODUCTS						
NOVOLOG INJ FLEXPEN U-100/ML	7,675	2,099	$5,095,032.52	0.54	$18.22	$663.85
NOVOLOG INJ U-100/ML	4,530	944	$2,331,002.71	0.67	$17.62	$514.57
NOVOLOG INJ PENFILL U-100/ML	679	140	$352,793.53	0.47	$14.39	$519.58
FIASP FLEX INJ TOUCH U-100/ML	16	8	$8,915.67	0.42	$15.56	$557.23
FIASP INJ U-100/ML	9	1	$7,676.85	1	$28.43	$852.98
SUBTOTAL	**12,909**	**3,192**	**$7,795,421.28**	**0.58**	**$17.83**	**$603.87**
INSULIN ASPART/NPH COMBINATION PRODUCTS						
NOVOLOG MIX INJ FLEX 70/30 U-100/ML	712	200	$639,426.13	0.74	$26.01	$898.07
NOVOLOG MIX INJ 70/30 U-100/ML	263	62	$201,826.43	0.94	$25.88	$767.40
SUBTOTAL	**975**	**262**	**$841,252.56**	**0.79**	**$25.98**	**$862.82**
INSULIN DEGLUDEC PRODUCTS						
TRESIBA FLEX INJ U-200/ML	712	154	$610,167.39	0.4	$24.42	$856.98
TRESIBA FLEX INJ U-100/ML	448	117	$199,035.87	0.33	$9.84	$444.28
SUBTOTAL	**1,160**	**271**	**$809,203.26**	**0.37**	**$17.90**	**$697.59**
INSULIN DETEMIR PRODUCTS						
LEVEMIR INJ FLEXT U-100/ML	6,782	1,813	$3,654,548.99	0.48	$12.87	$538.86
LEVEMIR INJ U-100/ML	2,887	685	$1,364,594.25	0.53	$14.65	$472.67
SUBTOTAL	**9,669**	**2,498**	**$5,019,143.24**	**0.49**	**$13.31**	**$519.10**
INSULIN GLARGINE PRODUCTS						
LANTUS SOLOS INJ U-100/ML	12,213	3,159	$6,209,231.56	0.46	$11.68	$508.41
LANTUS INJ U-100/ML	5,707	1,201	$2,585,510.49	0.55	$14.22	$453.04
TOUJEO SOLO INJ U-300/ML	567	105	$453,959.25	0.32	$24.73	$800.63
BASAGLAR INJ U-100/ML	38	12	$10,752.33	0.48	$6.98	$282.96
TOUJEO MAX INJ U-300/ML	14	6	$15,395.71	0.43	$35.31	$1,099.69
SUBTOTAL	**18,539**	**4,483**	**$9,274,849.34**	**0.48**	**$12.64**	**$500.29**
INSULIN GLULISINE PRODUCTS						
APIDRA INJ SOLOSTAR U-100/ML	334	78	$242,024.29	0.57	$19.10	$724.62
APIDRA INJ U-100/ML	138	27	$53,303.04	0.51	$13.61	$386.25
SUBTOTAL	**472**	**105**	**$295,327.33**	**0.55**	**$17.80**	**$625.69**
INSULIN LISPRO PRODUCTS						
HUMALOG KWIK INJ U-100/ML	4,163	1,163	$2,914,922.30	0.56	$18.82	$700.20
HUMALOG INJ U-100/ML	3,142	704	$1,675,804.65	0.68	$17.60	$533.36
HUMALOG INJ U-100/ML	326	66	$185,023.80	0.53	$17.34	$567.56
HUMALOG JR INJ U-100/ML	203	51	$120,583.66	0.45	$15.55	$594.01
HUMALOG KWIK INJ U-200/ML	46	8	$75,266.19	0.81	$55.38	$1,636.22
SUBTOTAL	**7,880**	**1,992**	**$4,971,600.60**	**0.60**	**$18.42**	**$630.91**
INSULIN LISPRO/NPH COMBINATION PRODUCTS						
HUMALOG MIX INJ 75/25KWP U-100/ML	175	37	$155,073.98	0.88	$29.48	$886.14
HUMALOG MIX SUS 75/25 U-100/ML	77	16	$48,609.17	0.62	$17.01	$631.29
HUMALOG MIX INJ 50/50KWP U-100/ML	29	9	$26,875.13	0.78	$26.85	$926.73

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	COST/ DAY	COST/ CLAIM
HUMALOG MIX INJ 50/50 U-100/ML	14	2	$16,418.24	1.51	$41.25	$1,172.73
SUBTOTAL	**295**	**64**	**$246,976.52**	**0.82**	**$25.95**	**$837.21**
NPH (N) INSULIN PRODUCTS						
HUMULIN N INJ U-100/ML	471	171	$114,538.58	0.48	$7.09	$243.18
NOVOLIN N INJ U-100/ML	371	121	$83,272.01	0.47	$6.10	$224.45
NOVOLIN N INJ RELION U-100/ML	314	107	$15,593.10	0.52	$1.43	$49.66
HUMULIN N INJ U-100KWP	307	135	$152,686.88	0.43	$12.65	$497.35
SUBTOTAL	**1,463**	**534**	**$366,090.57**	**0.47**	**$6.93**	**$250.23**
REGULAR (R) INSULIN PRODUCTS						
HUMULIN R INJ U-100/ML	966	281	$221,006.74	0.51	$7.82	$228.79
NOVOLIN R INJ U-100/ML	532	147	$122,312.20	0.55	$7.63	$229.91
NOVOLIN R INJ RELION U-100/ML	263	83	$16,270.00	0.51	$1.72	$61.86
HUMULIN R INJ U-500/ML	230	51	$348,284.31	0.52	$48.03	$1,514.28
HUMULIN R INJ U-500/ML	11	3	$25,765.22	1.06	$75.78	$2,342.29
SUBTOTAL	**2,002**	**565**	**$733,638.47**	**0.52**	**$11.96**	**$366.45**
R/N INSULIN COMBINATION PRODUCTS						
HUMULIN INJ 70/30 U-100/ML	456	100	$170,216.46	0.79	$11.74	$373.28
NOVOLIN INJ 70/30 U-100/ML	300	92	$101,217.87	0.7	$9.71	$337.39
NOVOLIN 70/30 INJ RELION U-100/ML	223	67	$14,108.41	0.79	$1.94	$63.27
HUMULIN INJ 70/30KWP U-100/ML	186	54	$136,334.66	0.62	$19.05	$732.98
SUBTOTAL	**1,165**	**313**	**$421,877.40**	**0.76**	**$13.11**	**$362.13**
TOTAL	**56,529**	**7,821***	**$30,775,380.57**	**0.53**	**$14.83**	**$544.42**

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

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Appendix K

30-Day Notice to Prior Authorize Cablivi® (Caplacizumab-yhdp)

Oklahoma Health Care Authority
April 2019

Introduction[1,2,3]

Thrombotic thrombocytopenic purpura (TTP) is a thrombotic microangiopathy caused by severely reduced activity of the von Willebrand factor (vWF)-cleaving protease ADAMTS13. It is characterized by small-vessel platelet-rich thrombi that cause thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and sometimes organ damage. TTP is a medical emergency that is usually fatal if appropriate treatment is not initiated promptly. With appropriate treatment, survival rates of up to 90% are possible. TTP can be acquired, due to an autoantibody inhibitor, or hereditary, due to inherited mutations in *ADAMTS13*. The term acquired TTP (aTTP) is used to refer to the primary thrombotic microangiopathy (TMA) characterized by severe ADAMTS13 deficiency (typically, activity <10%) due to an autoantibody directed against ADAMTS13.

The usual presentation of aTTP is severe MAHA and thrombocytopenia in a previously healthy individual. Initial symptoms may include fatigue, dyspnea, petechiae, or other bleeding. Importantly, however, not all patients with aTTP are critically ill. They may present with complaints of weakness and dizziness, abdominal pain, easy bruising, or nausea and vomiting. In some patients, the diagnosis of aTTP may not be considered until the complete blood count (CBC) reveals severe thrombocytopenia and MAHA. Organ involvement in aTTP often affects the central nervous system (CNS) and/or gastrointestinal (GI) system. Renal involvement is seen on renal biopsy, but acute kidney injury is uncommon. Other organs such as the heart may also be affected. Pulmonary involvement is rare. Severely reduced ADAMTS13 activity (generally <10%) during an acute episode is a hallmark of aTTP, but should not be used in isolation for diagnosis.

The incidence of aTTP is approximately 3 cases per 1 million adults per year, based on data from the Oklahoma TTP-Hemolytic Uremic Syndrome (HUS) Registry. The median age for the diagnosis of aTTP is 41 years of age (range 9 to 78 years). It is estimated that the incidence of aTTP in children younger than 18 years of age is approximately 1 per 10 million per year (approximately 30-fold less common than in adults). Demographic features associated with an increased risk of aTTP include female gender and African-American race.

Current therapy for aTTP includes plasma exchange therapy to supplement ADAMTS13 and to remove anti-ADAMTS13 autoantibodies. Additionally, to suppress autoantibody production, corticosteroid therapy may be administered in conjunction with plasma exchange. Reports have also shown that rituximab is effective in patients with refractory or relapsed TTP. In February 2019, the U.S. Food and Drug Administration (FDA) approved Sanofi's Nanobody®- based medicine, Cablivi® (caplacizumab-yhdp). Cablivi® is the first FDA-approved therapy specifically indicated for the treatment of aTTP.

Cablivi® (Caplacizumab-yhdp) Product Summary[4,5,6]

Indication(s): Cablivi® (caplacizumab-yhdp) is a vWF-directed antibody fragment indicated for the treatment of adult patients with aTTP, to be used in combination with plasma exchange and immunosuppressive therapy.

Dosing:

- Cablivi® for injection is supplied as a sterile, preservative-free, lyophilized powder in a single-dose vial (SDV). It is available in a carton containing (1) 11mg Cablivi® SDV, (1) 1mL sterile water for injection prefilled glass syringe (diluent for Cablivi®), 1 sterile vial adapter, 1 sterile hypodermic needle (30 gauge), and 2 individually packaged alcohol swabs.
- Caplacizumab vials should be refrigerated at 36 to 46°F (2 to 8°C) in the original carton to protect from light. Unopened vials may be stored in the original carton at room temperature up to 86°F (30°C) for a single period of up to 2 months.
- Caplacizumab should be administered upon the initiation of plasma exchange therapy.
- The recommended dosing for the first day of treatment is an 11mg intravenous (IV) bolus injection given at least 15 minutes prior to plasma exchange followed by an 11mg subcutaneous (sub-Q) injection after completion of plasma exchange on day 1.
- On subsequent days of treatment when daily plasma exchange is ongoing, the dosing is 11mg sub-Q once daily following plasma exchange.
- For treatment after the plasma exchange period, the dosing is 11mg sub-Q once daily continuing for 30 days following the last daily plasma exchange. If after the initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.
- Treatment should be discontinued if the patient experiences more than 2 recurrences of aTTP, while on caplacizumab.

Mechanism of Action: Caplacizumab is a vWF-directed antibody fragment that targets the A1-domain of vWF, and inhibits the interaction between vWF and platelets, thereby reducing both vWF-mediated platelet adhesion and platelet consumption.

Contraindication(s): Caplacizumab is contraindicated in patients with a previous severe hypersensitivity reaction to caplacizumab or to any of the excipients.

Warnings and Precautions:

- Bleeding: Caplacizumab increases the risk of bleeding. In clinical studies, severe bleeding adverse reactions of epistaxis, gingival bleeding, upper GI hemorrhage, and metrorrhagia were each reported in 1% of patients. Overall, bleeding events occurred in approximately 58% of patients on caplacizumab versus 43% of patients on placebo. Concomitant use of caplacizumab with any anticoagulant may increase the risk of bleeding. Caplacizumab should be withheld for 7 days prior to elective surgery, dental procedures, or other invasive interventions. If emergency surgery is needed, the use of vWF concentrate may be considered to correct hemostasis. After the risk of surgical

bleeding has resolved, and caplacizumab is resumed, the patient should be monitored closely for signs of bleeding.

Adverse Reactions:

- The most frequently reported adverse reactions (>15%) reported during caplacizumab clinical trials were epistaxis, headache, and gingival bleeding.
- As with all therapeutic proteins, there is potential for immunogenicity. The prevalence of pre-existing antibodies binding to caplacizumab observed during clinical studies and during evaluation of commercially available human samples varied between 4% and 63%. Treatment emergent anti-drug antibodies (TE ADA) against caplacizumab were detected in 3% of patients treated with caplacizumab. TE ADA had no clinically apparent impact on clinical efficacy or safety.

Use in Specific Populations:

- Pregnancy: There are no available data on caplacizumab use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. However, there are potential risks of hemorrhage in the mother and fetus associated with use of caplacizumab. Two separate reproduction studies were conducted in pregnant guinea pigs with administration of caplacizumab during the organogenesis period. In both studies, with doses up to 40mg/kg/day [corresponding to a drug exposure of approximately 30 times the area under the curve (AUC) in humans], no maternal toxicity or adverse developmental outcomes to the fetus were observed.
- Lactation: There is no information regarding the presence of caplacizumab in human milk, the effects on the breastfed child, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of caplacizumab in pediatric patients have not been established.
- Geriatric Use: Clinical studies of caplacizumab did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.
- Hepatic Impairment: No formal studies with caplacizumab have been conducted in patients with severe acute or chronic hepatic impairment and no data regarding the use of caplacizumab in these populations are available. Due to a potential increased risk of bleeding, patients being treated with caplacizumab who have severe hepatic impairment should be closely monitored for bleeding.

Efficacy: The efficacy of caplacizumab for the treatment of adult patients with aTTP in combination with plasma exchange and immunosuppressive therapy was established in a pivotal, multicenter, randomized, double-blind, placebo-controlled trial (HERCULES). A total of 145 patients were enrolled in the HERCULES study; the median age was 45 years (range 18 to 79). Patients were randomized to either caplacizumab (N=72) or placebo (N=73). Patients in both groups received plasma exchange and immunosuppressive therapy. Patients with sepsis, infection with *Escherichia coli*, atypical HUS, disseminated intravascular coagulation, or congenital thrombotic thrombocytopenic purpura were not eligible for enrollment.

Patients received a single 11mg caplacizumab IV bolus injection or placebo prior to the first plasma exchange, followed by a daily sub-Q injection of 11mg caplacizumab or placebo after completion of plasma exchange, for the duration of the daily plasma exchange period and for 30 days thereafter. If after the initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remained present, treatment was extended for 7-day intervals for a maximum of 28 days. The median treatment duration with caplacizumab was 35 days.

The primary endpoint was time to platelet count response, defined as platelet count $\geq 150 \times 10^9$/L within 5 days of stopping daily plasma exchange. Compared to patients treated with placebo, those on caplacizumab were >50% more likely to achieve a platelet response at any given time point (platelet count normalization rate 1.55, P<0.01). During the study drug treatment period, treatment with caplacizumab resulted in a 74% reduction in TTP-related death, recurrence of TTP, or a treatment-emergent major thromboembolic event (P<0.0001). During the overall study period, 28 patients in the placebo group experienced a recurrence versus 9 patients in the caplacizumab group, a 67% reduction (P<0.001). In all 6 caplacizumab-treated patients with a relapse during the follow-up period, ADAMTS13 activity was still <10% at stop of study drug, reflecting ongoing disease. The relapses after stopping the study drug in patients with ADAMTS13 activity <10% suggest that treatment should be continued until complete resolution of the underlying disease. No caplacizumab-treated patients were refractory to therapy, while 3 patients on placebo were refractory (P=0.057).

Cost: The Wholesale Acquisition Cost (WAC) of Cablivi® (caplacizumab) is $7,300 per vial. This results in an approximate cost per treatment of $299,300. This cost is based on a 10-day duration of plasma exchange followed by 30 days of caplacizumab treatment. Disease course may vary making plasma exchange duration patient-specific, so cost may vary. It is estimated that, on average, 7 to 10 days of plasma exchange may be required to achieve a response (indicated by normalization of the platelet count). Additionally, the cost provided does not include continued treatment beyond 30 days post-plasma exchange. In clinical trials, continued treatment for up to 28 days following the 30 days after plasma exchange was required for some patients who continued to have signs of persistent disease.

Recommendations

The College of Pharmacy recommends the prior authorization of Cablivi® (caplacizumab-yhdp) with the following criteria:

Cablivi® (Caplacizumab-yhdp) Approval Criteria:

1. An FDA approved diagnosis of acquired thrombotic thrombocytopenic purpura (aTTP); and
2. Member must be undergoing plasma exchange therapy; and
    a. Dates of initiation of plasma exchange therapy must be listed on the prior authorization request; and
    b. Authorizations will be for the duration of plasma exchange and for 30 days after discontinuation of plasma exchange; and

3. Member must be utilizing immunosuppressant therapy; and
4. Cablivi® must be prescribed by, or in consultation with, a hematologist; and
5. A quantity limit of 11mg per day will apply. Initial approvals will be for the duration of plasma exchange plus 30 days. Reauthorization, after completing 30 days post-plasma exchange, may be considered if the prescriber documents sign(s) of persistent underlying disease remain. Reauthorization will be for a maximum of 28 days.

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Appendix L

30-Day Notice to Prior Authorize Aldurazyme® (Laronidase) and Naglazyme® (Galsulfase)

Oklahoma Health Care Authority
April 2019

Introduction[1,2]

Mucopolysaccharidoses (MPS) are a group of lysosomal storage disorders caused by the deficiency of enzymes required for the breakdown of glycosaminoglycans (GAGs), previously known as mucopolysaccharides. GAGs are large, complex polymers of linear, repeating sulfated acidic and amino sugar disaccharide units attached to a protein core. GAGs are widely distributed in many tissues, including bone, cartilage, joint fluid, and the surface coating that initially binds growth factors to cells. Fragments of partially degraded GAGs accumulate in the lysosomes resulting in cellular dysfunction.

MPS are rare conditions, with an estimated total incidence of 1 in 20,000 live births for all types of MPS. All of the MPS are autosomal recessive disorders, except MPS II, which is X-linked. The MPS disorders are classified under 7 different types which are differentiated by their clinical features, age of presentation, and their associated enzyme deficiency. Signs and symptoms are usually not present at birth, with the exception of severe forms of MPS VII. Most present within the first few years of life, but some can present as late as adolescence to early adulthood.

MPS I is caused by the deficiency of the lysosomal hydrolase, alpha-L-iduronidase (IDUA), which is required for the degradation of heparan sulfate and dermatan. MPS I is caused by mutation(s) in the *IDUA* gene. The syndrome that results from the mutation(s) depends on the combination of mutations on both alleles and by the presence of polymorphisms within the gene. Hurler syndrome is the most severe form of MPS I, and is characterized by a broad spectrum of clinical symptoms including skeletal abnormalities, hepatosplenomegaly, and severe intellectual disability. Patients with Hurler syndrome typically die before the age of 10 years. Hurler-Scheie syndrome is intermediate in severity, and is less common than Hurler. The most common presenting complaint of Hurler-Scheie syndrome is joint pain, and patients typically live into their twenties. Scheie syndrome is the least severe form of MPS I. The most common presenting features are joint stiffness and corneal clouding. In general, average lifespan is longest with Scheie syndrome, compared to the other subtypes, with most living until middle age.

MPS VI, also known as Maroteaux-Lamy syndrome, is caused by mutations in the gene encoding arylsulfatase B. Maroteaux-Lamy syndrome primarily affects the skeleton and soft tissues. Severely affected children present between the ages of 1 and 6 years, but disease progression can be slower in attenuated forms of the disease. Death typically occurs in the second or third decade of life.

The treatment options vary based on the type of MPS and disease severity. Treatment options are classified as either supportive treatment, enzyme replacement therapy (ERT), or hematopoietic cell transplant (HCT). Many of the MPS types have an ERT approved by the U.S. Food and Drug Administration (FDA). Aldurazyme® (laronidase) was FDA approved in 2003 for the treatment of Hurler, Hurler-Scheie, and moderate-to-severe Scheie syndrome. Naglazyme® (galsulfase) was FDA approved in 2005 for the treatment of MPS VI, also known as Maroteaux-Lamy syndrome.

Aldurazyme® (Laronidase) Product Summary[3]

Indication(s): Aldurazyme® (laronidase) is indicated for patients with Hurler and Hurler-Scheie forms of MPS I and for patients with the Scheie form who have moderate-to-severe symptoms.

Dosing:

- Aldurazyme® is supplied as a sterile solution for single-use in a 5mL vial containing 2.9mg laronidase per 5mL.
- Laronidase should be refrigerated at 2 to 8°C (36 to 46°F) in the original container; diluted solution should be used immediately; storage after dilution should not exceed 48 hours from the time of preparation to the completion of infusion.
- The recommended dose of laronidase is 0.58mg/kg once weekly via intravenous (IV) infusion.
- Laronidase is recommended to be infused over approximately 3 to 4 hours.

Boxed Warning: Risk of Anaphylaxis
Life-threatening anaphylactic reactions have been observed in some patients during IV infusion with laronidase. Appropriate medical support should be readily available when laronidase is administered. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.

Mechanism of Action: Laronidase is a recombinant form of human IUDA intended to provide exogenous enzyme for uptake into lysosomes and increase the catabolism of GAGs.

Contraindication(s): None

Warnings and Precautions:

- Anaphylaxis and Allergic Reactions: Anaphylaxis and severe allergic reactions have been observed in patients during or up to 3 hours after laronidase infusions. Some of these reactions were life-threatening and included respiratory failure, respiratory distress, stridor, tachypnea, bronchospasm, obstructive airways disorder, hypoxia, hypotension, bradycardia, and urticaria. If anaphylactic or other severe allergic reactions occur, laronidase infusion should be discontinued and appropriate medical treatment should be initiated. Caution should be exercised if epinephrine is being considered for use in patients with MPS I due to the increased prevalence of coronary artery disease in these patients. In clinical studies and post-marketing safety experience with laronidase, approximately 1% of patients experienced severe or serious allergic reactions. Pre-

existing upper airway obstruction is common in patients with MPS I and may have contributed to the severity of some reactions.

- Acute Respiratory Complications Associated with Administration: Patients with sleep apnea, which is common in MPS I, or an acute febrile or respiratory illness at the time of laronidase infusion may be at greater risk for infusion reactions. Evaluation of airway patency should be considered prior to initiation of treatment with laronidase. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an infusion reaction or extreme drowsiness induced by antihistamine use.
- Risk of Acute Cardiorespiratory Failure: Caution should be exercised when administering laronidase to patients susceptible to fluid overload, or in patients with acute underlying respiratory illness or compromised cardiac and/or respiratory function for whom fluid restriction is indicated. These patients may be at risk of serious exacerbation of their cardiac or respiratory status during infusions.
- Infusion Reactions: Because of the potential for infusion reactions, patients should receive antipyretics and/or antihistamines prior to infusion. If an infusion reaction occurs, regardless of pretreatment, decreasing the infusion rate, temporarily stopping the infusion, or administering additional antipyretics and/or antihistamines may ameliorate the symptoms.

Adverse Reactions: The most common infusion reactions reported during clinical trials of laronidase included rash, flushing, pyrexia, headache, abdominal pain or discomfort, and injection site reaction(s). Less commonly reported infusion reactions included nausea, diarrhea, feeling hot or cold, vomiting, pruritus, arthralgia, and urticaria. Additional common adverse reactions included back pain and musculoskeletal pain.

Use in Specific Populations:

- Pregnancy: A developmental toxicity study has been performed in rats at doses up to 6.2 times the human dose and has revealed no evidence of impaired fertility or harm to the fetus due to laronidase. However, there are no adequate and well-controlled studies of laronidase in pregnant women.
- Lactation: It is not known whether laronidase is excreted in human milk.
- Pediatric Use: The safety and effectiveness of laronidase were assessed in a 52-week, open-label, uncontrolled clinical study in 20 patients with MPS I, ages 6 months to 5 years, and was found to be similar to the safety and effectiveness of laronidase in pediatric patients 6 to 18 years of age and in adults.
- Geriatric Use: Clinical studies of laronidase did not include patients 65 years of age and older. It is not known whether they respond differently from younger patients.

Efficacy: The safety and efficacy of laronidase were assessed in 3 clinical studies:

- Study 1: Study 1 was a randomized, double-blind, placebo-controlled study in 45 patients with MPS I, ages 6 to 43 years, including 1 patient with Hurler form, 37 patients with Hurler-Scheie form, and 7 patients with Scheie form of MPS I. All patients had a baseline percent predicted forced vital capacity (ppFVC) ≤77%. The primary efficacy outcome assessments were ppFVC and distance walked in 6 minutes (6-MWT). After 26

weeks, patients treated with laronidase showed improvement in median difference of ppFVC [2 (0.4, 7), P=0.02] and in median difference of 6-MWT [39 (-2, 79), P=0.07] compared to placebo-treated patients.

- Study 2: Study 2 was a 182-week, open-label, uncontrolled extension study of all 45 patients who completed Study 1. Patients received laronidase at 0.58mg/kg once weekly. For patients treated with laronidase, the mean increase in 6-MWT was maintained for an additional 182 weeks through completion of Study 2.
- Study 3: Study 3 was a 52-week, open-label, uncontrolled clinical study in 20 patients with MPS I, 6 months to 5 years of age (at enrollment), including 16 patients (80%) with Hurler form and 4 patients (20%) with Hurler-Scheie form. All 20 patients received laronidase 0.58mg/kg once weekly for 26 weeks. After 26 weeks of treatment, 16 patients continued to receive 0.58mg/kg once weekly through week 52, and 4 patients received 1.16mg/kg once weekly from week 26 through week 52. Reduction in mean urinary GAG levels was demonstrated at week 13 and was maintained through week 52.

Cost: The Wholesale Acquisition Cost (WAC) of Aldurazyme® is $176.00 per milliliter (mL), resulting in a cost per 28 days of $10,560 and a yearly cost of $137,280 for a 15kg patient. Dosing is weight-based; therefore, pricing will vary.

Naglazyme® (Galsulfase) Product Summary[4]

Indication(s): Naglazyme® (galsulfase) is a hydrolytic lysosomal GAG-specific enzyme indicated for patients with MPS VI (Maroteaux-Lamy syndrome).

Dosing:

- Naglazyme® is supplied as a sterile injection for IV infusion in 5mL single-use vials containing 1mg/1mL of galsulfase.
- Galsulfase should be stored at 2 to 8°C (36 to 46°F); diluted solution should be used immediately; storage after dilution should not exceed 48 hours from the time of preparation to the completion of infusion.
- The recommended dosage of galsulfase is 1mg/kg once weekly via IV infusion.
- Galsulfase is recommended to be infused over no less than 4 hours, and can be extended up to 20 hours if infusion reactions occur.
- Pretreatment with antihistamines with or without antipyretics is recommended 30 to 60 minutes prior to the start of the infusion.

Mechanism of Action: Galsulfase, an exogenous enzyme produced by recombinant DNA technology, increases the catabolism of GAG.

Contraindication(s): None

Warnings and Precautions:

- Anaphylaxis and Allergic Reactions: Anaphylaxis and allergic reactions have been observed in some patients during galsulfase infusions and up to 24 hours after infusion. Some of the reactions were life-threatening and included anaphylaxis, shock, respiratory distress, dyspnea, bronchospasm, laryngeal edema, and hypotension. In patients who

have experienced anaphylaxis or other severe allergic reactions during infusion with galsulfase, caution should be exercised upon re-challenge; appropriately trained personnel and equipment for emergency resuscitation should be available during infusion.

- Immune-Mediated Reactions: Type III immune complex-mediated reactions, including membranous glomerulonephritis have been observed with galsulfase, as with other ERTs. If immune-mediated reactions occur, discontinuation of galsulfase should be considered, and appropriate medical treatment initiated. The risks and benefits of re-administering galsulfase following an immune-mediated reaction should be considered.
- Risk of Acute Cardiorespiratory Failure: Caution should be exercised when administering galsulfase to patients susceptible to fluid volume overload (e.g., patients weighing ≤20kg, patients with acute underlying respiratory illness, patients with compromised cardiac and/or respiratory function).
- Acute Respiratory Complications Associated with Administration: Patients with acute febrile or respiratory illness at the time of galsulfase infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Prior to administration of galsulfase, careful consideration should be given to the patient's clinical status and the galsulfase infusion may need to be delayed. In patients with MPS VI, sleep apnea is common. Prior to initiation of treatment with galsulfase, an evaluation of airway patency should be considered. It is recommended that patients using supplemental oxygen or CPAP during sleep should have these treatments readily available during infusion in the event of an acute reaction or extreme drowsiness induced by antihistamine use.
- Infusion Reactions: Because of the potential for infusion reactions, patients should receive antihistamines with or without antipyretics prior to infusion. Despite routine pretreatment with antihistamines, infusion reactions, some severe, occurred in 33 of 59 (56%) patients treated with galsulfase. If severe infusion reactions occur, the infusion of galsulfase should be discontinued and appropriate treatment initiated. The risks and benefits of re-administering galsulfase following a severe reaction should be considered. No factors were identified that predisposed patients to infusion reactions. There was no association between severity of infusion reactions and titer of anti-galsulfase antibodies.
- Spinal or Cervical Cord Compression (SCC): SCC with resultant myelopathy is a known and serious complication of MPS VI and may occur in the natural history of the disease. There have been post-marketing reports of patients treated with galsulfase who experienced the onset or worsening of SCC requiring decompression surgery. Patients with MPS VI should be monitored for signs and symptoms of SCC (e.g., back pain, paralysis of limbs below the level of compression, urinary and fecal incontinence) and appropriate clinical care should be given.

Adverse Reactions:

- The most common adverse reactions observed in the placebo-controlled trial and the open-label trials of galsulfase included pruritus, urticaria, pyrexia, headache, nausea, vomiting, abdominal pain, ear pain, arthralgia, conjunctivitis, dyspnea, rash, chills, and chest pain.

- Serious adverse reactions included laryngeal edema, urticaria, angioedema, apnea, pyrexia, and respiratory distress.
- Severe adverse reactions included chest pain, dyspnea, laryngeal edema, conjunctivitis, urticaria, rash, and abdominal pain.

Use in Specific Populations:

- Pregnancy: Galsulfase is classified as pregnancy category B. Adequate and well-controlled studies have not been conducted with galsulfase in pregnant women. Reproduction studies have been performed in rats and rabbits at IV doses up to 3mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to galsulfase. Galsulfase should be used during pregnancy only if clearly needed.
- Lactation: It is not known whether galsulfase is excreted in human milk.
- Pediatric Use: The safety and effectiveness of galsulfase in pediatric patients 5 years of age and older have been established. Adequate and well-controlled trials in pediatric and adult patients support the use of galsulfase in patients 5 years of age and older. Clinical trials with galsulfase were conducted in 56 patients (range 5 to 29 years of age) with the majority of patients in the pediatric age group. In addition, an open-label study was conducted in 4 infants (3 months to 12.7 months) treated with 1mg/kg (N=2) or 2mg/kg (N=2) of galsulfase. Safety results in infants were consistent with results observed in patients 5 to 29 years of age.
- Geriatric Use: Clinical studies of galsulfase did not include patients older than 29 years of age. It is not known whether older patients respond differently than younger patients.

Efficacy: The efficacy of galsulfase was evaluated in a randomized, double-blind, multicenter, placebo-controlled clinical trial of 35 patients with MPS VI:

- The study only included patients with a 12-minute walk test (12-MWT) distance of 5 to 400 meters.
- Patients received 1mg/kg of galsulfase (N=19) or placebo (N=20) once weekly for 24 weeks.
- The galsulfase-treatment group showed a greater mean increase in the 12-MWT (92 ± 40 meters, P=0.025) and the rate of stair climbing in a 3-minute stair climb test (5.7 ± 2.9 stairs/minute, P=0.053) compared to placebo.
- Following the 24-week placebo-controlled study period, 38 patients received open-label galsulfase for 72 weeks. Among the 19 patients who were initially randomized to galsulfase and who continued to receive treatment for 72 weeks (total of 96 weeks), increases in the 12-MWT distance and in the rate of stair climbing were observed compared to the start of the open-label period (72 ± 116 meters and 5.6 ± 10.6 stairs/minute, respectively). Among the 19 patients who were randomized initially to placebo for 24 weeks and then crossed over to treatment with galsulfase, increases after 72 weeks of galsulfase treatment compared to the start of the open-label period were 118 ± 127 meters and 11.1 ± 10.0 stairs/minute, for the 12-MWT and the rate of stair climbing, respectively.

Cost: The WAC of Naglazyme® is $375.40 per mL, resulting in a cost per 28 days of $22,524 and a yearly cost of $292,812 for a 15kg patient. Dosing is weight-based; therefore, pricing will vary.

Recommendations

The College of Pharmacy recommends the prior authorization of Aldurazyme® (laronidase) and Naglazyme® (galsulfase) with the following criteria:

Aldurazyme® (Laronidase) Approval Criteria:

1. An FDA approved diagnosis of Hurler, Hurler-Scheie, or Scheie syndrome (mucopolysaccharidosis type I; MPS I) confirmed by:
    a. Enzyme assay demonstrating a deficiency of α-L-iduronidase enzyme activity; or
    b. Molecular genetic testing to confirm pathogenic mutations in the *IDUA* gene; and
2. For Scheie syndrome, the provider must document that the member has moderate-to-severe symptoms; and
3. Aldurazyme® must be administered by a health care professional prepared to manage anaphylaxis; and
4. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Naglazyme® (Galsulfase) Approval Criteria:

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

[1] Jones S, Wynn R. Mucopolysaccharidoses: Clinical features and diagnosis. *UpToDate*. Available online at: https://www.uptodate.com/contents/mucopolysaccharidoses-clinical-features-and-diagnosis?search=mucopolysaccharidosis&source=search_result&selectedTitle=1~63&usage_type=default&display_rank=1#H11. Last revised 02/01/2019. Last accessed 03/21/2019.

[2] Jones S, Wynn R. Mucopolysaccharidoses: Treatment. *UpToDate*. Available online at: https://www.uptodate.com/contents/mucopolysaccharidoses-treatment?sectionName=HEMATOPOIETIC%20CELL%20TRANSPLANTATION&search=mucopolysaccharidosis&topicRef=2931&anchor=H1119956597&source=see_link#H1119956597. Last revised 02/01/2019. Last accessed 03/21/2019.

[3] Aldurazyme® Prescribing Information. Biomarin Pharmaceuticals, Inc. Available online at: https://www.aldurazyme.com/. Last revised 04/2013. Last accessed 03/21/2019.

[4] Naglazyme® Prescribing information. Biomarin Pharmaceuticals, Inc. Available online at: https://www.naglazyme.com/. Last revised 03/2013. Last accessed 03/21/2019.

Appendix M

Calendar Year 2018 Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Consensi® (Amlodipine/Celecoxib) and Kapspargo™ Sprinkle [Metoprolol Succinate Extended-Release (ER)]

Oklahoma Health Care Authority
April 2019

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.

Direct Renin Inhibitors [Tekturna® (Aliskiren), Tekturna HCT® (Aliskiren/Hydrochlorothiazide)] 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.

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:

Byvalson® (Nebivolol/Valsartan) Approval Criteria:

1. A patient-specific, clinically significant reason the member cannot use the individual components, nebivolol (Bystolic®) and valsartan (Diovan®), separately; and
2. A quantity limit of 30 tablets per 30 days will apply.

Cardizem® CD (Diltiazem CD 360mg Capsules 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.

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; and
2. A patient-specific, clinically significant reason why the member cannot use the generic propranolol solutions (20mg/5mL and 40mg/5mL) which are available without prior authorization must be provided.

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

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

Prestalia® (Perindopril/Amlodipine) 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 patients 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.

Tekturna® (Aliskiren Oral Pellets) 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.

Vecamyl® (Mecamylamine) 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 tables 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**
irbesartan (Avapro®)	amlodipine/olmesartan (Azor®)	azilsartan (Edarbi®)
irbesartan/HCTZ (Avalide®)	amlodipine/valsartan/HCTZ (Exforge® HCT)	azilsartan/chlorthalidone (Edarbyclor®)
losartan (Cozaar®)	olmesartan (Benicar®)	candesartan (Atacand®)
losartan/HCTZ (Hyzaar®)	olmesartan/HCTZ (Benicar HCT®)	candesartan/HCTZ (Atacand® HCT)
telmisartan (Micardis®)	olmesartan/amlodipine/HCTZ (Tribenzor®)	eprosartan (Teveten®)
valsartan (Diovan®)		eprosartan/HCTZ (Teveten® HCT)
valsartan/amlodipine (Exforge®)		telmisartan/amlodipine (Twynsta®)
valsartan/HCTZ (Diovan HCT®)		telmisartan/HCTZ (Micardis® HCT)

HCTZ = hydrochlorothiazide

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
amlodipine (Norvasc®)	amlodipine/atorvastatin (Caduet®)	diltiazem CD 360mg (Cardizem® CD)
diltiazem (Cardizem®)	diltiazem LA (Cardizem® LA, Matzim® LA)	

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
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 ER		
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.

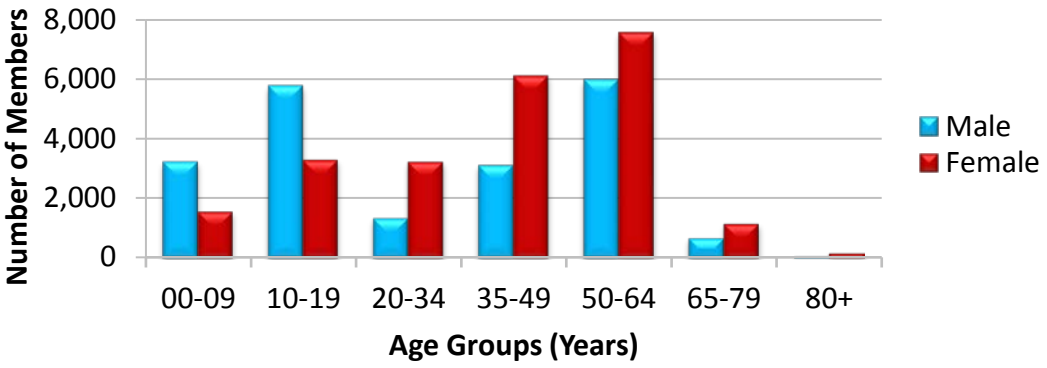
Utilization of Antihypertensive Medications: Calendar Year 2018

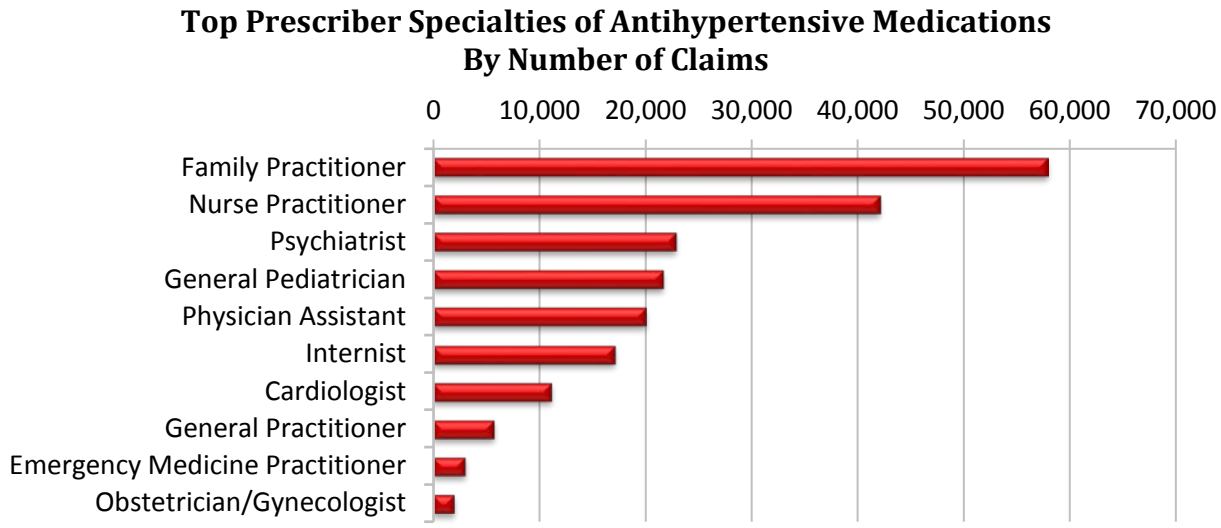
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	43,977	225,912	$3,093,652.61	$13.69	$0.34	11,126,670	9,003,584
2018	43,421	218,217	$2,952,266.32	$13.53	$0.33	11,121,408	9,025,024
% Change	**-1.30%**	**-3.40%**	**-4.60%**	**-1.20%**	**-2.90%**	**0.00%**	**0.20%**
Change	**-556**	**-7,695**	**-$141,386.29**	**-$0.16**	**-$0.01**	**-5,262**	**21,440**

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

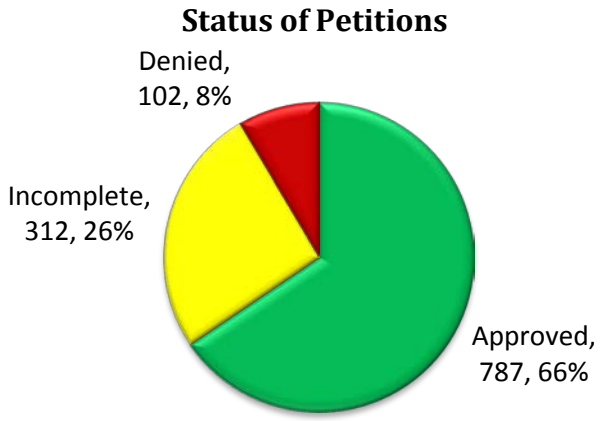
Demographics of Members Utilizing Antihypertensive Medications





Prior Authorization of Antihypertensive Medications

There were 1,201 prior authorization requests submitted for antihypertensive medications during calendar year 2018. 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 2018.



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

Anticipated Patent Expiration(s):

- Tekturna® (aliskiren tablets): August 2026
- Byvalson® (nebivolol/valsartan tablets): October 2027
- Edarbi® (azilsartan tablets): March 2028
- Tekturna HCT® [aliskiren/hydrochlorothiazide (HCTZ) tablets]: July 2028
- Hemangeol® (propranolol hydrochloride oral solution): October 2028
- Prestalia® (perindopril arginine/amlodipine tablets): October 2029
- Consensi® (amlodipine/celecoxib tablets): February 2030
- Edarbyclor® (azilsartan/chlorthalidone tablets): February 2030

- Kapspargo™ Sprinkle [metoprolol succinate extended-release (ER) capsules]: 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):

- **June 2018:** Kitov Pharma announced the FDA approval of Consensi® (amlodipine/ celecoxib tablets) for patients with osteoarthritis (OA) pain and hypertension (HTN).
- **August 2018:** Sun Pharmaceutical Industries Ltd. announced the launch of Kapspargo™ Sprinkle (metoprolol succinate ER capsules) for the treatment of HTN, angina pectoris, and heart failure (HF).

News:

- **August 2018:** Results of a clinical trial of 700 patients to assess whether a low-dose triple combination antihypertensive medication would achieve better blood pressure (BP) control versus usual care were published in the *Journal of the American Medical Association* (*JAMA)*. In this open-label trial, patients received a once-daily, fixed-dose, triple combination pill (20mg of telmisartan, 2.5mg of amlodipine, and 12.5mg of chlorthalidone) or usual care. The primary outcome was the proportion of patients achieving target systolic/diastolic BP [<140/90mmHg or <130/80mmHg in patients with diabetes or chronic kidney disease (CKD)] at 6 months. The triple combination pill increased the proportion of patients achieving target BP versus usual care at 6 months [70% vs. 55%, respectively; risk difference, 12.7%; 95% confidence interval (CI), 3.2% to 22.0%; P<0.001].
- **September 2018:** The American Heart Association updated its 2008 guidelines on detecting and managing resistant HTN, defined as an above goal BP (≥130/80mmHg) despite use of 3 antihypertensive medications, or controlled BP on a 4-drug regimen. The guidelines were published in *Hypertension* and contain several practical diagnostic and clinical management tips, including the following:
  - Health care providers should regularly ask patients with resistant HTN about their sleep patterns.
  - The role of lifestyle is emphasized as part of first-line management of resistant HTN.
  - If BP is above goal despite an optimal lifestyle and adherence to a 3-drug regimen, providers should consider switching from HCTZ to chlorthalidone or indapamide. If BP is still high after that, spironolactone may be considered as a fourth drug.
- **March 2019:** In January 2019, the FDA Commissioner and Director of the FDA Center for Drug Evaluation and Research released a statement updating the public on large-scale voluntary recalls of various products containing angiotensin II receptor blockers (ARBs). Two probable carcinogens, N-nitrosodimethylamine (NDMA) and N-nitrosodiethylamine (NDEA), had been identified in active pharmaceutical ingredients used by some manufacturers of irbesartan, losartan, and valsartan. The impurities arose during manufacture of the ingredients in 2 factories located in India and China. Most recently, a third impurity, N-nitroso-N-methyl-4-aminobutyric acid (NMBA) has been identified in

an ARB product, resulting in a new recall. Although not all products containing valsartan, losartan, or irbesartan that are marketed in the United States have been recalled, the scope of the exposure, the scale of the 20 recalls, and the impact on patient care are substantial. FDA officials believe that patients in the United States have been using ARBs containing carcinogenic impurities for approximately 4 years; they estimate that for every 8,000 patients taking the highest dose of an affected product for the full 4 years, 1 new cancer above the background incidence would be expected. The compounds triggering the recalls are known as genotoxic impurities because they have the potential to damage DNA. Although some products containing valsartan, irbesartan, or losartan remain commercially available in the United States, the lack of selected ARB products has placed pressure on the supply chain for nonrecalled ARBs. Furthermore, some unaffected manufacturers have increased valsartan prices threefold or more.

- **March 2019:** The FDA approved a new generic of Diovan® (valsartan) amid an ongoing series of tainted ARB drug recalls. In a news release, it was stated that "For this approval, the FDA evaluated the company's manufacturing processes and also made sure they used appropriate testing methods to demonstrate that the valsartan product approved today does not contain NDMA or NDEA. The FDA's assessment of the manufacturing processes for the product determined that there is no known risk for the formation of other nitrosamine impurities."

Consensi® (Amlodipine/Celecoxib Tablets) Product Summary[8,9]

Indication(s): Consensi® is a combination of amlodipine, a calcium channel blocker (CCB), and celecoxib, a nonsteroidal anti-inflammatory drug (NSAID), indicated for patients for whom treatment with amlodipine for HTN and celecoxib for OA pain are appropriate.

- Limitations of Use: Consensi® is only available in a celecoxib strength of 200mg and is only to be taken once daily.

Dosing:

- Consensi® (amlodipine/celecoxib) is supplied as 2.5mg/200mg, 5mg/200mg, or 10mg/200mg tablets.
- It is recommended to use the lowest effective dosage of celecoxib for the shortest duration consistent with treatment goals. If analgesic therapy is no longer indicated, it is recommended to discontinue Consensi® and initiate the patient on alternative antihypertensive therapy.
- The recommended starting dose is amlodipine 5mg/celecoxib 200mg (2.5mg/200mg for small, elderly, or frail patients, or patients with hepatic impairment) orally once daily. The dose may be titrated to 5mg/200mg or 10mg/200mg once daily as needed for BP control.
- Consensi® may be substituted for its individual components.

Boxed Warning: Risk of Serious Cardiovascular (CV) and Gastrointestinal (GI) Events

- NSAIDs cause an increased risk of serious CV thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use.
- Consensi® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.
- NSAIDs cause an increased risk of serious GI adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Contraindication(s):

- Known hypersensitivity to amlodipine, celecoxib, or any inactive ingredients of Consensi®
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs
- In the setting of CABG surgery
- Demonstrated allergic-type reactions to sulfonamide

Efficacy: During the development of this fixed-dose combination product, the central focus was to assess pharmacodynamic interactions related to BP effect between celecoxib and amlodipine. There are no studies of the combination of celecoxib and amlodipine demonstrating reductions in the signs and symptoms of OA, but celecoxib has demonstrated such effects. There are also no long-term studies to evaluate CV safety for the combination of amlodipine and celecoxib. The combination of amlodipine and celecoxib was studied in a randomized, double-blind, placebo- and active-controlled study in 152 patients with newly diagnosed HTN who required pharmacological therapy to control their HTN. The trial used commercial celecoxib capsules and amlodipine tablets that were individually over-encapsulated and then taken together or matching placebo. The patients were randomized 1.5:1.5:1:1 to 1 of 4 treatment arms: celecoxib 200mg + amlodipine 10mg, celecoxib 0mg + amlodipine 10mg, celecoxib 200mg + amlodipine 0mg, and celecoxib 0mg + amlodipine 0mg. All drugs were administered once daily for 14 days. The trial demonstrated that the combination of celecoxib and amlodipine provided similar BP reduction to an equal dose of amlodipine.

Cost and Product Availability: Cost information for Consensi® is currently unavailable. Kitov announced in January 2019 the signing of an exclusive marketing and distribution agreement with Coeptis Pharmaceuticals for commercialization of Consensi® in the United States.

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Consensi® (amlodipine/celecoxib tablet)	**Unknown**	**Unknown**	**Unknown**
amlodipine 10mg tablet	$0.02	$0.60	$7.20
celecoxib 200mg capsule	$0.20	$6.00	$72.00

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.

Kapspargo™ Sprinkle (Metoprolol Succinate ER Capsules) Product Summary[10]

Indication(s): Kapspargo™ Sprinkle is a beta$_1$-selective adrenoceptor blocking agent indicated for the treatment of:

- HTN, to lower BP
- Angina pectoris
- HF, to reduce the risk of CV mortality and HF hospitalization in patients with HF

Dosing:

- Kapspargo™ Sprinkle is supplied as 25mg, 50mg, 100mg, and 200mg ER capsules.
- The recommended dosage is based on indication:
  - Adult HTN: Usual initial dosage is 25mg to 100mg once daily; recommended to titrate weekly (or longer) to optimal BP
  - Pediatric HTN (6 Years of Age and Older): Recommended starting dose is 1mg/kg once daily and titrate to response; dose should not exceed a maximum initial dose of 50mg once daily
  - Angina Pectoris: Usual initial dosage is 100mg once daily; recommended to titrate weekly based on clinical response
  - HF: Recommended starting dose is 25mg once daily doubled every 2 weeks to the highest dose tolerated or up to 200mg
- Kapspargo™ Sprinkle pellets can be sprinkled over soft food (such as applesauce, yogurt, or pudding) or administered via a nasogastric tube.

Contraindication(s):

- Known hypersensitivity to product components
- Severe bradycardia, greater than first degree heart block, or sick sinus syndrome without a pacemaker
- Cardiogenic shock or decompensated HF

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Kapspargo™ Sprinkle (metoprolol succinate ER 100mg capsule)	**$1.92**	**$57.60**	**$691.20**
metoprolol succinate ER 100mg tablet	$0.20	$6.00	$72.00

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.

Recommendations

The College of Pharmacy recommends the prior authorization of Consensi® (amlodipine/ celecoxib) and Kapspargo™ Sprinkle (metoprolol succinate ER) with the following criteria:

Consensi® (Amlodipine/Celecoxib Tablets) 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.

Kapspargo™ Sprinkle [Metoprolol Succinate Extended-Release (ER) Capsules] 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.

Additionally, the College of Pharmacy recommends the following changes to the Antihypertensive Medication Product Based Prior Authorization (PBPA) category based on net cost:

1. Moving Benicar® (olmesartan), Benicar HCT® (olmesartan/hydrochlorothiazide), and Azor® (amlodipine/olmesartan) from Tier-2 to Tier-1.
2. Moving Atacand® (candesartan) and Micardis® HCT (telmisartan/hydrochlorothiazide) from Tier-3 to Tier-2.

The recommended changes are shown in red in the following tier charts:

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

HCTZ = hydrochlorothiazide

Utilization Details of Antihypertensive Medications: Calendar Year 2018

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	14,729	753,295	4,409	$135,394.21	$0.18	$9.19
AMLODIPINE TAB 5MG	11,766	548,106	3,814	$107,864.59	$0.20	$9.17
AMLODIPINE TAB 2.5MG	1,798	75,799	572	$17,138.06	$0.23	$9.53
NIFEDIPINE TAB 30MG ER	1,025	37,662	558	$18,495.77	$0.49	$18.04
NIFEDIPINE TAB 60MG ER	602	24,566	246	$12,350.06	$0.50	$20.52
NIFEDIPINE TAB 30MG ER	541	21,524	249	$10,983.05	$0.51	$20.30
NIFEDIPINE CAP 10MG	514	9,005	402	$23,836.65	$2.65	$46.37
VERAPAMIL TAB 240MG ER	424	19,889	102	$6,255.19	$0.31	$14.75
CARTIA XT CAP 180MG/24HR	404	18,903	116	$9,059.53	$0.48	$22.42
DILTIAZEM CAP 120MG ER	373	16,882	115	$7,800.85	$0.46	$20.91
CARTIA XT CAP 120/24HR	352	15,460	131	$6,909.01	$0.45	$19.63
NIFEDIPINE TAB 90MG ER	319	14,094	99	$8,667.71	$0.61	$27.17
DILTIAZEM CAP 240MG ER	303	13,406	81	$7,335.51	$0.55	$24.21
CARTIA XT CAP 240/24HR	293	13,931	91	$6,840.77	$0.49	$23.35
DILTIAZEM TAB 30MG	283	8,435	79	$4,725.10	$0.56	$16.70
DILTIAZEM CAP 180MG ER	244	10,389	77	$5,303.20	$0.51	$21.73
VERAPAMIL TAB 120MG ER	244	10,080	70	$4,012.68	$0.40	$16.45
VERAPAMIL TAB 180MG ER	235	10,807	68	$3,525.41	$0.33	$15.00
NIFEDIPINE TAB 60MG ER	230	9,349	121	$5,258.00	$0.56	$22.86
DILTIAZEM TAB 120MG	223	8,677	52	$5,133.81	$0.59	$23.02
DILTIAZEM TAB 60MG	212	6,941	62	$4,460.28	$0.64	$21.04

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
VERAPAMIL TAB 120MG	209	7,796	53	$2,449.68	$0.31	$11.72
VERAPAMIL TAB 80MG	191	6,462	57	$1,772.02	$0.27	$9.28
NIFEDIPINE TAB 90MG ER	175	9,017	62	$5,580.75	$0.62	$31.89
DILTIAZEM TAB 90MG	146	4,396	33	$3,454.01	$0.79	$23.66
NIFEDIPINE CAP 20MG	110	2,424	87	$12,677.22	$5.23	$115.25
VERAPAMIL TAB 40MG	109	3,482	38	$1,978.42	$0.57	$18.15
DILT-XR CAP 240MG	87	4,016	25	$2,807.41	$0.70	$32.27
DILT-XR CAP 180MG	68	3,184	20	$2,181.25	$0.69	$32.08
DILTIAZEM CAP 240MG/24HR	59	2,881	20	$1,935.94	$0.67	$32.81
DILTIAZEM CAP 300MG ER	55	2,787	17	$2,006.70	$0.72	$36.49
CARTIA XT CAP 300/24HR	53	2,421	16	$1,736.08	$0.72	$32.76
DILTIAZEM CAP 360MG ER	49	2,310	16	$1,776.07	$0.77	$36.25
DILT-XR CAP 120MG	45	1,987	18	$1,184.83	$0.60	$26.33
DILTIAZEM CAP 180MG/24HR	44	3,060	18	$1,450.70	$0.47	$32.97
DILTIAZEM CAP 120MG/24HR	36	1,440	17	$730.32	$0.51	$20.29
DILTIAZEM CAP 360MG/24HR	27	1,590	8	$1,087.14	$0.68	$40.26
DILTIAZEM CAP 240MG ER	27	1,230	9	$816.87	$0.66	$30.25
DILTIAZEM CAP 420MG/24HR	21	930	5	$1,376.62	$1.48	$65.55
FELODIPINE TAB 5MG ER	20	1,440	6	$521.65	$0.36	$26.08
FELODIPINE TAB 10MG ER	19	630	4	$355.75	$0.56	$18.72
DILTIAZEM CAP 300MG/24HR	19	1,334	9	$939.36	$0.70	$49.44
DILTIAZEM CAP 240MG CD	13	510	5	$266.68	$0.52	$20.51
NIMODIPINE CAP 30MG	12	312	8	$10,034.90	$32.16	$836.24
TAZTIA XT CAP 360MG/24HR	11	390	5	$333.25	$0.85	$30.30
DILTIAZEM CAP 120MG CD	10	300	3	$210.71	$0.70	$21.07
NIFEDICAL XL TAB 30MG	9	360	9	$180.10	$0.50	$20.01
DILTIAZEM CAP 180MG ER	8	480	4	$357.99	$0.75	$44.75
NICARDIPINE CAP 20MG	7	210	1	$931.07	$4.43	$133.01
TAZTIA XT CAP 180MG/24HR	6	180	1	$166.62	$0.93	$27.77
DILTIAZEM CAP 120MG ER	4	105	3	$106.87	$1.02	$26.72
NIFEDICAL XL TAB 60MG	3	90	2	$55.45	$0.62	$18.48
TAZTIA XT CAP 120MG/24HR	3	90	1	$12.00	$0.13	$4.00
AFEDITAB TAB 60MG CR	2	60	1	$36.74	$0.61	$18.37
DILTIAZEM CAP 180MG CD	2	120	1	$46.10	$0.38	$23.05
TAZTIA XT CAP 300MG/24HR	2	180	1	$119.55	$0.66	$59.78
NICARDIPINE CAP 30MG	1	20	1	$90.57	$4.53	$90.57
DILTIAZEM CAP 300MG CD	1	30	1	$28.09	$0.94	$28.09
NORVASC TAB 10MG	1	30	1	$258.05	$8.60	$258.05
CCB TIER-1 SUBTOTAL	**36,778**	**1,715,484**	**12,100**	**$473,402.97**	**$0.28**	**$12.87**
CCB TIER-2 UTILIZATION						
VERAPAMIL CAP 120MG SR	74	3,025	24	$4,306.74	$1.42	$58.20
DILTIAZEM CAP 120MG ER	72	2,436	21	$14,075.37	$5.78	$195.49
VERAPAMIL CAP 240MG SR	69	4,163	29	$5,608.55	$1.35	$81.28

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
VERAPAMIL CAP 180MG SR	64	4,030	21	$5,511.25	$1.37	$86.11
DILTIAZEM CAP 60MG ER	49	1,550	21	$5,847.05	$3.77	$119.33
AMLOD/ATORVA TAB 10-40MG	33	1,470	8	$5,893.22	$4.01	$178.58
VERAPAMIL CAP 360MG SR	30	1,385	10	$6,399.50	$4.62	$213.32
VERAPAMIL CAP 240MG ER	30	1,470	12	$2,105.09	$1.43	$70.17
VERAPAMIL CAP 180MG ER	24	870	7	$1,452.63	$1.67	$60.53
DILTIAZEM CAP 90MG ER	23	814	5	$3,239.04	$3.98	$140.83
VERAPAMIL CAP 120MG ER	22	840	7	$1,351.70	$1.61	$61.44
AMLOD/ATORVA TAB 10-80MG	21	1,350	4	$5,792.28	$4.29	$275.82
AMLOD/ATORVA TAB 10-20MG	19	940	3	$3,426.42	$3.65	$180.34
ISRADIPINE CAP 5MG	13	368	2	$2,040.95	$5.55	$157.00
CARDIZEM LA TAB 120MG	13	405	4	$1,942.16	$4.80	$149.40
ISRADIPINE CAP 2.5MG	13	380	2	$803.85	$2.12	$61.83
DILTIAZEM ER TAB 240MG	12	720	6	$1,827.83	$2.54	$152.32
VERAPAMIL CAP 100MG ER	10	300	1	$878.89	$2.93	$87.89
AMLOD/ATORVA TAB 5-40MG	10	900	3	$3,439.30	$3.82	$343.93
DILTIAZEM ER TAB 360MG	10	720	4	$2,464.49	$3.42	$246.45
DILTIAZEM ER TAB 180MG	10	600	3	$1,590.55	$2.65	$159.06
VERAPAMIL CAP 200MG ER	8	220	3	$384.74	$1.75	$48.09
MATZIM LA TAB 180MG/24HR	7	360	4	$826.13	$2.29	$118.02
AMLOD/ATORVA TAB 5-10MG	6	540	2	$1,482.57	$2.75	$247.10
VERELAN CAP 240MG SR	6	271	1	$2,089.80	$7.71	$348.30
AMLOD/ATORVA TAB 10-10MG	5	390	2	$1,144.32	$2.93	$228.86
MATZIM LA TAB 240MG/24HR	4	120	1	$318.04	$2.65	$79.51
MATZIM LA TAB 360MG/24HR	3	270	1	$950.12	$3.52	$316.71
CCB TIER-2 SUBTOTAL	**660**	**30,907**	**211**	**$87,192.58**	**$2.82**	**$132.11**
CCB SPECIAL PRIOR AUTHORIZATION (PA) UTILIZATION						
DILTIAZEM CAP 360MG CD	8	646	4	$2,946.67	$4.56	$368.33
CCB SPECIAL PA SUBTOTAL	**8**	**646**	**4**	**$2,946.67**	**$4.56**	**$368.33**
CCB TOTAL	**37,446**	**1,747,037**	**10,673***	**$563,542.22**	**$0.32**	**$15.05**
ANGIOTENSIN RECEPTOR BLOCKERS (ARB) AND COMBINATION PRODUCTS						
ARB TIER-1 UTILIZATION						
LOSARTAN POT TAB 50MG	4,589	218,897	1,455	$46,799.22	$0.21	$10.20
LOSARTAN POT TAB 100MG	3,423	188,351	1,059	$37,043.12	$0.20	$10.82
LOSARTAN POT TAB 25MG	2,750	134,357	904	$27,901.63	$0.21	$10.15
LOSARTAN/HCT TAB 100-25MG	1,431	81,191	447	$18,377.87	$0.23	$12.84
LOSARTAN/HCT TAB 50-12.5MG	1,241	61,454	398	$14,370.69	$0.23	$11.58
LOSARTAN/HCT TAB 100-12.5MG	666	36,710	209	$8,583.09	$0.23	$12.89
VALSARTAN TAB 160MG	297	14,079	119	$4,321.09	$0.31	$14.55
VALSARTAN TAB 80MG	269	12,220	98	$3,320.38	$0.27	$12.34
IRBESARTAN TAB 150MG	230	11,274	68	$3,472.95	$0.31	$15.10
VALSART/HCTZ TAB 320-25MG	194	11,134	58	$4,126.64	$0.37	$21.27
VALSART/HCTZ TAB 160-12.5MG	177	8,640	63	$2,894.71	$0.34	$16.35

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
VALSARTAN TAB 320MG	173	9,005	65	$2,920.72	$0.32	$16.88
VALSART/HCTZ TAB 160-25MG	161	9,259	58	$2,877.97	$0.31	$17.88
VALSART/HCTZ TAB 80-12.5MG	152	8,413	45	$2,283.97	$0.27	$15.03
VALSARTAN TAB 40MG	118	4,817	52	$1,580.97	$0.33	$13.40
AMLOD/VALSAR TAB 10-320MG	104	3,120	18	$2,562.67	$0.82	$24.64
IRBESARTAN TAB 300MG	103	6,360	46	$1,972.20	$0.31	$19.15
IRBESAR/HCTZ TAB 150-12.5MG	91	4,696	24	$1,903.05	$0.41	$20.91
TELMISARTAN TAB 40MG	75	3,562	23	$2,210.45	$0.62	$29.47
VALSART/HCTZ TAB 320-12.5MG	64	3,045	26	$1,192.99	$0.39	$18.64
IRBESARTAN TAB 75MG	56	2,775	20	$860.50	$0.31	$15.37
TELMISARTAN TAB 80MG	54	2,515	24	$1,551.93	$0.62	$28.74
IRBESAR/HCTZ TAB 300-12.5MG	37	2,190	13	$854.26	$0.39	$23.09
AMLOD/VALSAR TAB 5-160MG	33	990	9	$616.29	$0.62	$18.68
AMLOD/VALSAR TAB 5-320MG	22	660	3	$502.77	$0.76	$22.85
AMLOD/VALSAR TAB 10-160MG	19	570	7	$398.16	$0.70	$20.96
TELMISARTAN TAB 20MG	15	690	4	$394.76	$0.57	$26.32
COZAAR TAB 50MG	9	270	1	$1,506.20	$5.58	$167.36
DIOVAN TAB 160MG	8	300	1	$2,345.40	$7.82	$293.18
DIOVAN TAB 320MG	7	330	2	$3,236.39	$9.81	$462.34
MICARDIS TAB 40MG	3	270	1	$1,758.85	$6.51	$586.28
AMLOD/VALSAR TAB 5-160MG	33	990	9	$616.29	$0.62	$18.68
ARB TIER-1 SUBTOTAL	**16,571**	**842,144**	**5,320**	**$204,741.89**	**$0.24**	**$12.36**
ARB TIER-2 UTILIZATION						
OLMESA MEDOX TAB 40MG	114	5,580	30	$2,026.32	$0.36	$17.77
OLM MED/HCTZ TAB 40-25MG	102	5,150	27	$1,950.17	$0.38	$19.12
OLMESA MEDOX TAB 20MG	85	5,670	28	$1,419.12	$0.25	$16.70
OLM MED/HCTZ TAB 40-12.5MG	62	3,307	15	$1,244.30	$0.38	$20.07
OLM MED/HCTZ TAB 20-12.5MG	49	3,337	14	$904.91	$0.27	$18.47
AMLOD/VALSAR/HCTZ 10-320-25MG	34	1,080	6	$1,868.42	$1.73	$54.95
AMLOD/OLMESA TAB 5-40MG	24	1,260	5	$1,125.48	$0.89	$46.90
OLM MED/AMLO/HCTZ 40-10-25MG	23	1,150	5	$2,997.44	$2.61	$130.32
AMLOD/OLMESA TAB 10-40MG	22	885	5	$871.95	$0.99	$39.63
AMLOD/VALSAR/HCTZ 10-160-25MG	20	600	3	$1,032.12	$1.72	$51.61
AMLOD/OLMESA TAB 5-20MG	17	510	2	$486.48	$0.95	$28.62
AMLOD/VALSAR/HCTZ 5-160-12.5MG	14	404	3	$659.47	$1.63	$47.11
OLM MED/AMLO/HCTZ 20-5-12.5MG	12	480	3	$1,105.45	$2.30	$92.12
OLMESA MEDOX TAB 5MG	11	312	3	$126.36	$0.41	$11.49
OLM MED/AMLO/HCTZ 40-5-25MG	9	270	2	$697.39	$2.58	$77.49
OLM MED/AMLO/HCTZ 40-5-12.5MG	7	210	1	$532.87	$2.54	$76.12
AMLOD/VALSAR/HCTZ 5-160-25MG	6	180	3	$223.95	$1.24	$37.33
AMLOD/OLMESA TAB 10-20MG	4	360	1	$309.13	$0.86	$77.28
TRIBENZOR 40-10-25MG	3	210	1	$2,243.23	$10.68	$747.74
AMLOD/VALSAR/HCTZ 10-160-12.5MG	2	60	2	$114.85	$1.91	$57.43

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
OLM MED/AMLO/HCTZ 40-10-12.5MG	2	60	1	$160.15	$2.67	$80.08
BENICAR HCT TAB 20-12.5MG	2	60	1	$424.48	$7.07	$212.24
BENICAR TAB 40MG	1	90	1	$851.83	$9.46	$851.83
ARB TIER-2 SUBTOTAL	**625**	**31,225**	**162**	**$23,375.87**	**$0.75**	**$37.40**
ARB TIER-3 UTILIZATION						
CANDESARTAN TAB 8MG	38	1,470	10	$2,607.18	$1.77	$68.61
TELMISA/HCTZ TAB 80-12.5MG	32	1,140	4	$2,685.44	$2.36	$83.92
TELMISA/HCTZ TAB 80-25MG	29	1,470	6	$2,821.56	$1.92	$97.30
CANDESARTAN TAB 32MG	19	990	4	$1,965.51	$1.99	$103.45
CANDESARTAN TAB 4MG	19	690	10	$1,200.95	$1.74	$63.21
CANDESARTAN TAB 16MG	10	480	7	$704.24	$1.47	$70.42
EDARBYCLOR TAB 40-12.5MG	10	540	3	$3,198.32	$5.92	$319.83
TELMISA/HCTZ TAB 40-12.5MG	8	240	1	$516.90	$2.15	$64.61
EDARBYCLOR TAB 40-25MG	6	240	2	$1,423.70	$5.93	$237.28
EDARBI TAB 80MG	5	360	1	$2,240.53	$6.22	$448.11
EDARBI TAB 40MG	5	150	1	$900.89	$6.01	$180.18
ARB TIER-3 SUBTOTAL	**181**	**7,770**	**49**	**$20,265.22**	**$2.61**	**$111.96**
ARB TOTAL	**17,377**	**881,139**	**4,633***	**$248,382.98**	**$0.28**	**$14.29**
ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIs) AND COMBINATION PRODUCTS						
ACEI TIER-1 UTILIZATION						
LISINOPRIL TAB 20MG	16,431	781,197	5,168	$140,159.52	$0.18	$8.53
LISINOPRIL TAB 10MG	15,288	726,549	5,118	$131,386.51	$0.18	$8.59
LISINOPRIL TAB 40MG	7,990	418,272	2,302	$84,644.70	$0.20	$10.59
LISINOPRIL TAB 5MG	6,840	322,245	2,196	$58,085.00	$0.18	$8.49
LISINOP/HCTZ TAB 20-12.5MG	4,612	222,469	1,423	$40,394.74	$0.18	$8.76
LISINOP/HCTZ TAB 20-25MG	4,483	251,467	1,435	$40,676.26	$0.16	$9.07
LISINOPRIL TAB 2.5MG	3,070	138,231	994	$26,788.10	$0.19	$8.73
LISINOP/HCTZ TAB 10-12.5MG	2,737	140,871	943	$24,459.93	$0.17	$8.94
ENALAPRIL TAB 5MG	1,112	41,720	242	$22,672.21	$0.54	$20.39
ENALAPRIL TAB 20MG	1,024	41,808	216	$23,242.46	$0.56	$22.70
ENALAPRIL TAB 10MG	852	37,940	214	$15,894.16	$0.42	$18.66
LISINOPRIL TAB 30MG	842	42,085	270	$9,302.03	$0.22	$11.05
ENALAPRIL TAB 2.5MG	758	27,661	147	$14,329.30	$0.52	$18.90
BENAZEPRIL TAB 20MG	341	17,242	95	$3,388.27	$0.20	$9.94
BENAZEPRIL TAB 40MG	267	14,703	71	$2,739.92	$0.19	$10.26
BENAZEPRIL TAB 10MG	235	11,164	59	$2,285.15	$0.20	$9.72
RAMIPRIL CAP 10MG	179	7,585	36	$2,046.60	$0.27	$11.43
QUINAPRIL TAB 40MG	138	6,409	27	$2,111.04	$0.33	$15.30
ENALAPR/HCTZ TAB 10-25MG	134	6,775	31	$2,335.34	$0.34	$17.43
BENAZEP/HCTZ TAB 20-12.5MG	117	4,540	24	$4,757.76	$1.05	$40.66
BENAZEP/HCTZ TAB 10-12.5MG	90	4,377	23	$3,598.94	$0.82	$39.99
QUINAPRIL TAB 20MG	88	3,900	22	$1,302.32	$0.33	$14.80
RAMIPRIL CAP 5MG	69	3,330	19	$719.10	$0.22	$10.42

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ENALAPR/HCTZ TAB 5-12.5MG	68	2,915	16	$1,014.51	$0.35	$14.92
RAMIPRIL CAP 2.5MG	65	3,690	18	$805.25	$0.22	$12.39
BENAZEP/HCTZ TAB 20-25MG	59	2,869	18	$3,044.03	$1.06	$51.59
FOSINOPRIL TAB 10MG	52	2,161	9	$824.65	$0.38	$15.86
FOSINOPRIL TAB 40MG	49	1,800	8	$846.34	$0.47	$17.27
RAMIPRIL CAP 1.25MG	47	2,200	16	$737.93	$0.34	$15.70
BENAZEPRIL TAB 5MG	38	1,640	8	$338.86	$0.21	$8.92
FOSINOPRIL TAB 20MG	37	1,590	7	$556.19	$0.35	$15.03
QUINAPRIL TAB 10MG	34	1,740	9	$502.47	$0.29	$14.78
QNAPRIL/HCTZ TAB 20-12.5MG	10	540	2	$440.67	$0.82	$44.07
QUINAPRIL TAB 5MG	7	270	3	$82.50	$0.31	$11.79
QNAPRIL/HCTZ TAB 10-12.5MG	6	300	3	$172.24	$0.57	$28.71
PERINDOPRIL TAB 8MG	5	390	1	$246.89	$0.63	$49.38
QNAPRIL/HCTZ TAB 20-25MG	4	240	2	$138.58	$0.58	$34.65
BENAZEP/HCTZ TAB 5-6.25MG	3	270	1	$406.67	$1.51	$135.56
TRANDOLAPRIL TAB 4MG	2	100	1	$62.30	$0.62	$31.15
PERINDOPRIL TAB 4MG	1	30	1	$23.55	$0.79	$23.55
ACEI TIER-1 SUBTOTAL	**68,184**	**3,295,285**	**21,198**	**$667,562.99**	**$0.20**	**$9.79**
ACEI TIER-2 UTILIZATION						
CAPTOPRIL TAB 25MG	138	4,617	27	$7,911.00	$1.71	$57.33
CAPTOPRIL TAB 50MG	102	3,060	14	$9,277.55	$3.03	$90.96
CAPTOPRIL TAB 12.5MG	39	1,710	10	$2,774.29	$1.62	$71.14
CAPTOPR/HCTZ TAB 25-15MG	15	630	2	$900.99	$1.43	$60.07
CAPTOPR/HCTZ TAB 50-25MG	9	330	2	$719.45	$2.18	$79.94
CAPTOPR/HCTZ TAB 25-25MG	1	30	1	$26.01	$0.87	$26.01
CAPTOPRIL TAB 25MG	138	4,617	27	$7,911.00	$1.71	$57.33
ACEI TIER-2 SUBTOTAL	**304**	**10,377**	**56**	**$21,609.29**	**$2.08**	**$71.08**
ACEI SPECIAL PA UTILIZATION						
EPANED SOL 1MG/ML	772	29,923	177	$253,853.13	$8.48	$328.83
QBRELIS SOL 1MG/ML	54	2,184	13	$26,739.04	$12.24	$495.17
EPANED SOL 1MG/ML	9	324	5	$2,291.99	$7.07	$254.67
ACEI SPECIAL PA SUBTOTAL	**835**	**32,431**	**195**	**$282,884.16**	**$8.72**	**$338.78**
ACEI TOTAL	**69,323**	**3,338,093**	**18,597***	**$ 972,056.44**	**$0.29**	**$14.02**
ACEI AND CCB COMBINATION PRODUCTS						
ACEI AND CCB TIER-1 UTILIZATION						
AMLOD/BENAZP CAP 10-20MG	194	10,660	51	$3,685.20	$0.35	$19.00
AMLOD/BENAZP CAP 10-40MG	147	10,170	45	$3,471.76	$0.34	$23.62
AMLOD/BENAZP CAP 5-20MG	137	6,849	34	$2,161.33	$0.32	$15.78
AMLOD/BENAZP CAP 5-10MG	121	6,130	36	$2,121.10	$0.35	$17.53
AMLOD/BENAZP CAP 5-40MG	33	1,830	10	$706.34	$0.39	$21.40
AMLOD/BENAZP CAP 2.5-10MG	23	810	4	$329.95	$0.41	$14.35
ACEI/CCB TIER-1 SUBTOTAL	**655**	**36,449**	**180**	**$12,475.68**	**$0.34**	**$19.05**
ACEI/CCB TOTAL	**655**	**36,449**	**170***	**$12,475.68**	**$0.34**	**$19.05**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
DIRECT RENIN INHIBITORS (DRI)						
TEKTURNA TAB 300MG	5	450	2	$3,291.77	$7.32	$658.35
DRI TOTAL	**5**	**450**	**2***	**$3,291.77**	**$7.32**	**$658.35**
CLONIDINE PRODUCTS						
CLONIDINE UTILIZATION (NO PA REQUIRED)						
CLONIDINE TAB 0.1MG	56,620	1,767,977	12,314	$594,681.70	$0.34	$10.50
CLONIDINE TAB 0.2MG	21,200	671,618	3,729	$227,733.43	$0.34	$10.74
CLONIDINE TAB 0.3MG	5,148	163,688	817	$58,854.41	$0.36	$11.43
CLONIDINE DIS 0.1/24HR	172	4,737	68	$9,299.11	$1.96	$54.06
CLONIDINE DIS 0.2/24HR	125	3,501	35	$11,210.57	$3.20	$89.68
CLONIDINE DIS 0.3/24HR	108	3,020	25	$10,852.90	$3.59	$100.49
CLONIDINE TOTAL	**83,373**	**2,614,541**	**15,233***	**$912,632.12**	**$0.35**	**$10.95**
SOTALOL PRODUCTS						
SOTALOL UTILIZATION (NO PA REQUIRED)						
SOTALOL HCL TAB 80MG	200	6,243	41	$2,697.73	$0.43	$13.49
SOTALOL HCL TAB 120MG	152	4,642	27	$2,581.80	$0.56	$16.99
SOTALOL AF TAB 80MG	43	1,226	7	$599.81	$0.49	$13.95
SOTALOL HCL TAB 160MG	38	1,344	7	$718.58	$0.53	$18.91
SOTALOL SUBTOTAL	**433**	**13,455**	**82**	**$6,597.92**	**$0.49**	**$15.24**
SOTALOL SPECIAL PA UTILIZATION						
SOTYLIZE SOL 5MG/ML	72	2,233	12	$42,240.40	$18.92	$586.67
SOTALOL SPECIAL PA SUBTOTAL	**72**	**2,233**	**12**	**$42,240.40**	**$18.92**	**$586.67**
SOTALOL TOTAL	**505**	**15,688**	**84***	**$48,838.32**	**$3.11**	**$96.71**
PROPRANOLOL SOLUTION PRODUCTS						
PROPRANOLOL UTILIZATION (NO PA REQUIRED)						
PROPRANOLOL SOL 20MG/5ML	791	22,852	179	$21,115.38	$0.92	$26.69
PROPRANOLOL SOL 40MG/5ML	21	597	8	$667.89	$1.12	$31.80
PROPRANOLOL SUBTOTAL	**812**	**23,449**	**187**	**$21,783.27**	**$0.93**	**$26.83**
PROPRANOLOL SPECIAL PA UTILIZATION						
HEMANGEOL SOL 4.28MG/ML	12	460	6	$6,561.60	$14.26	$546.80
PROPRANOLOL SPECIAL PA	**12**	**460**	**6**	**$6,561.60**	**$14.26**	**$546.80**
PROPRANOLOL TOTAL	**824**	**23,909**	**188***	**$28,344.87**	**$14.26**	**$546.80**
SPIRONOLACTONE PRODUCTS						
SPIRONOLACTONE UTILIZATION (NO PA REQUIRED)						
SPIRONOLACT TAB 25MG	4,255	183,251	1,381	$45,287.75	$0.25	$10.64
SPIRONOLACT TAB 50MG	1,988	77,733	696	$33,441.99	$0.43	$16.82
SPIRONOLACT TAB 100MG	1,314	53,361	400	$29,464.40	$0.55	$22.42
SPIRONOLACT POW	44	734	5	$620.85	$0.85	$14.11
SPIRONOLACTONE SUBTOTAL	**7,601**	**315,079**	**2,482**	**$108,814.99**	**$0.35**	**$14.32**
SPIRONOLACTONE SPECIAL PA UTILIZATION						
CAROSPIR SUS 25MG/5ML	62	1,879	22	$16,455.75	$8.76	$265.42
SPIRONOLACTONE SPECIAL PA	**62**	**1879**	**22**	**$16,455.75**	**$8.76**	**$265.42**
SPIRONOLACTONE TOTAL	**7,663**	**316,958**	**2,269***	**125,271**	**$0.40**	**$16.35**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
MISCELLANEOUS (MISC) PRODUCTS						
MISC UTILIZATION (NO PA REQUIRED)						
BISOPRL/HCTZ TAB 5-6.25MG	233	11,183	55	$2,568.83	$0.23	$11.03
ATENOL/CHLOR TAB 50-25MG	232	11,155	56	$6,210.62	$0.56	$26.77
BISOPRL/HCTZ TAB 10-6.25MG	183	8,629	42	$2,315.08	$0.27	$12.65
ATENOL/CHLOR TAB 100-25MG	115	5,505	31	$3,975.64	$0.72	$34.57
BISOPRL/HCTZ TAB 2.5-6.25MG	98	5,600	30	$1,416.29	$0.25	$14.45
METOPRL/HCTZ TAB 50-25MG	69	3,328	23	$3,817.70	$1.15	$55.33
METOPRL/HCTZ TAB 100-25MG	54	2,435	17	$3,106.04	$1.28	$57.52
DUTOPROL TAB 50-12.5MG	17	690	4	$6,479.25	$9.39	$381.13
METOPRL/HCTZ TAB 100-50MG	10	780	4	$1,321.94	$1.69	$132.19
PROPRAN/HCTZ TAB 40/25MG	9	510	5	$506.52	$0.99	$56.28
PROPRAN/HCTZ TAB 80/25MG	9	255	1	$551.40	$2.16	$61.27
DUTOPROL TAB 100-12.5MG	7	210	2	$2,024.23	$9.64	$289.18
METHYLD/HCTZ TAB 250/15MG	4	120	2	$256.90	$2.14	$64.23
DUTOPROL TAB 25-12.5MG	4	180	2	$1,995.94	$11.09	$498.99
NADOLOL/BEND TAB 80-5MG	2	180	1	$884.80	$4.92	$442.40
MISC. TOTAL	**1,046**	**50,760**	**263***	**$37,431.18**	**$0.74**	**$35.79**
TOTAL	**218,217**	**9,025,024**	**43,421***	**$2,952,266.32**	**$0.33**	**$13.53**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Effective June 11, 2018, clonidine patches no longer require prior authorization.
Effective November 13, 2018, diltiazem sustained-release (Cardizem® SR), verapamil extended-release capsule (Verelan®), captopril (Capoten®), and captopril/hydrochlorothiazide (Capozide®) moved from Tier-1 to Tier-2; amlodipine/valsartan (Exforge®) and telmisartan (Micardis®) moved from Tier-2 to Tier-1.

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Appendix N

Industry News and Updates

Oklahoma Health Care Authority
April 2019

Introduction

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

News and Updates[1,2,3]

News:

- **Over-the-Counter (OTC) Insulin:** Insulin, such as insulin isophane suspension and 70% human isophane suspension/30% human insulin injection, is available OTC in 49 U.S. states and the District of Columbia. A national survey published in *The Journal of the American Medical Association* provided information about the sale and reasons for purchase of OTC insulin. The data represents perceptions of pharmacy employees, rather than actual sales data. The finding is that OTC insulin is sold more commonly at Walmart than at other chain pharmacies and likely reflects the fact that the Walmart brand is considerably less expensive than other brands of insulin sold at chain pharmacies. The inability to afford copays for prescription insulin was noted as a common reason for purchase of OTC insulin, particularly at Walmart pharmacies. Further research is needed to explore clinical and safety outcomes related to the use of OTC insulin.
- **Disposal Locations:** Google is partnering with the Drug Enforcement Administration, the Department of Health and Human Services, CVS, Walgreens, and state governments to display local drug disposal locations in Google Maps. The program will start with 3,500 locations nationwide. Disposal locations can be important in fighting the opioid crisis. According to the National Survey on Drug Use and Health in 2016, 53% of respondents indicated that they "obtained the last pain relievers they misused from a friend or relative."
- **Institute for Clinical and Economic Review (ICER):** ICER posted its revised protocol for conducting a new annual analysis to determine whether or not prescription drug price increases have been accompanied by new clinical evidence that could potentially support those increases. The first "Unsupported Price Increase" report is scheduled to be released in October 2019. ICER developed a draft protocol for how it will conduct its assessments with guidance from a multi-stakeholder advisory group, consisting of representatives from patient advocacy groups, pharmaceutical companies, and payers representing both Medicaid and the private market. The 2019 report will focus on at least 10 prescription drugs that experienced the most significant price increases in the United States over the past 24 months, based primarily on which net price increases resulted in the largest overall budget impact for the United States health system.

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Appendix O

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

FDA NEWS RELEASE

FDA approves a new generic valsartan

Agency prioritizing review of ARB applications to help mitigate shortage of valsartan

The FDA approved a new generic of Diovan® (valsartan). Valsartan is an angiotensin II receptor blocker (ARB) that treats high blood pressure and heart failure. The FDA prioritized the review of this drug application to help relieve the recent shortage of this critical medicine as a result of multiple recalls of generic valsartan products from several manufacturers due to the finding that certain lots of valsartan and other ARB medicines contain nitrosamine impurities.

Since last summer, the FDA has conducted a major investigation to address the presence of nitrosamine impurities in certain generic ARB products. The FDA has worked with companies to take swift action to remove any products with unacceptable impurities from the U.S. market, and continues evaluating other ARBs to ensure they are free of impurities. FDA scientists have made important strides in understanding how these impurities may form during the manufacturing process and the agency is working with international drug regulatory agencies to make new testing methods available. The FDA has also engaged drug manufacturers and helped facilitate manufacturing process changes to ensure ARBs are free of detectable levels of nitrosamine impurities. Now that this risk has been identified, the agency is implementing new requirements to guard against the development of these impurities in drugs.

In cases of severe shortages of critical medications, including the ongoing shortage of valsartan and now losartan products, the FDA plays an important role in mitigating these challenges. For example, the FDA can expedite review of a new or generic drug application that, if approved, may help mitigate or prevent such a shortage and to do so, prioritizes these inspections and reviews. The agency is also working closely with manufacturers to see if they can produce additional supplies of these medicines. FDA scientists are using the information learned from its investigation to evaluate all ARBs currently on the market and will also apply this information when assessing future applications to ensure that the manufacturing process can't form these impurities.

For this approval, the FDA evaluated the company's manufacturing processes and also made sure they used appropriate testing methods to demonstrate that the valsartan product approved does not contain NDMA or NDEA. The FDA's assessment of the manufacturing processes for the product determined that there is no known risk for the formation of other nitrosamine impurities.

The FDA continues to investigate ARB medicines that contain nitrosamine impurities and that do not meet the agency's quality standards. The agency will continue to update the lists on the FDA's website of recalled valsartan, losartan, and irbesartan products as more information becomes available from ongoing testing. If patients take an ARB drug product, they should check the lists periodically, as information may change. Not all ARB medicines have been recalled.

According to the National Heart, Lung, and Blood Institute, high blood pressure is a common disease in which blood flows through blood vessels, or arteries, at higher than normal pressures. Heart failure is a condition in which the heart can't pump enough blood to meet the body's needs.

The most common side effects associated with valsartan are dizziness, hypotension, high levels of potassium in the blood (hyperkalemia), and increased blood creatinine.

The approval of the new generic of Diovan® was granted to Alkem Laboratories Limited.

Safety Announcements

FDA Warns about the risks associated with the investigational use of Venclexta® in Multiple Myeloma

[03/21/2019] The FDA is alerting health care professionals, oncology clinical investigators, and patients about the risks associated with the investigational use of Venclexta® (venetoclax) for the treatment of patients with multiple myeloma based on data from a clinical trial. Venclexta® is not approved for the treatment of multiple myeloma.

The FDA reviewed data from the BELLINI clinical trial (NCT02755597, Study M14-031) evaluating the use of Venclexta® combined with bortezomib, a proteasome inhibitor, and dexamethasone in patients with multiple myeloma. The interim trial results demonstrated an increased risk of death for patients receiving Venclexta® as compared to the control group. On March 6, 2019, the FDA required no new patients be enrolled in the BELLINI trial. Patients who are receiving clinical benefit can continue treatment in the trial after they reconsent. This statement does not apply to patients taking Venclexta® for an approved indication. Patients taking Venclexta® for an approved indication should continue to take their medication as directed by their health care professional. Venclexta is safe and effective for its approved uses.

The FDA will be working directly with sponsors of Venclexta®, as well as other investigators conducting clinical trials in patients with multiple myeloma, to determine the extent of the safety issue. The agency will communicate any new information as appropriate.

Health care professionals and patients are encouraged to report any adverse events or side effects related to the use of these products and any drugs to FDA's MedWatch Adverse Event Reporting program.

Current Drug Shortages Index (as of March 29th, 2019):

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

Abciximab (ReoPro) Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azithromycin (Azasite) Ophthalmic Solution 1%	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bisoprolol Fumarate Tablets	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Buspirone HCl Tablets	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended Release Tablets	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cycloserine Capsules, USP	***Currently in Shortage***
Deferoxamine Mesylate for Injection, USP	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***

Diltiazem Hydrochloride ER (Twice-a-Day) Capsules	***Currently in Shortage***
Diphenhydramine Injection	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Sol	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Eflornithine Hydrochloride (Vaniqa) Cream	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Eprosartan Mesylate Tablets	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fludrocortisone Acetate Tablets	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Haloperidol Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxyprogesterone Caproate Injection	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Isocarboxazid Tablets	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride 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***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***Currently in Shortage***

Lidocaine Hydrochloride (Xylocaine) and Dextrose Inj Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methocarbamol Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLICHEW ER) ER Chew Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for ER Oral Suspension	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nelarabine (Arranon) Injection	***Currently in Shortage***
Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phenytoin Sodium Injection, USP	***Currently in Shortage***
Phosphate Injection Products	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Prednisolone Acetate 1% Ophthalmic Suspension	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Progesterone Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine Transdermal System	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***

Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Sterile Water	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Trifluoperazine Hydrochloride Tablets	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***