Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
April 11, 2018
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 Board Meeting – April 11th, 2018

DATE: March 29, 2018

NOTE: The DUR Board will meet at 4:00 p.m. 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/Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update – Appendix B

Action Item – Vote to Prior Authorize Ocrevus™ (Ocrelizumab) – Appendix C

Action Item – Vote to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl) – Appendix D

Action Item – Vote to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)] – Appendix E

Action Item – Vote to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib) – Appendix F

Annual Review of the SoonerCare Pharmacy Benefit – Appendix G

Action Item – Hepatitis C Medication Criteria Update – Appendix H

Action Item – Annual Review of Benlysta® (Belimumab) – Appendix I

Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Admelog® (Insulin Lispro), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin) – Appendix J

Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension) – Appendix K

Industry News and Updates – Appendix L

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – April 11, 2018 @ 4:00 p.m.

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 14, 2018 DUR Minutes – Vote
B. March 14, 2018 DUR Recommendations Memorandum
C. Correspondence

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

4. Update on Medication Coverage Authorization Unit/Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update – See Appendix B

A. Medication Coverage Activity for March 2018
B. Pharmacy Help Desk Activity for March 2018
C. Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update

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

5. Action Item – Vote to Prior Authorize Ocrevus™ (Ocrelizumab) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl) – See Appendix D

A. Introduction
B. Other AAV2 Clinical Studies
C. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)] – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib) – See Appendix F

A. Introduction
B. Recommendations

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

9. Annual Review of the SoonerCare Pharmacy Benefit – See Appendix G

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 Classes by Fiscal Year

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

10. Action Item – Hepatitis C Medication Criteria Update – See Appendix H

A. Introduction
B. Utilization of Hepatitis C Medications
C. College of Pharmacy Recommendations

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

11. Action Item – Annual Review of Benlysta® (Belimumab) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Benlysta® (Belimumab)
C. Prior Authorization of Benlysta® (Belimumab)
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Benlysta® (Belimumab)

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

12. Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Admelog® (Insulin Lispro), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Diabetes Medications
C. Prior Authorization of Diabetes Medications
D. Market News and Updates
E. Admelog® (Insulin Lispro) Product Summary
F. Fiasp® (Insulin Aspart) Product Summary
G. Ozempic® (Semaglutide) Product Summary
H. Steglatro™ (Ertugliflozin) Product Summary
I. Segluromet™ (Ertugliflozin/Metformin) Product Summary
J. Steglujan™ (Ertugliflozin/Sitagliptin) Product Summary
K. College of Pharmacy Recommendations
L. Utilization Details of Non-Insulin Diabetes Medications
M. Utilization Details of Insulin Medications

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

13. Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Antihypertensive Medications
C. Prior Authorization of Antihypertensive Medications
D. Market News and Updates

E. Prexxartan® (Valsartan Oral Solution) Product Summary
F. Tekturna® (Aliskiren Oral Pellets) Product Summary
G. CaroSpir® (Spironolactone Oral Suspension) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Antihypertensive Medications

Non-Presentation; Questions Only:

14. Industry News and Updates – See Appendix L

A. Introduction
B. News and Updates

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

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

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

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

No live meeting scheduled for May. May will be a packet only meeting.

A. Otic Anti-Infective Medications
B. Elaprase® (Idursulfase)
C. Kuvan® (Sapropterin)
D. Granulocyte Colony Stimulating Factors
E. Ophthalmic Anti-Inflammatories
F. Anti-Parasitic Medications
G. Bowel Preparation Medications

**Future business subject to change.*

17. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MARCH 14, 2018

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.	x	
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Anetta Harrell, Pharm.D.	x	
Ashley Huddleston, Pharm.D., BCOP		x
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, Pharm.D.	x	
James Osborne, Pharm.D.		x
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
Bruna Varalli-Claypool, MHS, PA-C	x	

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist		x
Stephanie Nichols, Pharm.D., BCGP; Clinical Pharmacist	x	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow		x
Leslie Robinson, D.Ph.; PA Coordinator		x
Sarah Schmidt, Pharm.D.; Clinical Assistant Professor	x	
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Christina Bulkley, Pharm.D.		x
Corby Thompson, Pharm.D.		x
Visiting Pharmacy Student(s): N/A		

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.; Assistant Pharmacy Director	x	
Kelli Brodersen, Marketing Coordinator		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	
Garth Splinter, M.D.; M.B.A.; Deputy Chief Executive Officer		x
Joseph Young, J.D.; Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Bob Atkins, Biogen	Jeff Knappen, Spark Therapeutics	Rei Nakamura, Spark Therapeutics
Quynh Doan, AbbVie	Tami Sova, Biogen	Garth Wright, Genentech
Lee Ding, Genentech	Mike Dunze, Genentech	James Gaustad, Purdue
Marc Parker, Sunovion	Jim Dunlap, PhRma	Rachel Gragg, Teva
Kari Suttee, Novartis	Nicole Wilkerson, Novartis	Travis Tate, HealthChoice
John Brynson, Impax	Ron Schnare, Shire	Brian Maves, Pfizer
Mai Duong, Novartis	Kim Wittle, AveXis	Gay Thomas, BMS

PRESENT FOR PUBLIC COMMENT:	
Rei Nakamura	Spark Therapeutics
Tami Sova	Biogen
Mike Dunze	Genentech

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. 13 SPEAKER: REI NAKAMURA

2B: AGENDA ITEM NO. 14 & 15 SPEAKER: TAMI SOVA

2C: AGENDA ITEM NO. 15 SPEAKER: MIKE DUNZE

ACTION: NONE REQUIRED

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

3A: FEBRUARY 14, 2018 DUR MINUTES – VOTE

3B: FEBRUARY 14, 2018 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

Dr. Harrell moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS**

4A: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2018

4B: PHARMACY HELP DESK ACTIVITY FOR FEBRUARY 2018

4C: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE TYMLOS™ (ABALOPARATIDE)**

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

Dr. Preslar moved to approve; seconded by Dr. Anderson

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE PREVYMIS™ (LETERMOVIR TABLETS AND INJECTION)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nichols

Dr. Preslar moved to approve; seconded by Dr. Hardzog-Britt

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE RHOPRESSA® (NETARSUDIL OPHTHALMIC SOLUTION) AND VYZULTA™ (LATANOPROSTENE BUNOD OPHTHALMIC SOLUTION)**

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nichols

Dr. Preslar moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE MEPSEVII™ (VESTRONIDASE ALFA-VJBK)**

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

Dr. Hardzog-Britt moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE ERGOMAR® (ERGOTAMINE SUBLINGUAL TABLETS)**

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

Dr. Harrell moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **VOTE TO PRIOR AUTHORIZE XADAGO® (SAFINAMIDE) AND GOCOVRI™ (AMANTADINE EXTENDED-RELEASE)**

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Anderson moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ARZERRA® (OFATUMUMAB), GAZYVA® (OBINUTUZUMAB), IMBRUVICA® (IBRUTINIB), VENCLEXTA™ (VENETOCLAX), AND ZYDELIG® (IDELALISIB)**

11A: INTRODUCTION

11B: UTILIZATION OF CLL MEDICATIONS

11C: MARKET NEWS AND UPDATES

11D: PRODUCT SUMMARIES

11E: RECOMMENDATIONS

11F: UTILIZATION DETAILS OF CLL MEDICATIONS

Materials included in agenda packet; presented by Dr. Schmidt

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF ERYTHROPOIETIN STIMULATING AGENTS (ESAs)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF ESAs

12C: PRIOR AUTHORIZATION OF ESAs

12D: MARKET NEWS AND UPDATES

12E: ESA COMPARISON

12F: COLLEGE OF PHARMACY RECOMMENDATIONS

12G: UTILIZATION DETAILS OF ESAs

Materials included in agenda packet; presented by Dr. Nichols

Dr. Preslar moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)

13A: INTRODUCTION
13B: MARKET NEWS AND UPDATES
13C: LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL) PRODUCT SUMMARY
13D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Dr. Muchmore recommends that criteria #6 [Member must not have used high-dose retinoid compounds (>7,500 retinal equivalent units or >3,300 IU per day of vitamin A) in the past 18 months] be removed from the criteria.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF SPINRAZA® (NUSINERSEN)

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF SPINRAZA® (NUSINERSEN)
14C: PRIOR AUTHORIZATION OF SPINRAZA® (NUSINERSEN)
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott
Dr. Garton moved to approve; seconded by Dr. Anderson
ACTION: MOTION CARRIED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF MULTIPLE SCLEROSIS (MS) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OCREVUS™ (OCRELIZUMAB)

15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF MS MEDICATIONS
15C: PRIOR AUTHORIZATION OF MS MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: INSTITUTE FOR CLINICAL EFFECTIVENESS AND ECONOMIC REVIEW (ICER): DISEASE MODIFYING THERAPIES FOR MS
15F: OCREVUS™ (OCRELIZUMAB) PRODUCT SUMMARY
15G: COLLEGE OF PHARMACY RECOMMENDATIONS
15H: UTILIZATION DETAILS OF MS MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF ALPHA$_1$-PROTEINASE INHIBITORS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PROLASTIN®-C LIQUID [ALPHA$_1$-PROTEINASE INHIBITOR (HUMAN)]

16A: ALPHA$_1$-ANTITRYPSIN DEFICIENCY
16B: CURRENT PRIOR AUTHORIZATION CRITERIA
16C: UTILIZATION OF ALPHA$_1$-PROTEINASE INHIBITORS
16D: PRIOR AUTHORIZATION OF ALPHA$_1$-PROTEINASE INHIBITORS
16E: MARKET NEWS AND UPDATES
16F: PROLASTIN®-C LIQUID [ALPHA$_1$-PROTEINASE INHIBITOR (HUMAN)] PRODUCT SUMMARY
16G: COLLEGE OF PHARMACY RECOMMENDATIONS
16H: UTILIZATION DETAILS OF ALPHA$_1$-PROTEINASE INHIBITORS

Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: INDUSTRY NEWS AND UPDATES

17A: INTRODUCTION
17B: NEWS AND UPDATES

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: 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. 19: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)

19A: ANNUAL REVIEW OF PHARMACY BENEFIT

19B: DIABETES MEDICATIONS

19C: ANTIHYPERTENSIVE MEDICATIONS

19D: BENLYSTA® (BELIMUMAB)

FUTURE BUSINESS SUBJECT TO CHANGE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: ADJOURNMENT

The meeting was adjourned at 5:18 pm.

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

Memorandum

Date: March 15, 2018

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

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

Subject: DUR Board Recommendations from Meeting of March 14, 2018

Recommendation 1: U.S. Food and Drug Administration Safety Alerts

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Tymlos™ (Abaloparatide)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Tymlos™ (abaloparatide) into the Special Prior Authorization (PA) Tier of the Osteoporosis Product Based Prior Authorization (PBPA) category with the following criteria:

Tymlos™ (Abaloparatide) Approval Criteria:

1. A diagnosis of postmenopausal osteoporosis confirmed by the following:
    a. History of vertebral fracture(s) or low trauma or fragility fracture(s) (e.g., prior fracture from minor trauma such as falling from standing height or less) within the past 5 years; or
    b. A Bone Mineral Density test (T-score at or below -2.5) within the last month in the spine, femoral neck, total hip, or 33% radius; or

c. Those with a T-score between -1.0 and -2.5 in the spine, femoral neck, total hip, or 33% radius, if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3%; and

2. One of the following [if a 12-month bisphosphonate trial is inappropriate for the member, the member must have a trial of Prolia® or a selective estrogen receptor modulator (SERM) or a patient-specific, clinically significant reason why Prolia® or a SERM is not appropriate]:
   a. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D; or
   b. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or
   c. A 12-month trial of a SERM, unless contraindicated, intolerant, or allergic, that did not yield adequate results; and
3. A patient-specific, clinically significant reason why the member cannot use Forteo® (teriparatide) must be provided; and
4. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
5. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy; and
6. A quantity limit of one pen per 30 days will apply.

The College of Pharmacy also recommends the following criteria updates noted in red based on the new U.S. Food and Drug Administration (FDA) approved indication for Xgeva® (denosumab) and net cost after rebates for Forteo® (teriparatide):

Xgeva® (Denosumab) Approval Criteria:

1. An FDA approved indication of one of the following:
   a. Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors; or
   b. Treatment of adults and skeletally mature adolescents with giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity; and
      i. Prescriber must document that tumor is unresectable or that surgical resection is likely to result in severe morbidity; or
   c. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy; and
      ii. Member must have albumin-corrected calcium of greater than 12.5mg/dL (3.1mmol/L) despite treatment with intravenous bisphosphonate therapy in the last 30 days prior to initiation of Xgeva® therapy.

Forteo® (Teriparatide) Approval Criteria:

1. ~~A Bone Mineral Density test (T-score at or below -2.5) within the last month; and~~
2. A diagnosis of one of the following:
   a. Treatment of postmenopausal women with osteoporosis at high risk for fracture; or
   b. To increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture; or

c. Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture; or
d. Treatment of non-healing fracture; and

3. ~~One of the following (if a 12-month bisphosphonate trial is inappropriate for the member, the member must have trial of Prolia® or a patient-specific, clinically significant reason why Prolia® is not appropriate):~~
4. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D or a patient-specific, clinically significant reason the member cannot use a bisphosphonate; and
   ~~a. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or~~
5. The diagnosis of non-healing fracture may be approved for 6 months; and
6. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
7. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy.

Finally, the College of Pharmacy recommends moving ibandronate tablets (Boniva®) from Tier-2 to Tier-1 based on national average drug acquisition cost (NADAC).

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

*Must be used in combination with a bisphosphonate to count as a Tier-1 trial.
tabs = tablets; inj = injection; soln = solution; DR = delayed-release
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendation 3: Vote to Prior Authorize Prevymis™ (Letermovir Tablets and Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Prevymis™ (letermovir tablets and injection) with the following criteria:

Prevymis™ (Letermovir Tablets and Injection) Approval Criteria:

1. An FDA approved indication of prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogenic hematopoietic stem cell transplant (HSCT); and

2. Member must be CMV R+; and
3. Member must have received a HSCT within the last 28 days; and
4. Members taking concomitant cyclosporine will only be approved for the 240mg dose; and
5. Members must not be taking the following medications:
    a. Pimozide; or
    b. Ergot alkaloids (e.g., ergotamine, dihydroergotamine); or
    c. Rifampin; or
    d. Atorvastatin, lovastatin, pitavastatin, simvastatin, or repaglinide when co-administered with cyclosporine; and
6. Prevymis™ must be prescribed by an oncology, hematology, infectious disease, or transplant specialist or advanced care practitioner with a supervising physician who is an oncology, hematology, infectious disease, or transplant specialist; and
7. Prescriber must verify the member will be monitored for CMV reactivation while on therapy; and
8. Approvals will be for the duration of 100 days post-transplant.
    a. For Prevymis™ vials, authorization will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
    b. Approval length for vial formulation will be based on duration of need.
9. A quantity limit of one tablet or vial per day will apply.

The College of Pharmacy also recommends the following changes to current antiviral product prior authorization criteria based on low net cost of acyclovir cream.

Sitavig® (Acyclovir Buccal Tablets), Xerese® (Acyclovir/Hydrocortisone Cream), and Denavir® (Penciclovir Cream) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets; and
3. A patient-specific, clinically significant reason why the member cannot use Zovirax® (acyclovir) cream.

Recommendation 4: Vote to Prior Authorize Rhopressa® (Netarsudil Ophthalmic Solution) and Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

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

1. The creation of a Special Prior Authorization (PA) category to account for very high net cost products.
    a. Placement of brimonidine (Alphagan-P® 0.15%), dorzolamide/timolol (Cosopt® PF), timolol maleate (Timoptic Ocudose®, Timoptic-XE®), netarsudil ophthalmic solution (Rhopressa®), and latanoprostene bunod ophthalmic solution (Vyzulta™) into the Special PA category of the Glaucoma PBPA category based on net cost.
2. Move echothiophate iodide (Phospholine Iodide®) from Tier-2 to Tier-1 based on low net cost.

3. Move pilocarpine (Isopto® Carpine®, Pilopine HS®) from Tier-1 to Tier-2 based on net cost. Current Tier-2 criteria will apply.

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

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must attempt at least three Tier-1 trials for a minimum of four weeks duration each within the last 120 days. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Glaucoma Special Prior Authorization (PA) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 or Tier-2 product; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 and Tier-2 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 and Tier-2 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Proposed changes can be seen in red in the following Tier chart:

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
Alpha-2 Adrenergic Agonists		
brimonidine (Alphagan® 0.2%)	apraclonidine (Iopidine®)	**brimonidine (Alphagan-P® 0.15%)**
brinzolamide/brimonidine (Simbrinza®)	brimonidine (Alphagan-P® 0.1%)	
	brimonidine/timolol (Combigan®)	
Beta-Blockers		
carteolol (Ocupress® 1%)	betaxolol (Betoptic® 0.5%, Betoptic-S®)	**dorzolamide/timolol (Cosopt® PF)**
dorzolamide/timolol (Cosopt®)	brimonidine/timolol (Combigan®)	**timolol maleate (Timoptic Ocudose®, Timoptic-XE®)**
levobunolol (Betagan®)	timolol (Betimol®)	
metipranolol (OptiPranolol®)		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
timolol maleate (Istalol®, Timoptic®)		
Carbonic Anhydrase Inhibitors		
acetazolamide (Diamox®)+		**dorzolamide/timolol (Cosopt® PF)**
brinzolamide (Azopt®)		
brinzolamide/brimonidine (Simbrinza®)		
dorzolamide (Trusopt®)		
dorzolamide/timolol (Cosopt®)		
methazolamide (Neptazane®)+		
Cholinergic Agonists/Cholinesterase Inhibitors		
echothiophate iodide (Phospholine Iodide®)	carbachol (Miostat®)	
	pilocarpine (Isopto® Carpine®, Pilopine HS®)	
Prostaglandin Analogs		
latanoprost (Xalatan®)	bimatoprost (Lumigan®)	**latanoprostene bunod (Vyzulta™)**
travoprost (Travatan-Z® 0.004%)	tafluprost (Zioptan™)	
	travoprost (Travatan® 0.004%)	
Rho Kinase Inhibitors		
		netarsudil (Rhopressa®)

*Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Indicates available oral medications.
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.

Recommendation 5: Vote to Prior Authorize Mepsevii™ (Vestronidase Alfa-vjbk)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Mepsevii™ (vestronidase alfa-vjbk) with the following criteria:

Mepsevii™ (Vestronidase Alfa-vjbk) Approval Criteria:

1. An FDA approved diagnosis of Sly syndrome (mucopolysaccharidosis type VII; MPS VII) confirmed by:
   a. Enzyme assay demonstrating a deficiency of beta-glucuronidase (GUS) activity; or
   b. Genetic testing to confirm diagnosis of MPS VII; and
2. Mepsevii™ must be administered by a healthcare professional prepared to manage anaphylaxis; and
3. Initial approvals will be for the duration of twelve months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

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.

Recommendation 6: Vote to Prior Authorize Ergomar® (Ergotamine Sublingual Tablets)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. Moving Zomig® (zolmitriptan nasal spray) from Tier-3 to Tier-2 of the Anti-Migraine Medication Product Based Prior Authorization (PBPA) category based on net cost. Current Tier-2 criteria would apply.
2. Brand name Relpax® (eletriptan) will be preferred over the generic formulation based on net cost. Approval of generic eletriptan would require a patient-specific, clinically significant reason why the member cannot use the brand formulation.
3. The placement of Ergomar® (ergotamine sublingual tablets) into the Special Prior Authorization (PA) Tier of the Anti-Migraine Medication PBPA category with the following criteria:
    a. **Ergomar® (Ergotamine Sublingual Tablets) Approval Criteria:**
        i. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
        ii. 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
        iii. A quantity limit of 20 tablets per 28 days will apply.

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

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan/naproxen (Treximet®)

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

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response; or
2. Documented adverse effect 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
2. Documented adverse effect to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days.
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 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® and 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.

Recommendation 7: Vote to Prior Authorize Xadago® (Safinamide) and Gocovri™ [Amantadine Extended-Release (ER)]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Xadago® (safinamide) and Gocovri™ (amantadine ER) with the following criteria:

Xadago® (Safinamide) Approval Criteria:

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

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, CrCl <15mL/min/1.73m^2); and
4. A minimum of a six-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 quantity limit of one 68.5mg capsule or two 137mg capsules per day will apply.

Recommendation 8: Annual Review of Chronic Lymphocytic Leukemia (CLL) Medications and 30-Day Notice to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Erythropoietin Stimulating Agents (ESAs)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of a patient-specific, clinically significant reason why the member cannot use Epogen® or Procrit® (epoetin alfa) to the approval criteria for Aranesp® (darbepoetin alfa). The following criteria would apply based on net cost after rebates:

Aranesp® (Darbepoetin Alfa) Approval Criteria:

1. An FDA approved diagnosis of anemia due to chemotherapy in patients with non-myeloid malignancies; or
2. An FDA approved diagnosis of anemia associated with chronic renal failure; and
    a. 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
3. Recent hemoglobin levels must be provided; and
4. A patient-specific, clinically significant reason why the member cannot use Epogen® or Procrit® (epoetin alfa); and
5. 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 less than 11g/dL.

Recommendation 10: 30-Day Notice to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Spinraza® (Nusinersen)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes shown in red to the Spinraza® (nusinersen) prior authorization criteria:

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
    a. Type I; or
    b. Type II; or
    c. Type III with symptoms; and

2. Molecular genetic testing to confirm biallelic pathogenic variants in the survival motor neuron gene 1 (*SMN1*); and
3. Member is not currently dependent on permanent ventilation; and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or be an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
6. Spinraza® must be administered in a healthcare facility by a specialist experienced in performing lumbar punctures; and
    a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
7. A baseline assessment must be provided using at least one of the following exams as functionally appropriate:
    a. Hammersmith Infant Neurological Exam (HINE); or
    b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
    c. Upper Limb Module (ULM) Test; or
    d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
8. Initial authorizations will be for the duration of six months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically-significant improvement or maintenance of function from pretreatment baseline status using the same exam as performed at baseline assessment:
    a. HINE; or
    b. CHOP-INTEND; or
    c. ULM Test; or
    d. HFMSE; and
9. Approval quantity will be based on Spinraza® prescribing information and FDA approved dosing regimen(s).
    a. Only one 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

Recommendation 12: Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Ocrevus™ (Ocrelizumab)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Alpha$_1$-Proteinase Inhibitors and 30-Day Notice to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)]

NO ACTION REQUIRED.

Recommendation 14: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 15: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

February 21, 2018

Barbara Pasternik-Ikard, Medicaid Director
Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

Re: Importance of Medicaid Formulary Access for Rare Disease Patients

Dear Director Pasternik-Ikard:

As organizations representing millions of Americans with rare diseases, we are writing to you about the importance of preserving patient access to orphan therapies in your Medicaid program. In sending this letter, we hope to foster a dialogue with you on the best way to engage with patient organizations and other rare disease experts to improve patient access to innovative new medicines.

Any disease affecting fewer than 200,000 Americans is considered rare. With nearly 7,000 rare diseases identified and 30 million Americans affected, the population represented by our organizations is incredibly diverse. It is likely that your Medicaid program has only encountered rare diseases within the context of coverage decisions for individual disorders. Even in isolation, however, individual coverage determinations can have widespread effects on the health of rare disease patients by creating new norms for coverage of breakthrough medicines approved by the Food and Drug Administration (FDA).

In making coverage decisions for individual drugs, our organizations recognize that states are under immense pressure to control health care costs in Medicaid in order to protect services for all beneficiaries. However, we believe that these decisions disproportionately affect rare disease patients because they are not suffering from a more prevalent condition even though they are no less deserving of treatment options. Further, we believe the rare disease community has not done enough to inform state Medicaid agencies about the regulatory approval process for breakthrough treatments, especially pertaining to the use of surrogate endpoints in approval decisions.

As a first step in addressing these important concerns, we wish to provide further context about the obstacles encountered by rare disease patients in seeking coverage for new treatments, and the tools FDA uses to accelerate the approval of medicines for untreated conditions.

The Impact of Adverse Medicaid Utilization Decisions on Rare Disease Patients

In an effort to better control Medicaid costs, several states are seeking to use 1115 waivers to enact “commercial-style” formulary restrictions for their programs. Our organizations have seen firsthand how such restrictions can overrule the prescribing decisions of physicians, resulting in patients being unable to access the medicines best suited to treat their condition. These restrictions inhibit quality care by causing lapses in medication adherence and delays in use of

medicines that provide an enhanced clinical benefit.[1] Over time, this will not only result in poorer health outcomes for beneficiaries but raise health care costs for states.

Formulary utilization measures can certainly promote the use of lower cost medicines, including generics. However, there are instances when these restrictions are applied even if there are no cheaper therapeutically equivalent medicines available for patients to take. In these instances, patient access is blocked for the only FDA-approved medicine available to treat their condition.

Further, the underlying assumption supporting the use of formulary restrictions– that they will significantly lower costs – is not borne out by recent research analyzing the impact of orphan therapies used to treat rare diseases on overall health care spending. Nationwide, the volume of prescriptions for orphan drugs is relatively low because of the small patient populations. The orphan drug share of the total volume of pharmaceutical use in the U.S. was just 0.3% in 2016.[2] Additionally, nationwide spending on orphan drugs accounted for only 7.9% of all drug purchases.[3] Looking specifically at the Medicaid program in 2016, spending on rare disease medicines accounted for only 1% of all Medicaid spending.[4]

State Concerns Regarding Medications Approved Via FDA's Accelerated Approval Program

Our organizations are aware that your state may also be broadly concerned about its role in providing access to breakthrough medications approved by FDA via its Accelerated Approval Program. As organizations that work closely with FDA and Congress to improve approval pathways for innovative treatments, we can shed light on this program in regard to the safety and effectiveness of new drugs to treat rare diseases.

Accelerated Approval was created over 25 years ago to facilitate and speed the availability of new treatment options for serious conditions that fill an unmet need by analyzing "surrogate endpoints" when it is not possible to analyze more traditional indicators. It is often impossible to conduct large-scale, randomized, placebo-controlled trials within rare diseases as there simply are not enough patients to participate and, in some diseases, reliable clinical endpoints may not exist that can be measured in a reasonable timeframe. With overwhelming bipartisan Congressional support and approval, FDA has implemented innovative methods to evaluate orphan therapies. Without these unique tools for FDA to evaluate orphan therapies, individuals with rare diseases would be left without any treatment because traditional clinical trials would be impossible to conduct.

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[1] Streeter, S.B., Schwartzberg, L., Husain, N.,Johnsrud, M. "Patient and plan characteristics affecting abandonment of oral oncolytic prescriptions." American Journal of Managed Care. 2011. 175 (5 Spec No.): SP38---SP44.

[2] Need citation for this figure

[3] Trends in Orphan Drug Costs and Expenditures Do Not Support Revisions in the Orphan Drug Act: Background and History. National Organization for Rare Disorders. October 2017. https://rarediseases.org/wp-content/uploads/2017/10/NORD-IMS-Report_FNL.pdf

[4] Coverage of Rare Disease Therapies in Medicaid and Medicare and the Impact on Patient Care. Jay Greissing, Dir. U.S. Government Relations and Policy, Shire. February 2016. http://www.cbinet.com/sites/default/files/files/Greissing_Jay_pres.pdf

The use of surrogate endpoints is one these innovative tools. These endpoints are scientifically accepted indicators of patient health used to determine drug effectiveness. For example, surrogate endpoints, such as tumor shrinkage, have been used to support the accelerated approval of cancer drugs for over two decades. Moreover, every treatment for HIV/AIDS on the market was approved using a surrogate endpoint (HIV viral load and patient CD4 count), because it was not possible to identify an underlying clinical endpoint. Other examples include the use of blood pressure and cholesterol to examine the effectiveness of medications to treat heart disease. As with these examples, the surrogate endpoints used to approve breakthrough treatments for rare diseases must demonstrate substantial evidence of effectiveness from adequate and well-controlled clinical investigations.

FDA and Congress have repeatedly affirmed that drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval and do not represent a lower standard.[5] As such, accelerated approval is a full approval, not a partial, interim, or conditional approval. If states misinterpret the accelerated approval pathway or reject the rigorous process used by FDA to evaluate innovative treatments, the net effect is to turn back the clock to a time in which rare disease patients have no role in determining what is best for their own health and little hope for new medical breakthroughs to fight their disease. Before making judgements on which patients should or should not benefit from new medicines, we implore Medicaid agencies to better understand FDA's process for approving innovative treatments and facilitate enhanced engagement with rare disease patients and the organizations that represent them.

How States and Rare Disease Patient Organizations Can Support Patients

There are several actions that can be taken to help states address these issues. First, as your state considers seeking 1115 waivers from the Centers for Medicaid and Medicare Services (CMS), we encourage you to strongly consider the implications for rare disease patients before proposing any restrictions to accessing newly approved orphan therapies. Specifically, waivers that seek an exemption to Section 1927 of the Social Security Act (42 U.S.C. §1396a(a)(54)) may harm patients seeking coverage for new medications that provide an enhanced clinical benefit over existing treatment options. Moreover, excluding coverage for drugs that utilize FDA's expedited programs like accelerated approval could rob rare disease patients, many of whom are children, of access to FDA-approved medicines that may be their *only* treatment option.

Second, and as previously noted, our organizations are seeking better opportunities to engage with you about the orphan drug approval process and specific coverage decisions. To that end, Tim Boyd at the National Organization for Rare Disorders (NORD) is available to facilitate contacts with any of our organizations to discuss the issues raised within this letter (Tim can be reach via email at tboyd@rarediseases.org). Please also feel free to reach out to each organization directly to discuss our specific patient populations.

[5] Food and Drug Administration Safety and Innovation Act (FDASIA) § 901

Finally, given the Federal prioritization of innovative orphan product development, our organizations believe policies should be explored that provide states additional assistance to cover these products for Medicaid beneficiaries. We would appreciate feedback from your state on the necessity and potential structure of such assistance, and on other opportunities to innovate when it comes to meeting the needs of the rare disease community.

On behalf of our patients, thank you for your consideration of this letter and for your continued commitment to improving patient access in the Medicaid program. We look forward to further collaboration with you on these important issues.

Sincerely,

Acid Maltase Deficiency Association (AMDA)
ADNP Kids Research Foundation
Adrenal Insufficiency United
Adult Polyglucosan Body Disease Research Foundation
Alpha-1 Foundation
ALS Association
American Autoimmune Related Diseases Association (AARDA)
American Syringomyelia and Chiari Alliance Project
Amyloidosis Foundation
Amyloidosis Research Consortium
Amyloidosis Support Groups
Angelman Biomarkers and Outcome Measures Alliance
APS Foundation of America, Inc
Association for Creatine Deficiencies
Autoinflammatory Alliance
Benign Essential Blepharospasm Research Foundation
Bridge the Gap - SYNGAP Education and Research Foundation
CdLS Foundation
Children's Cardiomyopathy Foundation
Children's PKU Network
Children's Tumor Foundation
Chloe's Fight Rare Disease Foundation
CJD Aware!
CMTC-OVM the Netherlands
Congenital Hyperinsulinism International
Cooley's Anemia Foundation
cureCADASIL
CureCMT4J/Talia Duff Foundation
CurePSP

The Degos Disease Support Network
Dravet Syndrome Foundation
Dystonia Advocacy Network
Dystonia Medical Research Foundation
Fabry Support & Information Group
FACES: The National Craniofacial Association
Fat Disorders Research Society
Fibrolamellar Cancer Foundation
FOD (Fatty Oxidation Disorders) Family Support Group
Foundation Fighting Blindness
Foundation for a Angelman Syndrome Therapeutics
Foundation for Atypical HUS
Foundation for Prader-Willi Research
Friedreich's Ataxia Research Alliance (FARA)
GBS|CIDP Foundation International
Glut1 Deficiency Foundation
The Guthy-Jackson Charitable Foundation
HCU Network America
Hereditary Neuropathy Foundation
Hermansky-Pudlak Syndrome Network Inc.
Histiocytosis Association
HSAN1E Society
The Hyper IgM Foundation
Immune Deficiency Foundation
Indian Organization for Rare Diseases
International Fibrodysplasia Ossificans Progressiva (FOP) Association
International Foundation for CDKL5 Research
International FOXG1 Foundation
International Pemphigus & Pemphigoid Foundation
International Rett Syndrome Foundation
International Waldenstrom's Macroglobulinemia Foundation (IWMF)
Interstitial Cystitis Association
The Jansen's Foundation
Kids With Heart National Association for Children's Heart Disorders, Inc.
Klippel-Feil Syndrome Freedom
LAL D Aware
The Life Raft Group
Li-Fraumeni Syndrome Association (LFSA / LFS Association)
Lung Transplant Foundation

Lymphangiomatosis & Gorham's Disease Alliance
MEBO Research, Inc.
Mila's Miracle Foundation
MLD Foundation
Moebius Syndrome Foundation
The M.O.R.G.A.N. Project
MPN (Myeloproliferative Neoplasms) Research Foundation
The Myasthenia Gravis Foundation of America
The Myelin Project
The Myositis Association
The National Adrenal Diseases Foundation
National Ataxia Foundation
National Eosinophilia Myalgia Syndrome Network
National Fabry Disease Foundation
National MPS Society
National Niemann-Pick Disease Foundation
National Organization for Rare Disorders (NORD)
National Tay-Sachs & Allied Diseases Association
National Urea Cycle Disorders Foundation
National Spasmodic Dysphonia Association
NephCure Kidney International
Neurofibromatosis Northeast
The Oral Cancer Foundation
Organic Acidemia Association
PANDAS Network
PANDAS/PANS Advocacy and Support
Phelan-McDermid Syndrome Foundation
PKD Foundation
Platelet Disorder Support Association
Prader-Willi Syndrome Association (USA)
Prevent Blindness
Pulmonary Hypertension Association
Rare and Undiagnosed Network (RUN)
Rare Army
RASopathies Network USA
Rett Syndrome Research Trust
Rothmund-Thomson Syndrome Foundation
RYR-1 Foundation
Scleroderma Foundation

Shwachman-Diamond Syndrome Foundation
The Snyder-Robinson Foundation
Soft Bones, Inc.: The U.S. Hypophosphatasia Foundation
Spastic Paraplegia Foundation
Spinal CSF Leak Foundation
SSADH Association
Stiff Person Syndrome Support Group
Tarlov Cyst Disease Foundation
Tom Wahlig Foundation
The Transverse Myelitis Association
Tuberous Sclerosis Alliance
Turner Syndrome Society of the United States
United Leukodystrophy Foundation
US Hereditary Angioedema Association
Vasculitis Foundation
Vestibular Disorders Association
VHL Alliance
Wilhelm Foundation
Worldwide Syringomyelia & Chiari Task Force

March 29, 2018

Tim Boyd, MPH
Director of State Policy
tboyd@rarediseases.org

Oklahoma Health Care Authority
DUR Committee
Oklahoma University Health Sciences Center

Transmitted via email

Re: Patient Access to Treatment for Inherited Retinal Dystrophies and Other FDA-Approved Rare Disease Treatments

Dear Members of the Committee:

On behalf of the 1-in-10 Oklahoma residents with one of the nearly 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) writes in regard to the proposed prior authorization requirements for voretigene neparvovec-rzyl (brand name Luxturna), a treatment for inherited retinal dystrophies that may cause blindness. NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. We are committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

NORD was recently contacted by multiple ophthalmologists regarding concerns that the Oklahoma Health Care Authority's (OHCA) proposed prior authorization requirements for voretigene neparvovec- rzyl might exclude patients who suffer from inherited retinal dystrophies and are in need of treatment by restricting coverage based on disease progression counter to the Food and Drug Administration's (FDA) approved indication. Specifically, we are concerned that restricting coverage of this medication based on visual acuity and visual field could render patients untreatable at later stages of the disease because their retinal cells degenerate beyond repair.

NORD recognizes that prior authorization and other formulary utilization measures can promote the use of lower cost generic medicines by patients and, therefore, help lower overall health care costs. However, Luxturna is the first ever treatment for inherited retinal dystrophies approved by FDA, and there are no therapeutically equivalent versions of it available for patients to take. As the agency noted in granting approval for this medicine, "[p]atients with biallelic RPE65 mutation-associated retinal dystrophy now have a chance for improved vision, where little hope previously existed."[1]

1

Given these circumstances, restricting use of this medicine to only patients at certain point in their disease progression — counter to FDA indication for adult and pediatric patients (12 months or older) — serves only to reduce costs by restricting patient access to a medically necessary treatment.

In order to remedy this issue, NORD urges the OHCA (and the DUR Committee) to consult with disease experts and patient groups in order to ensure that patients with inherited retinal dystrophies are not denied access to medically necessary treatment. As a national umbrella organization for rare diseases, NORD can assist in this matter by facilitating contact with appropriate patient groups and disease experts, such as our member organization Foundation Fighting Blindness (http://www.blindness.org).

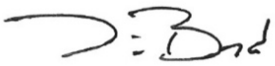
State Concerns Regarding Medications Approved Via FDA Accelerated Approval

In addition to the Oklahoma Healthcare Authority's consideration of Luxturna, NORD is aware that the OHCA is broadly concerned about its role in providing access to breakthrough medications approved by FDA via its Accelerated Approval pathway. Last month, NORD joined 125 rare disease patient organizations in sending a letter to Medicaid Directors all across the country highlighting the importance of Medicaid formulary access for rare disease patients (a copy of the letter sent to Oklahoma is attached along with this correspondence).

With this letter, it is our hope to start a dialogue with the OHCA regarding ways to interact with patient organizations and rare disease experts in order to improve patient access to innovative new medicines.

Thank you for your attention in this matter. Please feel free to contact me at tboyd@rarediseases.org.Thank you for your attention in this matter. Please feel free to contact me at tboyd@rarediseases.org.

Sincerely,



Tim Boyd, MPH
Director of State Policy

1779 Massachusetts Ave. NW, Suite 500 • Washington, DC 20036
T 202.588.5700 • F 202.588.5701
rarediseases.org • orphan@rarediseases.org

CULLEN EYE INSTITUTE

Baylor College of Medicine

J. Timothy Stout, M.D., Ph.D., M.B.A.

Sid W. Richardson Professor,
Margarett Root Brown Chair, and
Director, Cullen Eye Institute

March 28, 2018

Dear DUR committee, OHCA, OUHSC

Thank you for considering approval of Luxturna (Voretigene) in Oklahoma. I have recently read your board packet that includes your recommendations for its use. As you know, SPARK Inc. is planning on limiting the number of centers able to dose this drug to patients with biallelic RPE65 deficiency. As I am the surgeon at Baylor College of Medicine that will be dosing these patients (and am closest to Oklahoma) it is likely that I will be treating patients from your state. While I applaud your recommendation to approve, I have one concern about your approval criteria – specifically the requirement that patients must have a best corrected visual acuity of 20/60 or worse and or visual fields less than 20° in both eyes.

I was the principal investigator in one of the clinical trials to test gene therapy for RPE65 deficiency. We found that the younger the patient was, the better the long term outcome. I could imagine a scenario where a patient might have 20/40 or 20/50 vision (better than 20/60) who might very well merit treatment. As you know the FDA guidelines have indicated that the approval criteria is limited to patients 1) with biallelic RPE 65 deficiency and 2) viable retina who are 12 months of age or older. They purposefully did not want to set visual acuity parameters for this very reason. I'd ask that you reconsider the requirement for specific acuity or field decrement to be treated.

Thank you for your consideration. Should you have any questions, please do not hesitate to contact me directly.

Sincerely,

J. Timothy Stout, MD PhD MBA
Sid W. Richardson Professor
Margarett Root Brown Chair
Director, Cullen Eye Institute and
Chair, Department of Ophthalmology
at Baylor College of Medicine and
Chief of Service at CHI-BSLMC

JTS:bjl

SOFIA SEES HOPE
PO Box 705 | Ledyard, CT 06339
860-556-3119 | info@sofiaseeshope.org
www.sofiaseeshope.org

Submitted to: DUR committee, OHCA, OUHSC via email on March 30, 2018

Re: Patient Access to Treatment for Inherited Retinal Dystrophies and Other FDA-Approved Rare Disease Treatments

Dear Members of the Committee:

We write today to strongly urge you to not restrict access to voretigene neparvovecrzyl (brand name Luxturna) for those with biallelic RPE65 mutation-associated retinal dystrophy. Requiring a certain degree of blindness in an individual before treatment will be allowed not only goes against federal health recommendations, but it flies in the face of basic humanity.

Sofia Sees Hope is a nonprofit advocacy organization that works on behalf of those with rare inherited retinal diseases (IRDs). We are dedicated to patient advocacy and education to advance research to cure blindness caused by rare inherited retinal disease. We represent families across the United States. We full support the principle that all FDA-approved treatments should be made available to all those who will benefit from such treatments.

The proposed prior authorization requirements for Luxturna would exclude many individuals who suffer from life-altering vision loss due to RPE65 genetic mutation. As it stands now, Oklahoma requirements state the “member must have best corrected visual acuity of 20/60 or worse in both eyes and/or visual field less than 20 degrees in any meridian in both eyes”. We are asking this VA/VF requirement be stricken as it serves only to reduce cost by restricting access.

As per the FDA, the optimal window for reversing vision loss is during the early phase of the disease. Any withholding of treatment increases the potential for failure and increases the likelihood of recurrent disease activity. Access to a full range of options is essential for people with IRDs to effectively manage their own disease course, and for their physicians to make the most optimal treatment decisions. We urge the DUR committee, OHCA, and OUHSC to continue to allow physicians to have the ability to choose the best product and the timing of prescribing the treatment for their patients.

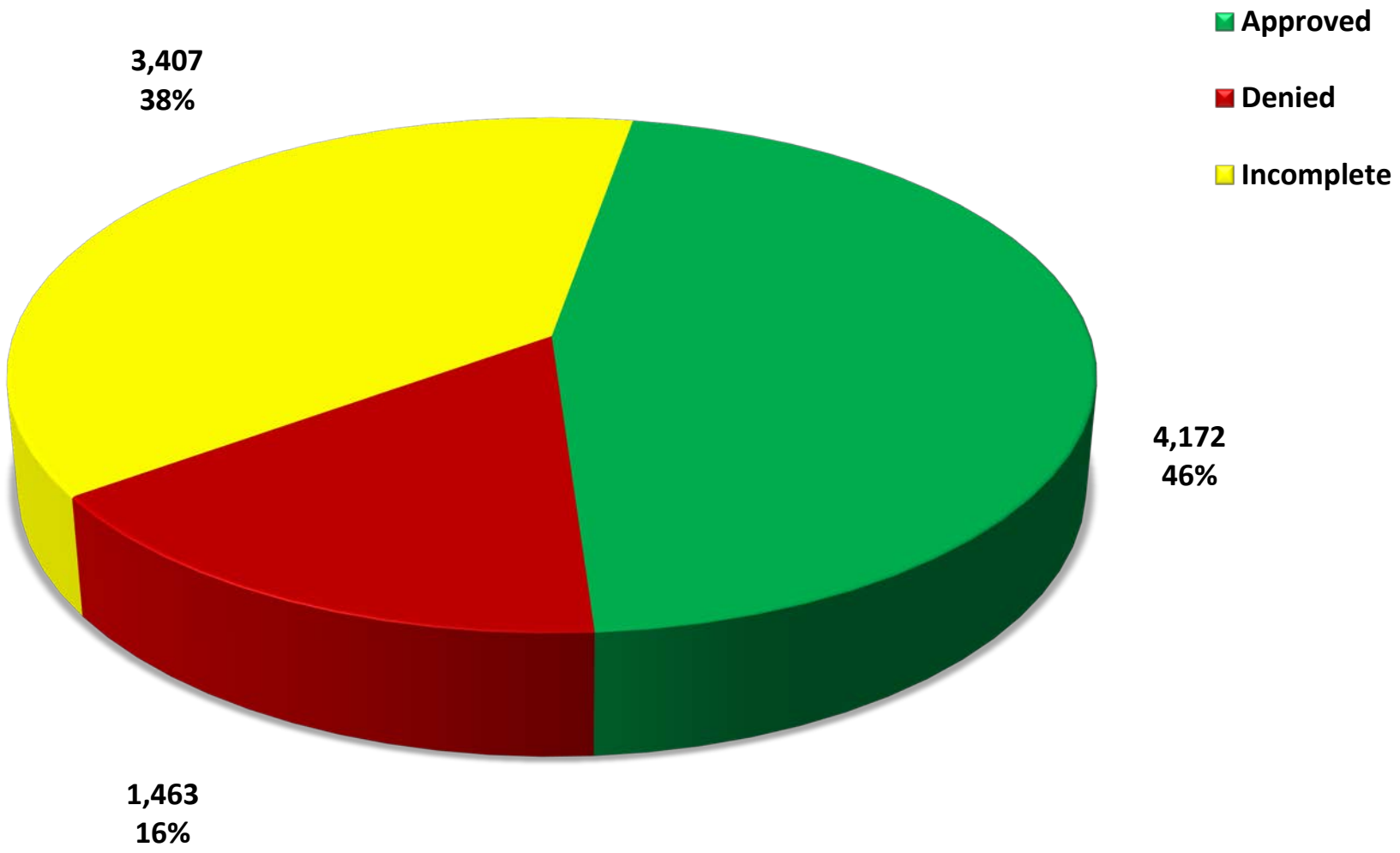
We would be happy to provide more information for the Committee as it considers these proposals. Please feel free to contact me danielle@sofiaseeshope.org or 860-556-3119.

Sincerely,

Danielle Chiaraluce, COO

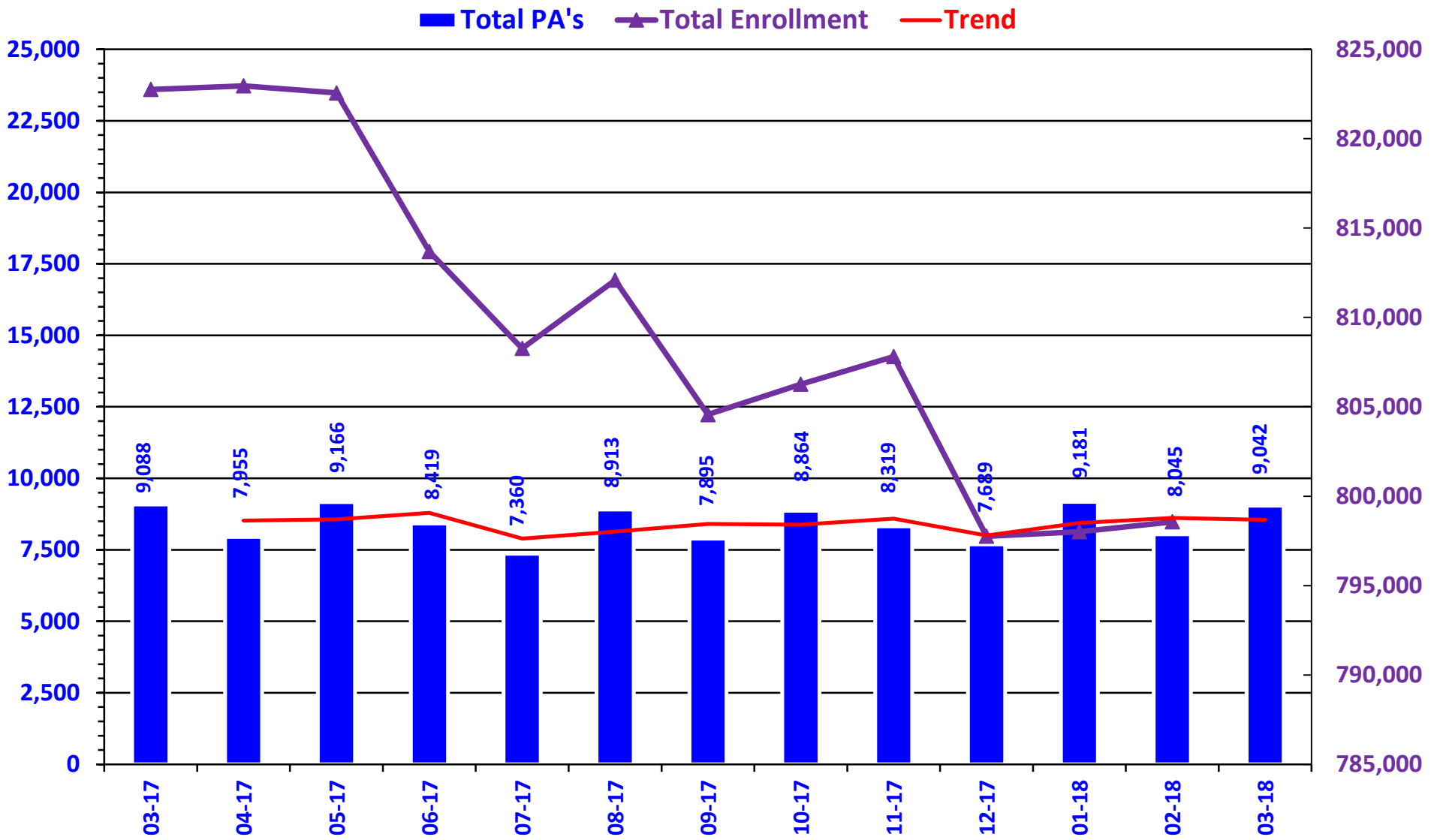
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH 2018



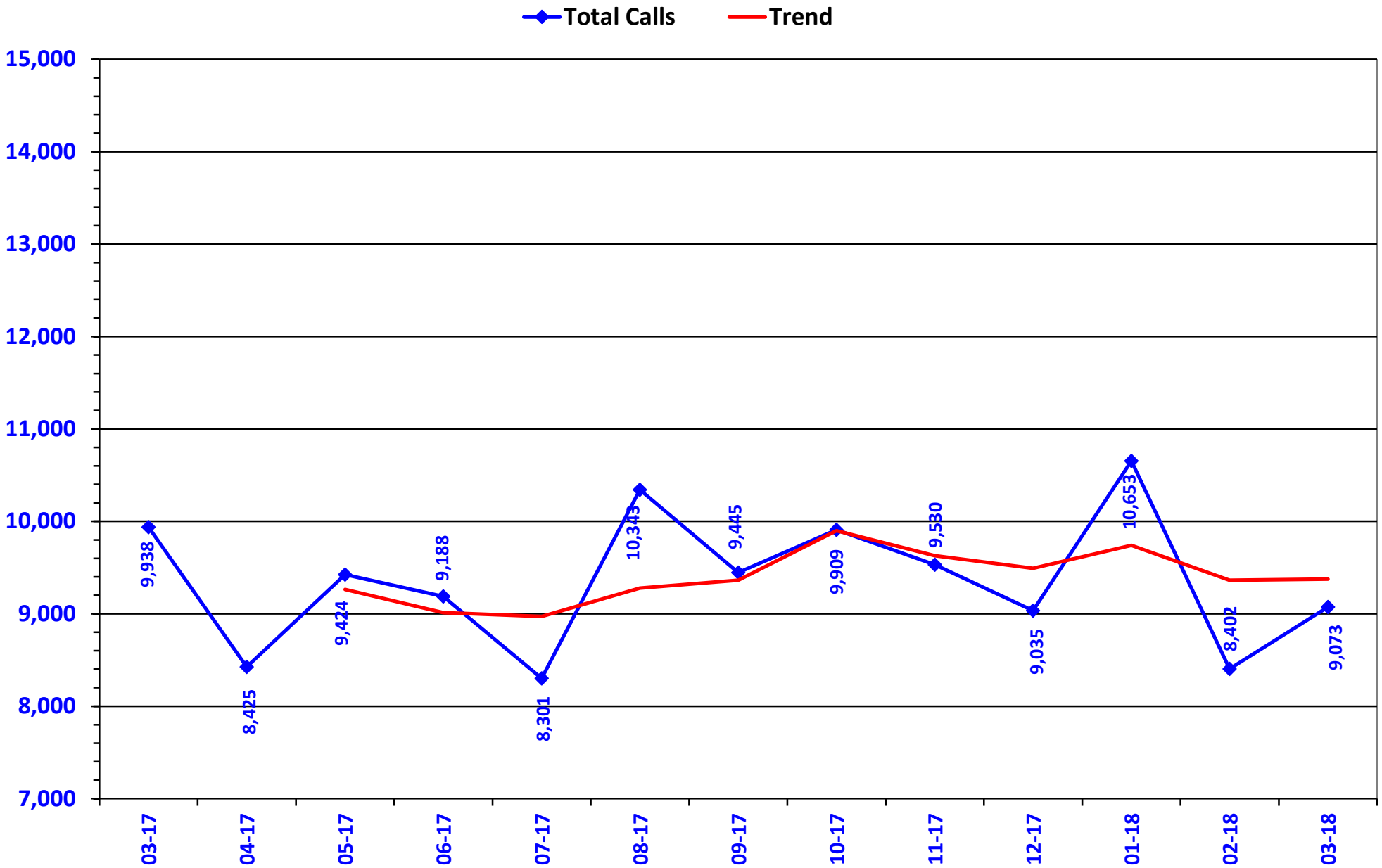
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MARCH 2017 – MARCH 2018



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MARCH 2017 – MARCH 2018



Prior Authorization Activity

3/1/2018 Through 3/31/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	238	13	57	168	358
Analgesic - NonNarcotic	40	0	6	34	0
Analgesic, Narcotic	433	218	44	171	164
Angiotensin Receptor Antagonist	21	6	4	11	310
Antiasthma	61	12	15	34	337
Antibiotic	26	15	1	10	201
Anticonvulsant	133	59	21	53	318
Antidepressant	188	54	32	102	330
Antidiabetic	251	98	52	101	344
Antigout	10	5	2	3	358
Antihistamine	33	6	15	12	313
Antimigraine	47	7	13	27	215
Antineoplastic	99	54	14	31	157
Antiparasitic	13	0	3	10	0
Antiulcers	209	57	72	80	107
Anxiolytic	82	37	11	34	246
Atypical Antipsychotics	210	98	21	91	330
Biologics	131	87	11	33	304
Bladder Control	57	10	17	30	268
Blood Thinners	242	143	16	83	326
Botox	38	20	12	6	358
Buprenorphine Medications	326	231	15	80	75
Cardiovascular	134	52	20	62	283
Chronic Obstructive Pulmonary Disease	192	37	59	96	306
Constipation/Diarrhea Medications	167	26	71	70	212
Contraceptive	13	10	0	3	357
Dermatological	400	187	81	132	271
Diabetic Supplies	475	286	21	168	202
Endocrine & Metabolic Drugs	114	71	7	36	136
Erythropoietin Stimulating Agents	13	8	2	3	109
Fibric Acid Derivatives	16	2	1	13	360
Fibromyalgia	253	32	140	81	324
Gastrointestinal Agents	113	36	21	56	188
Growth Hormones	100	85	4	11	151
Hematopoietic Agents	10	6	0	4	96
Hepatitis C	229	172	11	46	9
HFA Rescue Inhalers	64	5	26	33	238
Insomnia	46	7	17	22	151
Insulin	142	33	24	85	316
Miscellaneous Antibiotics	20	2	2	16	52
Multiple Sclerosis	68	34	11	23	192
Muscle Relaxant	48	8	22	18	22
Nasal Allergy	91	12	25	54	153
Neurological Agents	131	33	32	66	215
NSAIDs	178	27	55	96	221
Ocular Allergy	47	10	16	21	83
Ophthalmic Anti-infectives	14	3	5	6	16
Osteoporosis	30	14	3	13	320
Other*	349	89	63	197	261
Otic Antibiotic	24	2	3	19	5

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Respiratory Agents	23	15	2	6	245
Statins	23	2	6	15	360
Stimulant	804	372	84	348	343
Synagis	61	29	12	20	59
Testosterone	49	20	13	16	341
Topical Antifungal	27	3	6	18	40
Topical Corticosteroids	63	3	22	38	74
Vitamin	89	23	43	23	269
Pharmacotherapy	102	83	0	19	258
Emergency PAs	1	1	0	0	
Total	**7,611**	**3,070**	**1,384**	**3,157**	
Overrides					
Brand	36	27	1	8	295
Compound	24	18	1	5	20
Cumulative Early Refill	5	5	0	0	180
Diabetic Supplies	9	7	1	1	88
Dosage Change	330	312	3	15	13
High Dose	2	1	0	1	87
Ingredient Duplication	16	12	0	4	9
Lost/Broken Rx	80	75	0	5	18
NDC vs Age	289	204	24	61	247
Nursing Home Issue	41	35	0	6	10
Opioid Quantity	20	16	3	1	155
Other*	48	32	8	8	16
Quantity vs. Days Supply	525	356	38	131	245
STBS/STBSM	24	15	3	6	61
Stolen	17	16	0	1	9
Temporary Unlock	1	1	0	0	28
Third Brand Request	22	16	2	4	15
Overrides Total	**1,431**	**1,102**	**79**	**250**	
Total Regular PAs + Overrides	**9,042**	**4,172**	**1,463**	**3,407**	

Denial Reasons	
Unable to verify required trials.	2,563
Does not meet established criteria.	1,484
Lack required information to process request.	804
Other PA Activity	
Duplicate Requests	605
Letters	10,485
No Process	4
Changes to existing PAs	768
Helpdesk Initiated Prior Authorizations	644
PAs Missing Information	20

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

Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update

Oklahoma Health Care Authority
April 2018

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

Tardive dyskinesia (TD) is a serious, potentially disabling and possibly irreversible movement disorder that has been associated with prolonged use of dopamine receptor blocking agents (DRBAs), primarily antipsychotic medications and the antiemetic drug, metoclopramide (Reglan®). Metoclopramide is indicated in adults with symptomatic gastroesophageal reflux (GERD) that has failed to respond to conventional therapy and is the only medication approved by the U.S. Food and Drug Administration (FDA) to treat adults with acute and recurrent diabetic gastroparesis. The most common clinical manifestation of metoclopramide-induced TD is acute dystonia. In 2009, the FDA announced that manufacturers of metoclopramide must add a boxed warning to drug labels regarding the risk of TD with long-term or high-dose use. The gastroparesis management guidelines from the American College of Gastroenterology (ACG) recommend metoclopramide as first-line pharmacologic therapy for gastroparesis with the caveat that it should be administered at the lowest effective dose for no longer than a 12-week period unless the therapeutic benefits outweigh the potential risks. The ACG also recommends that patients be counseled to discontinue metoclopramide therapy if they develop TD symptoms.

Prescriber Mailing Summary

In July 2017, the College of Pharmacy and the Oklahoma Health Care Authority (OHCA) sent an educational letter to 114 prescribers of 131 unique members who had more than three paid claims for metoclopramide during the analysis period of January 1, 2017 through June 30, 2017.

Prescribers were notified of the potential risk of TD associated with prolonged use of metoclopramide and were encouraged to review the member list provided for medication efficacy, adverse events, and need for continued therapy. Prescribers were provided recommendations for TD prevention and for counseling patients on the signs of TD.

Metoclopramide Mailing Results

Of the 131 members included in the mailing, 7.6% were 10 years of age or younger, 33.6% were 55 years of age or older, and 54.2% were female. The majority of patients (94.7%) included had at least 120 days worth of medication over the 180-day study period. The total number of claims for metoclopramide from the 131 members was 920, with an average day supply of 28.1 days per claim and a total cost of $27,733.01.

The post-analysis of the mailing reviewed claims from July 21, 2017 to January 17, 2018. Results found 109 prescribers accounting for 124 unique members with more than three paid claims

for metoclopramide during the analysis period. The 124 members accounted for 839 claims with an average day supply of 28.3 days per claim and a total cost of $27,884.52; this resulted in a 5.3% decline in the number of SoonerCare members with more than three metoclopramide claims, and an 8.8% decline in the number of claims for those members. The majority of patients (94.4%) included had at least 120 days worth of medication over the 180-day study period. Approximately half of the prescribers included in the mailing no longer had patients included in the post-mailing analysis [N=56 (49.1%)]. Similarly, 57.2% of members in the post-mailing analysis were included in the original mailing population, indicating that 42.8% of members in the mailing were no longer chronic users of metoclopramide. The member demographic break down among chronic metoclopramide users was similar to prior to the mailing with 56.5% of members being female, 32.3% age 55 years or older, and 8.9% age 10 years or younger.

Conclusions

Analysis of the metoclopramide safety mailing revealed a modest decrease in the number of members receiving chronic metoclopramide therapy as well as a decline in the number of claims in members receiving more than three claims for metoclopramide. Additionally, approximately half of the prescribers who received an educational letter no longer had members receiving chronic metoclopramide therapy in the post-mailing analysis. While these results are promising, it cannot be confirmed that the decline is a result of the mailing, as prescribers may be following ACG recommendations that metoclopramide should be administered at the lowest effective dose for no longer than a 12-week period unless the therapeutic benefits outweigh the potential risks. The College of Pharmacy and OHCA will continue to monitor chronic metoclopramide use, with potential intervention opportunities brought to the Drug Utilization Review (DUR) Board where appropriate.

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[1] Tarsy D. Tardive Dyskinesia: Etiology and Epidemiology. *UpToDate*. Available online at: http://www.uptodate.com/contents/tardive-dyskinesia-etiology-and-epidemiology?source=search_result&search=tardive+dyskinesia&selectedTitle=3%7E150. Last revised 12/14/2016. Last accessed 03/12/2018.

[2] Reglan® (Metoclopramide) Prescribing Information. Ani Pharmaceuticals, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017854s062lbl.pdf. Last revised 08/2017. Last accessed 03/14/2018.

[3] Cloud LF, Zutshi D, Factor SA. Tardive Dyskinesia: Therapeutic Options for an Increasingly Common Disorder. *Neurotherapeutics* 2014; 11(1):166-176.

[4] Tarsy D. Tardive Dyskinesia: Prevention and Treatment. *UpToDate*. Available online at: http://www.uptodate.com/contents/tardive-dyskinesia-prevention-and-treatment?source=see_link&sectionName=PHARMACOLOGIC+TREATMENT&anchor=H5#H1. Last revised 02/07/2018. Last accessed 03/14/2018.

[5] Camilleri M et al. Clinical Guideline: Management of Gastroparesis. *Am J Gastroenterol* 2013; 108:18-37.

[6] Kanto WP. An FDA Warning About Metoclopramide. *New England Journal of Medicine*. Available online at: http://www.jwatch.org/pa200903180000001/2009/03/18/fda-warning-about-metoclopramide. Issued 03/18/2009. Last accessed 03/14/2018.

Appendix C

Vote to Prior Authorize Ocrevus™ (Ocrelizumab)

Oklahoma Health Care Authority
April 2018

Introduction[1]

Ocrevus™ (ocrelizumab) is a CD20-directed cytolytic antibody indicated for the treatment of patients with relapsing (R) or primary progressive (PP) forms of multiple sclerosis (MS). Ocrevus™ is supplied as 300mg/10mL single-dose vials. The recommended initial dosage is 300mg via intravenous (IV) infusion over a minimum period of 2.5 hours, followed two weeks later by a second 300mg IV infusion. Recommended maintenance dosing is a single 600mg IV infusion over a minimum period of 3.5 hours every six months. Ocrelizumab should be administered under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions. Patients should be observed for at least one hour after the completion of the infusion. Prior to every infusion, patients should be assessed for active infection. In the case of active infection, infusion of ocrelizumab should be delayed until the infection resolves. Prior to initiating ocrelizumab, hepatitis B virus (HBV) screening should be performed. Ocrelizumab is contraindicated in patients with active HBV infection.

Cost:

Medication	Cost Per Dose*	Cost Per Year[+]
Ocrevus™ (ocrelizumab)	**$32,500.00**	**$65,000.00**

*Cost based on Wholesale Acquisition Cost (WAC) and does not reflect rebated price or net cost.
[+]Cost per year based on maintenance dosing after loading dosing complete.

Recommendations

The College of Pharmacy recommends the prior authorization of Ocrevus™ (ocrelizumab) with the following criteria:

Ocrevus™ (Ocrelizumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing or primary progressive forms of Multiple Sclerosis (MS); and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Ocrevus™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for one hour after each infusion; and
4. Prescriber must verify hepatitis B virus (HBV) testing has been performed prior to initiating Ocrevus™ therapy and member does not have active HBV; and
5. Verification from the prescriber that member has no active infection(s); and

6. Verification from the prescriber that female members are not currently pregnant and will use contraception while receiving Ocrevus™ therapy and for six months after the last infusion of Ocrevus™; and
7. Compliance will be checked for continued approval.

[1] Ocrevus™ Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/ocrevus_prescribing.pdf. Last revised 03/2017. Last accessed 03/08/2018.

Appendix D

Vote to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl)

Oklahoma Health Care Authority
April 2018

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

Luxturna™ (voretigene neparvovec-rzyl) is a live, non-replicating adeno-associated virus serotype 2 (AAV2) vector-based gene therapy, designed to deliver a normal copy of the gene encoding the human retinal pigment epithelial 65 kDa protein (*RPE65*) to cells of the retina in patients with reduced or absent levels of biologically active *RPE65*. The U.S. Food and Drug Administration (FDA) approved Luxturna™, a one-time gene therapy product, in December 2017 for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy that leads to vision loss and may cause complete blindness in certain patients. Patients must have viable retinal cells as determined by the treating physician(s). Mutations in the *RPE65* gene lead to reduced or absent levels of *RPE65* isomerohydrolase activity, blocking the visual cycle and resulting in impairment of vision. The absence of *RPE65* eventually leads to the accumulation of toxic precursors and damage to the RPE cells, which, over time, results in damage to the photoreceptors, which depend on the RPE cells for cellular metabolism. Patients with untreated *RPE65*-mediated inherited retinal dystrophy eventually lose the ability to detect light of any intensity. Retinal diseases caused by biallelic *RPE65* mutations include some forms of Leber congenital amaurosis (LCA) and retinitis pigmentosa (RP), among other disorders, with mutations in *RPE65* estimated to be responsible for 7 to 9% of LCA cases and 1 to 2% of RP cases.[8] Injection of Luxturna™ into the subretinal space results in transduction of some RPE cells with complementary DNA (cDNA) encoding normal human *RPE65* protein, thus providing the potential to restore the visual cycle. This does not repair or eliminate the defective gene, but rather introduces a normal copy of the gene into the cell. While Luxturna™ is a one-time therapy, long-term efficacy remains a question for this treatment. Individuals with an *RPE65* mutation have significant retinal degeneration leading to worse functional vision over time. The therapeutic effects of gene therapy may not be permanent. Visual improvements past three years have been described by clinical experts, but no published data exist beyond one year. Even if improvements persist in treated cells, it remains unclear whether long-term retinal degeneration is impacted by gene therapy.

The anticipated cost of Luxturna™ is $850,000 per patient ($425,000 per single-dose vial). An analysis published in January 2018 from the Institute for Clinical and Economic Review (ICER) states the $850,000 list price for Luxturna™ is about four times too high for the value the drug provides. ICER is an independent, non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. In its report, ICER said a cost-effective price for Luxturna™ would be $153,000 to $217,000 and cited a lack of data that Luxturna™ causes permanent improvements in vision as a key reason that its developer, Spark

Therapeutics, should not be charging so much. ICER reached its suggested list price for Luxturna™ by assuming that a 15 year old patient (the average age of the patients enrolled in the clinical trials) would experience improvements for a decade or two and taking into account the benefits to the health care system. ICER added that when it also took into account the benefits related to education, caregiver burdens, and productivity, the drug's list price should still be cut in half.

Luxturna™ is an intraocular suspension for subretinal injection that must be diluted prior to use and should be prepared within 4 hours of administration using sterile technique under aseptic conditions in a Class II vertical laminar flow biological safety cabinet (*refer to Luxturna™ prescribing information for a complete list of dilution, preparation, and administration steps*). Each carton of Luxturna™ contains one single-dose vial of Luxturna™ and two vials of diluent; Luxturna™ and diluent should be stored frozen at ≤ -65°C prior to dilution and administration. Luxturna™ does not contain preservatives. Luxturna™ should be administered by subretinal injection to each eye on separate days within a close interval, but no fewer than 6 days apart, and is to be administered at selected Ocular Gene Therapy Treatment Centers in the United States by leading retinal surgeons, who will receive surgical training provided by the pharmaceutical company on the administration procedure. Systemic oral corticosteroids equivalent to prednisone 1mg/kg/day (maximum of 40mg/day) are recommended for a total of 7 days (starting 3 days before administration of Luxturna™ to the first eye), and followed by tapering the dose during the following 10 days. The same corticosteroid regimen applies for the administration of Luxturna™ to the second eye.

The efficacy and safety of Luxturna™ in pediatric and adult patients with biallelic *RPE65* mutation-associated retinal dystrophy were evaluated in an open-label, two-center, randomized Phase 3 clinical trial. Patients had to have a confirmed genetic diagnosis of *RPE65* gene mutation and sufficient viable retinal cells as determined by retinal thickness on spectral domain optical coherence tomography (>100 microns within the posterior pole), fundus photography, and clinical examination, in order to be included in the study. The study was open to patients ages 3 years and older; however, the youngest patient included in the study was 4 years of age. Treatment with Luxturna™ is not recommended in patients younger than 12 months of age because retinal cells are still undergoing cell proliferation, and Luxturna™ would potentially be diluted or lost during cell proliferation. The average age of the randomized patients in the study was 15 years (range 4 to 44 years), and the intervention group included 20 patients, with nine patients younger than 10 years of age. The control group included nine patients who did not receive Luxturna™, but participated in the same efficacy outcome testing as did the intervention group. To be included in the study, patients had to have best corrected visual acuity (BCVA) of 20/60 or worse in each eye, or visual field less than 20 degrees in any meridian in each eye, or both. The best bilateral (both eyes averaged) BCVA at baseline of the patients included in the intervention group was 20/105. Patients also had to have the ability to perform multi-luminance mobility testing (MLMT) within the luminance range to be included in the study. The MLMT was developed by members of the sponsor and study team, with input from the FDA, to study Luxturna™ in these low-vision patients with nyctalopia. The MLMT uses a 5-foot by 10-foot course surrounded by a 1-foot border to

evaluate an individual's ability to navigate a marked path, while avoiding obstacles in or adjacent to the path, negotiating raised steps, and identifying a door, all while relying on vision. Patients were excluded from the study if they had participated in a previous gene therapy or investigational drug study, used high-dose retinoid compounds in the past 18 months, had intraocular surgery in the past 6 months, had known sensitivity to medications planned for use in the perioperative period, or had ocular or systemic conditions that would interfere with study interpretation. Women who were pregnant or any patients unwilling to use effective contraception for 4 months after vector administration were also ineligible for the study.

The intervention group received bilateral, subretinal injections of Luxturna™, administered sequentially in two separate surgical procedures with an interval of 6 to 18 days. The primary efficacy endpoint was 1-year change from baseline in bilateral MLMT performance (change in lux score for the lowest passing light level), measuring functional vision at specified light levels. Baseline testing established the lowest level of illumination at which each patient could pass the MLMT. A positive change score indicates passing the MLMT at a lower light level. At one year, mean bilateral MLMT change score was 1.8 light levels in the intervention group and 0.2 in the control group, for a difference of 1.6 [95% confidence interval (CI): 0.72 to 2.41; P=0.0013]. The response to bilateral administration of Luxturna™ in the intervention group was rapid; mean MLMT lux score improved by the day 30 visit and remained stable throughout one year. At one year, the best bilateral (both eyes averaged) BCVA, a secondary endpoint, of the patients included in the intervention group was 20/54. No product-related serious adverse events or deleterious immune responses occurred, and most ocular events were mild in severity.

Other AAV2 Clinical Studies[9,10,11,12]

The following are publications reviewing other clinical studies using AAV2 vectors (not Luxturna™) for the treatment of *RPE65* mutation-associated retinal dystrophy:

- An article published in *The New England Journal of Medicine (NEJM)* examined the long-term effects of patients with *RPE65*-associated LCA treated by subretinal delivery of recombinant AAV2 vectors carrying human *RPE65* cDNA in two clinical studies. Both studies reported on Phase 1-2 open-label clinical trials.
    - The first study described the 5-to-6-year post treatment follow-up of three patients with *RPE65*-associated LCA (16 to 23 years of age at enrollment) who were given a single subretinal injection into one eye, with the contralateral eye serving as the control. All three patients had improvement in visual sensitivity in the treated region, which peaked at 1 to 3 years after treatment but declined thereafter for up to 5 to 6 years after treatment, alongside a continuing loss of photoreceptors. The degeneration continued at much the same rate as in the untreated retina, despite the initial improvement.
    - The second study involved 12 patients with *RPE65*-associated LCA (6 to 23 years of age at enrollment) who were treated with a similar AAV2-*RPE65* vector and single subretinal injection into one eye, although in this study the investigators sought to include the fovea, to try to improve central as well as foveal vision. Four patients were administered a lower dose of the vector, and eight were administered a

higher dose. Six of the 12 treated patients (5 of 8 given the higher dose and 1 of 4 given the lower dose) had modest improvements in visual sensitivities, which peaked at 6 to 12 months after treatment, but the effect again declined or was lost by 3 years after treatment. No clear correlation between response and the age of the patient was identified. The greatest improvements were evident in older patients, and contrary to expectation, improvements in retinal sensitivity were of lower magnitude in younger participants who had the greatest preservation of retinal structure. Also, despite the vector having been delivered to the fovea in the majority of patients (10 of 12), there was no improvement in foveal function. Additionally, with the exception of one patient who had an apparent improvement in visual acuity in the study eye accompanied by a similar improvement in the contralateral untreated eye, no consistent improvement in visual acuity was evident. Furthermore, two patients had clinically significant deterioration of visual acuity.

- An article published in the *Proceedings of the National Academy of Sciences of the United States of America* analyzed advancing retinal degeneration despite visual improvements with gene therapy in patients with *RPE65*-LCA. The visual function and retinal degeneration in treated and untreated eyes of patients with *RPE65*-LCA and in the dog model of this disease were evaluated. Gene therapy resulted in improvements in visual function that persisted for up to 3 years, but serial measurements of outer photoreceptor nuclear layer (ONL) thickness showed continuing progression of photoreceptor loss. Therefore, the analyses of ONL supported the conclusion that gene therapy has not modified the natural history of progressive retinal degeneration in *RPE65*-LCA patients. It was deduced that treatment of *RPE65*-LCA should evolve into a two-pronged intervention that not only leads to visual restoration in the short term but also, slowed retinal degeneration and improved photoreceptor survival in the long term.

Recommendations

The College of Pharmacy recommends the prior authorization of Luxturna™ (voretigene neparvovec-rzyl) with the following criteria with changes noted in red based on recommendations by the Drug Utilization Review (DUR) Board:

Luxturna™ (Voretigene Neparvovec-rzyl) Approval Criteria:

1. An FDA approved diagnosis of biallelic *RPE65* mutation-associated retinal dystrophy; and
    a. Diagnosis must be confirmed by genetic testing; and
2. Member must have sufficient viable retinal cells in both eyes as determined by the treating physician(s); and
3. Member must have best corrected visual acuity of 20/60 or worse in both eyes and/or visual field less than 20 degrees in any meridian in both eyes; and
4. Member must be four years of age or older; and
5. Member must not have participated in a previous *RPE65* gene therapy study or have previously received treatment with Luxturna™; and
6. ~~Member must not have used high-dose retinoid compounds (>7,500 retinal equivalent units or >3,300 IU per day of vitamin A) in the past 18 months; and~~

7. Member must not have had intraocular surgery in the past 6 months; and
8. Female members of child bearing age must not be pregnant and must have a negative pregnancy test immediately prior to administration of Luxturna™; and
9. Male and female members of child bearing age must be willing to use effective contraception during treatment with Luxturna™ and for at least 4 months after administration of Luxturna™; and
10. Member must take the recommended systemic oral corticosteroid regimen, starting 3 days prior to administration of Luxturna™ to each eye, and continuing after administration of Luxturna™, as per package labeling of Luxturna™; and
11. Luxturna™ must be prescribed and administered by a retinal surgeon with expertise in the treatment of biallelic *RPE65* mutation-associated retinal dystrophy and in the administration of Luxturna™ at an Ocular Gene Therapy Treatment Center; and
    a. Luxturna™ must be shipped via cold chain supply shipping and delivery to the Ocular Gene Therapy Treatment Center where the member is scheduled to receive treatment; and
    b. Luxturna™ must be stored frozen prior to preparation for administration (Luxturna™ should be administered within 4 hours of preparation); and
    c. The receiving facility must have in place a mechanism to track patient-specific Luxturna™ from receipt to storage to administration; and
12. Luxturna™ must be administered subretinally to each eye on separate days within a close interval, but no fewer than 6 days apart; and
    a. The scheduled procedure date for each eye must be provided; and
13. Only one single-dose vial per eye will be approved per member per lifetime; and
    a. Each single-dose vial of Luxturna™ is to be dispensed immediately prior to the scheduled procedure for the specific eye.

[1] U.S. Food and Drug Administration (FDA) News Release: FDA Approves Novel Gene Therapy to Treat Patients with a Rare Form of Inherited Vision Loss. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm589467.htm. Issued 12/19/2017. Last accessed 01/31/2018.

[2] Luxturna™ Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/luxturna/. Last revised 01/02/2018. Last accessed 03/22/2018.

[3] Luxturna™ Prescribing Information. Spark Therapeutics. Available online at: http://sparktx.com/luxturna_us_prescribing_information. Last accessed 03/22/2018.

[4] Russell S, Bennett J, Wellman JA, et al. Efficacy and Safety of Voretigene Neparvovec (AAV2-hRPE65v2) in Patients with *RPE65*-Mediated Inherited Retinal Dystrophy: A Randomized, Controlled, Open-Label, Phase 3 Trial. *The Lancet* 2017; 390(10097):849-860.

[5] Sagonowsky E. Spark Sets Off Gene Therapy Debate with $850K Sticker on Luxturna™. *FiercePharma.* Available online at: https://www.fiercepharma.com/pharma/spark-prices-gene-therapy-luxturna-at-850k-grabbing-top-spot-pharma-s-costliest-drugs. Issued 01/03/2018. Last accessed 01/31/2018.

[6] Spark Therapeutics News Release: FDA Approves Spark Therapeutics' Luxturna™ (Voretigene Neparvovec-rzyl), a One-Time Gene Therapy for Patients with Confirmed Biallelic *RPE65* Mutation-Associated Retinal Dystrophy. *Globe Newswire*. Available online at: http://ir.sparktx.com/news-releases/news-release-details/fda-approves-spark-therapeutics-luxturnatm-voretigene-neparvovec. Issued 12/19/2017. Last accessed 01/31/2018.

[7] Banken R, Rind D, Cramer G, et al. Voretigene Neparvovec for Biallelic *RPE65*-Mediated Retinal Disease: Effectiveness and Value. *Institute for Clinical and Economic Review (ICER)*. Available online at: http://icer-review.org/wp-content/uploads/2017/06/MWCEPAC_VORETIGENE_EVIDENCE_REPORT_01122018.pdf. Issued 01/12/2018. Last accessed 03/22/2018.

[8] Lewis R. FDA Panel Backs Gene Therapy for Inherited Blindness. *Medscape*. Available online at: https://www.medscape.com/viewarticle/887022. Issued 10/13/2017. Last accessed 03/23/2018.

[9] Wright AF. Long-Term Effects of Retinal Gene Therapy in Childhood Blindness. *N Engl J Med* 2015; 372:1954-1955.

[10] Jacobson SG, Cideciyan AV, Roman AJ, et al. Improvement and Decline in Vision with Gene Therapy in Childhood Blindness. *N Engl J Med* 2015; 372:1920-1926.

[11] Bainbridge JWB, Mehat MS, Sundaram V, et al. Long-Term Effect of Gene Therapy on Leber's Congenital Amaurosis. *N Engl J Med* 2015; 372:1887-1897.

[12] Cideciyan AV, Jacobson SG, Beltran WA, et al. Human Retinal Gene Therapy for Leber Congenital Amaurosis Shows Advancing Retinal Degeneration Despite Enduring Visual Improvement. *Proc Natl Acad Sci USA* 2013; 110(6):E517-E525.

Appendix E

Vote to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)]

Oklahoma Health Care Authority
April 2018

Introduction[1]

Prolastin®-C Liquid is an alpha$_1$-proteinase inhibitor (human) (alpha$_1$-PI) indicated for chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe alpha$_1$-antitrypsin deficiency (AATD). The effect of augmentation therapy with any alpha$_1$-PI, including Prolastin®-C Liquid, on pulmonary exacerbations and on the progression of emphysema in alpha$_1$-PI deficiency has not been conclusively demonstrated in randomized, controlled clinical trials. Clinical data demonstrating the long-term effects of chronic augmentation or maintenance therapy with Prolastin®-C Liquid are not available. Prolastin®-C Liquid is not indicated as therapy for lung disease in patients in whom severe AATD has not been established. It is supplied in a 1,000mg (approximate) single-use vial containing 20mL of solution for injection. The recommended dosage of Prolastin®-C Liquid is 60mg/kg given intravenously (IV) once weekly. It is recommended to infuse at a rate of 0.08mL/kg/min as determined by patient response and comfort. Each infusion takes approximately 15 minutes. Prolastin®-C Liquid is contraindicated in immunoglobulin A (IgA) deficient patients with antibodies against IgA, due to the risk of severe hypersensitivity, and in patients with a history of anaphylaxis or other severe systemic reaction(s) to alpha$_1$-PI.

The efficacy data for Prolastin®-C Liquid is based on the predecessor product, Prolastin®-C. A randomized, double-blind, crossover trial was performed comparing Prolastin®-C Liquid to Prolastin®-C and was conducted in 32 adult subjects 44 to 71 years of age with severe AATD. This pharmacokinetic (PK) study determined bioequivalence between the two products.

Cost Comparison:

Medication	Cost Per mg	Cost Per Month$^{\Delta}$	Cost Per Year$^{\Delta}$
Prolastin®-C Liquid	**$0.50**	**$9,000.00**	**$108,000.00**
Prolastin®-C	$0.50	$9,000.00	$108,000.00
Aralast NP™	$0.53	$9,540.00	$114,480.00
Glassia®	$0.53	$9,540.00	$114,480.00
Zemaira®	$0.52	$9,360.00	$112,320.00

Costs do not reflect rebated price or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
$^{\Delta}$Cost for treatment based on a weekly dosing of 60mg/kg for a 75kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Prolastin®-C Liquid [alpha$_1$-proteinase inhibitor (human)] with the following criteria:

Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
    a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
    b. Serum levels of AAT less than 11µmol/L; and
    c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C, Aralast NP™, Glassia®, and Zemaira®; 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.

The College of Pharmacy also recommends adding Zemaira® to the current Aralast NP™ and Glassia® criteria based on net cost after rebates.

Aralast NP™, ~~and~~ Glassia®, and Zemaira® [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
    a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
    b. Serum levels of AAT less than 11µmol/L; and
    c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C; 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.

[1] Prolastin®-C Liquid Prescribing Information. Grifols Therapeutics Inc. Available online at: https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM209676.pdf. Last revised 09/2017. Last accessed 03/20/2018.

Appendix F

Vote to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib)

Oklahoma Health Care Authority
April 2018

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

Arzerra® (Ofatumumab):

- **Therapeutic Class:** CD20-directed cytolytic monoclonal antibody
- **Indication(s):** Treatment of chronic lymphocytic leukemia (CLL) in the following scenarios:
  - In combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate
  - In combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL
  - For extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL
  - For the treatment of patients with CLL refractory to fludarabine and alemtuzumab
- **How Supplied:** 100mg/5mL or 1,000mg/50mL single-use vials for intravenous (IV) infusion
- **Dose:**
  - Previously Untreated, Relapsed: IV Cycle 1: 300mg on day 1, followed by 1,000mg on day 8; Subsequent Cycles: 1,000mg on day 1 every 28 days
    - Previously Untreated Patients: Maximum 12 cycles
    - Relapsed: In combination with fludarabine and cyclophosphamide, maximum 6 cycles
  - Refractory: IV Cycle 1: 300mg on day 1, followed by 2,000mg on day 8, continued once weekly for 7 doses, followed 4 weeks later by 200mg once every 4 weeks for 4 doses
  - Extended Treatment: IV Cycle 1: 300mg on day 1, followed by 1,000mg on day 8, followed by 1,000mg 7 weeks later and then every 8 weeks for a maximum of 2 years
- **Cost:** The state maximum allowable cost (SMAC) for ofatumumab is $564.70 per 5mL vial and $5,647.00 per 50mL vial

Gazyva® (Obinutuzumab):

- **Therapeutic Class:** CD20-directed cytolytic monoclonal antibody
- **Indication(s):**
  - In combination with chlorambucil, for the treatment of patients with previously untreated CLL

- In combination with bendamustine followed by obinutuzumab monotherapy, for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen
- In combination with chemotherapy followed by obinutuzumab monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated Stage II bulky, III, or IV FL

- **How Supplied:** 1,000mg/40mL (25mg/mL) single-dose vial for IV infusion
- **Dose:**
  - Untreated CLL: Cycle 1: 100mg on day 1, followed by 900mg on day 2, followed by 1,000mg weekly for 2 doses (days 8 and 15); Cycles 2 through 6: 1,000mg on day 1 every 28 days for 5 doses
- **Cost:** The SMAC for obinutuzumab is $6,064.00 per 40mL vial

Imbruvica® (Ibrutinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
  - CLL/small lymphocytic lymphoma (SLL)
  - CLL/SLL with 17p deletion
  - Waldenström's macroglobulinemia (WM)
  - Patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
  - Chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy
- **How Supplied:** 70mg and 140mg oral capsules
- **Dose:**
  - MCL and MZL: 560mg once daily (four 140mg capsules)
  - CLL/SLL, WM, and cGVHD: 420mg once daily (three 140mg capsules)
- **Cost:** The wholesale acquisition cost (WAC) of ibrutinib is $135.33 per 140mg capsule, resulting in a daily cost ranging from $405.99 to $541.32

Venclexta™ (Venetoclax):

- **Therapeutic Class:** B-cell lymphoma-2 (BCL-2) inhibitor
- **Indication(s):** Treatment of patients with CLL with 17p deletion, as detected by an FDA-approved test, who have received at least one prior therapy
- **How Supplied:** 10mg, 50mg, and 100mg oral tablets
- **Dose:** Initial dosing is 20mg once daily for 7 days, followed by a weekly ramp-up dosing schedule to the recommended daily dose of 400mg
- **Cost:** The WAC of venetoclax is $92.91 per 100mg tablet, resulting in a daily cost of $371.64

Zydelig® (Idelalisib):

- **Therapeutic Class:** Kinase inhibitor

- **Indication(s):**
  - Relapsed CLL, in combination with rituximab, in patients for whom rituximab alone would be considered inappropriate therapy due to other co-morbidities
  - Relapsed follicular B-cell non-Hodgkin lymphoma in patients who have received at least two prior systemic therapies
  - Relapsed SLL in patients who have received at least two prior systemic therapies
- **How Supplied:** 100mg and 150mg oral tablets
- **Dose:** 150mg administered twice daily
- **Cost:** The WAC of idelalisib is $170.28 per 150mg tablet, resulting in a daily cost of $340.56

Recommendations

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

1. As first-line treatment of CLL in combination with chlorambucil or bendamustine; or
2. For relapsed or refractory disease as a single-agent or in combination with fludarabine and cyclophosphamide; or
3. As maintenance therapy as second-line extended dosing following complete or partial response to relapsed or refractory therapy (maximum 2 years).

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

1. For previously treated disease that does not respond to primary therapy or for progressive or relapsed disease; and
2. As a single-agent or combination therapy; and
3. Member is rituximab-intolerant.

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

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

Gazyva® (Obinutuzumab) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 or 2 patients with Stage I (≥7cm), contiguous Stage II (≥7cm), noncontiguous Stage II, Stage III, or Stage IV patients (first, second, or subsequent therapy); and
2. In combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine; and
3. When used for maintenance therapy a total of 12 doses will be approved.

Gazyva® (Obinutuzumab) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy in combination with bendamustine; or

2. Maintenance therapy as second-line consolidation or extended dosing in rituximab-refractory patients treated with obinutuzumab and bendamustine for a total of 12 doses.

Imbruvica® (Ibrutinib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 or 2 FL; and
2. As subsequent therapy (third-line or greater) for histologic transformation to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Graft-Versus-Host Disease (cGVHD) Diagnosis]:

1. A diagnosis of cGVHD after failure of one or more lines of therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Histologic Transformation of Marginal Zone Lymphoma (MZL) to Diffuse Large B-Cell Lymphoma Diagnosis]:

1. As third-line or greater therapy for patients who have transformed to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. Used as a single-agent or in combination with rituximab or lenalidomide/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Diffuse Large B-Cell Lymphoma Diagnosis or Acquired Immunodeficiency Syndrome (AIDS)-Related B-Cell Lymphoma Diagnosis]:

1. A diagnosis of non-germinal center diffuse large B-cell lymphoma; and
2. As second-line or subsequent therapy; and
3. Member is not a candidate for high-dose therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Post-Transplant Lymphoproliferative Disorders Diagnosis]:

1. As second-line and subsequent therapy in patients with partial response, persistent, or progressive disease; and
2. Non-germinal center B-cell type.

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

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

Imbruvica® (Ibrutinib) Approval Criteria [Hairy Cell Leukemia Diagnosis]:

1. As a single-agent in patients with indication for treatment for progression.

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

1. As first or subsequent therapy; and
2. As a single-agent.

Venclexta™ (Venetoclax) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. As a single-agent only.

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

1. For relapsed/refractory disease; and
2. In combination with rituximab or as a single-agent.

Zydelig® (Idelalisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 to 2 FL; and
2. As second-line or subsequent therapy for refractory or progressive disease; and
3. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease; and
2. Refractory to both alkylator and rituximab therapy.

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

1. For relapsed or refractory disease; and
2. In combination with rituximab or rituximab/bendamustine; or
3. As a single-agent.

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[1] Arzerra® Prescribing Information. Novartis Pharmaceuticals. Available online at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/arzerra.pdf. Last revised 08/2016. Last accessed 03/08/2018.

[2] Gazyva® Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/gazyva_prescribing.pdf. Last revised 11/2017. Last accessed 03/08/2018.

[3] Imbruvica® Prescribing Information. Janssen Biotech, Inc. Available online at: https://www.imbruvica.com/docs/librariesprovider7/default-document-library/prescribing-information.pdf. Last revised 02/2018. Last accessed 03/08/2018.

[4] Venclexta™ Prescribing Information. AbbVie, Inc. Available online at: http://www.rxabbvie.com/pdf/venclexta.pdf. Last revised 12/2017. Last accessed 03/08/2018.

[5] Zydelig® Prescribing Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~/media/Files/pdfs/medicines/oncology/zydelig/zydelig_pi.pdf. Last revised 01/2018. Last accessed 03/08/2018.

Appendix G

Fiscal Year 2017 Annual Review of the SoonerCare Pharmacy Benefit

Oklahoma Health Care Authority
April 2018

Summary[1,2,3]

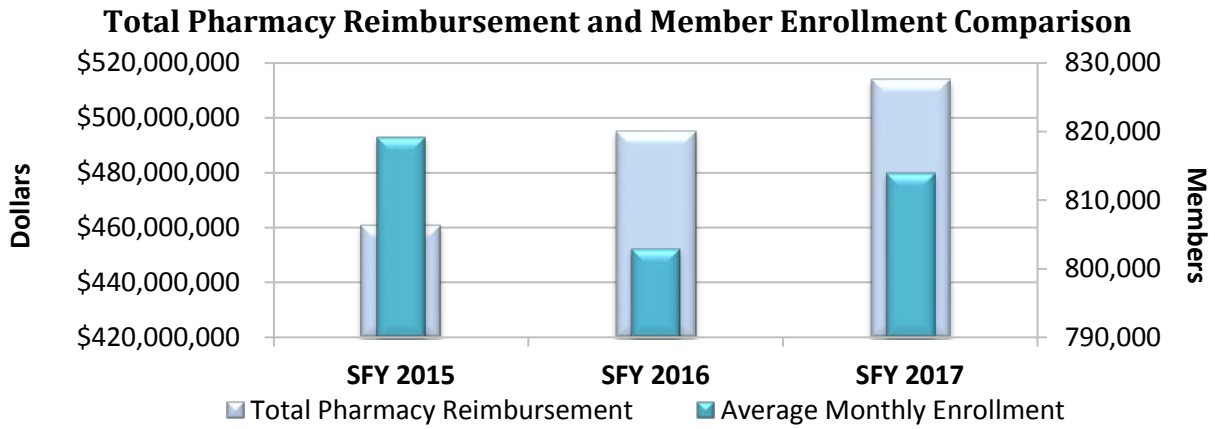
During State Fiscal Year (SFY) 2017, prescription drugs accounted for $514 million of the approximate $5.2 billion in total SoonerCare funding. According to the Centers for Medicare and Medicaid Services (CMS), national health spending is projected to grow at an average rate of 5.6% annually. Comparing SoonerCare pharmacy data from SFY 2016 and 2017, the total reimbursement increased by 3.8%, which is less than anticipated. The cost per total members increased from $470.33 in SFY 2016 to $506.47 in SFY 2017, a 7.7% increase. Reimbursement increases per member can largely be attributed to the increase in cost per claim for specialty medications as well as an increase in the number of claims for specialty mediations. 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 Oklahoma Medicaid spent 37.7% of total pharmacy expenditures on 0.84% of claims for medications costing greater than $1,000 per claim.

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 effective 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 2017 with previous fiscal years, IHS data was excluded from the analysis.

SFY	Members	Average Monthly Enrollment	Utilizers*	Claims	Reimbursement	Days	Cost/ Claim	Cost/ Day
2015	1,021,359	819,193	541,116	5,842,175	$461,040,791	144,683,680	$78.92	$3.19
2016	1,052,826	802,916	542,290	5,891,156	$495,171,030	149,086,518	$84.05	$3.32
2017	1,014,983	813,969	541,021	5,897,218	$514,062,769	150,979,625	$87.17	$3.40

*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 two years. Calendar year (CY) 2017 saw a 2.8% increase from 2016 in overall PMPY.

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

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 2016, ESI's Medicaid PMPY was $1,196 – 67% higher than OHCA's $715. If OHCA had experienced the same PMPY as ESI for CY 2016, it would have cost over $342 million more than the $511 million spent. Similarly, for CY 2017, ESI's Medicaid PMPY was $1,241 – 69% higher than OHCA's $735. At the ESI PMPY rate, it would have cost over $359 million more than the $521 million spent during CY 2017 for pharmacy reimbursement.

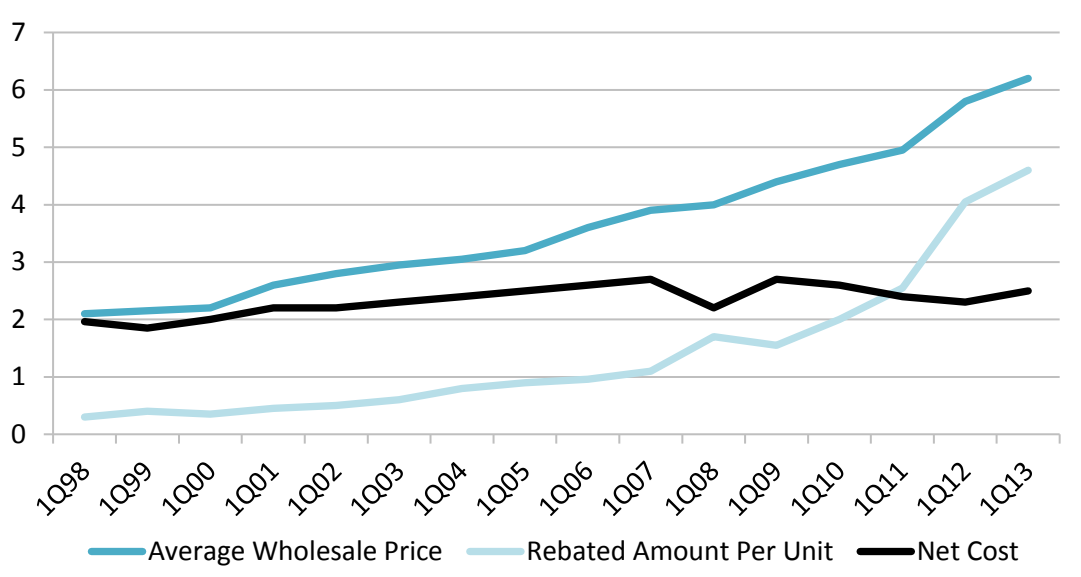
Calendar Year	ESI	OHCA	Percent Difference
2016	$1,196	$715	67%
2017	$1,241	$735	69%

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 both years. As a return on investment (ROI), using the overage generated by the ESI PMPY rate, for CY 2016 the ROI is $68 to $1 and for 2017 it is $72 to $1.

Medicaid Drug Rebate Program[4,5,6]

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

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



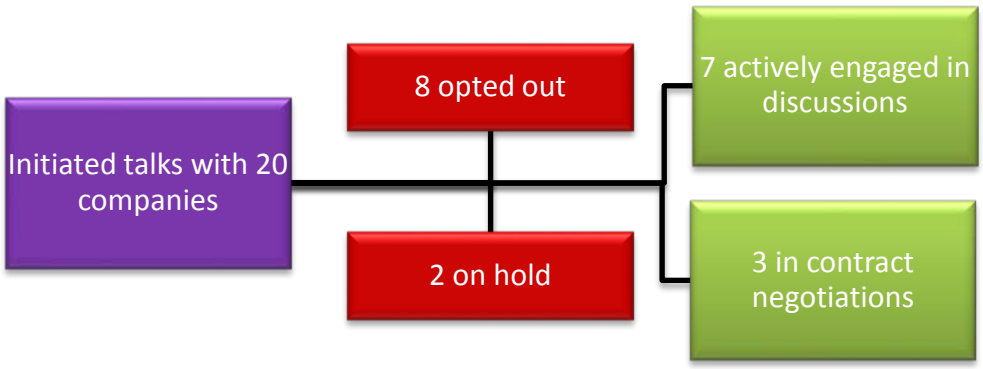
Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. In SFY 2017, OHCA collected $283 million in federal rebates and $22 million in state supplemental rebates, both of which increased from SFY 2016 ($275 million federal; $14 million state). These rebates are collected after reimbursement for the medication and are not reflected in this report.

Alternative Payment Models[7,8,9,10,11]

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 two types of APMs:

- **Financial APM:** Where 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:** Payments for medications are tied to clinical outcomes or measurements; these type of contracts are often referred to as "value-based contracts". Health outcome-based APMs require additional planning and data collection, but do have the potential to increase the quality and value of treatments.
    - Examples: Outcomes guarantee, conditional coverage, PMPY guarantees, event avoidance (e.g., hospitalizations)

Thus far, 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 20 companies regarding APMs. Three companies are currently in contract negotiations and seven are actively engaged in conversations. PMC and OHCA have a proposed value-based agreement with a pharmaceutical manufacturer pending CMS approval. Future considerations include the expectation that initial value-based contracts will set the precedent for further collaboration among manufacturers and state agencies.



Drug Approval Trends[12,13]

During SFY 2017, 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 three years. Other key first time generic approvals during SFY 2017 include Seroquel XR® [quetiapine extended-release (ER)] in May 2017, Tamiflu® (oseltamivir capsules) in August 2016, and Focalin XR® (dexmethylphenidate ER) in November 2016.

A total of 31 new drugs were approved by the FDA during SFY 2017. Of the new drugs approved, eight were novel oncology medications. There were five non-oncology drugs approved that have orphan drug designations: Radicava® (edaravone), Austedo® (deutetrabenazine), Emflaza® (deflazacort), Spinraza® (nusinersen), and Exondys 51® (eteplirsen).

Select Novel Drugs Approved During SFY 2017

Drug Name	Date Approved	FDA-Approved Indication	Estimated Annual Cost*
Kevzara® (sarilumab)	05/22/2017	Treatment of adults with moderate-to-severe rheumatoid arthritis (RA)	$36,000
Tymlos™ (abaloparatide)	04/28/2017	Treatment of postmenopausal women with osteoporosis at risk for fracture	$20,651
Ingrezza® (valbenazine)	04/11/2017	Treatment for adults with tardive dyskinesia (TD)	$74,700
Austedo® (deutetrabenazine)	04/03/2017	Treatment of chorea associated with Huntington's disease or TD in adults	$118,368
Dupixant® (dupilumab)	03/28/2017	Treatment for adults with moderate-to-severe eczema	$35,577
Symproic® (naldemedine)	03/23/2017	Treatment of opioid-induced constipation	$3,822
Xadago® (safinamide)	03/21/2017	Treatment of Parkinson's disease (PD)	$8,762
Siliq® (brodalumab)	02/15/2017	Treatment for adults with moderate-to-severe plaque psoriasis	$45,500
Emflaza® (deflazacort)	02/09/2017	Treatment of Duchenne muscular dystrophy (DMD)	$51,480 - $191,232
Trulance® (plecanatide)	01/19/2017	Treatment of chronic idiopathic constipation in adults	$4,457
Spinraza® (nusinersen)	12/23/2016	Treatment of spinal muscular atrophy (SMA) in pediatric and adult patients	$750,000
Eucrisa® (crisaborole)	12/14/2016	Treatment of mild-to-moderate eczema in patients age 2 years and older	$7,142
Exondys 51® (eteplirsen)	09/19/2016	Treatment of DMD	$416,000 - $1,664,000

*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. Costs reflect first year of therapy and include loading doses. Subsequent years may have a lower estimated annual cost.

Traditional Versus Specialty Pharmacy Products

Traditional pharmaceuticals include products that are typically non-injectable and do not require special transportation, storage, administration, and are not typically indicated for rare diseases requiring unique management. These products treat many common chronic diseases such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). Traditional pharmaceuticals carry the bulk of the reimbursement costs accounting for 82.5% of the total pharmacy reimbursement in SFY 2017 and 99% of utilizers. 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. The percent of total pharmacy reimbursement for specialty pharmaceuticals increased in SFY 2017 to 17.5%, compared to 16.6% in SFY 2016. Recently, the specialty pharmaceutical products total pharmacy reimbursement has been on the incline due to new emerging therapies and the high costs associated with these therapies.

Top 10 Therapeutic Classes by Reimbursement: Fiscal Year 2017[14,15,16,17]

Traditional Top 10 Classes by Reimbursement			
Therapeutic Class	**SFY 2015**	**SFY 2016**	**SFY 2017**
Anti-Infective Agents	$62,972,086.06	$64,753,193.00	$63,996,676.99
ADHD Agents	$59,222,643.32	$59,210,124.93	$62,118,533.40
Anti-Asthmatic Agents	$40,250,424.00	$42,407,875.09	$43,565,926.25
Antipsychotics/Antimanic Agents	$53,508,208.93	$53,434,190.89	$39,977,374.37
Anti-Diabetic Agents	$30,259,419.12	$35,416,629.46	$38,298,122.04
Analgesic Agents	$23,157,175.88	$24,729,391.27	$25,210,044.42
Anticonvulsant Agents	$21,264,626.03	$22,587,039.07	$24,851,122.19
Endocrine Agents	$20,090,703.73	$19,378,355.51	$22,954,966.66
Topical Agents	$12,977,166.54	$17,927,089.21	$20,067,381.33
Cardiovascular Agents	$13,348,962.64	$13,942,125.97	$14,665,236.10

SFY = state fiscal year; ADHD = attention-deficit/hyperactivity disorder
Reimbursement does not reflected rebated costs or net costs.

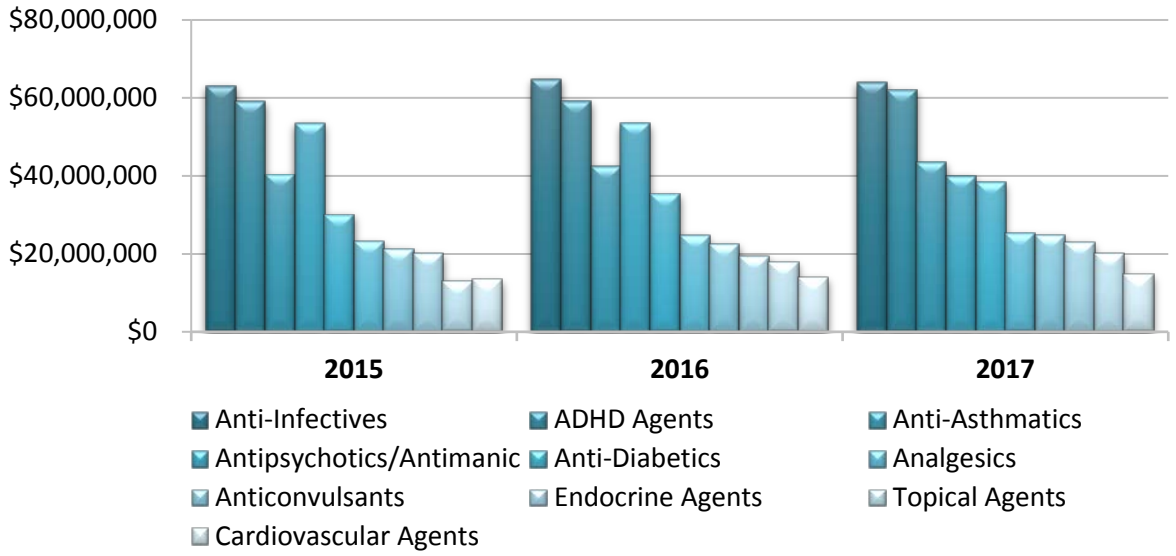
The ranking of the top 10 traditional therapeutic classes by reimbursement remained similar from SFY 2016 to SFY 2017 with the exception of antipsychotics/antimanic agents falling from 3rd to 4th. Traditional pharmaceutical classes that showed the most significant change included antipsychotic/antimanic agents and endocrine agents.

- The antipsychotic/antimanic agents category dropped from 3rd to 4th in SFY 2017 after a 25% decrease in reimbursement from SFY 2016 to SFY 2017. The FDA approved the first generic formulation of Abilify® (aripiprazole) tablets in April 2015; however, the cost for the generic remained high and comparable to that of the brand, resulting in SoonerCare preferring the branded product based on net cost. On January 1, 2017, SoonerCare began preferring the generic aripiprazole tablets due to a significant reduction in price. Even though this change occurred halfway through SFY 2017, the reimbursement for aripiprazole tablet formulations decreased by $16,334,891 from SFY 2016, a change of 88%. Costs in this

report do not reflect rebated prices provided by medication manufacturers and therefore do not reflect net costs.

- Endocrine agents saw an increase in reimbursement in SFY 2017 as a result of more flexible prior authorization restrictions on progesterone products indicated to prevent pre-term birth (Makena®, Crinone®, and Endometrin®). Changes were implemented after recommendations from the Oklahoma Perinatal Quality Improvement Collaborative (OPQIC) and internal OHCA review determined reduced medical costs would offset the increased utilization and subsequent pharmacy reimbursement.
- Anti-infective agents reimbursement can largely be attributed to the costly therapies for the treatment of hepatitis C. The decrease in reimbursement in SFY 2017 can be accounted for by a decrease in combination regimen use of multiple direct acting antiviral agents (DAAs) as well as the increased availability of products indicated for shortened treatment durations. Continual efforts are made to ensure optimal treatment regimens with cost-effective outcomes.

Top 10 Traditional Therapeutic Classes by Reimbursement

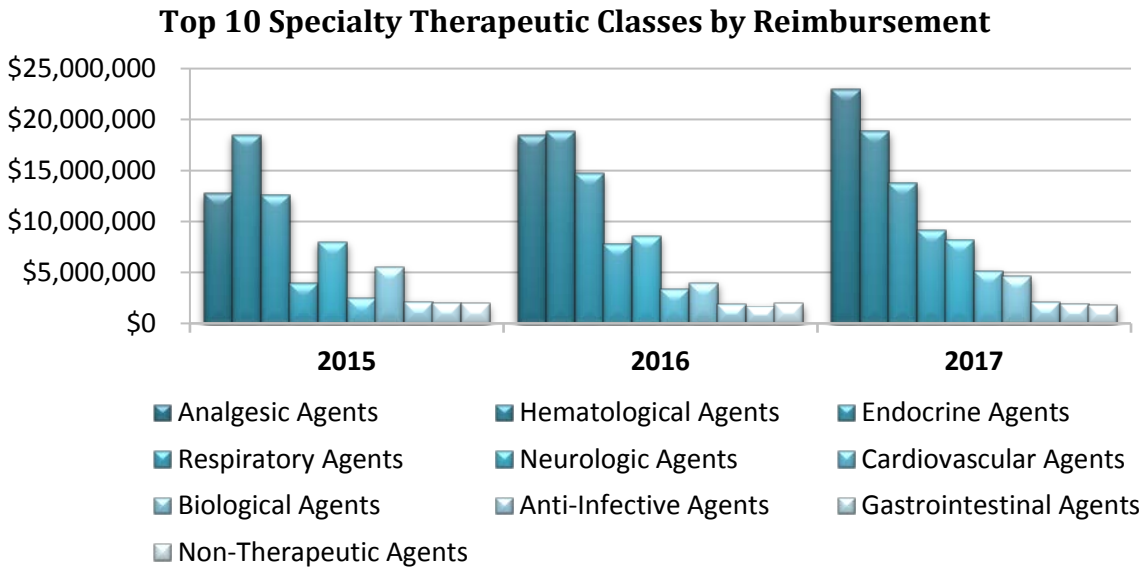


Specialty Top 10 Classes by Reimbursement			
Therapeutic Class	**SFY 2015**	**SFY 2016**	**SFY 2017**
Analgesic Agents	$12,732,939.34	$18,481,116.06	$22,988,676.02
Hematological Agents	$18,497,494.10	$18,852,788.36	$18,813,132.66
Endocrine Agents	$12,528,464.19	$14,684,343.06	$13,782,182.00
Respiratory Agents	$3,959,014.79	$7,754,987.89	$9,093,408.80
Neurological Agents	$7,930,952.10	$8,540,617.18	$8,139,124.40
Cardiovascular Agents	$2,441,564.38	$3,387,174.02	$5,143,843.17
Biological Agents	$5,459,825.55	$3,935,198.64	$4,581,237.28
Anti-Infective Agents	$2,086,175.75	$1,865,601.04	$2,060,759.57
Gastrointestinal Agents	$1,962,601.23	$1,642,701.27	$1,856,032.89
Non-Therapeutic Agents	$1,930,027.69	$1,928,230.30	$1,780,090.76

SFY = state fiscal year
Reimbursement does not reflected rebated costs or net costs.

The high costs of specialty therapeutic products can largely be attributed to the orphan drug therapies indicated for rare diseases. Specialty 2017 therapeutic class reimbursement rankings differ from the previous fiscal year with analgesic agents and hematological agents switching places in the 1st and 2nd positions, respiratory agents and neurological agents switching places in the 4th and 5th positions, biological agents falling from 6th to 7th, and non-therapeutic products falling from 8th to 10th in SFY 2017. Specialty pharmaceutical classes that displayed the most significant change from SFY 2016 to SFY 2017 include analgesic agents, cardiovascular agents, respiratory agents, and endocrine agents. Continuous review and management of anti-infective agents, biological agents, and gastrointestinal agents has promoted minimal reimbursement increases other than expected yearly price increases by product manufacturers and declines in reimbursement for hematological agents, neurological agents, and non-therapeutic agents.

- The cost of specialty analgesic medications had an overall increase of $4.5 million from the last fiscal year, which is attributable to the increase in reimbursement of targeted immunomodulatory agents, such as Humira® (adalimumab), Enbrel® (etanercept), Cimzia® (certolizumab), Orencia® (abatacept), Xeljanz® (tofacitinib), and Actemra® (tocilizumab). With the emergence of biosimilar FDA approvals, current branded product manufacturers raised their prices in anticipation of more market competition. There are currently five biosimilar products approved by the FDA: Inflectra® (infliximab-dyyb), Erelzi™ (etanercept-szzs), Amjevita™ (adalimumab-atto), Cyltezo™ (adalimumab-adbm), and Renflexis™ (infliximab-abda). Despite biosimilar products receiving FDA approval, several of these products are not yet available on the market due to ongoing litigation from the brand manufacturers over possible patent infringement. Once biosimilar products become more readily available, this class may see a significant reduction in costs as a result of increased market competition. During SFY 2017, the majority of utilization for the specialty pain medication category was seen in Tier-2 medications, which are supplementally rebated medications. Supplementally rebated prices and therefore net costs are not reflected in this analysis.
- Reimbursement for the specialty cardiovascular agents is largely comprised of medications indicated to treat pulmonary arterial hypertension (PAH). Both the number of members utilizing these high cost medications as well as the number of claims increased in SFY 2017 compared to SFY 2016 accounting for virtually all of the $1.7 million increase.
- Specialty pharmaceutical respiratory agents include medications for CF, idiopathic pulmonary fibrosis (IPF), and emphysema. Orkambi® (lumacaftor/ivacaftor) 200mg/125mg is a medication that was approved by the FDA in July 2015 for CF patients 12 years of age and older with two copies of the *F508del* mutation in their CF transmembrane regulator (CFTR) gene. In September 2016, the FDA approved Orkambi® 100mg/125mg for pediatric patients 6 to 11 years of age. Orkambi® accounted for $6,580,339 of total reimbursement for SFY 2017, compared to $2,693,284 in SFY 2016.
- The reduction in reimbursement for specialty endocrine agents can be accounted for by utilization changes of H.P. Acthar® Gel (corticotropin injection) and a reduction in use for diagnoses other than infantile spasms.



Top 10 Medications by Reimbursement: Fiscal Year 2017

The top 10 medications by reimbursement typically contain highly utilized medications such as albuterol inhalers and maintenance asthma medications. Abilify® (aripiprazole) was ranked 2nd in drugs by reimbursement during SFY 2016; however, due to the significant reduction in cost for the generic aripiprazole, SoonerCare started preferring generic over brand in January 2017, causing Abilify® to drop off the top 10 list of drugs by reimbursement. The top products in SFY 2017 include medications from the psychotherapeutic class, such as atypical antipsychotics and attention deficit therapies; the respiratory class, including rescue asthma therapies; the anti-infective class, which includes antiviral medications for hepatitis C; the antidiabetic class, including long-acting insulin; the targeted immunomodulator class; and growth hormone replacement. Top drug reimbursement rankings change from year to year only slightly for several reasons: high utilization, broad use between age demographics, and high costs of new therapies such as hepatitis C medications.

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

*Includes brand and generic where applicable.
SFY = state fiscal year; inj = injection; ER = extended-release

Cost Per Claim

Claims for generic medications made up 83.8% of the volume while only accounting for 28.9% of the reimbursement amount. The SoonerCare cost per claim of traditional medications rose by 2.6% in SFY 2017 in comparison to SFY 2016, and the cost per specialty claim increased by 6.8%. As mentioned previously, specialty costs are largely driven by the significant cost associated with medications for rare diseases as well as price increases of drugs that will soon face biosimilar competition.

Drug Class	SFY 2015	SFY 2016	SFY 2017
Traditional	$67.05	$70.31	$72.13
Specialty	$4,363.31	$4,984.75	$5,321.87

Reimbursement does not reflected rebated costs or net costs.

Conclusion

New prior authorization categories and product-based criteria implemented during SFY 2017 include: bowel preparation medications, prostate cancer medications, H.P. Acthar® Gel (corticotropin injection), anthelmintic medications, skin cancer medications, iron overload medications, pancreatic enzyme medications, phosphate binding medications, actinic keratosis medications, alpha$_1$-proteinase inhibitors, lung cancer medications, Huntington's disease medications, Kuvan® (sapropterin), topical acne products, atopic dermatitis medications, Exondys 51® (eteplirsen), Zinplava™ (bezlotoxumab), Kanuma® (sebelipase alfa), Ocaliva® (obeticholic acid), Spinraza® (nusinersen), Defitelio® (defibrotide), Veltassa® (patiromer), Lumizyme® (alglucosidase alfa), Elaprase® (idursulfase), Ingrezza® (valbenazine), Radicava® (edaravone), Vimizim® (elosulfase alfa), and Brineura™ (cerliponase alfa); additional class reviews and product additions to existing classes were also conducted. When new drugs are FDA approved and cost information is available, a cost-effective analysis is performed to ensure spending is minimized while maintaining appropriate clinical care. The goal of the SoonerCare program is to provide members with the most appropriate healthcare in a fiscally responsible manner. For the pharmacy benefit, this is accomplished by the use of a robust prior authorization program, limiting the number of total prescriptions and the number of brand name prescriptions allowed each month for non-institutionalized adults, 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 2017		SFY 2016	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Lisdexamfetamine	Vyvanse	1	$23,950,300.47	1	$21,437,249.59
Ledipasvir/Sofosbuvir	Harvoni	2	$14,625,414.97	3	$18,960,609.67
Paliperidone Injection	Invega Trinz/Sust	3	$14,324,277.92	6	$11,701,288.42
Methylphenidate	Multiple Products	4	$14,212,027.73	4	$13,649,664.47
Albuterol	Multiple Products	5	$13,947,480.75	5	$13,081,866.22

Top 100 Reimbursed Drugs By Fiscal Year		SFY 2017		SFY 2016	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Adalimumab	Humira	6	$13,348,634.96	8	$10,502,062.31
Atomoxetine	Strattera	7	$13,125,663.38	7	$11,669,131.17
Insulin Glargine	Lantus/Toujeo	8	$9,174,361.56	9	$9,471,187.65
Oseltamivir	Tamiflu*	9	$8,731,144.29	48	$2,092,380.83
Somatropin	Multiple Products	10	$8,304,384.02	12	$7,846,393.01
Fluticasone Inhalation	Flovent	11	$8,251,271.87	11	$8,025,005.06
Lurasidone	Latuda	12	$8,021,225.51	13	$7,099,561.41
Insulin Aspart	Novolog	13	$7,605,974.39	15	$6,623,353.96
Sofosbuvir/Velpatasvir	Epclusa	14	$7,069,087.91	NA	****
Oxycodone	Multiple Products	15	$6,964,899.25	14	$7,005,649.53
Lumacaftor/Ivacaftor	Orkambi	16	$6,580,338.71	37	$2,693,283.71
Etanercept	Enbrel	17	$6,348,980.27	21	$4,762,240.68
Hydroxyprogesterone Caproate	Makena	18	$5,943,296.09	20	$4,886,735.63
Fluticasone/Salmeterol	Advair	19	$5,405,558.38	23	$4,646,692.64
Epinephrine Injection	Multiple Products	20	$5,380,870.61	18	$5,491,294.00
Ciprofloxacin/Dexamethasone Otic	Ciprodex	21	$5,188,025.55	27	$3,979,274.42
Insulin Detemir	Levemir	22	$4,906,607.94	22	$4,671,403.13
Aripiprazole	Abilify*	23	$4,635,547.54	2	$20,701,912.16
Insulin Lispro	Humalog	24	$4,589,958.49	25	$4,246,366.75
Amphetamine/Dextroamphetamine	Multiple Products	25	$4,548,721.03	16	$5,662,120.75
Dexmethylphenidate	Focalin*	26	$4,419,315.74	19	$4,952,936.42
Blood Glucose Test Strip	Multiple Products	27	$4,394,441.78	26	$4,164,695.47
Buprenorphine/Naloxone	Multiple Products	28	$4,140,795.80	30	$3,616,867.59
Antihemophilic Factor (Recombinant)	Multiple Products	29	$4,112,292.00	17	$5,614,917.62
Pregabalin	Lyrica	30	$4,098,800.00	24	$4,539,268.75
Lacosamide	Vimpat	31	$3,642,713.25	31	$3,272,798.24
Hydrocodone/Acetaminophen	Multiple Products	32	$3,335,169.90	29	$3,680,715.15
Clobazam	Onfi	33	$3,311,213.10	40	$2,496,949.76
Dornase Alfa	Pulmozyme	34	$3,037,127.57	36	$2,860,441.54
Tiotropium	Spiriva	35	$3,000,855.71	34	$2,916,142.89
Antihemophilic Factor rAHF-PFM	Advate	36	$2,823,984.84	33	$2,917,940.57
Palivizumab	Synagis	37	$2,786,474.72	39	$2,543,042.20
Ivermectin Lotion	Sklice	38	$2,693,211.37	105	$914,281.12
Budesonide Inhalation	Pulmicort*	39	$2,515,855.49	28	$3,757,897.68
Anti-Inhibitor Coagulant Complex	Feiba	40	$2,497,213.00	50	$1,967,685.24
Quetiapine	Seroquel*	41	$2,495,465.41	32	$3,073,186.57
Pancrelipase	Multiple Products	42	$2,469,781.19	47	$2,133,366.46
Glatiramer Acetate	Multiple Products	43	$2,427,922.48	35	$2,911,594.04
Sitagliptin	Januvia	44	$2,412,513.31	43	$2,276,186.86
Beclomethasone Inhalation	Qvar	45	$2,228,840.71	49	$2,084,832.73
Amoxicillin	Amoxil*	46	$2,215,278.70	53	$1,864,456.73
Vigabatrin	Sabril	47	$2,133,072.37	74	$1,316,496.46
Montelukast	Singulair*	48	$2,110,128.71	54	$1,832,620.42

Top 100 Reimbursed Drugs By Fiscal Year		SFY 2017		SFY 2016	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Canakinumab	Ilaris	49	$2,062,531.33	55	$1,820,996.15
Cefdinir	Omnicef*	50	$2,040,751.59	41	$2,482,258.90
Azithromycin	Zithromax*	51	$1,993,999.52	44	$2,252,906.25
Rifaximin	Xifaxan	52	$1,981,604.43	51	$1,937,844.84
Cetirizine	Multiple Products	53	$1,922,236.91	63	$1,573,117.88
Liraglutide	Victoza	54	$1,901,436.32	67	$1,486,447.80
Oxycodone/Acetaminophen	Multiple Products	55	$1,900,595.74	45	$2,247,087.52
Sapropterin	Kuvan	56	$1,872,591.33	81	$1,202,462.18
Dasatinib	Sprycel	57	$1,848,594.31	72	$1,371,022.90
Paliperidone Tablet	Invega*	58	$1,788,805.07	42	$2,471,478.48
Sildenafil	Revatio*	59	$1,787,647.45	111	$862,896.25
Corticotropin Injection	H.P. Acthar	60	$1,721,095.62	38	$2,568,844.91
Eculizumab	Soliris	61	$1,711,063.67	57	$1,729,571.78
Amoxicillin/Clavulanate	Augmentin*	62	$1,679,469.47	56	$1,777,543.55
Ipratropium/Albuterol	Combivent*	63	$1,658,156.47	58	$1,704,110.17
Deferasirox	Jadenu/Exjade	64	$1,642,546.27	52	$1,870,992.02
Dimethyl Fumarate	Tecfidera	65	$1,627,492.10	68	$1,468,432.45
Budesonide/Formoterol Fumarate	Symbicort	66	$1,590,711.89	59	$1,664,440.67
Sofosbuvir	Sovaldi	67	$1,556,611.65	10	$9,195,711.00
Elbasvir/Grazoprevir	Zepatier	68	$1,543,340.25	NA	****
Rufinamide	Banzel	69	$1,502,656.87	77	$1,251,142.14
Tazarotene	Tazorac	70	$1,500,452.68	70	$1,381,398.62
Varenicline	Chantix	71	$1,439,536.89	91	$1,059,831.32
Oxcarbazepine	Multiple Products	72	$1,431,645.76	73	$1,359,189.16
Ivacaftor	Kalydeco	73	$1,403,634.25	61	$1,580,816.57
Antihemophilic Factor (Recombinant)	Eloctate	74	$1,392,066.37	134	$666,828.85
Tobramycin Inhalation	Multiple Products	75	$1,383,885.46	69	$1,407,819.63
Gabapentin	Neurontin*	76	$1,377,246.57	78	$1,206,847.26
Abacavir/Dolutegravir/Lamivudine	Triumeq	77	$1,352,124.88	119	$798,175.71
Palbociclib	Ibrance	78	$1,335,746.00	100	$996,665.65
Sulfamethoxazole/Trimethoprim	Bactrim*	79	$1,296,150.52	71	$1,381,371.56
Leuprolide Acetate	Lupron Depot	80	$1,285,342.68	108	$890,502.75
Asfotase Alfa	Strensiq	81	$1,268,376.77	231	$326,488.76
Guanfacine	Intuniv*	82	$1,266,794.03	87	$1,089,087.06
Divalproex	Depakote*	83	$1,248,777.71	64	$1,511,501.70
Clozapine	Multiple Products	84	$1,245,870.51	65	$1,490,919.24
Infliximab	Remicade	85	$1,231,500.38	92	$1,053,320.60
Emtricitabine/Tenofovir DF	Truvada	86	$1,205,663.93	66	$1,486,652.60
Coagulation Factor VIIa	Novoseven	87	$1,200,060.60	152	$583,582.08
Interferon Beta-1a	Rebif/Avonex	88	$1,198,386.46	62	$1,577,109.06
Fluticasone Propionate Nasal	Flonase*	89	$1,190,109.01	96	$1,017,765.94
Levothyroxine	Multiple Products	90	$1,172,182.24	94	$1,026,108.06
Efavirenz/Emtricitabine/Tenofovir DF	Atripla	91	$1,153,329.19	60	$1,636,427.63

Top 100 Reimbursed Drugs By Fiscal Year		SFY 2017		SFY 2016	
Generic Name	**Brand Name**	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Chlorpromazine	Thorazine*	92	$1,130,711.94	83	$1,177,724.17
C1 Esterase Inhibitor (Human)	Multiple Products	93	$1,090,565.65	98	$1,003,742.26
Hydrocodone ER	Multiple Products	94	$1,085,736.51	129	$733,538.79
Filgrastim	Neupogen	95	$1,072,940.83	113	$857,402.11
Etonogestrel Ethinyl Estradiol VA Ring	Nuvaring	96	$1,062,690.16	95	$1,017,916.74
Levetiracetam	Keppra*	97	$1,044,804.96	102	$980,238.45
Rivaroxaban	Xarelto	98	$1,029,104.84	114	$839,850.15
Asenapine	Saphris	99	$1,002,762.72	101	$995,258.39
Permethrin	Multiple Products	100	$998,804.43	80	$1,204,152.74

*Includes brand and generic where applicable.

NA = not applicable; Trinz = Trinza; Sust = Sustenna; DF = disoproxil fumarate; ER = extended-release; VA = vaginal

Reimbursement does not reflect rebated costs or net costs.

Top 50 Medications by Total Number of Claims: Fiscal Year 2017

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	228,327	97,400	$13,946,039.48	2.32	$61.08	2.34	11.03%
2	Cetirizine	Multiple	215,802	93,001	$1,921,935.26	2.98	$8.91	2.32	1.52%
3	Amoxicillin	Amoxil*	215,227	157,576	$2,214,918.94	11.66	$10.29	1.37	1.75%
4	Hydrocodone/Acetaminophen	Multiple	184,057	68,580	$3,334,053.87	4.02	$18.11	2.68	2.64%
5	Montelukast	Singulair*	134,726	39,077	$2,110,013.99	1	$15.66	3.45	1.67%
6	Azithromycin	Zithromax*	113,578	86,977	$1,993,497.78	3	$17.55	1.31	1.58%
7	Fluticasone Propionate Nasal	Flonase*	99,317	54,445	$1,189,896.82	0.44	$11.98	1.82	0.94%
8	Lisdexamfetamine	Vyvanse	95,286	17,015	$23,950,300.47	1	$251.35	5.6	18.94%
9	Gabapentin	Neurontin*	90,129	19,366	$1,376,994.68	3.17	$15.28	4.65	1.09%
10	Clonidine	Catapres*	84,290	15,273	$730,397.89	1.45	$8.67	5.52	0.58%
11	Methylphenidate	Multiple	80,691	12,708	$14,211,904.52	1.36	$176.13	6.35	11.24%
12	Omeprazole	Prilosec*	72,269	22,335	$729,470.58	1.23	$10.09	3.24	0.58%
13	Sertraline HCl	Zoloft*	72,088	18,274	$689,455.37	1.16	$9.56	3.94	0.55%
14	Ondansetron	Zofran*	68,835	54,277	$850,278.84	2.13	$12.35	1.27	0.67%
15	Loratadine	Multiple	64,629	28,137	$637,173.33	2.6	$9.86	2.3	0.50%
16	Alprazolam	Xanax*	63,449	10,617	$497,109.98	2.32	$7.83	5.98	0.39%
17	Ibuprofen	Motrin*	63,373	43,480	$582,889.36	3.05	$9.20	1.46	0.46%
18	Fluoxetine	Prozac*	62,899	15,006	$804,880.54	1.24	$12.80	4.19	0.64%
19	Trazodone	Desyrel*	62,587	15,201	$632,218.38	1.21	$10.10	4.12	0.50%
20	Prednisone	Multiple	62,264	45,700	$535,525.21	1.98	$8.60	1.36	0.42%
21	Amoxicillin/Clavulanate	Augmentin*	61,789	51,647	$1,679,273.95	8.34	$27.18	1.2	1.33%
22	Cefdinir	Omnicef*	61,722	48,025	$2,040,620.56	6.71	$33.06	1.29	1.61%
23	Oxycodone/Acetaminophen	Multiple	56,125	24,204	$1,899,483.29	3.76	$33.84	2.32	1.50%
24	Lisinopril	Multiple	54,416	14,801	$354,485.02	1.09	$6.51	3.68	0.28%
25	Amphetamine/Dextroamphetamine	Multiple	54,236	8,496	$4,548,721.03	1.44	$83.87	6.38	3.60%
26	Cephalexin	Keflex*	54,076	46,781	$948,632.32	9.45	$17.54	1.16	0.75%
27	Sulfamethoxazole/Trimethoprim	Bactrim*	53,178	42,937	$1,295,544.16	7.59	$24.36	1.24	1.02%
28	Levothyroxine	Multiple	52,084	10,561	$1,172,001.37	1	$22.50	4.93	0.93%
29	Triamcinolone Topical	Multiple	50,094	35,886	$657,724.65	4.38	$13.13	1.4	0.52%
30	Quetiapine	Seroquel*	49,198	8,882	$2,495,162.15	1.45	$50.72	5.54	1.97%
31	Oseltamivir	Tamiflu*	47,820	45,843	$8,730,223.44	10.48	$182.56	1.04	6.90%

Top 50 Medications by Total Number of Claims									
Rank	**Generic Name**	**Brand Name**	**Claims**	**Members**	**Cost**	**Units/ Day**	**Cost/ Claim**	**Claims/ Member**	**% Cost+**
32	Risperidone	Risperdal*	46,470	8,136	$646,064.67	1.52	$13.90	5.71	0.51%
33	Guanfacine Extended-Release	Intuniv*	45,773	7,707	$1,266,682.55	1	$27.67	5.94	1.00%
34	Metformin	Multiple	44,770	10,985	$314,063.91	2.02	$7.02	4.08	0.25%
35	Tramadol	Ultram*	44,144	17,396	$342,791.63	3.92	$7.77	2.54	0.27%
36	Prednisolone Sodium Phosphate	Multiple	43,159	33,054	$744,264.20	6.82	$17.24	1.31	0.59%
37	Mupirocin	Bactroban*	41,519	35,496	$593,256.22	2.19	$14.29	1.17	0.47%
38	Cyclobenzaprine	Flexeril	40,324	19,558	$283,395.03	2.43	$7.03	2.06	0.22%
39	Oxycodone	Multiple	39,867	6,249	$6,964,747.25	3.06	$174.70	6.38	5.51%
40	Citalopram	Celexa*	39,306	10,931	$293,556.70	1.01	$7.47	3.6	0.23%
41	Clonazepam	Klonopin*	39,015	7,960	$365,488.55	2.14	$9.37	4.9	0.29%
42	Fluticasone Propionate Inhalation	Flovent	38,955	16,028	$8,250,693.55	0.34	$211.80	2.43	6.52%
43	Ranitidine	Zantac*	37,191	16,251	$378,426.74	3.38	$10.18	2.29	0.30%
44	Escitalopram	Lexapro*	36,323	9,414	$401,569.64	1.05	$11.06	3.86	0.32%
45	Acetaminophen/Codeine	Multiple	36,024	22,909	$512,151.20	5.13	$14.22	1.57	0.40%
46	Prednisolone Syrup	Prelone*	34,872	27,976	$330,616.38	6.84	$9.48	1.25	0.26%
47	Dexmethylphenidate	Focalin*	34,219	4,578	$4,419,315.74	1.22	$129.15	7.47	3.49%
48	Promethazine HCl	Multiple	34,168	21,707	$364,263.64	5.3	$10.66	1.57	0.29%
49	Polyethylene Glycol	Multiple	32,973	18,199	$684,093.73	17.2	$20.75	1.81	0.54%
50	Topiramate	Multiple	32,455	7,422	$562,809.21	2.06	$17.34	4.37	0.44%

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 Classes by Fiscal Year

Top 10 Traditional Therapeutic Classes by Fiscal Year*

Anti-Infective Agents	2017		2016	
	Total Claims	Total Paid	Total Claims	Total Paid
Antiviral Agents	69,559	$44,630,471.24	33,265	$43,941,879.75
Anti-Infectives	95,818	$5,489,975.24	98,842	$5,880,375.05
Penicillins	288,122	$4,166,293.25	302,095	$3,947,091.25
Cephalosporins	124,983	$3,582,541.00	128,215	$3,979,890.91
Macrolide Antibiotics	116,667	$2,728,190.67	133,904	$3,136,033.16
Antifungal Agents	27,144	$1,110,881.32	27,008	$1,135,502.45
Anthelmintic Agents	3,416	$1,011,380.48	3,061	$1,102,667.35
Tetracyclines	23,935	$673,516.86	23,043	$814,555.61
Antimalarial Agents	4,045	$314,267.14	3,921	$538,171.05
Fluoroquinolones	19,560	$197,638.15	24,153	$221,386.12
Antimycobacterial Agents	357	$45,386.84	354	$33,150.86
Aminoglycosides	422	$44,789.23	393	$21,367.47
Sulfonamides	5	$1,345.57	3	$1,121.97
Amebicides	0	$0.00	0	$0.00
Total:	**774,033**	**$63,996,676.99**	**778,257**	**$64,753,193.00**

Attention Deficit Hyperactivity Disorder (ADHD) Agents	2017		2016	
	Total Claims	Total Paid	Total Claims	Total Paid
ADHD/Anti-Narcolepsy Agents	344,360	$62,118,533.40	336,815	$59,210,124.93
Total:	**344,360**	**$62,118,533.40**	**336,815**	**$59,210,124.93**

Anti-Asthmatic and Bronchodilator Agents	2017		2016	
	Total Claims	Total Paid	Total Claims	Total Paid
Anti-Asthmatic and Bronchodilator Agents	481,600	$43,565,926.25	481,147	$42,407,875.09
Total:	**481,600**	**$43,565,926.25**	**481,147**	**$42,407,875.09**

Antipsychotics	2017		2016	
	Total Claims	Total Paid	Total Claims	Total Paid
Antipsychotics	206,343	$39,977,374.37	199,798	$53,434,190.89
Total:	**206,343**	**$39,977,374.37**	**199,798**	**$53,434,190.89**

Anti-Diabetic Agents		2017		2016	
		Total Claims	Total Paid	Total Claims	Total Paid
Anti-Diabetic Agents		133,142	$38,298,122.04	128,651	$35,416,629.46
	Total:	**133,142**	**$38,298,122.04**	**128,651**	**$35,416,629.46**
Analgesic Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Analgesics - Narcotic		409,330	$22,109,625.16	444,940	$22,098,031.55
Analgesics - Anti-Inflammatory		141,741	$2,222,487.80	149,352	$1,552,699.76
Analgesics - Non-Narcotic		10,232	$429,555.90	15,040	$464,824.70
Migraine Agents		11,521	$270,920.00	11,539	$427,239.57
Gout Agents		5,990	$171,071.95	5,994	$175,818.52
Local Anesthetics - Parenteral		440	$4,551.19	1,361	$7,101.16
General Anesthetics		76	$1,832.42	120	$3,676.01
	Total:	**579,330**	**$25,210,044.42**	**628,346**	**$24,729,391.27**
Anticonvulsant Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticonvulsant Agents		328,780	$24,851,122.19	320,804	$22,587,039.07
	Total:	**328,780**	**$24,851,122.19**	**320,804**	**$22,587,039.07**
Endocrine Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Endocrine Agents		19,542	$8,307,015.77	19,528	$7,812,325.83
Contraceptives		103,888	$5,895,596.07	101,539	$6,105,358.72
Progestins		6,297	$3,945,781.83	4,896	$684,218.10
Corticosteroids		176,846	$2,416,613.80	175,994	$2,568,861.88
Thyroid Agents		55,479	$1,288,052.21	53,656	$1,116,262.82
Estrogens		9,756	$947,412.23	9,967	$901,337.09
Androgen - Anabolic Agents		560	$127,409.73	557	$152,660.84
Oxytocics		207	$27,085.02	268	$37,330.23
	Total:	**372,575**	**$22,954,966.66**	**366,405**	**$19,378,355.51**
Topical Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological Agents		208,935	$11,976,602.74	205,867	$10,823,750.41
Otic Agents		28,049	$5,460,502.74	31,731	$4,539,614.73

Ophthalmic Agents		63,020	$2,167,976.60	67,703	$2,137,738.43
Mouth/Throat/Dental Agents		23,981	$340,849.43	23,448	$293,594.13
Anorectal Agents		1,396	$121,449.82	1,514	$132,391.51
	Total:	**325,381**	**$20,067,381.33**	**330,263**	**$17,927,089.21**
Cardiovascular Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Vasopressors		10,000	$5,423,811.71	10,535	$5,536,685.77
Antihypertensives		221,860	$2,636,721.04	218,766	$2,082,327.07
Beta Blockers		81,632	$2,041,709.01	78,229	$1,816,175.02
Antihyperlipidemics		73,629	$1,627,116.74	72,406	$2,383,832.37
Antianginal Agents		7,698	$774,851.53	8,136	$762,320.31
Other Cardiovascular Agents		899	$711,190.51	388	$127,352.69
Diuretics		52,724	$693,395.04	51,709	$538,373.15
Calcium Channel Blockers		37,364	$485,892.64	36,513	$406,346.80
Cardiotonics		3,314	$149,608.75	3,489	$172,429.87
Antiarrhythmic Agents		2,419	$120,939.13	2,242	$116,282.92
	Total:	**491,539**	**$14,665,236.10**	**482,413**	**$13,942,125.97**

Top 10 Specialty Therapeutic Classes by Fiscal Year*

Pain Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Analgesics - Anti-Inflammatory		4,634	$22,987,786.81	4,193	$18,480,210.27
Local Anesthetics - Parenteral		45	$889.21	35	$905.79
	Total:	**4,679**	**$22,988,676.02**	**4,228**	**$18,481,116.06**
Hematological Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Hematological Agents		709	$16,422,436.53	698	$16,463,906.42
Hematopoietic Agents		670	$2,390,696.13	629	$2,388,881.94
	Total:	**1,379**	**$18,813,132.66**	**1,327**	**$18,852,788.36**
Endocrine Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Endocrine Agents		3,158	$11,561,298.40	3,053	$10,243,991.35

Progestins		596	$2,220,883.60	1,188	$4,440,351.71
	Total:	**3,754**	**$13,782,182.00**	**4,241**	**$14,684,343.06**
Specialized Respiratory Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Specialized Respiratory Agents		1,233	$9,093,408.80	1,150	$7,754,987.89
	Total:	**1,233**	**$9,093,408.80**	**1,150**	**$7,754,987.89**
Psychotherapeutic/Neurologic Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Psychotherapeutic & Neurological Agents		1,378	$8,139,124.40	1,522	$8,540,617.18
	Total:	**1,378**	**$8,139,124.40**	**1,522**	**$8,540,617.18**
Cardiovascular Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Cardiovascular Agents		1,058	$5,143,843.17	835	$3,387,174.02
	Total:	**1,058**	**$5,143,843.17**	**835**	**$3,387,174.02**
Biological Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Passive Immunizing Agents		2,154	$4,033,455.79	2,001	$3,565,034.09
Other Biological Agents		14	$547,781.49	11	$370,164.55
	Total:	**2,168**	**$4,581,237.28**	**2,012**	**$3,935,198.64**
Anti-Infective Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Aminoglycosides		340	$1,383,885.46	307	$1,407,819.63
Other Anti-Infective Agents		86	$666,053.61	66	$423,791.39
Antivirals		3	$10,820.50	10	$33,990.02
	Total:	**429**	**$2,060,759.57**	**383**	**$1,865,601.04**
Gastrointestinal Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Gastrointestinal Agents		348	$1,856,032.89	332	$1,642,701.27
	Total:	**348**	**$1,856,032.89**	**332**	**$1,642,701.27**
Non-Therapeutic Agents		**2017**		**2016**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidotes		257	$1,780,090.76	312	$1,928,230.30

			Total:	257	$1,780,090.76	312	$1,928,230.30

Total	2017		2016	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Top 10 Traditional and Specialty Therapeutic Classes	4,053,766	$443,943,871.30	4,069,241	$434,858,772.22

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

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Appendix H

Hepatitis C Medication Criteria Update

Oklahoma Health Care Authority
April 2018

Introduction[1,2]

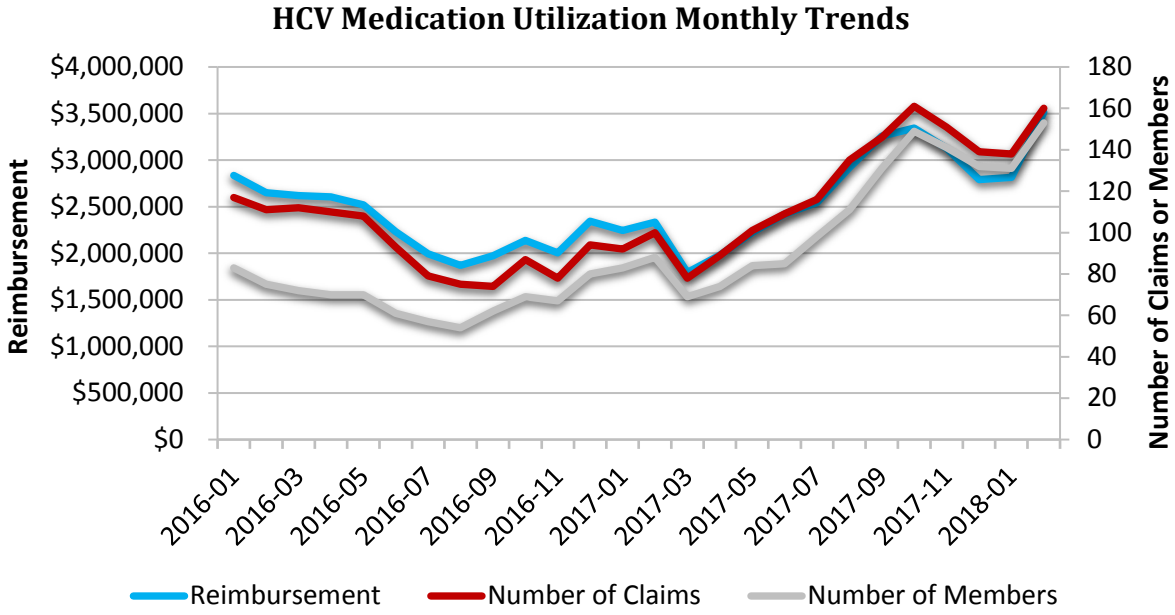
Hepatitis C virus (HCV) infection can be acute or chronic. The Centers for Disease Control and Prevention (CDC) estimates that approximately 15% to 25% of patients infected with HCV will clear the virus spontaneously without treatment and do not develop chronic HCV infection. Predictors of spontaneous clearance include jaundice, elevated alanine aminotransferase (ALT) level, hepatitis B virus surface antigen (HBsAg) positivity, female sex, younger age, HCV genotype 1, and host genetic polymorphisms. The HCV guidance for testing, managing, and treating created by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) estimate a higher percentage, stating that 20% to 50% of patients spontaneously clear the infection. Further, the guidance estimates that only 11% of those who remain viremic at 6 months will spontaneously clear the infection at a later time. Therefore, detectable HCV RNA at 6 months after the time of infection will identify most persons who should receive antiviral therapy.

HCV infection can be detected by HCV antibody screening tests approximately 4 to 10 weeks after infection. A positive test result for HCV antibody indicates either current HCV infection, past infection that has resolved, or a false-positive result. An HCV nucleic acid test (NAT) to detect viremia is necessary to confirm active HCV infection and guide clinical management, including initiation of HCV treatment. An FDA-approved quantitative or qualitative NAT with a detection level of 25 IU/mL or lower should be used to detect HCV RNA. A positive HCV RNA test in the setting of a negative HCV antibody test is indicative of an acute HCV infection. In rare instances such as immunosuppressed individuals, these approaches may be misleading due to impaired antibody production. When baseline HCV antibody and RNA testing are both positive, the person most likely has chronic HCV infection.

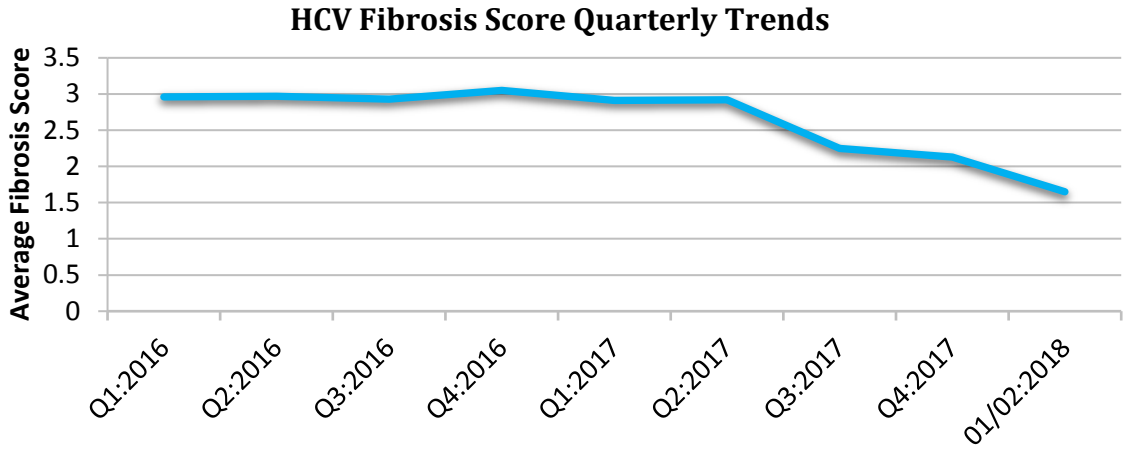
HCV antibodies can be detected in more than 97% of people by 6 months after exposure. Current treatment guidelines do not recommend treatment of acute HCV. Patients with acute HCV infection should be followed and only considered for treatment if HCV RNA persists after 6 months. Additionally, pharmacologic prophylaxis with antiviral therapy following exposure or pre-exposure to HCV is not recommended. Prescribers are instead recommended to encourage regular laboratory monitoring in the setting of acute HCV. Patients should be monitored for 6 to 12 months to determine spontaneous clearance versus persistence of HCV infection. Patients who spontaneously clear the virus should not be treated with antiviral therapy. However, they should be counseled about the possibility of reinfection and tested routinely if risk behaviors are ongoing. All currently U.S. Food and Drug Administration (FDA) approved direct acting antivirals (DAAs) indicated for the treatment of HCV are specifically indicated to treat chronic HCV. SoonerCare HCV medications current prior authorization criteria states that the member must have a diagnosis of chronic HCV and does not specify testing requirements.

Utilization of Hepatitis C Medications: Trends 2016-2018

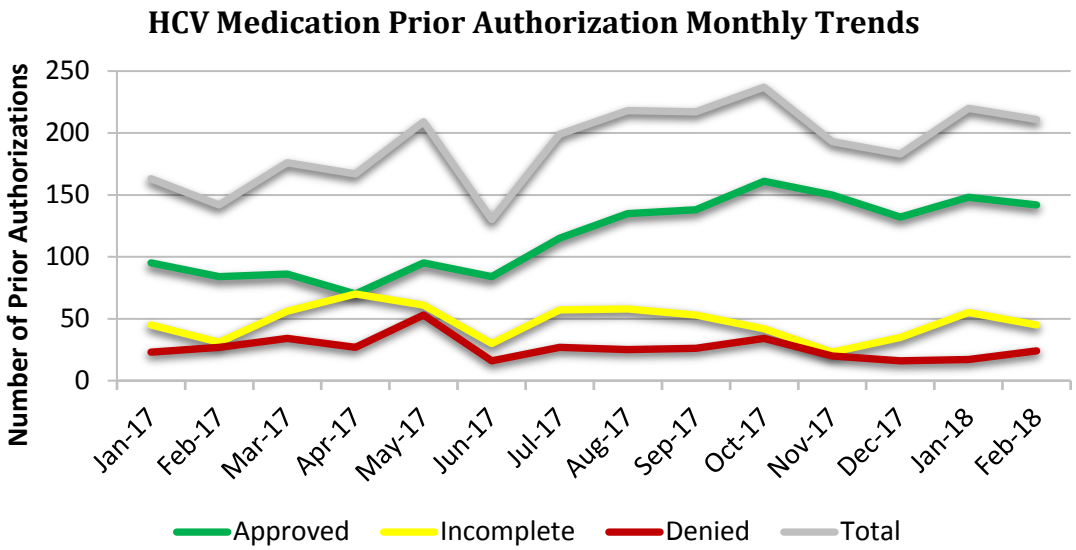
In December 2016, the Drug Utilization Review (DUR) Board voted to lower the minimum fibrosis score requirement for authorization of SoonerCare reimbursement for chronic HCV therapy from a METAVIR equivalent F2 to F1 effective July 1, 2017, and to F0 effective January 1, 2018. The following is a line graph representing the monthly trend in reimbursement, number of claims, and number of members for HCV medications since January 2016. A steep increase can be seen following the F2 to F1 change, and again following the change to F0. The combined monthly totals for January and February 2017 in comparison to January and February 2018 resulted in a 38.28% increase in reimbursement and a 55.21% and 66.08% increase in the number of claims and members, respectively.



The following graph outlines the trends in average fibrosis score by quarter and the first two months of 2018. An immediate decline in average fibrosis score can be seen following the change to F1 in July 2017, and again following the change to F0 in January 2018. The average fibrosis score dropped by 44.3% from quarter one 2016 (Q1:2016) to January and February 2018 (01/02:2018).



Prior authorization requests as well as approvals increased following the F1 and F0 transitions. From January 2017 to January 2018, total requests increased by 35.0%. Additionally, the percentage of approved prior authorizations per month increased from 58.3% to 67.2%. Incomplete prior authorizations are typically a result of incomplete prior authorization submissions, or failure to complete the prior authorization form. Denials are rare and most commonly a result of the member being dual eligible in which their primary prescription drug plan would reimburse for the medication. Approvals are granted for 28 days of therapy each time, so members will have a prior authorization request for each refill of therapy.



Recommendations

The College of Pharmacy recommends adding the following criteria to all prior authorized hepatitis C virus (HCV) medications regarding confirmation of chronic HCV infection:

1. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only one detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least six months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test six months after date of positive HCV antibody test; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least six months apart.

[1] Centers for Disease Control and Prevention (CDC). Hepatitis C FAQs for Health Professionals. Available online at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1. Last revised 02/2018. Last accessed 03/08/2018.
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Appendix I

Calendar Year 2017 Annual Review of Benlysta® (Belimumab)

Oklahoma Health Care Authority
April 2018

Current Prior Authorization Criteria

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical claim only benefit while the subcutaneous (subQ) formulation will be covered as a pharmacy only benefit; and
2. An FDA approved indication of the treatment of adults with active, autoantibody-positive, systemic lupus erythematosus (SLE) already receiving standard therapy; and
3. Documented inadequate response to at least two of the following medications:
    a. High-dose oral corticosteroids; or
    b. Methotrexate; or
    c. Azathioprine; or
    d. Mycophenolate; or
    e. Cyclophosphamide; and
4. Member must not have severe active lupus nephritis or severe active central nervous system lupus; and
5. Benlysta® will not be approved for combination use with biologic therapies or IV cyclophosphamide.

Utilization of Benlysta® (Belimumab): Calendar Year 2017

Calendar Year 2017 Utilization of Benlysta® (Belimumab): Pharmacy Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Claims/Member
2	4	$14,162.20	$3,540.55	2

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Please note, the subcutaneous formulation of Benlysta® was approved by the U.S. Food and Drug Administration (FDA) in July 2017; therefore, there was no pharmacy utilization of Benlysta® during calendar year 2016.

Calendar Year 2017 Utilization of Benlysta® (Belimumab): Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Claims/Member
16	119	$355,794.59	$2,989.87	7.4

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

Demographics of Members Utilizing Benlysta® (Belimumab)

- There were 17 unique members utilizing Benlysta® (belimumab) during calendar year 2017, and all members were female and in the 20 to 64 year old age group. One member had both medical and pharmacy claims for Benlysta®.

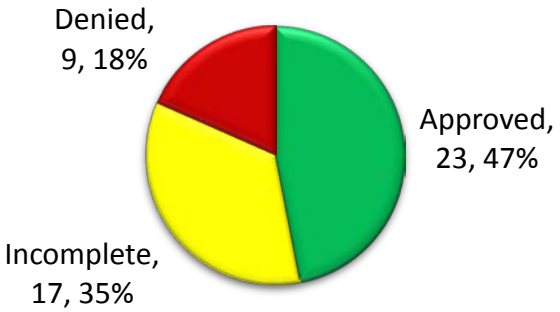
Top Prescriber Specialties of Benlysta® (Belimumab) by Number of Claims

- The only prescriber specialties listed on paid claims for Benlysta® (belimumab) during calendar year 2017 was rheumatologist and physician assistant. Upon further research, the supervising physician for the physician assistant was a rheumatologist.

Prior Authorization of Benlysta® (Belimumab)

There were 49 prior authorization requests submitted for 25 unique members for Benlysta® (belimumab) during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



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

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

- **July 2017:** The FDA approved a subcutaneous (subQ) formulation of Benlysta® (belimumab) for the treatment of adult patients with active, antibody-positive systemic lupus erythematosus (SLE) who are receiving standard therapy. This approval marks the first subQ self-injection treatment option for patients with SLE. After training from their healthcare provider, patients will be able to self-administer Benlysta® as a once weekly subQ injection of 200mg, either from a single-dose prefilled syringe or from a single-dose autoinjector. The recommended dosage is 200mg once weekly given as a subQ injection in the abdomen or thigh; subQ dosing is not based on weight. Benlysta® was first FDA approved for the treatment of SLE in 2011 as an intravenous (IV) formulation. The recommended maintenance dosage for the IV formulation is 10mg/kg every 4 weeks (given as a 1-hour IV infusion). If transitioning from IV Benlysta® to subQ Benlysta®, the first subQ dose should be administered 1 to 4 weeks after the last IV dose. The current PA criteria for Benlysta® has been updated to include the subQ formulation (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).

Pipeline:

- **Anifrolumab:** Positive Phase 2 data was published for AstraZeneca's anifrolumab for the treatment of moderate-to-severe SLE. Anifrolumab is an investigational, fully human monoclonal antibody that binds to subunit 1 of the type I interferon (IFN) receptor,

inhibiting the activity of all type I IFNs, which play a central role in lupus. Anifrolumab is the only anti-type-I IFN receptor approach currently in development for SLE. Anifrolumab is being developed with a type I IFN gene signature test designed to identify patients who may be more likely to benefit from treatment. The study met its primary and secondary endpoints, with anifrolumab treatment resulting in significantly greater rates of improvement across a broad range of composite and organ-specific disease measures, as well as a reduction in oral corticosteroid use, compared to placebo. Anifrolumab (IV formulation) is currently in Phase 3 trials and has been granted Fast Track designation from the FDA for the treatment of SLE. The filing of a Biologics License Application (BLA) for anifrolumab is anticipated in 2019. Anifrolumab is also currently in Phase 2 trials for a subQ formulation for the treatment of SLE, and in Phase 2 trials for the treatment of lupus nephritis.

- **Blisibimod:** A Phase 3 trial of Anthera's blisibimod did not reach its primary endpoint at week 52 for the treatment of SLE. Blisibimod is an inhibitor of B-cell activating factor (BAFF). The Phase 3 CHABLIS-SC1 trial evaluated blisibimod in a "responder population" identified from prior studies with this drug class. The primary endpoint at week 52 was the SLE Responder Index-6 (SRI-6). Response rates to blisibimod were equivalent to past trials of BAFF inhibitors, but the placebo response was greater. Blisibimod was well tolerated, and modest benefits of blisibimod were observed on serological effects and corticosteroid tapering. BAFF has been shown to be elevated in a variety of B-cell mediated autoimmune diseases, including immunoglobulin A nephropathy (IgAN), SLE, and others. Blisibimod is currently in development for the treatment of IgAN, also known as Berger's disease, and has received Orphan Drug designation from the FDA for the treatment of IgAN.
- **Lupuzor™:** New data from an ongoing Phase 3 trial continues to demonstrate that ImmuPharma's Lupuzor™ is safe for the treatment of SLE patients. After the trial completion, the company expects to gather sufficient safety and efficacy information to support a regulatory submission to the FDA and the European Medicines Agency (EMA). Lupuzor™, also known as IPP-201101 or rigerimod, was designed to modulate the activation of auto-reactive T-cells. Other attempts to modulate the immune response in SLE have been done further downstream in the immune cascade, most notably in the regulation of B-cells. However, in targeting upstream T-cell activation, Lupuzor™ presents a novel approach in modulating this unwelcome autoimmune reaction. This targeted approach marks a paradigm shift in treating autoimmune disease. The FDA has granted Lupuzor™ Fast Track designation for the treatment of SLE.

Recommendations

The College of Pharmacy recommends the changes shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report, based on the recent FDA approval of the subQ formulation of Benlysta® (belimumab).

Utilization Details of Benlysta® (Belimumab): Calendar Year 2017

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
BENLYSTA SUBQ INJ 200MG/ML PREFILLED SYRINGE	2	1	$7,081.10	$3,540.55	2
BENLYSTA SUBQ INJ 200MG/ML AUTO-INJECTOR	2	1	$7,081.10	$3,540.55	2
TOTAL	**4**	**2***	**$14,162.20**	**$3,540.55**	**2**

*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
BELIMUMAB INJ J0490	119	16	$355,794.59	$2,989.87	7.4
TOTAL	**119**	**16***	**$355,794.59**	**$2,989.87**	**7.4**

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

[1] GlaxoSmithKline (GSK) Press Release: GSK Receives FDA Approval for a New Self-Injectable Formulation of Benlysta® (Belimumab) for Systemic Lupus Erythematosus. Available online at: https://www.gsk.com/en-gb/media/press-releases/gsk-receives-fda-approval-for-a-new-self-injectable-formulation-of-benlysta-belimumab-for-systemic-lupus-erythematosus/#. Issued 07/21/2017. Last accessed 03/22/2018.

[2] Benlysta® (Belimumab) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/benlysta/. Last revised 07/20/2017. Last accessed 03/22/2018.

[3] Benlysta® (Belimumab) Prescribing Information. GlaxoSmithKline (GSK). Available online at: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Benlysta/pdf/BENLYSTA-PI-MG.PDF. Last revised 07/2017. Last accessed 03/22/2018.

[4] AstraZeneca Press Release: *Arthritis and Rheumatology* Publishes Positive Phase II Data on Anifrolumab in Lupus. Available online at: https://www.astrazeneca.com/media-centre/medical-releases/Arthritis-and-Rheumatology-publishes-positive-Phase-II-data-on-anifrolumab-in-lupus-14112016.html. Issued 11/14/2016. Last accessed 03/22/2018.

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[6] Merrill J, Martin RS, Shanahan WR, et al. SAT0240 Phase 3 Trial Results with Blisibimod, a Selective Inhibitor of B-Cell Activating Factor, in Subjects with Systemic Lupus Erythematosus (SLE). *Ann Rheum Dis* 2017; 76:864.

[7] Anthera Pipeline: Blisibimod. Available online at: https://www.anthera.com/blisibimod/. Last accessed 03/23/2018.

[8] Anthera Press Release: Anthera Announces FDA Orphan Drug Designation for Blisibimod for the Treatment of IgA Nephropathy. Available online at: http://investor.anthera.com/news-releases/news-release-details/anthera-announces-fda-orphan-drug-designation-blisibimod. Issued 08/09/2017. Last accessed 03/23/2018.

[9] ImmuPharma PLC Press Release: ImmuPharma Initiates Preparation of Lupuzor's Regulatory Submissions. Available online at: http://otp.investis.com/clients/uk/immu_pharma/rns/regulatory-story.aspx?cid=1554&newsid=930234. Issued 09/26/2017. Last accessed 03/23/2018.

[10] ImmuPharma Pipeline: Lupuzor™. Available online at: http://www.immupharma.co.uk/folio/lupuzor/. Last accessed 03/23/2018.

Appendix J

Calendar Year 2017 Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Admelog® (Insulin Lispro), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/ Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin)

Oklahoma Health Care Authority
April 2018

Current Prior Authorization Criteria

Diabetes Medications Tier-2 Approval Criteria:

1. A trial of a Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier-2 medications may be approved based on current American Association of Clinical Endocrinologists (AACE) or American Diabetes Association (ADA) guidelines.
3. A clinical exception will apply for medications with the FDA approved diagnosis to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (DM) and CV disease for patients with the diagnosis of type 2 DM 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 a 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.)

Diabetes Medications Special Prior Authorization (PA) Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least three other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member.

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 indication 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).

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.

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).

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), 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).

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors acarbose (Precose®) **Biguanides** metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®) **Glinides** repaglinide (Prandin®)	**DPP-4 Inhibitors** saxagliptin (Onglyza®) saxagliptin/metformin (Kombiglyze®) sitagliptin (Januvia®) sitagliptin/metformin (Janumet®) sitagliptin/metformin ER (Janumet® XR) **Glinides** nateglinide (Starlix®) repaglinide/metformin (Prandimet®) **GLP-1 Agonists** exenatide (Byetta®) exenatide ER (Bydureon®) liraglutide (Victoza®)	**Alpha-Glucosidase Inhibitors** miglitol (Glyset®) **Dopamine Agonists** bromocriptine (Cycloset®) **DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto®)	**Amylinomimetics** pramlintide (Symlin®) **Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®) **DPP-4 Inhibitors** linagliptin/metformin ER (Jentadueto® XR) **SGLT-2 Inhibitors** canagliflozin/metformin ER (Invokamet® XR)

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Sulfonylureas chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide micronized (Micronase®) tolbutamide (Orinase®) **Thiazolidinediones** pioglitazone (Actos®)	**SGLT-2 Inhibitors** dapagliflozin (Farxiga®) dapagliflozin/metformin ER (Xigduo® XR) empagliflozin (Jardiance®) empagliflozin/metformin (Synjardy®) empagliflozin/metformin ER (Synjardy® XR)	**GLP-1 Agonists** albiglutide (Tanzeum®) dulaglutide (Trulicity®) lixisenatide (Adlyxin™) **GLP-1 Agonists/Insulin** insulin degludec/ liraglutide (Xultophy® 100/3.6) insulin glargine/ lixisenatide (Soliqua® 100/33) **SGLT-2 Inhibitors** canagliflozin (Invokana®) canagliflozin/metformin (Invokamet®) **SGLT-2/DPP-4 Inhibitors** dapagliflozin/saxagliptin (Qtern®) empagliflozin/linagliptin (Glyxambi®) **Thiazolidinediones** pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met® XR) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®)	

*Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
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 Diabetes Medications: Calendar Year 2017

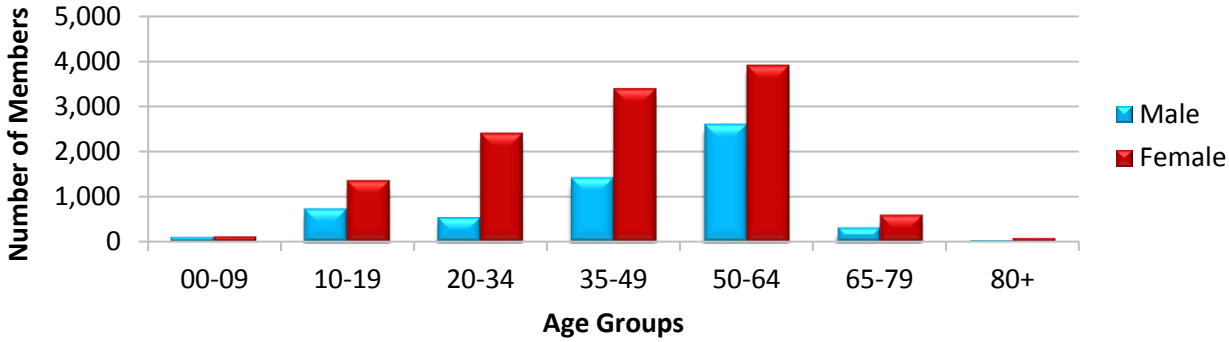
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	17,373	128,810	$36,737,084.00	$285.20	$8.18	5,428,620	4,490,402
2017	17,572	132,823	$37,846,163.02	$284.94	$8.07	5,613,378	4,692,088
% Change	**1.10%**	**3.10%**	**3.00%**	**-0.10%**	**-1.30%**	**3.40%**	**4.50%**
Change	**199**	**4,013**	**$1,109,079.02**	**-$0.26**	**-$0.11**	**184,758**	**201,686**

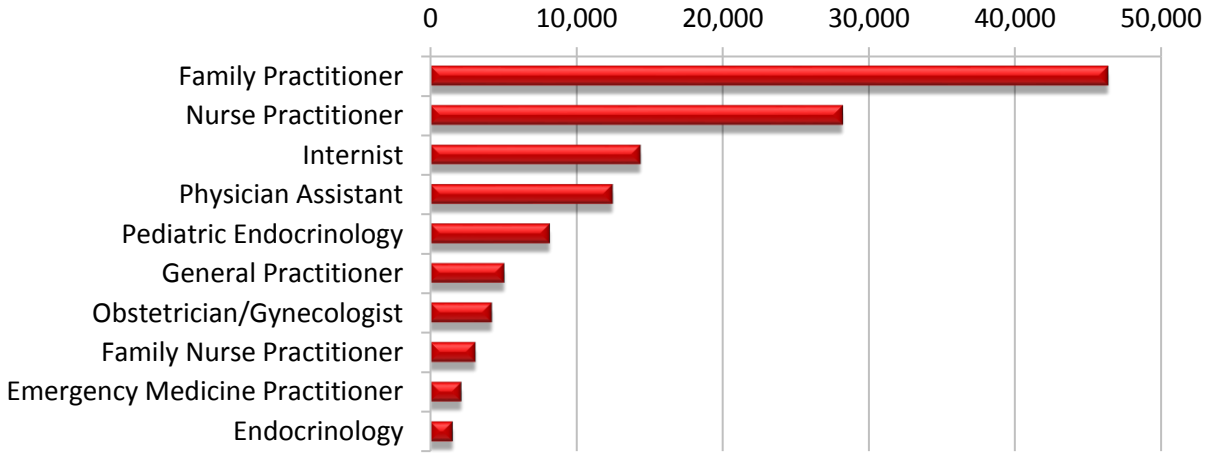
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Please note, due to new federal regulations, a new pricing methodology for pharmacy claims reimbursement was implemented by SoonerCare 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 effective 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.

Demographics of Members Utilizing Diabetes Medications

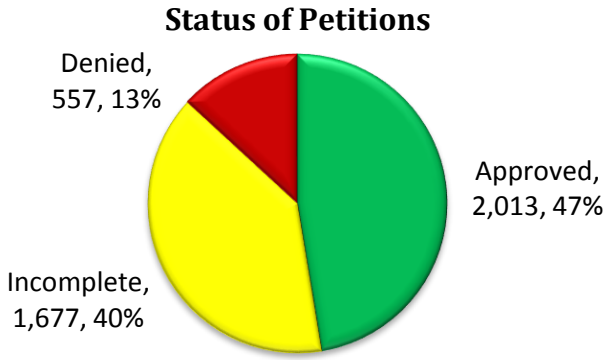


Top Prescriber Specialties of Diabetes Medications by Number of Claims



Prior Authorization of Diabetes Medications

There were 4,247 prior authorization requests submitted for diabetes medications during calendar year 2017. Of the 4,247 total prior authorizations submitted, 2,557 were for non-insulin diabetic medications and 1,690 were for insulin products. 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 2017.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32]

Anticipated Patent Expiration(s):

- Byetta® (exenatide): January 2020
- Avandia® (rosiglitazone): October 2020
- Apidra® (insulin glulisine): January 2023
- Riomet® (metformin oral solution): September 2023
- Kombiglyze® XR [saxagliptin/metformin extended-release (ER)]: July 2025
- Actoplus Met XR® (pioglitazone/metformin ER): July 2026
- Januvia® (sitagliptin): November 2026
- Janumet XR® (sitagliptin/metformin ER): November 2026
- Synjardy® (empagliflozin/metformin): April 2027
- Synjardy XR® (empagliflozin/metformin ER): April 2027
- Lantus® (insulin glargine): March 2028
- Janumet® (sitagliptin/metformin): July 2028
- Onglyza® (saxagliptin): November 2028
- Invokana® (canagliflozin): February 2029
- Invokamet® (canagliflozin/metformin): February 2029
- Invokamet XR® (canagliflozin/metformin ER): February 2029
- Jardiance® (empagliflozin): October 2029
- Glyxambi® (empagliflozin/linagliptin): October 2029
- Qtern® (dapagliflozin/saxagliptin): December 2029
- Farxiga® (dapagliflozin): May 2030
- Bydureon® (exenatide ER): May 2030
- Jentadueto® (linagliptin/metformin): June 2030
- Bydureon BCise® (exenatide ER): October 2030
- Xigduo® XR (dapagliflozin/metformin ER): November 2030
- Tradjenta® (linagliptin): March 2031
- Toujeo® (insulin glargine): May 2031
- Ozempic® (semaglutide): February 2032
- Tresiba® (insulin degludec): February 2032
- Ryzodeg® 70/30 (insulin degludec/insulin aspart): February 2032
- Xultophy® (insulin degludec/liraglutide): February 2032
- Cycloset® (bromocriptine): April 2032
- Soliqua® (insulin glargine/lixisenatide): May 2032
- Afrezza® (insulin human inhalation powder): July 2032

- Adlyxin® (lixisenatide): August 2032
- Victoza® (liraglutide): September 2032
- Jentadueto XR® (linagliptin/metformin ER): March 2033

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

- **July 2017:** The FDA granted tentative approval for Lusduna™ Nexvue® (insulin glargine injection), a follow-on biologic basal insulin, for treatment of type 1 and type 2 diabetes mellitus (DM).
- **September 2017:** The FDA approved Fiasp® (insulin aspart injection) for the treatment of type 1 and type 2 DM in adults.
- **December 2017:** The FDA approved Admelog® (insulin lispro injection) to improve glycemic control in adults and children 3 years of age and older with type 1 DM and adults with type 2 DM.
- **December 2017:** The FDA approved Ozempic® (semaglutide injection) for the treatment of adults with type 2 DM.
- **December 2017:** The FDA approved Steglatro™ (ertugliflozin), and combination products Steglujan™ (ertugliflozin/sitagliptin) and Segluromet™ (ertugliflozin/metformin) for the treatment of adults with type 2 DM.

New FDA Approved Indication(s) and Formulation(s):

- **June 2017:** The FDA approved Humalog® Junior KwikPen® for the treatment of type 1 and type 2 DM. The Humalog® Junior KwikPen® is a prefilled pen with half-unit dosing capability, enabling finer dose adjustments.
- **August 2017:** The FDA approved a new indication for Victoza® (liraglutide) to reduce the risk of major adverse cardiovascular (CV) events, myocardial infarction (MI), cerebrovascular accident (CVA), and CV death in adults with type 2 DM and established cardiovascular disease (CVD).
- **October 2017:** The FDA approved once-weekly Bydureon® BCise™ (exenatide ER injectable suspension) as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM. Bydureon® BCise™ is an auto-injector pen with a hidden needle that removes the need for attaching the needle and depressing a plunger as is the case with Bydureon® pen. Additionally, BCise™ only requires 15 seconds of shaking for preparation compared to the pen which requires tapping at least 80 times.
- **March 2018:** The FDA approved Toujeo® (insulin glargine 300 units/mL) Max SoloStar®, the highest capacity long-acting insulin pen that will be available on the market. The new pen holds 900 units of Toujeo® and provides up to 160 units/mL of Toujeo® in a single injection. It may reduce the number of pens needed, allowing for fewer refills and related copays. The maximum dose of up to 160 units/mL may also help reduce the number of injections needed to deliver the required Toujeo® dosage. Toujeo® Max SoloStar® will be available at the same price as the original Toujeo® SoloStar® per insulin unit. Toujeo® Max SoloStar® is expected to launch in the third quarter of 2018.

Guideline Update(s):

- **November 2017:** The American Diabetes Association (ADA) released a new consensus report standardizing clinically meaningful outcome measures for type 1 DM, beyond using hemoglobin A_{1c} (HbA_{1c}) testing. In the report, consensus definitions were developed for hypoglycemia, hyperglycemia, time in range [proportion of time in glucose target ranges during continuous glucose monitoring (CGM)], and diabetic ketoacidosis (DKA). The following are highlights from the report:
  - Hypoglycemia in patients with type 1 DM was defined in three levels: Level 1 (glucose <70mg/dL but ≥54mg/dL); Level 2 (glucose <54mg/dL); Level 3 (a severe event characterized by altered mental and/or physical status requiring assistance).
  - Hyperglycemia in patients with type 1 DM was defined in two levels: Level 1 (glucose >180mg/dL and ≤250mg/dL) and Level 2 (>250mg/dL).
- **December 2018:** The ADA released the 2018 Standards of Medical Care in Diabetes which included several notable updates:
  - Based on the results of multiple CV outcome trials, new treatment recommendations were included for adults with type 2 DM and CVD. After lifestyle management and metformin, it is recommended to include a medication validated to improve CV health.
  - Based on four major, randomized controlled trials that compared intensive versus standard hypertension (HTN) treatment, the ADA recommends that most adults with DM and HTN should have a target blood pressure of <140/90mmHg. A new algorithm illustrating the recommended antihypertensive treatment approach has been included in the update. Additionally, it is recommended that all patients with DM and HTN monitor their blood pressure at home to help identify potential discrepancies between office and home blood pressure and to improve medication behavior.
  - Updated recommendations emphasize testing for prediabetes and type 2 DM should be considered in children and adolescents younger than 18 years of age who are overweight or obese (BMI >85^{th} percentile, or weight >120% of ideal for height) and have one or more additional risk factors for DM such as (1) maternal history of DM or gestational DM during the child's gestation; (2) family history of type 2 DM in first- or second-degree relative; (3) race/ethnicity; and (4) signs of insulin resistance or conditions associated with insulin resistance.
  - Additional recommendations included that all pregnant women with preexisting type 1 or type 2 DM should consider daily low-dose aspirin starting at the end of the first trimester in order to reduce the risk of pre-eclampsia.

News:

- **June 2017:** A multicenter, prospective, open-label, randomized parallel clinical trial conducted by researchers in Japan investigated the therapeutic effects of sodium glucose cotransporter-2 (SGLT-2) inhibitors on atherosclerosis and endothelial function. Patients with type 2 DM (N=80) who had a HbA_{1c} level of ≥6% to <8% were randomly assigned to receive 750mg of metformin supplemented with 5mg of dapagliflozin or 1,500mg of metformin for 16 weeks. Primary endpoints were comparing changes from

baseline in glycemic control, lipid levels, body composition, and atherosclerosis-related markers between the two groups. Both groups had significant declines in HbA_{1c}, fasting plasma glucose, and in body weight; however, the dapagliflozin group also had significant decreases in levels of an oxidative stress biomarker, urine 8-OHdG, compared with the metformin group (–0.63 ± 1.82 vs. 1.13 ± 2.17ng/mg, respectively; P<0.001).

- **June 2017:** The CANVAS program, which was comprised of two similar trials with over 10,000 patients, assessed the efficacy, safety, and durability of canagliflozin in patients with type 2 DM and a history of CVD, or at least two CV risk factors. Compared to placebo, canagliflozin reduced the risk of the composite primary endpoint (CV mortality, nonfatal MI, and nonfatal CVA) by 14% [hazard ratio (HR): 0.85; 95% confidence interval (CI): 0.75-0.97]. In addition, treatment with canagliflozin lowered the risk of hospitalization for heart failure (HF) by 33% (HR: 0.67; 95% CI: 0.52-0.87). Canagliflozin also showed potential renal protective effects, delays in progression of albuminuria, and reduction in the risk of clinically important renal composite outcomes by 40% (HR: 0.60; 95% CI: 0.47-0.77). However, with regards to adverse events, an increased risk of amputations was noted in the canagliflozin arm of both trials, with patients with prior history of amputation or peripheral vascular disease being found to be at greatest risk.
- **June 2017:** A study in *The New England Journal of Medicine (NEJM)* showed that among high-risk patients with type 2 DM, insulin degludec is non-inferior to insulin glargine in terms of the incidence of CV events. The study randomized 7,637 patients with type 2 DM [85.2% with established CVD, chronic kidney disease (CKD), or both] to receive either insulin degludec (N=3,818) or insulin glargine U-100 (N=3,819) once daily between dinner and bedtime. The results indicated that for the primary outcome of first occurrence of an adjudicated major CV event, CV events occurred in 8.5% and 9.3% of patients in the insulin degludec group and insulin glargine U-100 group, respectively (P<0.001 for non-inferiority). The mean HbA_{1c} level was 7.5 ± 1.2% in both groups at 24 months, however the insulin degludec group had a significantly lower mean fasting plasma glucose level (128 ± 56mg/dL vs. 136 ± 57mg/dL; P<0.001).
- **September 2017:** A retrospective study of claims from 52,544 patients covered by Aetna who had two physician claims or one hospitalization with a type 2 DM diagnosis showed apparent diabetes failures may in fact be attributable to non-adherence. The researchers found that of 22,956 patients given second-line treatment, only 8.2% had evidence of recommended use of metformin (first-line treatment) in the past 60 days, and 28% had no prior claims evidence of having taken metformin. An additional second-line antihyperglycemic medication or insulin was more likely in patients given their initial second-line medication without evidence of recommended use of metformin (P<0.001).
- **September 2017:** A study published in *Diabetes, Obesity and Metabolism* reported no increased risk of below-knee lower extremity (BKLE) amputation for patients newly initiated on canagliflozin versus non-SGLT-2 inhibitor antihyperglycemics in patients with type 2 DM. A total of 118,018 patients newly exposed to SGLT-2 inhibitors (of which 73,024 were exposed to canagliflozin) and 226,623 patients newly exposed to non-SGLT-2 inhibitors were included in the analysis. The incidence rate of BKLE amputation was 1.22 events per 1,000 person-years (PY) with SGLT-2 inhibitors, 1.26

events per 1,000 PY with canagliflozin, and 1.87 events per 1,000 PY with non-SGLT-2 inhibitors. In a comparative analysis that matched 63,845 new canagliflozin users with new non-SGLT-2 inhibitor users, the incidence rate of BKLE amputation was 1.18 events per 1,000 PY versus 1.12 events per 1,000 PY (P=0.92).

- **September 2017:** A new study published in *The NEJM* reported that in patients with type 2 DM, the incidence of major CV events is similar for those receiving exenatide or placebo. The study randomized 14,752 patients with type 2 DM (73.1% with previous CVD) to receive exenatide ER or placebo once weekly. The results showed 11.4% of patients in the exenatide group and 12.2% in the placebo group had a primary composite event. Exenatide was non-inferior to placebo in terms of safety, but was not superior with respect to efficacy. There was no significant difference between the groups in the rates of death from CV causes, fatal or non-fatal MI, fatal or non-fatal CVA, HF hospitalization, or acute coronary syndrome hospitalization.
- **September 2017:** New data shows that Xultophy® (insulin degludec/liraglutide) significantly decreased the number of risk factors associated with increased risk of CVD in patients with type 2 DM compared to basal insulin. A post-hoc analysis of two randomized-controlled trials compared insulin degludec/liraglutide to insulin degludec and to insulin glargine, given with metformin for 26 weeks. The data indicated Xultophy®-treated patients had significantly lower systolic blood pressure, lower total cholesterol, and lower low-density lipoprotein (LDL) cholesterol versus patients treated with basal insulin.
- **October 2017:** A new study that evaluated data from 14,671 patients in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) study found that among patients with type 2 DM and atherosclerotic cardiovascular disease (ASCVD), sudden death was the most common category of CV mortality. The researchers identified 1,084 deaths and characterized 530 of them as CV (1.2/100 PY; 49% of deaths), 338 as non-CV (0.77/100 PY; 31% of deaths), and 216 as unknown (0.49/100 PY; 20% of deaths). Sudden death was the most common CV death (27% of CV deaths), followed by acute MI/CVA (21% of CV deaths), and HF (12% of CV deaths). For non-CV deaths, malignancy was the most common (46% of non-CV deaths).
- **November 2017:** Results from the CANVAS clinical trial program showed canagliflozin improved renal outcomes and showed potential renal protective effects in patients with type 2 DM who either have or are at risk for CVD. The results showed that when compared to placebo, canagliflozin was associated with a reduced risk of renal disease progression, including significantly reducing urinary albumin excretion (18% lower in all participants; 34% lower in those with baseline microalbuminuria; 36% lower in those with baseline macroalbuminuria), and stabilizing estimated glomerular filtration rate (eGFR) (rate gradually increasing with canagliflozin over 6.5 years compared to progressive decline with placebo). Canagliflozin reduced rates of several pre-specified major renal composite endpoints [i.e., end-stage renal disease (ESRD), doubled serum creatinine, renal death] by up to 47% (HR: 0.53; 95% CI: 0.33-0.84).
- **December 2017:** Companion Medical announced the launch of the InPen® system, a prescription-only insulin injector pen with a smartphone app and bolus advisor, for the management of DM. The InPen® is compatible for use with Humalog® U-100 (insulin

lispro) and NovoLog® (insulin aspart) 3mL insulin cartridges and single-use detachable and disposable needles in patients 12 years of age and older. The InPen® can monitor insulin doses, including priming, and transmit data to the user's mobile device via Bluetooth®. The system is also able to calculate and recommend optimal insulin dosing, track time of doses for one year, monitor insulin temperature, remind users to take insulin, and display last dose and insulin-on-board. InPen® can also create reports for healthcare providers.

- **December 2017:** The researchers at the deprescribing project, based at the Bryère Research Institute, published a deprescribing algorithm focused on antihyperglycemic agents in patients age 65 years of age and older. The aim of the algorithm is to guide healthcare professionals in stopping, switching, or lowering the dose of these drugs in patients at risk for hypoglycemia or other antihyperglycemic adverse effects or in whom the drug's benefit is uncertain due to frailty, dementia, or limited life expectancy.
- **January 2018:** A report published in *Diabetes Care* showed unstable housing is associated with an increased likelihood of DM-related emergency department (ED) visits and hospitalization. Data from the nationally representative 2014 Health Center Patient Survey was examined to determine whether unstable housing (defined as not having enough money to pay rent/mortgage, moving two or more times in the past 12 months, or staying at a place one does not own/rent) was associated with risk for DM-related ED visits or inpatient hospitalizations. Overall, 37% of the 1,087 participants were unstably housed. The study found that 13.7% of participants reported a DM-related ED visit or inpatient hospitalization in the previous 12 months. Unstable housing was correlated with increased odds of DM-related ED use or hospitalization after adjustments for multiple potential confounders (adjusted odds ratio, 5.17).

Product Discontinuation(s):

- **January 2018:** Novo Nordisk announced that the NovoFine® 30G 8mm pen needles will be discontinued on or before April 30, 2018. This decision was not due to any safety issues related to the product.
- **January 2018:** GlaxoSmithKline (GSK) announced Tanzeum® (albiglutide), a glucagon-like peptide-1 (GLP-1) receptor agonist, is being discontinued due to limited prescribing and not because of safety concerns. According to GSK, the product will be no longer available as of May 2018.

Pipeline:

- **Bexagliflozin:** Bexagliflozin is a SGLT-2 inhibitor currently in Phase 3 trials for the treatment of type 2 DM. Results of clinical trials of bexagliflozin show no increase in genital infection rates relative to placebo, unlike other SGLT-2 inhibitors.
- **Farxiga® (Dapagliflozin) in Type 1 DM:** In September 2017, AstraZeneca announced results of a Phase 3 trial of dapagliflozin for adjunct treatment to insulin in patients with type 1 DM. The trial showed that dapagliflozin, when given as an oral adjunct to adjustable insulin in patients with inadequately-controlled type 1 DM, demonstrated significant and clinically-relevant reductions from baseline in HbA_{1c}, weight reductions, and lowered total daily insulin dose at 24 weeks compared to placebo at both the 5mg and 10mg dose.

- **Oral Semaglutide:** In February 2018, Novo Nordisk announced positive results of a Phase 3 trial for an oral formulation of semaglutide, which would be the first oral GLP-1 agonist. The company states that the trial met its primary goal by demonstrating "significant and superior" improvements in long-term blood glucose levels and weight loss compared to placebo. The company also noted that mild-to-moderate nausea was only reported in 5% to 16% of patients, which is less than nausea levels observed with the injectable formulation.
- **Ready-to-Use Glucagon:** Xeris Pharmaceuticals announced completion of two Phase 3 trials of an investigational ready-to-use rescue glucagon pen for severe hypoglycemia in patients with DM. The findings of the studies will not be released until later this year; however, the company stated that the trials were successful and have plans to submit a New Drug Application (NDA) by the second quarter of 2018.
- **Sotagliflozin:** Sotagliflozin is a novel, first in class, oral SGLT type 1 and 2 (SGLT1/2) inhibitor currently in Phase 3 trials for type 1 and type 2 DM. In one of the Phase 3 trials, adult subjects with type 1 DM on background insulin showed statistically significant reductions in HbA_{1c} at 24 weeks with sotagliflozin compared to placebo. Results of the trial also showed statistically significant results in all of the secondary endpoints, compared to placebo, including net benefit (proportion of patients with HbA_{1c} <7.0% at week 24 and no episode of severe hypoglycemia and no episode of DKA) and reduction in body weight, bolus insulin dose, fasting plasma glucose, Diabetes Treatment Satisfaction Questionnaire status (DTSQs) score, and 2-item Diabetes Distress Screening Scale (DDS2) questionnaire score.

Admelog® (Insulin Lispro) Product Summary[33]

Indication(s): Admelog® (insulin lispro) is a rapid-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients 3 years of age and older with type 1 and type 2 DM.

Dosing:

- Admelog® is supplied as a 100 units/mL (U-100) solution in a 10mL multiple-dose vial (MDV) or as a 3mL single-patient-use SoloStar® prefilled pen for subcutaneous (SQ) or intravenous (IV) use.
- The dose of Admelog® should be individualized based on route of administration, individual's metabolic needs, blood glucose monitoring results, and glycemic control.
- If a patient is being changed from another insulin lispro product to Admelog®, the dose of Admelog® should be the same as the other insulin lispro product.
- For SQ administration: Admelog® should be administered within 15 minutes before a meal or immediately after a meal.
- For IV administration: Admelog® should be diluted with 0.9% sodium chloride and administered only under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hypokalemia.
- Admelog® MDV and SoloStar® pens should be stored refrigerated until opened, and once opened, they may be stored at room temperature for up to 28 days. Admelog® SoloStar® pens should not be refrigerated once opened.

Efficacy: The safety and effectiveness of Admelog® have been established based on adequate and well controlled studies of another insulin lispro U-100 product in adult and pediatric patients 3 years of age and older with type 1 DM and adult patients with type 2 DM.

Cost:

Medication	Cost Per Unit*	Cost Per Package^
Admelog® vial (insulin lispro)	**$23.35**	**$233.50**
Admelog® SoloStar® (insulin lispro)	**$30.06**	**$450.90**
Humalog® vial (insulin lispro)	$26.39	$263.90
Humalog® KwikPen® (insulin lispro)	$33.99	$509.88

Costs do not reflect rebated prices or net costs.
^Vial package size = 10mL, SoloStar® package size = 15mL, and KwikPen® package size = 15mL
*Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Fiasp® (Insulin Aspart) Product Summary[34]

Indication(s): Fiasp® (insulin aspart) is a rapid-acting human insulin analog indicated to improve glycemic control in adults with DM. It contains niacinamide (vitamin B_3) to increase the speed of initial absorption and a formulation-stabilizing amino acid (L-arginine).

Dosing:

- Fiasp® is supplied as a U-100 solution in a 10mL MDV or as a 3mL single-patient-use FlexTouch® prefilled pen for SQ or IV use.
- The dose of Fiasp® should be individualized based on route of administration, individual's metabolic needs, blood glucose monitoring results, and glycemic control.
- For SQ administration: Fiasp® should be administered at the start of a meal or within 20 minutes after starting a meal.
- For IV administration: Fiasp® should be diluted with 0.9% sodium chloride or 5% dextrose and administered only under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hypokalemia.
- Fiasp® MDV and FlexTouch® pens should be stored refrigerated until opened. Once opened, they may be stored at room temperature or refrigerated for up to 28 days.

Efficacy: The efficacy of Fiasp® was evaluated in three randomized, active-controlled trials of 18 to 26 weeks duration. For type 1 DM, subjects (N=1,143) were randomized to either blinded mealtime Fiasp®, blinded mealtime NovoLog®, or open-label post-meal Fiasp® for patients already on insulin detemir. For type 2 DM, subjects (N=689) were randomized to either mealtime Fiasp® or to mealtime NovoLog®, both in combination with insulin glargine and metformin in a basal-bolus regimen. In adult subjects with type 1 DM, mealtime Fiasp® and post-meal Fiasp® was found to be non-inferior to mealtime NovoLog® in glycemic control, both in combination with insulin detemir. In adult subjects with type 2 DM, mealtime Fiasp® provided non-inferior glycemic control compared to mealtime NovoLog®, both in combination with metformin. In addition, mealtime Fiasp® in a basal-bolus regimen, in combination with metformin, also provided statistically significant improvement in overall glycemic control compared to basal insulin therapy alone with metformin in adult patients with type 2 DM.

Cost:

Medication	Cost Per Unit*	Cost Per Package^
Fiasp® vial (insulin aspart)	**$27.56**	**$275.60**
Fiasp® FlexTouch® (insulin aspart)	**$35.48**	**$532.20**
NovoLog® vial (insulin aspart)	$26.48	$264.80
NovoLog® FlexPen® (insulin aspart)	$34.10	$511.50

Costs do not reflect rebated prices or net costs.
^Vial package size = 10mL, FlexTouch® package size = 15mL, and FlexPen® package size = 15mL
*Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Ozempic® (Semaglutide) Product Summary[35]

Indication(s): Ozempic® (semaglutide) is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM.

- Limitations of Use:
  - Ozempic® is not recommended as first-line therapy for patients inadequately controlled on diet and exercise.
  - Ozempic® has not been studied in patients with a history of pancreatitis.
  - Ozempic® is not indicated for use in type 1 DM or for the treatment of DKA.

Boxed Warning: Risk of Thyroid C-Cell Tumors

- In rodents, semaglutide caused thyroid C-cell tumors. It is unknown whether Ozempic® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. Ozempic® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

Dosing:

- Ozempic® is supplied as an injection containing 2mg of semaglutide in a 1.5mL pre-filled, single-patient-use pen injector packaged in a carton containing either one or two pens.
  - Carton of 1 Pen: Pen delivers dose of 0.25mg or 0.5mg per injection and is intended for treatment initiation at the 0.25mg dose and maintenance treatment at the 0.5mg dose.
  - Carton of 2 Pens: Pen delivers dose of 1mg per injection and is intended for the maintenance treatment at the 1mg dose only.
- The recommended starting dose is 0.25mg via SQ injection once weekly, with or without meals, for four weeks.
  - The 0.25mg dose is intended for treatment initiation and is not effective for glycemic control. After four weeks on the 0.25mg dose, the dose should be increased to 0.5mg once weekly. If additional glycemic control is needed after at least four weeks on the 0.5mg dose, the dose may be increased to the maximum dose of 1mg once weekly.
  - Ozempic® should be administered once weekly, on the same day each week, at any time of the day. The day of weekly administration can be changed if necessary as long as the time between two doses is at least two days (>48 hours).

Efficacy: Ozempic® has been studied as monotherapy and in combination with metformin, metformin and sulfonylureas, metformin and/or thiazolidinediones (TZD), and basal insulin in patients with type 2 DM. The efficacy of Ozempic® was compared with placebo, sitagliptin, exenatide ER, and insulin glargine. Most trials evaluated the use of Ozempic® 0.5mg and 1mg, with the exception of the trial comparing Ozempic® and exenatide ER, where only the 1mg dose was studied. Results of the trials showed statistically significant reduction in HbA_{1c} with Ozempic® compared to placebo, sitagliptin, exenatide ER, and insulin glargine. A CV outcome study, including 3,297 patients with type 2 DM with high risk of CV events was done to compare Ozempic® to placebo, in addition to standard-of-care. The primary composite endpoint was the time from randomization to first occurrence of a major adverse cardiovascular event (MACE): CV death, non-fatal MI, or non-fatal CVA. The total number of primary composite MACE endpoints was 108 (6.6%) in Ozempic® group compared to 146 (8.9%) in placebo group. There was no increased risk for MACE observed with Ozempic®.

Cost:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Ozempic® (semaglutide) 0.25mg/0.2mL	**$450.67**	**$676.01**	**$8,112.12**
Ozempic® (semaglutide) 1mg/0.75mL	**$225.33**	**$675.99**	**$8,111.88**
Bydureon® (exenatide ER) 2mg/0.65mL	$158.46	$633.84	$7,606.08
Victoza® (liraglutide) 18mg/3mL	$86.11	$258.33	$3,099.96

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.

Steglatro™ (Ertugliflozin) Product Summary[36]

Indication(s): Steglatro™ (ertugliflozin) is an SGLT-2 inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM.

- Limitations of Use: Steglatro™ is not indicated for the treatment of type 1 DM or DKA.

Dosing:

- Steglatro™ is supplied as an oral tablet in two strengths: 5mg and 15mg.
- The recommended starting dose is 5mg once daily, taken in the morning, with or without food. The dose should be increased to the maximum recommended dose of 15mg once daily in those tolerating Steglatro™ and needing additional glycemic control.
- Renal function should be assessed before initiation of Steglatro™ and periodically thereafter.
    - Steglatro™ should not be used in patients with an eGFR <30mL/min/1.73m^2.
    - Initiation of Steglatro™ is not recommended in patients with an eGFR of 30 to <60mL/min/1.73m^2. Continued use is not recommended in patients with an eGFR persistently between 30 to <60mL/min/1.73m^2.

Efficacy: The efficacy and safety of Steglatro™ was studied in seven multicenter, randomized, double-blind, placebo- or active-comparator (glimepiride) controlled studies involving 4,863 patients with type 2 DM. Steglatro™ was studied as monotherapy and in combination with metformin and/or a dipeptidyl peptidase-4 (DPP-4) inhibitor (sitagliptin). In patients with type 2

DM, Steglatro™ reduced HbA_{1c} compared to placebo; however, in patients with type 2 DM and moderate renal impairment, treatment with Steglatro™ did not result in reduction in HbA_{1c} compared to placebo.

Cost:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Steglatro™ (ertugliflozin) both strengths	**$8.94**	**$268.20**	**$3,218.40**
Farxiga® (dapagliflozin) 10mg	$14.87	$446.10	$5,353.20
Jardiance® (empagliflozin) 25mg	$14.94	$448.20	$5,378.40

Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Segluromet™ (Ertugliflozin/Metformin) Product Summary[37]

Indication(s): Segluromet™ (ertugliflozin/metformin) is a combination product containing an SGLT-2 inhibitor (ertugliflozin) and a biguanide (metformin) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin.

- Limitations of Use: Segluromet™ is not indicated for the treatment of type 1 DM or DKA.

Boxed Warning: Lactic Acidosis

- Post-marketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. Symptoms included malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Laboratory abnormalities included elevated blood lactate levels, anion gap acidosis, increased lactate/pyruvate ratio, and metformin plasma levels generally >5mcg/mL. Risk factors include renal impairment, concomitant use of certain drugs, 65 years of age or older, radiological studies with contrast, surgery and other procedures, hypoxic states, excessive alcohol intake, and hepatic impairment. If lactic acidosis is suspected, Segluromet™ should be discontinued and general supportive measures should be instituted in a hospital setting.

Dosing:

- Segluromet™ is supplied as an oral tablet in four strengths (ertugliflozin/metformin): 2.5mg/500mg, 2.5mg/1,000mg, 7.5mg/500mg, and 7.5mg/1,000mg.
- The maximum recommended dose is 7.5mg ertugliflozin/1,000mg metformin twice daily with meals.
- Renal function should be assessed before initiation of Segluromet™ and periodically thereafter.
  - Segluromet™ should not be used in patients with an eGFR <30mL/min/1.73m^2.
  - Initiation of Segluromet™ is not recommended in patients with an eGFR of 30 to <60mL/min/1.73m^2. Continued use is not recommended in patients with an eGFR persistently between 30 to <60mL/min/1.73m^2.
  - Segluromet™ may need to be discontinued at time of, or prior to, iodinated contrast imaging procedures.

Efficacy: The efficacy and safety of Segluromet™ was studied in four multicenter, randomized, double-blind, placebo- and active comparator-controlled clinical studies involving 3,643 patients with type 2 DM. When ertugliflozin 5mg and 15mg were studied with glimepiride (mean dose of 3mg) as the active comparator as a add on to metformin (≥1,500mg/day), ertugliflozin 15mg was found to be non-inferior to glimepiride after 52 weeks of treatment. In patients with type 2 DM, treatment with Segluromet™ resulted in a statistically significant reduction in HbA_{1c} compared to placebo.

Cost:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Segluromet™ (ertugliflozin/metformin) all strengths	**$4.47**	**$268.20**	**$3,218.40**
Invokamet® (canagliflozin/metformin) 150mg/1,000mg	$7.41	$444.60	$5,335.20

Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Steglujan™ (Ertugliflozin/Sitagliptin) Product Summary[38]

Indication(s): Steglujan™ (ertugliflozin/sitagliptin) is a combination product containing an SGLT-2 inhibitor (ertugliflozin) and a DPP-4 inhibitor (sitagliptin) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM when treatment with both ertugliflozin and sitagliptin is appropriate.

- Limitations of Use:
  - Steglujan™ is not indicated for the treatment of type 1 DM or DKA.
  - Steglujan™ has not been studied in patients with a history of pancreatitis.

Dosing:

- Steglujan™ is supplied as an oral tablet in two strengths (ertugliflozin/sitagliptin): 5mg/100mg and 15mg/100mg.
- The recommended starting dose is 5mg ertugliflozin/100mg sitagliptin once daily, taken in the morning, with or without food. The dose should be increased to 15mg ertugliflozin/100mg sitagliptin in those tolerating Steglujan™ 5mg/100mg and needing additional glycemic control.
- Renal function should be assessed before initiation of Steglujan™ and periodically thereafter.
  - Steglujan™ should not be used in patients with an eGFR <30mL/min/1.73m^2.
  - Initiation of Steglujan™ is not recommended in patients with an eGFR of 30 to <60mL/min/1.73m^2. Continued use is not recommended in patients with an eGFR persistently between 30 to <60mL/min/1.73m^2.

Efficacy: The efficacy and safety of Steglujan™ was studied in three multicenter, randomized, double-blind, placebo- and active comparator-controlled clinical trials involving 1,985 patients with type 2 DM. In patients with type 2 DM, Steglujan™ reduced HbA_{1c} compared to placebo or active comparator.

Cost:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Steglujan™ (ertugliflozin/sitagliptin) both strengths	**$17.45**	**$523.50**	**$6,282.00**
Glyxambi® (empagliflozin/linagliptin) both strengths	$17.45	$523.50	$6,282.00

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 Admelog® (insulin lispro), Humulin® R (insulin human 500 units/mL) U-500 vials, and Fiasp® (Insulin Aspart) with the following criteria:

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.

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

1. 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.

Fiasp® (Insulin Aspart) Approval Criteria:

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

The College of Pharmacy also recommends the following changes to the diabetes medications Product Based Prior Authorization (PBPA) criteria based on net costs after rebates:

1. Add Bydureon® BCise™ (exenatide ER) into the Special Prior Authorization (PA) tier.
    a. Authorization of Bydureon® BCise™ will require tier trials be met and a patient-specific, clinically significant reason why the member cannot use the vial or pen formulations must be provided. Current Special PA criteria will apply.
2. Place Ozempic® (semaglutide), Steglatro™ (ertugliflozin), Segluromet™ (ertugliflozin/metformin), and Steglujan™ (ertugliflozin/sitagliptin) into Tier-3. Current Tier-3 criteria will apply.
3. Add a patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with an alternative GLP-1 receptor agonist to the Soliqua® (insulin glargine/lixisenatide) criteria.
4. Add a patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with Victoza® (liraglutide) to the Xultophy® (insulin degludec/ liraglutide) criteria.

5. Add a patient-specific, clinically significant reason why the member cannot take the immediate-release formulation to the Invokamet® XR (canagliflozin/metformin ER) and Jentadueto® XR (linagliptin/metformin ER) criteria.

The recommended changes are shown in red in the following criteria and tier chart.

Diabetes Medications Special Prior Authorization (PA) Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least three 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); or
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.

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 GLP-1 receptor agonist must be provided.
3. Current Tier-3 criteria will apply.

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) or Levemir® (insulin detemir) with Victoza® (liraglutide) must be provided.
3. Current Tier-3 criteria will apply.

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors acarbose (Precose®)	**DPP-4 Inhibitors** saxagliptin (Onglyza®) saxagliptin/metformin (Kombiglyze®) sitagliptin (Januvia®) sitagliptin/metformin (Janumet®) sitagliptin/metformin ER (Janumet XR®)	**Alpha-Glucosidase Inhibitors** miglitol (Glyset®)	**Amylinomimetics** pramlintide (Symlin®)
Biguanides metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®)	**Glinides** nateglinide (Starlix®) repaglinide/metformin (Prandimet®)	**Dopamine Agonists** bromocriptine (Cycloset®)	**Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®)
Glinides repaglinide (Prandin®)		**DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto®)	**DPP-4 Inhibitors** linagliptin/metformin ER (Jentadueto® XR)
			GLP-1 Agonists **exenatide ER (Bydureon® BCise™)**

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Sulfonylureas chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide micronized (Micronase®) Tolbutamide (Orinase®) **Thiazolidinediones** pioglitazone (Actos®)	**GLP-1 Agonists** exenatide (Byetta®) exenatide ER (Bydureon® pen and vial) liraglutide (Victoza®) **SGLT-2 Inhibitors** dapagliflozin (Farxiga®) dapagliflozin/metformin ER (Xigduo® XR) empagliflozin (Jardiance®) empagliflozin/metformin (Synjardy®) empagliflozin/metformin ER (Synjardy® XR)	**GLP-1 Agonists** albiglutide (Tanzeum®) dulaglutide (Trulicity®) lixisenatide (Adlyxin™) **semaglutide (Ozempic®)** **GLP-1 Agonists/Insulin** insulin degludec/ liraglutide (Xultophy® 100/3.6) insulin glargine/ lixisenatide (Soliqua™ 100/33) **SGLT-2 Inhibitors** canagliflozin (Invokana®) canagliflozin/metformin (Invokamet®) **ertugliflozin (Steglatro™)** **ertugliflozin/metformin (Segluromet™)** **SGLT-2/DPP-4 Inhibitors** dapagliflozin/saxagliptin (Qtern®) empagliflozin/linagliptin (Glyxambi®) **ertugliflozin/sitagliptin (Steglujan™)** **Thiazolidinediones** pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®)	**SGLT-2 Inhibitors** canagliflozin/metformin ER (Invokamet® XR)

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

SR = sustained-release, ER = extended-release, DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT-2 = sodium-glucose cotransporter-2

Utilization Details of Non-Insulin Diabetes Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
ALPHA-GLUCOSIDASE INHIBITOR PRODUCTS						
ACARBOSE TAB 25MG	100	26	$2,489.82	2.85	3.85	$24.90
ACARBOSE TAB 50MG	32	8	$968.48	3.22	4	$30.27
ACARBOSE TAB 100MG	18	3	$589.52	3	6	$32.75
GLYSET TAB 100MG	5	2	$1,380.39	3	2.5	$276.08
SUBTOTAL	**155**	**37**	**$5,428.21**	**2.95**	**4.19**	**$35.02**
AMYLINOMIMETIC PRODUCTS						
SYMLINPEN 60 INJ 1000MCG	1	1	$790.73	0.1	1	$790.73
SUBTOTAL	**1**	**1**	**$790.73**	**0.1**	**1**	**$790.73**
BIGUANIDE PRODUCTS						
METFORMIN TAB 500MG	20,872	5,818	$179,675.20	2.04	3.59	$8.61
METFORMIN TAB 1000MG	17,047	4,121	$143,715.69	1.96	4.14	$8.43
METFORMIN TAB 500MG ER	5,062	1,541	$48,614.49	2.17	3.28	$9.60
METFORMIN TAB 850MG	1,301	345	$11,513.63	2.01	3.77	$8.85
METFORMIN TAB 750MG ER	711	212	$9,903.37	1.58	3.35	$13.93
RIOMET SOL 500MG/5ML	25	4	$11,463.58	13.72	6.25	$458.54
METFORMIN ER TAB 1000MG	6	2	$3,351.98	2	3	$558.66
METFORMIN TAB 500MG ER	1	1	$5,343.41	4	1	$5,343.41
SUBTOTAL	**45,025**	**10,843**	**$413,581.35**	**2.02**	**4.15**	**$9.19**
DPP-4 INHIBITOR PRODUCTS						
JANUVIA TAB 100MG	3,335	762	$1,864,683.00	1.01	4.38	$559.13
TRADJENTA TAB 5MG	1,303	232	$484,520.79	1	5.62	$371.85
JANUVIA TAB 50MG	899	219	$531,737.27	1.16	4.11	$591.48
ONGLYZA TAB 5MG	200	53	$121,058.87	1.05	3.77	$605.29
JANUVIA TAB 25MG	165	42	$77,763.04	1.05	3.93	$471.29
ALOGLIPTIN TAB 25MG	24	9	$5,496.07	1	2.67	$229.00
NESINA TAB 25MG	20	3	$9,454.54	1	6.67	$472.73
ONGLYZA TAB 2.5MG	15	8	$13,741.33	1	1.88	$916.09
SUBTOTAL	**5,961**	**1,245**	**$3,108,454.91**	**1.03**	**4.79**	**$521.47**
DPP-4 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
JANUMET TAB 50-1000MG	1,176	208	$448,963.56	1.94	5.65	$381.77
JANUMET XR TAB 50-1000MG	368	72	$124,467.21	1.78	5.11	$338.23
JANUMET XR TAB 100-1000MG	323	54	$122,592.22	1	5.98	$379.54
JANUMET TAB 50-500MG	192	36	$73,234.81	1.96	5.33	$381.43
JENTADUETO TAB 2.5-1000MG	83	18	$38,398.58	2	4.61	$462.63
KOMBIGLYZ XR TAB 2.5-1000MG	50	9	$19,105.76	2	5.56	$382.12
KOMBIGLYZ XR TAB 5-1000MG	38	6	$18,325.57	1	6.33	$482.25
JANUMET XR TAB 50-500MG	23	6	$4,701.50	1.04	3.83	$204.41
KOMBIGLYZ XR TAB 5-500MG	12	2	$4,472.32	1	6	$372.69
JENTADUETO TAB 2.5-500MG	9	4	$6,293.41	2	2.25	$699.27
JENTADUETO TAB 2.5-850MG	5	2	$3,708.68	1.54	2.5	$741.74

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
ALOGLIPTIN/METFORM 12.5-1000MG	2	1	$407.07	2	2	$203.54
SUBTOTAL	**2,281**	**391**	**$864,670.69**	**1.76**	**5.83**	**$379.08**
DPP-4 INHIBITOR/TZD COMBINATION PRODUCTS						
ALOG/PIOGLIT TAB 25-30MG	6	2	$2,656.12	1	3	$442.69
OSENI TAB 25-30MG	4	1	$4,344.42	1	4	$1,086.11
SUBTOTAL	**10**	**3**	**$7,000.54**	**1**	**3.33**	**$700.05**
GLINIDE PRODUCTS						
REPAGLINIDE TAB 1MG	49	10	$1,315.33	2.5	4.9	$26.84
NATEGLINIDE TAB 120MG	41	12	$2,515.22	3.1	3.42	$61.35
NATEGLINIDE TAB 60MG	22	6	$1,383.34	3	3.67	$62.88
REPAGLINIDE TAB 2MG	14	5	$579.26	4.3	2.8	$41.38
REPAGLINIDE TAB 0.5MG	5	3	$139.64	2.6	1.67	$27.93
SUBTOTAL	**131**	**33**	**$5,932.79**	**2.99**	**3.97**	**$45.29**
GLP-1 AGONIST PRODUCTS						
VICTOZA INJ 18MG/3ML	3,158	684	$2,155,831.14	0.26	4.62	$682.66
TRULICITY INJ 1.5MG/0.5ML	421	74	$267,089.22	0.07	5.69	$634.42
BYDUREON PEN INJ 2MG	351	65	$212,211.84	0.14	5.4	$604.59
TRULICITY INJ 0.75MG/0.5ML	122	37	$79,121.28	0.07	3.3	$648.54
BYDUREON INJ 2MG	85	22	$50,983.51	0.14	3.86	$599.81
BYETTA INJ 10MCG	66	21	$50,505.32	0.08	3.14	$765.23
TANZEUM INJ 50MG	58	9	$28,908.27	0.14	6.44	$498.42
BYETTA INJ 5MCG	34	17	$21,977.56	0.04	2	$646.40
TANZEUM INJ 30MG	18	6	$8,644.18	0.14	3	$480.23
SUBTOTAL	**4,313**	**871**	**$2,875,272.32**	**0.22**	**4.95**	**$666.65**
GLP-1 AGONIST/INSULIN COMBINATION PRODUCTS						
XULTOPHY INJ 100U/ML/3.6MG/ML	9	5	$8,654.07	0.34	1.8	$961.56
SOLIQUA INJ 100U/ML/33MCG/ML	5	1	$3,083.15	0.3	5	$616.63
SUBTOTAL	**14**	**6**	**$11,737.22**	**0.33**	**2.33**	**$838.37**
SGLT-2 INHIBITOR PRODUCTS						
INVOKANA TAB 300MG	682	142	$280,920.69	1	4.8	$411.91
INVOKANA TAB 100MG	467	143	$193,359.87	1	3.27	$414.05
JARDIANCE TAB 25MG	421	84	$173,014.14	1	5.01	$410.96
JARDIANCE TAB 10MG	274	60	$115,090.58	1	4.57	$420.04
FARXIGA TAB 10MG	150	25	$62,402.55	1	6	$416.02
FARXIGA TAB 5MG	34	7	$14,182.85	1	4.86	$417.14
SUBTOTAL	**2,028**	**407**	**$838,970.68**	**1**	**4.98**	**$413.69**
SGLT-2 INHIBITOR/BIGUANIDE COMBINATION PRODUCTS						
INVOKAMET TAB 150-1000MG	79	18	$32,540.52	1.97	4.39	$411.91
SYNJARDY 12.5-1000MG	54	11	$22,777.22	2	4.91	$421.80
XIGDUO XR TAB 10-1000MG	39	7	$16,210.43	1	5.57	$415.65
INVOKAMET TAB 50-1000MG	39	11	$16,128.27	2	3.55	$413.55
XIGDUO XR TAB 5-1000MG	19	4	$7,986.64	2	4.75	$420.35
INVOKAMET XR TAB 150-1000MG	9	3	$3,369.03	1.78	3	$374.34

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
INVOKAMET TAB 150-500MG	8	2	$3,300.78	2	4	$412.60
SYNJARDY TAB 5-1000MG	5	1	$2,101.55	2	5	$420.31
SYNJARDY TAB 5-500MG	3	1	$1,228.37	2	3	$409.46
INVOKAMET TAB 50-500MG	3	2	$1,212.09	2	1.5	$404.03
SUBTOTAL	**258**	**55**	**$106,854.90**	**1.83**	**4.69**	**$414.17**
SULFONYLUREA PRODUCTS						
GLYBURIDE TAB 5MG	2,836	710	$44,995.81	2.17	3.99	$15.87
GLIPIZIDE TAB 5MG	2,625	758	$23,163.72	1.5	3.46	$8.82
GLIPIZIDE TAB 10MG	2,521	634	$21,822.03	1.86	3.98	$8.66
GLIMEPIRIDE TAB 4MG	1,449	369	$18,245.30	1.43	3.93	$12.59
GLIMEPIRIDE TAB 2MG	1,034	291	$11,537.87	1.31	3.55	$11.16
GLYBURIDE TAB 2.5MG	786	369	$10,122.51	1.37	2.13	$12.88
GLIPIZIDE ER TAB 10MG	531	180	$11,837.28	1.25	2.95	$22.29
GLIPIZIDE ER TAB 5MG	528	186	$8,103.93	1.23	2.84	$15.35
GLIMEPIRIDE TAB 1MG	481	128	$5,132.84	1.19	3.76	$10.67
GLIPIZIDE ER TAB 2.5MG	287	95	$5,237.58	1.15	3.02	$18.25
GLIPIZIDE XL TAB 10MG	244	102	$5,323.54	1.36	2.39	$21.82
GLIPIZIDE XL TAB 5MG	197	102	$3,209.03	1.34	1.93	$16.29
GLYBURIDE TAB 1.25MG	96	43	$1,390.26	1.4	2.23	$14.48
GLIPIZIDE XL TAB 2.5MG	53	32	$942.05	1.11	1.66	$17.77
GLYBURID MCR TAB 6MG	48	8	$523.90	1.84	6	$10.91
GLYBURID MCR TAB 3MG	39	12	$365.82	1.33	3.25	$9.38
GLYBURID MCR TAB 1.5MG	4	2	$58.72	2	2	$14.68
CHLORPROPAM TAB 100MG	1	1	$31.61	1	1	$31.61
GLIPIZIDE XL TAB 5MG	1	1	$19.62	1	1	$19.62
SUBTOTAL	**13,761**	**3,507**	**$172,063.42**	**1.6**	**3.92**	**$12.50**
SULFONYLUREA/BIGUANIDE COMBINATION PRODUCTS						
GLYB/METFORM TAB 5-500MG	402	65	$5,256.79	3.14	6.18	$13.08
GLIP/METFORM TAB 5-500MG	155	33	$5,539.00	2.2	4.7	$35.74
GLIP/METFORM TAB 2.5-500MG	95	19	$4,350.50	2.66	5	$45.79
GLYB/METFORM TAB 2.5-500MG	87	23	$1,098.64	2.53	3.78	$12.63
GLIP/METFORM TAB 2.5-250MG	10	3	$274.77	1.5	3.33	$27.48
GLYB/METFORM TAB 1.25-250MG	1	1	$10.11	2	1	$10.11
SUBTOTAL	**750**	**139**	**$16,529.81**	**2.78**	**5.4**	**$22.04**
SGLT-2 INHIBITOR/DPP-4 INHIBITOR COMBINATION PRODUCTS						
GLYXAMBI TAB 25-5MG	94	16	$46,265.69	1	5.88	$492.19
GLYXAMBI TAB 10-5MG	16	4	$8,118.30	1	4	$507.39
SUBTOTAL	**110**	**20**	**$54,383.99**	**1**	**5.5**	**$494.40**
TZD PRODUCTS						
PIOGLITAZONE TAB 30MG	912	234	$13,864.42	0.99	3.9	$15.20
PIOGLITAZONE TAB 15MG	653	195	$8,948.57	1.07	3.35	$13.70
PIOGLITAZONE TAB 45MG	415	117	$6,546.84	1	3.55	$15.78
AVANDIA TAB 4MG	5	3	$970.24	1.2	1.67	$194.05

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
SUBTOTAL	**1,985**	**494**	**$30,330.07**	**1.02**	**4.02**	**$15.28**
TZD/BIGUANIDE COMBINATION PRODUCTS						
PIOGLITA/MET TAB 15-850MG	37	6	$3,548.08	1.76	6.17	$95.89
PIOGLITA/MET TAB 15-500MG	14	3	$1,256.97	2	4.67	$89.78
ACTOPLUS MET TAB XR 15-1000MG	5	1	$3,113.02	2	5	$622.60
SUBTOTAL	**56**	**10**	**$7,918.07**	**1.83**	**5.6**	**$141.39**
TZD/SULFONYLUREA COMBINATION PRODUCTS						
PIOGLIT/GLIM TAB 30-4MG	3	1	$866.97	1	3	$288.99
SUBTOTAL	**3**	**1**	**$866.97**	**1**	**3**	**$288.99**
TOTAL	**76,842**	**13,370***	**$8,520,786.67**	**1.7**	**5.75**	**$110.89**

*Total number of unduplicated members.
Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.
ER = extended-release, DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT-2 = sodium-glucose cotransporter-2, XL = extended-release, XR = extended-release, TZD = thiazolidinedione

Utilization Details of Insulin Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
INSULIN ASPART PRODUCTS						
NOVOLOG INJ FLEXPEN 100U/ML	7,461	2,018	$4,952,096.34	0.56	3.7	$663.73
NOVOLOG INJ 100U/ML	4,829	1,038	$2,365,561.56	0.67	4.65	$489.87
NOVOLOG INJ PENFILL 100U/ML	611	133	$308,573.58	0.48	4.59	$505.03
SUBTOTAL	**12,901**	**2,961**	**$7,626,231.48**	**0.59**	**4.36**	**$591.13**
INSULIN ASPART/NPH COMBINATION PRODUCTS						
NOVOLOG MIX INJ FLEXPEN 70/30	707	200	$633,669.61	0.74	3.54	$896.28
NOVOLOG MIX INJ 70/30	217	58	$167,601.22	0.86	3.74	$772.36
SUBTOTAL	**924**	**249**	**$801,270.83**	**0.77**	**3.71**	**$867.18**
INSULIN DEGLUDEC PRODUCTS						
TRESIBA FLEX INJ 200U/ML	420	100	$349,256.01	0.42	4.2	$831.56
TRESIBA FLEX INJ 100U/ML	183	58	$86,558.43	0.42	3.16	$473.00
SUBTOTAL	**603**	**154**	**$435,814.44**	**0.42**	**3.92**	**$722.74**
INSULIN DETEMIR PRODUCTS						
LEVEMIR INJ FLEXTOUCH 100U/ML	6,690	1,799	$3,566,460.80	0.49	3.72	$533.10
LEVEMIR INJ 100U/ML	2,729	644	$1,222,768.39	0.53	4.24	$448.06
SUBTOTAL	**9,419**	**2,330**	**$4,789,229.19**	**0.5**	**4.04**	**$508.46**
INSULIN GLARGINE PRODUCTS						
LANTUS INJ SOLOSTAR 100U/ML	11,522	3,041	$5,607,961.44	0.46	3.79	$486.72
LANTUS INJ 100U/ML	6,453	1,336	$2,825,115.68	0.57	4.83	$437.80
TOUJEO SOLO INJ 300U/ML	601	112	$413,153.71	0.31	5.37	$687.44
BASAGLAR INJ 100U/ML	3	2	$264.23	0.44	1.5	$88.08
LANTUS INJ SOLOSTAR 100U/ML	1	1	$522.66	1	1	$522.66
SUBTOTAL	**18,580**	**4,183**	**$8,847,017.72**	**0.49**	**4.44**	**$476.16**
INSULIN GLULISINE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
APIDRA INJ SOLOSTAR U-100	357	91	$236,845.82	0.57	3.92	$663.43
APIDRA INJ U-100	178	39	$67,034.98	0.5	4.56	$376.60
SUBTOTAL	**535**	**126**	**$303,880.80**	**0.55**	**4.25**	**$568.00**
INSULIN LISPRO PRODUCTS						
HUMALOG KWIK INJ 100/ML	4,025	1,133	$2,706,389.31	0.55	3.55	$672.39
HUMALOG INJ 100U/ML	3,190	725	$1,647,174.54	0.7	4.4	$516.36
HUMALOG INJ 100U/ML	409	87	$198,131.61	0.51	4.7	$484.43
HUMALOG KWIK INJ 200U/ML	27	6	$58,523.32	1.43	4.5	$2,167.53
HUMALOG JR INJ 100U/ML	16	11	$10,246.40	0.47	1.45	$640.40
SUBTOTAL	**7,667**	**1,805**	**$4,620,465.18**	**0.6**	**4.25**	**$602.64**
INSULIN LISPRO/NPH COMBINATION PRODUCTS						
HUMALOG MIX INJ 75/25KWP	202	51	$195,531.33	0.81	3.96	$967.98
HUMALOG MIX SUS 75/25	100	22	$64,739.25	0.7	4.55	$647.39
HUMALOG MIX INJ 50/50KWP	57	17	$51,896.67	0.93	3.35	$910.47
HUMALOG MIX INJ 50/50	20	4	$23,191.23	1.36	5	$1,159.56
SUBTOTAL	**379**	**94**	**$335,358.48**	**0.82**	**4.03**	**$884.85**
NPH (N) INSULIN PRODUCTS						
HUMULIN N INJ U-100	546	189	$143,475.00	0.54	2.89	$262.77
NOVOLIN N INJ U-100	367	110	$80,171.79	0.49	3.34	$218.45
NOVOLIN N INJ RELION U-100	323	115	$16,598.18	0.53	2.81	$51.39
HUMULIN N INJ U-100KWP	279	142	$152,045.09	0.43	1.96	$544.96
SUBTOTAL	**1,515**	**506**	**$392,290.06**	**0.5**	**2.99**	**$258.94**
REGULAR (R) INSULIN PRODUCTS						
HUMULIN R INJ U-100	1,080	290	$243,950.70	0.55	3.72	$225.88
NOVOLIN R INJ U-100	615	169	$130,612.99	0.55	3.64	$212.38
NOVOLIN R INJ RELION U-100	269	92	$13,824.43	0.49	2.92	$51.39
HUMULIN R INJ U-500	139	30	$217,252.91	0.59	4.63	$1,562.97
HUMULIN R INJ U-500	60	21	$101,117.08	0.67	2.86	$1,685.28
SUBTOTAL	**2,163**	**560**	**$706,758.11**	**0.55**	**3.86**	**$326.75**
R/N INSULIN COMBINATION PRODUCTS						
HUMULIN INJ 70/30	536	111	$190,265.84	0.79	4.83	$354.97
NOVOLIN INJ 70/30	289	95	$97,380.31	0.71	3.04	$336.96
HUMULIN INJ 70/30KWP	262	56	$162,656.09	0.62	4.68	$620.82
NOVOLIN 70/30 INJ RELION	202	57	$14,448.24	0.79	3.54	$71.53
SUBTOTAL	**1,289**	**293**	**$464,750.48**	**0.41**	**4.4**	**$360.55**
TOTAL	**55,977**	**7,801***	**$29,324,571.85**	**0.54**	**7.18**	**$523.87**

*Total number of unduplicated members.

Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

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Appendix K

Calendar Year 2017 Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension)

Oklahoma Health Care Authority
April 2018

Current Prior Authorization Criteria

There are seven 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 two 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 two 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 six months and at least four 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.
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 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. Authorization requires a patient-specific, clinically significant reason why the member cannot use two 180mg Cardizem® CD (diltiazem CD) capsules.

Catapres TTS® Patch (Clonidine Transdermal Patch) Approval Criteria:

1. An FDA approved indication for the treatment of hypertension in adults; and
2. A patient-specific, clinically significant reason why the member cannot take oral clonidine immediate-release tablets.

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.

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

1. Authorization requires a patient-specific, clinically significant reason why the member cannot use the individual components.

Prestalia® (Perindopril/Amlodipine) Approval Criteria:

1. An FDA approved diagnosis; and
2. Documented trials of inadequate response to two 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; and
4. A quantity limit of 30 tablets per 30 days will apply.

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.

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; and
3. A quantity limit of 64mL per day or 1,920mL per 30 days will apply.

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 six 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 four-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®)		enalapril oral solution (Epaned®)
captopril (Capoten®)		lisinopril oral solution (Qbrelis®)
enalapril (Vasotec®)		
enalaprilat (Vasotec® IV)		
fosinopril (Monopril®)		
lisinopril (Prinivil®, Zestril®)		
moexipril (Univasc®)		
perindopril erbumine (Aceon®)		
quinapril (Accupril®)		
ramipril (Altace®)		
trandolapril (Mavik®)		

IV = intravenous

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

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

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)
valsartan (Diovan®)	olmesartan/amlodipine/HCTZ (Tribenzor®)	eprosartan (Teveten®)
valsartan/HCTZ (Diovan HCT®)	telmisartan (Micardis®)	eprosartan/HCTZ (Teveten® HCT)
	valsartan/amlodipine (Exforge®)	telmisartan/amlodipine (Twynsta®)
		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)	
diltiazem (Tiazac®, Taztia XT®)	isradipine (Dynacirc®, Dynacirc CR®)	
diltiazem CD (Cardizem® CD)*	nicardipine (Cardene® SR)	
diltiazem ER (Cartia XT®, Diltia XT®)	nisoldipine (Sular®)	
diltiazem SR (Cardizem® SR)	verapamil (Covera-HS®)	
diltiazem XR (Dilacor® XR)	verapamil ER (Verelan® PM)	
felodipine (Plendil®)		
nicardipine (Cardene®)		
nifedipine (Adalat®, Procardia®)		
nifedipine ER (Adalat® CC)		

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
nifedipine ER		
nifedipine XL (Nifedical XL®, Procardia XL®)		
nimodipine (Nimotop®)		
verapamil (Calan®, Isoptin®, Verelan®)		
verapamil SR (Calan® SR, Isoptin® SR)		

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

Utilization of Antihypertensive Medications: Calendar Year 2017

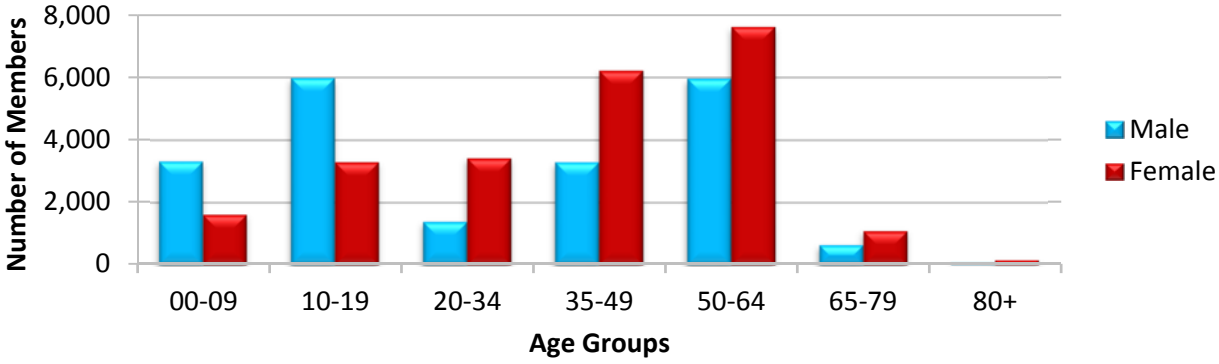
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	43,068	223,155	$2,053,922.57	$9.20	$0.24	10,813,916	8,705,138
2017	43,968	225,852	$3,092,989.63	$13.69	$0.34	11,125,516	9,002,579
% Change	**2.10%**	**1.20%**	**50.60%**	**48.80%**	**41.70%**	**2.90%**	**3.40%**
Change	**900**	**2,697**	**$1,039,067.06**	**$4.49**	**$0.10**	**311,600**	**297,441**

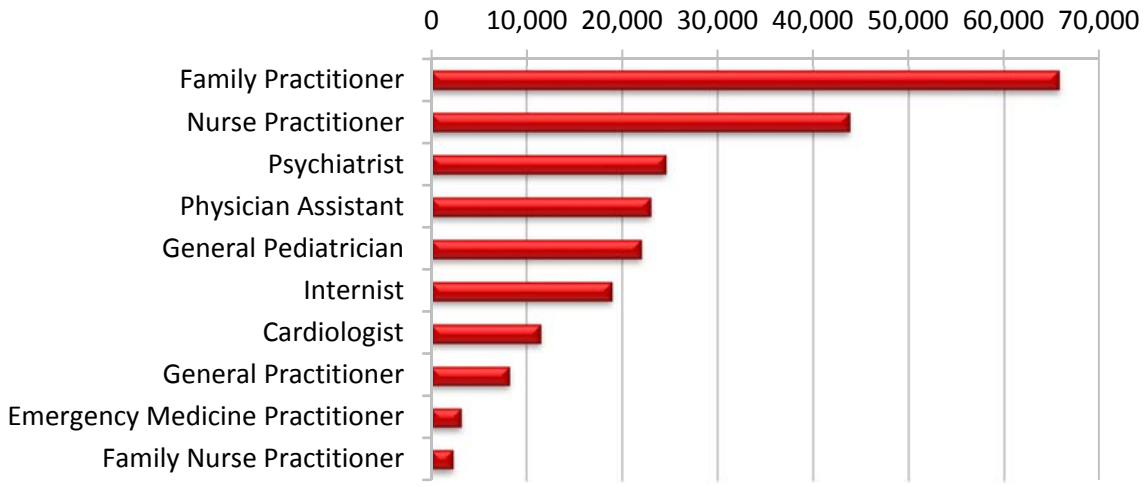
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Please note, due to new federal regulations, a new pricing methodology for pharmacy claims reimbursement was implemented by SoonerCare 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 effective 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.

Demographics of Members Utilizing Antihypertensive Medications



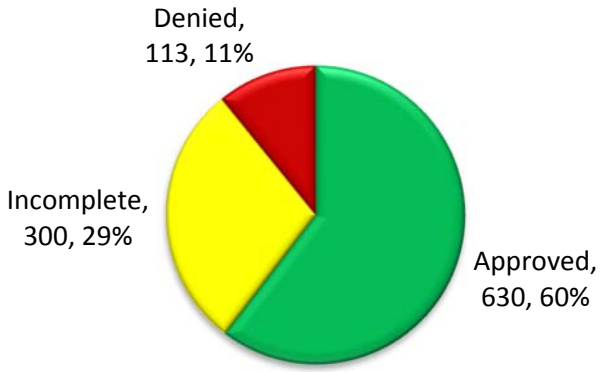
Top Prescriber Specialties of Antihypertensive Medications by Number of Claims



Prior Authorization of Antihypertensive Medications

There were 1,043 prior authorization requests submitted for antihypertensive medications during calendar year 2017. 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 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Tekturna® (aliskiren tablets): August 2026
- Byvalson™ (nebivolol/valsartan tablets): October 2027
- Edarbi® (azilsartan tablets): March 2028
- Tekturna HCT® (aliskiren/hydrochlorothiazide tablets): July 2028
- Hemangeol™ (propranolol hydrochloride oral solution): October 2028
- Prestalia® (perindopril arginine/amlodipine tablets): October 2029
- Edarbyclor® (azilsartan/chlorthalidone tablets): February 2030
- Qbrelis® (lisinopril oral solution): November 2035
- Epaned® (enalapril oral solution): March 2036

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

- CaroSpir® (spironolactone oral suspension): August 2017
- Tekturna® (aliskiren oral pellets): November 2017
- Prexxartan® (valsartan oral solution): December 2017

Guideline Update(s):

- **August 2017:** The American Academy of Pediatrics (AAP) issued updated clinical practice guidelines for the diagnosis and management of high blood pressure (BP) in children. The update replaces the 2004 pediatric hypertension (HTN) guidelines. Key points of the updated guidelines include new normative BP tables, revised screening protocols, and recommendations for initiating antihypertensive medication. The updated BP tables are based on normal-weight children only, which replaces previous tables, which included BP measurements in overweight and obese children and adolescents. According to Dr. Kaelber, MD, PhD, from the department of pediatrics at Case Western Reserve University School of Medicine and MetroHealth System, additional important points include:
    - Initiating antihypertensive medication when lifestyle changes alone do not sufficiently lower BP
    - A change in the term "prehypertension" to "elevated blood pressure"
    - For children 13 years of age and older, the table is designed to align with cut-offs from adult abnormal BP developed by the American Heart Association (AHA) and American College of Cardiology (ACC)
- **November 2017:** The AHA and ACC released the 2017 guideline for HTN with key changes to the threshold, treatment algorithm, and BP measurement. The national guidelines have reduced the goal from 140/90mmHg to 130/80mmHg for the general population, including community-dwelling seniors. Normal BP remains below 120mmHg; however, HTN has been split into Stage 1 (130/80 to 139/89mmHg) and Stage 2 (140/90 mmHg and higher). The new target is expected to increase the overall prevalence of HTN among U.S. adults to 45.6% compared with 31.9% based on the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) 140/90mmHg threshold. Targets were the same for older and younger adults, with the exception that treatment decisions should be individualized for seniors with a high comorbidity burden and limited life expectancy. The change was based mostly on findings from the SPRINT trial that indicated a target <120mmHg reduced heart attack, stroke, or death in higher-risk older adults, with clear benefit and no evidence of increased risk of falls or orthostatic HTN in elderly individuals in the trial. The SPRINT researchers cautioned that BP measurements were taken with a careful automated process and in a clinical trial setting with a motivated population, such that their finding should not be directly applied to usual practice. Other changes included the BP target for treatment moved to <130/80mmHg, and there are differences in the recommended treatment based on HTN category. For Stage 1 HTN, nonpharmacologic therapy (predominantly lifestyle) was recommended unless the patient has clinical cardiovascular disease (CVD) or at least a 10% 10-year risk of CVD based on the ACC/AHA atherosclerotic CVD risk calculator. For Stage 2 HTN, BP medication is recommended regardless of 10-year risk of CVD status. Non-pharmacologic attention to lifestyle therapy was recommended for elevated BP in the 120 to 129mmHg systolic

range. Lifestyle measures included weight loss, DASH diet, reducing sodium, increasing potassium through diet, physical activity, and moderate alcohol consumption. The guidelines reiterated proper BP measurement techniques and provided a new recommendation for out-of-office BP measurement to confirm the diagnosis of HTN and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions.

News:

- **November 2017:** Consumer advocacy group, Public Citizen, requested the FDA to remove the sale of olmesartan stating that the medication puts patients' health at risk. According to the group, the medication can cause sprue-like enteropathy and research has connected the medication to more than 150 cases of the disorder worldwide.
- **December 2017:** A Danish study suggests that patients taking hydrochlorothiazide (HCTZ) may be more likely to get skin cancer. The medication can increase the risk of sunburns, but the current study shows that it may also increase the risk of basal cell carcinoma and squamous cell carcinoma. Researchers examined national prescription registry data for HCTZ from 1995 to 2012 as well as cancer registry records on diagnosed skin malignancies from 2004 to 2012. The study found people who took HCTZ daily for at least six years were 29% more likely to develop basal cell carcinoma and almost four times more likely to get squamous cell carcinoma than people who did not take the medication. Dr. Elizabeth Martin, president of Pure Dermatology and Aesthetics in Alabama, stated that the findings add to the evidence suggesting that patients taking HCTZ should take extra precautions to protect their skin from sun damage. The study author, Anton Pottegard of the University of Southern Denmark, cautioned that patients taking HCTZ should not stop taking their medication without first consulting with their doctor. He said that patients already taking HCTZ will not meaningfully alter their skin cancer risk by staying on the medication for a few months until a physician can advise them.
- **March 2018:** According to results of a new study presented at the ACC 18 Scientific Sessions, a triple drug combination can significantly reduce BP among individuals with HTN compared with usual care. Researchers conducted the study in Sri Lanka to examine whether initial treatment with a low-dose triple therapy would safely achieve BP targets. Participants were randomized to a fixed-dose combination of telmisartan 20mg, amlodipine 2.5mg, and chlorthalidone 12.5mg (Triple Pill group) or a usual care group. The primary outcome was defined as a BP ≤140/90mmHg, or ≤130/80mmHg in patients with diabetes or chronic kidney disease. At 6 months, 83% of participants in the Triple Pill group were still on all three medications. At 6 months, the Triple Pill regimen helped participants achieve the primary outcome compared with usual care (70% vs. 55%), with the largest difference seen at 6 weeks of treatment (68% vs. 44%). Adverse events were similar between the groups (38.7% vs. 34.7%).

Pipeline:

- **Consensi™:** Kitov Pharmaceuticals announced the FDA granted permission to the manufacturer to use the brand name Consensi™ to market KIT-302. Consensi™ is a combination of celecoxib and amlodipine besylate indicated to simultaneously treat osteoarthritis pain and HTN. The FDA accepted Kitov's New Drug Application (NDA) in

September 2017 and set a Prescription Drug User Fee Act (PDUFA) target date of May 31, 2018.

- **EZR-104:** The FDA accepted the NDA for EZR-104, an investigational product for the treatment of HTN and heart failure (HF), in January 2017. EZR-104 combines valsartan with the Rubireten™ delivery technology. The Rubireten™ delivery technology allows for a more controlled drug release in the body.

Prexxartan® (Valsartan Oral Solution) Product Summary[12]

Indication(s): Prexxartan® (valsartan oral solution) is an angiotensin II receptor blocker (ARB) indicated for the following:

- HTN in adults and pediatric patients 6 years of age and older, to lower BP
- HF (NYHA Class II to IV); Prexxartan® significantly reduces hospitalization for HF in patients who are unable to swallow valsartan tablets
- Stable left ventricular failure or left ventricular dysfunction following myocardial infarction (MI); Prexxartan® reduces cardiovascular mortality in patients who are unable to swallow valsartan tablets

Dosing:

- Prexxartan®, 4mg/mL solution, is supplied in bottles containing 473mL, bottles containing 120mL, and unit dose cups containing 20mL.
- Prexxartan® is not therapeutically equivalent to the tablet formulation of Diovan®. The peak concentration of valsartan with Prexxartan® is higher than with Diovan®.
- For the treatment of HTN in adults, the recommended initial dose is 40 or 80mg twice daily.
- For the treatment of HTN in pediatric patients 6 to 16 years of age, the recommended starting dose is 0.65mg/kg twice daily (up to 40mg total daily dose). Doses higher than 1.35mg/kg twice daily (or greater than 160mg total daily dose) have not been studied in pediatric patients 6 to 16 years of age.
- The recommended initial dose for HF is 40mg twice daily.
- The recommended starting dose post-MI is 20mg twice daily. Prexxartan® may be initiated as early as 12 hours after an MI.

Boxed Warning: Fetal Toxicity
Valsartan oral solution should be discontinued as soon as possible when pregnancy is detected. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

Contraindication(s):

- Patients with known hypersensitivity to any component
- Co-administration of aliskiren with Prexxartan® in patients with diabetes

Use in Specific Populations:

- Pregnancy: Prexxartan® can cause fetal harm when administered to a pregnant woman. Medications that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduce fetal renal function and increase fetal and neonatal morbidity and death.

- Lactation: There is no information regarding the presence of Prexxartan® in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for valsartan to affect postnatal renal development in nursing infants, women should be advised not to breastfeed during treatment with Prexxartan®.
- Pediatric Use: Valsartan is not recommended for pediatric patients younger than 6 years of age due to safety findings for which a relationship to treatment could not be excluded.
- Geriatric Use: No overall difference in the efficacy or safety of valsartan were observed in patients 65 years of age or older, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: The safety and effectiveness of valsartan in patients with severe renal impairment [creatinine clearance (CrCl) ≤30mL/min] have not been established. No dose adjustment is required in patients with mild (CrCl 60 to 90mL/min) or moderate (CrCl 30 to 60 mL/min) renal impairment.
- Hepatic Impairment: No dose adjustment is required for patients with mild-to-moderate liver disease. No dosing recommendations can be provided for patients with severe liver disease.

Clinical Studies: Studies evaluating the antihypertensive effects of valsartan were conducted with a formulation that is not therapeutically equivalent to Prexxartan®.

Cost: The cost of Prexxartan® is not available at this time.

Tekturna® (Aliskiren Oral Pellets) Product Summary[13,14,15]

Indications: Tekturna® (aliskiren) is a renin inhibitor indicated for the treatment of HTN in adults and children 6 years of age and older to lower BP.

Dosing:

- Tekturna® tablets are supplied as tablets containing 150 or 300mg of aliskiren. Tekturna® 37.5mg oral pellets are supplied as capsules, each containing 12 pellets; each pellet contains 3.125mg of aliskiren, equivalent to 3.453mg of aliskiren hemifumarate.
- For the treatment of adult HTN, the recommended starting dose is 150mg once daily with a routine pattern with regard to meals. If BP remains uncontrolled, the dose may be increased to 300mg.
- For the treatment of pediatric HTN in patients 6 to 17 years of age, the recommended dosage is based on patient's weight. For patients weighing <20kg, aliskiren is not recommended. For patients weighing 20 to 50kg, the recommended starting dose is 37.5 or 75mg once daily; the maximum recommended dose is 150mg. For patients weighing ≥50kg, the recommended dose is the same as in adults.
- For patients unable to swallow tablets, Tektruna® oral pellets can be used. Tekturna® oral pellets are provided in a dispensing capsule. The capsules containing the oral pellets should not be swallowed. The oral pellets may be taken by opening the dispensing capsule, emptying the contents into a spoon, and then administering by mouth, followed immediately by milk or water without chewing or crushing.

Boxed Warning: Fetal Toxicity

- Aliskiren should be discontinued as soon as possible when pregnancy is detected. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

Contraindication(s):

- Co-administration of aliskiren with ARBs or ACEIs in patients with diabetes
- Hypersensitivity to any of the components
- Pediatric patients younger than 2 years of age

Use in Specific Populations:

- Pregnancy: Aliskiren can cause fetal harm when administered to a pregnant woman. Medications that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduce fetal renal function and increase fetal and neonatal morbidity and death.
- Lactation: There is no information regarding the presence of aliskiren in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions, nursing women should be advised that breastfeeding is not recommended during treatment with aliskiren.
- Pediatric Use: The safety and effectiveness of aliskiren have not been established in pediatric patients younger than 6 years of age. Preclinical studies indicate a potential for substantial increase in exposure to aliskiren in pediatric patients; therefore, aliskiren is contraindicated in children younger than 2 years of age and should not be used in children age 2 years to younger than 6 years of age.
- Geriatric Use: No overall difference in the efficacy or safety of aliskiren was observed in patients 65 years of age or older, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: The safety and effectiveness of aliskiren in patients with severe renal impairment (CrCl <30mL/min) have not been established as these patients were excluded in clinical trials.

Clinical Studies: Please refer to the Tekturna® prescribing information for a complete summary of clinical studies related to the antihypertensive effects of Tekturna®. Information presented below pertains to the expanded indication for Tekturna® that was approved by the FDA in November 2017 to include the treatment of HTN in children 6 years of age and older.

- **Pediatric HTN:** The efficacy of aliskiren was evaluated in an 8-week randomized, double-blind trial in 267 pediatric hypertensive patients between 6 and 17 years of age. In the initial 4-week, dose-response phase of the trial patients were randomized to weight-based low, mid, and high dosing groups. The low dose ranged from 6.25mg to 25mg of aliskiren, the mid dose ranged from 37.5mg to 150mg of aliskiren, and the high dose ranged from 150mg to 600mg of aliskiren. Patients received aliskiren dispensing capsules containing minitablets (3.125mg per minitablet). At the end of this phase, patients were entered into a 4-week randomized withdrawal phase in which they were re-randomized in each weight category in a 1:1 ratio to continue the same dose of aliskiren or take placebo. During the initial dose-response phase, aliskiren reduced both systolic and diastolic BP in a weight-based dose-dependent manner. The trial's primary endpoint was sitting systolic BP and was reduced by 4.8, 5.6, and 8.7mmHg from

baseline in the low, mid, and high dosing groups, respectively. In the randomized withdrawal phase, the mean difference between the high dose group of aliskiren and placebo in the mean change in sitting systolic BP was -2.7mmHg. After the 8-week trial, 208 subjects were enrolled in a 52-week extension trial. Patients were randomized 1:1 to receive either aliskiren or enalapril. The extension study included three dose levels based on weight, and optional dose titrations were allowed during the study to control BP. At the end of the 52 weeks, reductions in BP from baseline were similar in patients receiving aliskiren and enalapril.

Cost: The cost of Tekturna® oral pellets is not available at this time.

CaroSpir® (Spironolactone Oral Suspension) Product Summary[16,17]

Indication(s): CaroSpir® (spironolactone oral suspension) is an antagonist of aldosterone indicated for the following:

- Treatment of NYHA Class III to IV HF and reduced ejection fraction to increase survival, manage edema, and to reduce the need for hospitalization for HF
- As an add-on therapy for the treatment of HTN to lower BP
- Management of edema in adult cirrhotic patients when edema is not responsive to fluid and sodium restrictions

Dosing:

- CaroSpir® 25mg/5mL oral suspension is a white to off-white, opaque, banana-flavored suspension.
- CaroSpir® is not therapeutically equivalent to Aldactone®. For an equivalent dose, CaroSpir® results in 15 to 37% higher serum concentration compared to Aldactone® tablets. Information about the dose proportionality of spironolactone tablets is limited and, based on the results of studies comparing the suspension formulation to the tablet formulation, doses of the suspension higher than 100mg might result in spironolactone concentrations that could be higher than expected. Therefore, in patients requiring a dose greater than 100mg, another formulation should be used.
- The recommended initial dose for HF is 20mg once daily.
- The recommended initial dose for HTN is 20 to 75mg daily in either single or divided doses.
- The recommended initial dose for edema associated with hepatic cirrhosis is 75mg in either single or divided doses. Therapy should be initiated in a hospital setting and titrated slowly.

Contraindication(s):

- Hyperkalemia
- Addison's disease
- Concomitant use of eplerenone

Use in Specific Populations:

- Pregnancy: Based on the mechanism of action and findings in animal studies, spironolactone may affect sex differentiation of the male during embryogenesis. Based

on the potential risk to the male fetus due to anti-androgenic properties of spironolactone and animal data, spironolactone should be avoided in pregnant women or pregnant women should be advised of the risk to a male fetus.

- Lactation: Spironolactone is not present in breastmilk; however, limited data from a lactating woman at 17 days postpartum reported the presence of the active metabolite, canrenone, in human breastmilk in low amounts that are expected to be clinically inconsequential. In this case, there were no adverse effects reported for the breastfed infant after short-term exposure to spironolactone; however, long-term effects on a breastfed infant are unknown. There are no data on the effects of spironolactone on milk production.
- Pediatric Use: The safety and effectiveness of spironolactone in pediatric patients have not been established.
- Geriatric Use: Spironolactone is substantially excreted by the kidney, and the risk of adverse reactions to this medication may be greater in patients with impaired renal function. Elderly patients are more likely to have decreased renal function, therefore renal function should be monitored.
- Renal Impairment: Spironolactone is substantially excreted by the kidney and the risk of adverse reactions to this medication may be greater in patients with impaired renal function. Patients with renal impairment are at increased risk of hyperkalemia. Potassium should be monitored closely.
- Hepatic Impairment: Spironolactone can cause sudden alterations of fluid and electrolyte balance which may precipitate impaired neurological function, worsening hepatic encephalopathy, and coma in patients with hepatic disease with cirrhosis and ascites. In these patients, spironolactone should be initiated in the hospital.

Efficacy: Clinical studies for the treatment of HTN and HF were conducted with a formulation of spironolactone that is not therapeutically equivalent to CaroSpir®.

Handling: The National Institute for Occupational Safety and Health (NIOSH) recommends appropriate procedures for handling of spironolactone tablets in healthcare settings. When cutting, crushing, manipulating, or handling uncoated tablets, NIOSH recommends the use of double gloves and a protective gown.

Cost Comparison:

Medication	Cost Per Unit*	Cost Per Month^	Cost Per Year
CaroSpir® 25mg/5mL (spironolactone oral suspension)	**$2.05**	**$246.00**	**$2,952.00**
spironolactone 25mg tablet	$0.06	$1.80	$21.60

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 unit for CaroSpir® based on 1mL and cost for spironolactone tablet based on one 25mg tablet.
^Cost per month for CaroSpir® based on 20mg per day dose and cost per month for spironolactone based on 25mg per day dose. CaroSpir® is not therapeutically equivalent to spironolactone tablets.

Recommendations

The College of Pharmacy recommends the prior authorization of Prexxartan® (valsartan oral solution), Tekturna® (aliskiren oral pellets), and CaroSpir® (spironolactone oral suspension) with the following criteria:

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.

Tekturna® (Aliskiren Oral Pellets) Approval Criteria:

1. An FDA approved indication; and
2. A recent trial, within the previous six months and at least four 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.

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.

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 Cardizem® SR (diltiazem SR), Verelan® (verapamil ER capsule), Capoten® (captopril), and Capozide® (captopril/HCTZ) from Tier-1 to Tier-2. Current Tier-2 criteria would apply.
2. Moving Exforge® (amlodipine/valsartan) and Micardis® (telmisartan) from Tier-2 to Tier-1.

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

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®)		

Angiotensin Converting Enzyme Inhibitors (ACEIs)		
Tier-1	**Tier-2**	**Special PA**
ramipril (Altace®)		
trandolapril (Mavik®)		

IV = intravenous

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®)		

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)	
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)		

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
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
*All strengths other than 360mg.

Utilization Details of Antihypertensive Medications: Calendar Year 2017

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	14,593	699,067	4,212	$135,101.89	$0.19	$9.26
AMLODIPINE TAB 5MG	12,032	527,055	3,733	$109,236.82	$0.21	$9.08
AMLODIPINE TAB 2.5MG	1,823	74,414	574	$17,499.22	$0.24	$9.60
NIFEDIPINE TAB 30MG ER	853	30,760	448	$17,089.92	$0.56	$20.04
NIFEDIPINE TAB 60MG ER	660	26,617	250	$14,739.40	$0.55	$22.33
NIFEDIPINE CAP 10MG	647	11,846	506	$32,345.98	$2.73	$49.99
NIFEDIPINE TAB 30MG ER	480	18,622	231	$10,577.17	$0.57	$22.04
VERAPAMIL TAB 240MG ER	440	20,155	101	$6,930.40	$0.34	$15.75
DILTIAZEM CAP 120MG ER	350	16,035	117	$7,848.26	$0.49	$22.42
CARTIA XT CAP 180/24HR	348	15,473	101	$7,795.57	$0.50	$22.40
CARTIA XT CAP 120/24HR	337	15,170	120	$7,473.59	$0.49	$22.18
NIFEDIPINE TAB 90MG ER	330	15,347	105	$10,449.14	$0.68	$31.66
CARTIA XT CAP 240/24HR	316	15,372	89	$8,295.15	$0.54	$26.25
VERAPAMIL TAB 120MG ER	309	11,929	93	$5,491.21	$0.46	$17.77
DILTIAZEM TAB 60MG	265	8,059	68	$5,327.14	$0.66	$20.10
DILTIAZEM TAB 120MG	262	10,556	57	$6,389.68	$0.61	$24.39
VERAPAMIL TAB 80MG	260	8,575	75	$2,725.39	$0.32	$10.48
DILTIAZEM CAP 240MG ER	247	10,745	81	$6,275.72	$0.58	$25.41
VERAPAMIL TAB 180MG ER	247	11,130	65	$3,782.84	$0.34	$15.32
NIFEDIPINE TAB 60MG ER	236	9,205	99	$6,937.48	$0.75	$29.40
DILTIAZEM CAP 180MG ER	229	9,544	79	$5,459.56	$0.57	$23.84
VERAPAMIL TAB 120MG	212	8,158	53	$2,354.66	$0.29	$11.11
DILTIAZEM TAB 30MG	194	5,985	57	$3,230.92	$0.54	$16.65
NIFEDICAL XL TAB 30MG	172	5,657	98	$3,282.24	$0.58	$19.08
DILTIAZEM TAB 90MG	154	4,684	35	$3,613.31	$0.77	$23.46
DILTIAZEM CAP 240MG CD	151	6,368	55	$3,821.10	$0.60	$25.31

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
NIFEDIPINE CAP 20MG	135	2,315	108	$13,850.70	$5.98	$102.60
NIFEDIPINE TAB 90MG ER	125	6,600	46	$5,071.87	$0.77	$40.57
DILT-XR CAP 240MG	110	4,475	23	$3,304.88	$0.74	$30.04
DILTIAZEM CAP 360MG ER	107	5,370	27	$4,425.79	$0.82	$41.36
VERAPAMIL CAP 240MG SR	102	5,880	28	$7,994.55	$1.36	$78.38
VERAPAMIL TAB 40MG	97	3,045	35	$1,785.23	$0.59	$18.40
NIFEDICAL XL TAB 60MG	91	3,548	58	$2,093.12	$0.59	$23.00
VERAPAMIL CAP 240MG ER	80	3,584	20	$5,097.56	$1.42	$63.72
VERAPAMIL CAP 360MG SR	71	3,315	19	$13,499.07	$4.07	$190.13
DILTIAZEM CAP 240MG ER	69	2,878	19	$1,972.51	$0.69	$28.59
DILTIAZEM CAP 180MG/24HR	65	3,392	18	$2,022.85	$0.60	$31.12
VERAPAMIL CAP 120MG SR	63	2,870	29	$3,759.89	$1.31	$59.68
DILT-XR CAP 120MG	62	2,616	16	$1,633.07	$0.62	$26.34
DILTIAZEM CAP 240MG/24HR	62	2,195	15	$1,945.17	$0.89	$31.37
DILTIAZEM CAP 120MG ER	61	2,185	20	$13,161.62	$6.02	$215.76
DILT-XR CAP 180MG	60	2,803	22	$1,929.47	$0.69	$32.16
DILTIAZEM CAP 180MG CD	54	2,600	31	$1,382.35	$0.53	$25.60
VERAPAMIL CAP 120MG ER	53	2,040	19	$3,333.82	$1.63	$62.90
DILTIAZEM CAP 120MG CD	52	2,154	22	$1,086.20	$0.50	$20.89
DILTIAZEM CAP 60MG ER	50	1,505	14	$5,266.63	$3.50	$105.33
VERAPAMIL CAP 180MG SR	47	2,360	20	$3,287.94	$1.39	$69.96
DILTIAZEM CAP 300MG ER	41	2,320	16	$1,756.38	$0.76	$42.84
DILTIAZEM CAP 120MG/24HR	39	1,830	15	$999.85	$0.55	$25.64
DILTIAZEM CAP 90MG ER	37	1,365	11	$5,067.62	$3.71	$136.96
DILTIAZEM CAP 180MG ER	36	1,580	14	$919.31	$0.58	$25.54
CARTIA XT CAP 300/24HR	31	1,365	9	$1,105.56	$0.81	$35.66
DILTIAZEM CAP 300MG/24HR	26	1,614	6	$1,345.42	$0.83	$51.75
FELODIPINE TAB 10MG ER	24	1,000	6	$520.76	$0.52	$21.70
FELODIPINE TAB 5MG ER	22	1,440	8	$551.16	$0.38	$25.05
DILTIAZEM CAP 300MG CD	22	970	7	$780.84	$0.80	$35.49
DILTIAZEM CAP 420MG/24HR	18	930	4	$1,289.83	$1.39	$71.66
VERAPAMIL CAP 180MG ER	14	660	8	$870.70	$1.32	$62.19
NICARDIPINE CAP 20MG	12	360	1	$1,596.12	$4.43	$133.01
DILTIAZEM CAP 120MG ER	10	437	8	$267.99	$0.61	$26.80
NIMODIPINE CAP 30MG	8	388	5	$4,177.35	$10.77	$522.17
AFEDITAB TAB 30MG CR	7	210	5	$133.04	$0.63	$19.01
VERELAN CAP 240MG SR	7	354	1	$2,724.36	$7.70	$389.19
AFEDITAB TAB 60MG CR	6	180	3	$189.52	$1.05	$31.59
TAZTIA XT CAP 360MG/24HR	4	360	1	$129.41	$0.36	$32.35
NIFEDIPINE POW	3	44	2	$49.10	$1.12	$16.37

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TAZTIA XT CAP 300MG/24HR	2	60	1	$65.09	$1.08	$32.55
DILTIAZEM CAP 360MG/24HR	1	30	1	$29.04	$0.97	$29.04
CCB TIER-1 SUBTOTAL	**38,133**	**1,681,755**	**12,243**	**$566,546.50**	**$0.34**	**$14.86**
CCB TIER-2 UTILIZATION						
AMLOD/ATORVA 10-40MG	47	2,400	8	$10,307.41	$4.29	$219.31
AMLOD/ATORVA 10-80MG	26	1,680	6	$8,768.43	$5.22	$337.25
AMLOD/ATORVA 10-20MG	21	1,180	5	$5,357.45	$4.54	$255.12
MATZIM LA TAB 180MG/24HR	20	660	4	$2,082.03	$3.15	$104.10
ISRADIPINE CAP 2.5MG	14	420	2	$896.76	$2.14	$64.05
DILTIAZEM ER TAB 360MG	14	720	4	$2,532.99	$3.52	$180.93
VERAPAMIL CAP 100MG ER	13	630	3	$1,061.13	$1.68	$81.63
CARDIZEM LA TAB 120MG	12	540	3	$2,057.68	$3.81	$171.47
ISRADIPINE CAP 5MG	10	300	1	$1,694.92	$5.65	$169.49
AMLOD/ATORVA 5-40MG	9	750	2	$3,646.38	$4.86	$405.15
MATZIM LA TAB 240MG/24HR	7	330	3	$848.79	$2.57	$121.26
VERAPAMIL CAP 200MG ER	7	405	2	$636.06	$1.57	$90.87
DILTIAZEM ER TAB 180MG	7	330	2	$1,074.74	$3.26	$153.53
AMLOD/ATORVA 5-10MG	4	360	1	$1,213.50	$3.37	$303.38
AMLOD/ATORVA 10-10MG	4	360	1	$1,135.42	$3.15	$283.86
MATZIM LA TAB 360MG/24HR	4	300	1	$1,056.28	$3.52	$264.07
DILTIAZEM ER TAB 240MG	4	280	3	$662.28	$2.37	$165.57
AMLOD/ATORVA 5-20MG	2	120	1	$513.39	$4.28	$256.70
VERAPAMIL CAP 300MG ER	1	30	1	$57.23	$1.91	$57.23
CCB TIER-2 SUBTOTAL	**226**	**11795**	**53**	**$45,602.87**	**$3.87**	**$201.78**
CCB TOTAL	**38,359**	**1,693,550**	**10,567***	**$612,149.37**	**$0.36**	**$15.96**
ANGIOTENSIN RECEPTOR BLOCKERS (ARB) AND COMBINATION PRODUCTS						
ARB TIER-1 UTILIZATION						
LOSARTAN POT TAB 50MG	4,426	196,320	1,317	$45,806.89	$0.23	$10.35
LOSARTAN POT TAB 100MG	2,999	153,836	900	$33,517.44	$0.22	$11.18
LOSARTAN POT TAB 25MG	2,416	113,107	739	$24,936.04	$0.22	$10.32
LOSARTAN/HCT TAB 100-25MG	1,346	71,763	365	$16,982.49	$0.24	$12.62
LOSARTAN/HCT 50-12.5MG	1,040	53,055	333	$12,637.00	$0.24	$12.15
LOSARTAN/HCT 100-12.5MG	560	29,434	164	$7,320.72	$0.25	$13.07
VALSARTAN TAB 160MG	483	22,649	139	$7,370.18	$0.33	$15.26
VALSARTAN TAB 80MG	349	15,380	106	$4,881.26	$0.32	$13.99
VALSART/HCTZ 160-12.5MG	320	14,330	78	$5,275.44	$0.37	$16.49
IRBESARTAN TAB 150MG	253	11,718	55	$4,035.89	$0.34	$15.95
VALSART/HCTZ 160-25MG	244	12,895	73	$4,899.02	$0.38	$20.08
VALSART/HCTZ 320-25MG	236	12,212	68	$5,069.55	$0.42	$21.48

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
VALSART/HCTZ TAB 80-12.5MG	228	11,085	57	$3,461.38	$0.31	$15.18
VALSARTAN TAB 320MG	218	12,070	61	$4,276.01	$0.35	$19.61
VALSARTAN TAB 40MG	113	4,777	49	$1,593.37	$0.33	$14.10
VALSART/HCTZ 320-12.5MG	95	4,470	29	$2,016.20	$0.45	$21.22
IRBESARTAN TAB 300MG	95	4,750	29	$1,861.83	$0.39	$19.60
IRBESARTAN TAB 75MG	68	2,420	14	$970.57	$0.40	$14.27
IRBESAR/HCTZ 150-12.5MG	68	3,180	15	$1,397.85	$0.44	$20.56
IRBESAR/HCTZ 300-12.5MG	34	1,853	9	$836.37	$0.45	$24.60
COZAAR TAB 50MG	10	330	1	$1,789.38	$5.42	$178.94
DIOVAN TAB 160MG	9	270	1	$1,956.84	$7.25	$217.43
DIOVAN TAB 320MG	2	60	2	$545.24	$9.09	$272.62
ARB TIER-1 SUBTOTAL	**15,612**	**751,964**	**4,604**	**$193,436.96**	**$0.26**	**$12.39**
ARB TIER-2 UTILIZATION						
AMLOD/VALSAR 10-320MG	114	3,420	19	$3,061.50	$0.90	$26.86
OLMESA MEDOX 40MG	103	4,620	18	$10,731.62	$2.32	$104.19
OLMESA MEDOX 20MG	73	4,560	22	$7,583.28	$1.66	$103.88
OLM MED/HCTZ 40-25MG	71	3,840	14	$8,463.09	$2.20	$119.20
TELMISARTAN TAB 80MG	63	2,640	15	$1,843.22	$0.70	$29.26
TELMISARTAN TAB 40MG	55	2,700	10	$1,851.05	$0.69	$33.66
OLM MED/HCTZ 40-12.5MG	52	2,640	10	$5,667.83	$2.15	$109.00
OLM MED/HCTZ 20-12.5MG	50	3,720	16	$5,565.89	$1.50	$111.32
AMLO/VALS/HCTZ 10-320-25MG	41	1,320	10	$4,016.96	$3.04	$97.97
OLM/AMLO/HCTZ 40-10-25MG	36	1,620	9	$6,405.57	$3.95	$177.93
AMLOD/OLMESA 5-40MG	30	1,260	5	$1,457.90	$1.16	$48.60
AMLOD/OLMESA 10-40MG	29	870	5	$1,252.78	$1.44	$43.20
AMLOD/VALSAR 5-160MG	28	840	5	$565.21	$0.67	$20.19
AMLO/VALS/HCTZ 5-160-12.5MG	24	720	6	$1,472.24	$2.04	$61.34
AMLOD/VALSAR 10-160MG	18	540	8	$453.55	$0.84	$25.20
AMLO/VALSA/HCTZ 10-160-25MG	17	510	4	$1,522.95	$2.99	$89.59
AMLOD/OLMESA 5-20MG	17	810	3	$910.51	$1.12	$53.56
AMLOD/VALSAR 5-320MG	15	450	3	$373.41	$0.83	$24.89
TELMISARTAN 20MG	14	660	4	$420.23	$0.64	$30.02
AMLO/VALSAR/HCTZ 5-160-25MG	9	270	3	$643.71	$2.38	$71.52
BENICAR HCT TAB 20-12.5MG	9	390	2	$2,410.43	$6.18	$267.83
AZOR TAB 5-40MG	8	240	2	$2,354.72	$9.81	$294.34
TRIBENZOR 40-10-25MG	7	201	1	$2,038.52	$10.14	$291.22
OLM/AMLO/HCTZ 40-10-12.5MG	5	150	1	$647.50	$4.32	$129.50
OLM/AMLO/HCTZ 20-5-12.5MG	4	120	1	$335.56	$2.80	$83.89

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
MICARDIS TAB 40MG	3	270	1	$1,661.00	$6.15	$553.67
BENICAR TAB 40MG	2	60	1	$527.52	$8.79	$263.76
AZOR TAB 5-20MG	2	180	1	$1,394.98	$7.75	$697.49
EXFORGE TAB 10-320MG	2	60	1	$674.82	$11.25	$337.41
BENICAR HCT TAB 40-25MG	2	120	2	$1,027.90	$8.57	$513.95
BENICAR TAB 20MG	2	180	1	$1,120.86	$6.23	$560.43
BENICAR HCT TAB 40-12.5MG	1	90	1	$779.97	$8.67	$779.97
AZOR TAB 10-40MG	1	30	1	$298.80	$9.96	$298.80
OLMESA MEDOX TAB 5MG	1	30	1	$122.80	$4.09	$122.80
AMLOD/OLMESA 10-20MG	1	90	1	$93.04	$1.03	$93.04
ARB TIER-2 SUBTOTAL	**909**	**40,221**	**207**	**$79,750.92**	**$1.98**	**$87.73**
ARB TIER-3 UTILIZATION						
TELMISA/HCTZ 80-25MG	53	1,770	5	$4,076.53	$2.30	$76.92
TELMISA/HCTZ TAB 80-12.5MG	24	960	4	$2,790.30	$2.91	$116.26
CANDESARTAN TAB 4MG	23	1,284	8	$2,646.27	$2.06	$115.06
CANDESARTAN TAB 32MG	19	1,050	6	$3,244.94	$3.09	$170.79
TELMISA/HCTZ TAB 40-12.5MG	11	450	3	$1,255.14	$2.79	$114.10
EDARBYCLOR TAB 40-12.5MG	10	600	2	$3,490.84	$5.82	$349.08
EDARBI TAB 80MG	10	300	1	$1,863.38	$6.21	$186.34
EDARBYCLOR TAB 40-25MG	7	390	3	$2,208.22	$5.66	$315.46
CANDESARTAN TAB 16MG	7	330	2	$692.19	$2.10	$98.88
CANDESARTAN TAB 8MG	6	540	3	$1,122.85	$2.08	$187.14
ARB TIER-3 SUBTOTAL	**170**	**7,674**	**37**	**$23,390.66**	**$3.05**	**$137.59**
ARB TOTAL	**16,691**	**799,859**	**4,216***	**$296,578.54**	**$0.37**	**$17.77**
ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIs) AND COMBINATION PRODUCTS						
ACEI TIER-1 UTILIZATION						
LISINOPRIL TAB 20MG	17,114	781,382	5,334	$144,721.85	$0.19	$8.46
LISINOPRIL TAB 10MG	16,307	726,706	5,235	$136,385.59	$0.19	$8.36
LISINOPRIL TAB 40MG	8,552	420,951	2,362	$88,977.41	$0.21	$10.40
LISINOPRIL TAB 5MG	7,140	318,388	2,271	$59,321.34	$0.19	$8.31
LISINOP/HCTZ 20-25MG	5,208	274,591	1,643	$45,513.30	$0.17	$8.74
LISINOP/HCTZ TAB 20-12.5MG	5,151	237,778	1,608	$44,784.28	$0.19	$8.69
LISINOPRIL TAB 2.5MG	3,300	143,149	1,019	$28,537.26	$0.20	$8.65
LISINOP/HCTZ TAB 10-12.5MG	3,157	151,550	1,054	$27,444.31	$0.18	$8.69
ENALAPRIL TAB 20MG	1,289	50,853	253	$33,671.08	$0.66	$26.12
ENALAPRIL TAB 5MG	1,238	45,780	262	$27,910.44	$0.61	$22.54
ENALAPRIL TAB 10MG	1,072	45,591	253	$21,230.04	$0.47	$19.80
LISINOPRIL TAB 30MG	972	46,503	293	$11,227.00	$0.24	$11.55

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ENALAPRIL TAB 2.5MG	790	28,514	160	$15,704.62	$0.55	$19.88
BENAZEPRIL TAB 20MG	430	19,391	98	$3,976.38	$0.21	$9.25
BENAZEPRIL TAB 40MG	319	15,125	75	$3,282.45	$0.22	$10.29
BENAZEPRIL TAB 10MG	255	11,329	58	$2,396.50	$0.21	$9.40
RAMIPRIL CAP 10MG	223	9,724	48	$2,856.22	$0.29	$12.81
ENALAPR/HCTZ TAB 10-25MG	169	7,426	38	$2,641.08	$0.36	$15.63
QUINAPRIL TAB 40MG	126	6,540	31	$2,000.70	$0.31	$15.88
CAPTOPRIL TAB 50MG	125	3,762	21	$12,014.49	$3.19	$96.12
QUINAPRIL TAB 20MG	120	5,475	28	$1,888.16	$0.34	$15.73
RAMIPRIL CAP 2.5MG	116	5,060	30	$1,457.93	$0.29	$12.57
CAPTOPRIL TAB 25MG	112	3,928	28	$6,907.30	$1.76	$61.67
RAMIPRIL CAP 5MG	100	4,505	26	$1,159.48	$0.26	$11.59
ENALAPR/HCTZ TAB 5-12.5MG	95	3,613	20	$1,254.56	$0.35	$13.21
CAPTOPRIL TAB 12.5MG	82	3,353	26	$4,533.17	$1.35	$55.28
BENAZEP/HCTZ TAB 20-12.5MG	79	3,240	19	$3,496.87	$1.08	$44.26
RAMIPRIL CAP 1.25MG	78	3,370	21	$1,224.84	$0.36	$15.70
BENAZEP/HCTZ TAB 20-25MG	76	4,050	18	$3,938.78	$0.97	$51.83
FOSINOPRIL TAB 40MG	61	2,385	14	$1,099.75	$0.46	$18.03
FOSINOPRIL TAB 10MG	60	2,881	11	$1,048.23	$0.36	$17.47
BENAZEP/HCTZ TAB 10-12.5MG	59	3,057	18	$3,039.36	$0.99	$51.51
BENAZEPRIL TAB 5MG	52	2,410	13	$469.54	$0.19	$9.03
FOSINOPRIL TAB 20MG	37	1,350	8	$481.74	$0.36	$13.02
QUINAPRIL TAB 10MG	34	1,560	8	$514.93	$0.33	$15.15
QUINAPRIL TAB 5MG	18	540	3	$228.43	$0.42	$12.69
QNAPRIL/HCTZ TAB 20-12.5MG	16	754	3	$616.32	$0.82	$38.52
CAPTOPR/HCTZ TAB 50-25MG	16	840	4	$1,685.91	$2.01	$105.37
CAPTOPR/HCTZ TAB 25-15MG	13	720	3	$955.14	$1.33	$73.47
QNAPRIL/HCTZ TAB 10-12.5MG	11	390	2	$275.08	$0.71	$25.01
QNAPRIL/HCTZ TAB 20-25MG	9	450	2	$289.95	$0.64	$32.22
CAPTOPRIL TAB 100MG	9	450	2	$1,262.61	$2.81	$140.29
TRANDOLAPRIL TAB 1MG	5	210	2	$121.01	$0.58	$24.20
PERINDOPRIL TAB 8MG	4	360	1	$228.03	$0.63	$57.01
MOEXIPR/HCTZ TAB 15-25MG	3	270	1	$222.09	$0.82	$74.03
TRANDOLAPRIL TAB 2MG	1	30	1	$12.97	$0.43	$12.97
CAPTOPR/HCTZ TAB 25-25MG	1	30	1	$26.01	$0.87	$26.01
ACEI TIER-1 SUBTOTAL	**74,204**	**3,400,314**	**22,429**	**$753,034.53**	**$0.22**	**$10.15**
SPECIAL PRIOR AUTHORIZATION (PA) UTILIZATION						
EPANED SOL 1MG/ML	550	22,670	130	$210,873.10	$9.30	$383.41

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
EPANED SOL 1MG/ML	137	5,639	73	$38,603.72	$6.85	$281.78
QBRELIS SOL 1MG/ML	19	720	6	$8,499.65	$11.81	$447.35
ACEI SPECIAL PA SUBTOTAL	**706**	**29,029**	**209**	**$257,976.47**	**$8.89**	**$365.41**
ACEI TOTAL	**74,910**	**3,429,343**	**19,579***	**$1,011,011.00**	**$0.29**	**$13.50**
ACEI AND CCB COMBINATION PRODUCTS						
ACEI AND CCB TIER-1 UTILIZATION						
AMLOD/BENAZP CAP 10-20MG	209	10,753	55	$4,487.08	$0.42	$21.47
AMLOD/BENAZP CAP 10-40MG	193	10,853	51	$4,772.47	$0.44	$24.73
AMLOD/BENAZP CAP 5-20MG	179	6,900	33	$2,974.37	$0.43	$16.62
AMLOD/BENAZP CAP 5-10MG	72	3,900	24	$1,652.94	$0.42	$22.96
AMLOD/BENAZP CAP 5-40MG	51	2,490	11	$1,089.20	$0.44	$21.36
AMLOD/BENAZP 2.5-10MG	12	420	4	$239.19	$0.57	$19.93
ACEI/CCB TIER-1 SUBTOTAL	**716**	**35,316**	**178**	**$15,215.25**	**$0.43**	**$21.25**
ACEI AND CCB TIER-2 UTILIZATION						
TRANDO/VERAP TAB 4-240 ER	7	350	1	$2,271.92	$6.49	$324.56
ACEI/CCB TIER-2 SUBTOTAL	**7**	**350**	**1**	**$2,271.92**	**$6.49**	**$324.56**
ACEI/CCB TOTAL	**723**	**35,666**	**167***	**$17,487.17**	**$0.49**	**$24.19**
DIRECT RENIN INHIBITORS (DRI)						
TEKTURNA TAB 300MG	6	420	2	$2,854.84	$6.80	$475.81
TEKTURNA HCT TAB 300-25MG	3	270	1	$1,829.24	$6.77	$609.75
TEKTURNA HCT TAB 150-12.5MG	1	60	1	$323.64	$5.39	$323.64
DRI TOTAL	**10**	**750**	**3***	**$5,007.72**	**$6.68**	**$500.77**
CLONIDINE PRODUCTS						
CLONIDINE UTILIZATION (NO PA REQUIRED)						
CLONIDINE TAB 0.1MG	58,457	1,806,259	12,536	$618,604.06	$0.34	$10.58
CLONIDINE TAB 0.2MG	21,623	680,289	3,809	$234,916.58	$0.35	$10.86
CLONIDINE TAB 0.3MG	4,773	151,357	785	$56,308.81	$0.37	$11.80
CATAPRES TAB 0.2MG	6	180	1	$1,943.38	$10.80	$323.90
CLONIDINE POW	4	120	2	$43.92	$0.37	$10.98
CLONIDINE SUBTOTAL	**84,863**	**2,638,205**	**17,133**	**$911,816.75**	**$0.35**	**$10.74**
CLONIDINE SPECIAL PA UTILIZATION						
CLONIDINE DIS 0.2/24HR	142	4,033	37	$13,810.45	$3.42	$97.26
CLONIDINE DIS 0.1/24HR	130	3,634	31	$8,622.83	$2.37	$66.33
CLONIDINE DIS 0.3/24HR	98	2,780	24	$11,447.51	$4.12	$116.81
CLONIDINE SPECIAL PA SUBTOTAL	**370**	**10447**	**92**	**$33,880.79**	**$3.24**	**$91.57**
CLONIDINE TOTAL	**85,233**	**2,648,652**	**15,449***	**$945,697.54**	**$0.36**	**$11.10**
SOTALOL PRODUCTS						
SOTALOL UTILIZATION (NO PA REQUIRED)						
SOTALOL HCL TAB 80MG	244	7,601	54	$3,064.18	$0.40	$12.56

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
SOTALOL HCL TAB 120MG	154	4,780	22	$2,547.32	$0.53	$16.54
SOTALOL HCL TAB 160MG	39	1,229	6	$710.26	$0.58	$18.21
SOTALOL AF TAB 80MG	35	1,347	7	$450.84	$0.33	$12.88
SOTALOL AF TAB 120MG	8	240	1	$118.53	$0.49	$14.82
SORINE TAB 80MG	4	120	1	$64.80	$0.54	$16.20
SOTALOL SUBTOTAL	**484**	**15,317**	**91**	**$6,955.93**	**$0.45**	**$14.37**
SOTALOL SPECIAL PA UTILIZATION						
SOTYLIZE SOL 5MG/ML	57	1,642	13	$29,563.11	$18.00	$518.65
SOTALOL SUBTOTAL	**57**	**1,642**	**13**	**$29,563.11**	**$18.00**	**$518.65**
SOTALOL TOTAL	**541**	**16,959**	**98***	**$36,519.04**	**$2.15**	**$67.50**
PROPRANOLOL SOLUTION PRODUCTS						
PROPRANOLOL UTILIZATION (NO PRIOR AUTHORIZATION REQUIRED)						
PROPRANOLOL SOL 20MG/5ML	711	20,807	189	$17,660.27	$0.85	$24.84
PROPRANOLOL SOL 40MG/5ML	15	460	6	$346.44	$0.75	$23.10
PROPRANOLOL INJ 1MG/ML	2	2	2	$222.50	$111.25	$111.25
PROPRANOLOL SUBTOTAL	**728**	**21,269**	**197**	**$18,229.21**	**113**	**$25.04**
PROPRANOLOL SPECIAL PA UTILIZATION						
HEMANGEOL SOL 4.28/ML	15	503	5	$8,328.49	$16.56	$555.23
PROPRANOLOL SUBTOTAL	**15**	**503**	**5**	**$8,328.49**	**$16.56**	**$555.23**
PROPRANOLOL TOTAL	**743**	**21,772**	**195***	**$26,557.70**	**$1.22**	**$35.74**
SPIRONOLACTONE PRODUCTS						
SPIRONOLACTONE UTILIZATION (NO PRIOR AUTHORIZATION REQUIRED)						
SPIRONOLACT TAB 25MG	4,106	173,367	1,295	$41,469.78	$0.24	$10.10
SPIRONOLACT TAB 50MG	2,083	79,850	675	$36,983.10	$0.46	$17.75
SPIRONOLACT TAB 100MG	1,337	50,148	386	$30,810.48	$0.61	$23.04
SPIRONOLACT POW	32	704	5	$585.88	$0.83	$18.31
SPIRONOLACTONE SUBTOTAL	**7,558**	**304,069**	**2,361**	**$109,849.24**	**2**	**$14.53**
SPIRONOLACTONE SPECIAL PA UTILIZATION						
CAROSPIR SUS 25MG/5ML	1	50	1	$280.55	$5.61	$280.55
SPIRONOLACTONE SUBTOTAL	**1**	**50**	**1**	**$280.55**	**$5.61**	**$280.55**
SPIRONOLACTONE TOTAL	**7,559**	**304,119**	**2,191***	**$110,129.79**	**$0.36**	**$14.57**
MISCELLANEOUS (MISC.) PRODUCTS						
MISC. UTILIZATION (NO PRIOR AUTHORIZATION REQUIRED)						
BISOPRL/HCTZ TAB 5-6.25MG	277	11,957	73	$3,005.90	$0.25	$10.85
ATENOL/CHLOR TAB 50-25MG	267	13,691	76	$6,971.72	$0.51	$26.11
BISOPRL/HCTZ TAB 10-6.25MG	145	6,785	39	$1,385.51	$0.20	$9.56
ATENOL/CHLOR 100-25MG	132	6,128	35	$4,235.52	$0.69	$32.09
BISOPRL/HCTZ TAB 2.5-6.25MG	79	4,630	23	$823.46	$0.18	$10.42
METOPRL/HCTZ TAB 50-25MG	75	3,828	19	$4,497.11	$1.17	$59.96

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL DAYS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
METOPRL/HCTZ 100-25MG	47	2,040	14	$2,849.60	$1.40	$60.63
PROPRAN/HCTZ TAB 40-25MG	16	540	5	$724.89	$1.34	$45.31
PROPRAN/HCTZ TAB 80-25MG	15	450	2	$966.15	$2.15	$64.41
METOPRL/HCTZ 100-50MG	11	930	3	$1,568.73	$1.69	$142.61
METHYLD/HCTZ TAB 250-15MG	7	210	2	$288.19	$1.37	$41.17
NADOLOL/BEND TAB 80-5MG	4	360	1	$1,431.70	$3.98	$357.93
DUTOPROL TAB 25-12.5MG	3	120	2	$1,079.09	$8.99	$359.70
DUTOPROL TAB 50-12.5MG	3	180	1	$1,275.09	$7.08	$425.03
DUTOPROL TAB 100-12.5MG	2	60	1	$749.10	$12.49	$374.55
MISC. TOTAL	**1,083**	**51,909**	**285***	**$31,851.76**	**$0.61**	**$29.41**
TOTAL	**225,852**	**9,002,579**	**43,968***	**$3,092,989.63**	**$0.34**	**$13.69**

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

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Appendix L

Industry News and Updates

Oklahoma Health Care Authority
April 2018

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:

- **Heroin Vaccine:** According to researchers at The Scripps Research Institute (TSRI), a novel vaccine to treat heroin addiction and block lethal overdose is almost ready for human testing. In February 2018, their research was published in the journal *Molecular Pharmaceuticals*. The vaccine works by training immune system antibodies to recognize and bind heroin molecules; in turn, the drug is prevented from reaching the brain to cause a "high". The researchers explained that because the "high" sensation is blocked, recovering addicts might be less motivated to relapse into using heroin.
- **Neurology Medications:** New documents released by the U.S. Food and Drug Administration (FDA) in February 2018 provide more flexibility to manufacturers in trial endpoints for Alzheimer's disease, Duchenne muscular dystrophy (DMD) and related conditions, amyotrophic lateral sclerosis (ALS), migraine, and pediatric epilepsy. For Alzheimer's medications, biomarker effects will be allowed to be the primary endpoint in patients with Alzheimer's pathology but no current symptoms. For migraines, the FDA stated that manufacturers will only need two primary endpoints (i.e., pain reduction, effects on individual patients' "most bothersome symptoms") instead of addressing four different classes of symptoms (i.e., pain, nausea, photophobia, phonophobia). For medications for children 4 years of age and older with partial onset seizures, the FDA will not require efficacy studies in children as the agency will now consider efficacy data from adult patients to be sufficient for pediatric approval. For medications used for "dystrophinopathies" such as DMD, the guidance highlighted the difficulties in designing trials for these conditions. Patients with these conditions vary considerably in age and functional ability and as trials progress, the participants get older and typically lose functional ability. Therefore, a functional measure such as walking ability may be confounded by both participants' growth and some of the participants may transition to wheelchairs. The DMD guideline did not allow for approval based solely on biomarkers such as dystrophin level; however, effects on other objective measures such as respiratory and cardiac muscle function may be used to support approval. For ALS, the guidance offered more clarity but did not include any major changes. Efficacy must be demonstrated at "clinically meaningful" levels for survival, function, or symptoms and

for safety, trials only need to include enough patients and enough drug exposure for adequate assessment of adverse effects.

- **Asthma:** A new study published in *The New England Journal of Medicine* finds that the practice of temporarily increasing the dose of inhaled corticosteroids (ICS) in children with mild-to-moderate asthma when the condition deteriorates fails to effectively prevent severe exacerbations and may also have the adverse effect of slowing growth. The study led by the University of Wisconsin School of Medicine points out that higher doses of ICS are routinely recommended when patients present with symptoms such as wheezing, shortness of breath, and coughing; however, the study states that whether this approach was safe or effective in pediatric mild-to-moderate asthma had not previously been rigorously tested. Researchers followed 254 children between the ages of 5 to 11 years with mild-to-moderate asthma for one year. The children were treated with low-dose ICS, but when participants experienced signs of asthma flare-up researchers divided them into two groups – continuing low-dose ICS or quintupling the dosage of ICS. The patients received ICS twice daily for 7 days during each episode. The high-dose group received 14% more exposure to ICS than the low-dose group, yet did not suffer fewer severe flare-ups. Researchers determined that the number of asthma symptoms, length of time until the first severe flare-up, and the use of rescue medication were not significantly different between the two groups. The study authors warned that children who use high-dose ICS more frequently or for longer periods of time could suffer even more dramatic effects on their growth. Study leader, Dr. Daniel Jackson, MD, stated that "these findings suggest that a short-term increase to high-dose inhaled steroids should not be routinely included in asthma treatment plans for children with mild-moderate asthma who are regularly using low-dose inhaled corticosteroids."

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[1] Han DH. Researchers Hope to Test Heroin Vaccine in Humans Soon. *MPR*. Available online at: https://www.empr.com/news/heroin-vaccine-addiction-overdose-immune-response/article/744289/. Issued 02/14/2018. Last accessed 02/26/2018.

[2] Gever J. FDA Eases Approval Path for Migraines, Pediatric Epilepsy Drugs. *MedPage Today*. Available online at: https://www.medpagetoday.com/neurology/generalneurology/71209. Issued 02/16/2018. Last accessed 02/26/2018.

[3] U.S. Pharmacist Staff. Higher Steroids Don't Prevent Asthma Flare-Ups in Mild/Moderate Pediatric Cases. *U.S. Pharmacist*. Available online at: https://www.uspharmacist.com/article/higher-steroids-dont-prevent-asthma-flareups-in-mild-moderate-pediatric-cases/?wc_mid=4:553283&wc_rid=4:7349994. Issued 03/14/2018. Last accessed 03/15/2018.

Appendix M

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

FDA NEWS RELEASE

For Immediate Release: March 20th, 2018

FDA expands approval of Adcetris® for first-line treatment of Stage III or IV classical Hodgkin lymphoma in combination with chemotherapy

The FDA approved Adcetris® (brentuximab vedotin) to treat adult patients with previously untreated stage III or IV classical Hodgkin lymphoma (cHL) in combination with chemotherapy. Lymphoma is a cancer that begins in the lymph system, which is part of the immune system that helps the body fight infection and disease. Lymphoma can begin almost anywhere in the body and can spread to nearby lymph nodes. The two main types of lymphoma are Hodgkin lymphoma (also called Hodgkin disease) and non-Hodgkin lymphoma. Most people with Hodgkin lymphoma have the classical type. With this type, there are large, abnormal lymphocytes (a type of white blood cell) in the lymph nodes called Reed-Sternberg cells. With early intervention, patients with Hodgkin lymphoma can usually experience long-term remission. The National Cancer Institute at the National Institutes of Health estimates that 8,260 people in the United States were diagnosed with Hodgkin lymphoma last year and approximately 1,070 patients with non-Hodgkin lymphoma died from the disease in 2017.

Adcetris® combines an antibody and drug, allowing the antibody to direct the drug to a target on lymphoma cells known as CD30. Adcetris® has also been previously approved by the FDA to treat cHL after relapse, cHL after stem cell transplant when a patient is at a high risk of relapse or progression, systemic anaplastic large cell lymphoma (ALCL) after failure of other treatment, and primary cutaneous ALCL after failure of other treatment.

The approval for adult patients with previously untreated stage III or IV cHL was based on a clinical trial comparing Adcetris® plus chemotherapy [Adriamycin® (doxorubicin), vinblastine and dacarbazine, or AVD] to a chemotherapy-only regimen common for cHL treatment (AVD plus bleomycin, also known as ABVD). The trial measured modified progression-free survival (mPFS), which considers the length of time it took for the disease to progress, death to occur, or new therapy to be initiated in patients who did not achieve a complete response. In the trial of 1,334 patients, after patients received an average of six 28-day cycles of treatment, those treated with Adcetris® plus AVD were 23% less likely to experience progression, death, or initiation of new therapy compared with those receiving ABVD. There were 117 (18%) patients on the Adcetris® plus AVD arm who experienced disease progression, death, or began new therapy compared to 146 (22%) patients on the ABVD arm.

Common side effects of Adcetris® include low levels of certain blood cells (neutropenia, anemia), nerve damage causing numbness or weakness in the hands and feet (peripheral neuropathy), nausea, fatigue, constipation, diarrhea, vomiting, and fever (pyrexia). In the above clinical trial, 67% of patients treated with Adcetris® plus chemotherapy experienced damage to the peripheral nervous system (peripheral neuropathy). In addition, neutropenia occurred in 91% of patients treated with Adcetris® plus chemotherapy, which was associated with a 19% rate of febrile neutropenia (neutropenia and fever). Preventative treatment with G-CSF, a growth factor for the bone marrow to produce white blood cells, is recommended with Adcetris® plus chemotherapy for the first-line treatment of Stage III or IV cHL.

Adcetris® has a boxed warning that highlights the risk of John Cunningham virus infection resulting in progressive multifocal leukoencephalopathy, or PML, a rare but serious brain infection that can result in death. Serious risks of Adcetris® include peripheral neuropathy; severe allergic (anaphylaxis) or infusion-site reactions; damage to the blood, lungs and liver (hematologic, pulmonary and hepato-toxicities); serious or opportunistic infections; metabolic abnormalities (tumor lysis syndrome); serious dermatologic reactions; and gastrointestinal complications. Adcetris® can cause harm to a developing fetus and newborn baby; women should be advised of the potential risk to the fetus and to use effective contraception, and to avoid breastfeeding while taking Adcetris®.

The FDA granted this application Priority Review and Breakthrough Therapy designations.

The FDA granted the approval of Adcetris® to Seattle Genetics, Inc.

FDA NEWS RELEASE

For Immediate Release: March 29th, 2018

FDA expands approval of Blincyto® for treatment of a type of leukemia in patients who have a certain risk factor for relapse

The FDA granted accelerated approval to Blincyto® (blinatumomab) to treat adults and children with B-cell precursor acute lymphoblastic leukemia (ALL) who are in remission but still have minimal residual disease (MRD). MRD refers to the presence of cancer cells below a level that can be seen under the microscope. In patients who have achieved remission after initial treatment for this type of ALL, the presence of MRD means they have an increased risk of relapse.

"This is the first FDA-approved treatment for patients with MRD-positive ALL," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Because patients who have MRD are more likely to relapse, having a treatment option that eliminates even very low amounts of residual leukemia cells may help keep the cancer in remission longer. We look forward to furthering our understanding about the reduction in MRD after treatment with Blincyto®. Studies are being conducted to assess how Blincyto® affects long-term survival outcomes in patients with MRD."

B-cell precursor ALL is a rapidly progressing type of cancer in which the bone marrow makes too many B-cell lymphocytes, an immature type of white blood cell. The National Cancer Institute estimates that approximately 5,960 people in the United States will be diagnosed with ALL this year and approximately 1,470 will die from the disease.

Blincyto® works by attaching to CD19 protein on the leukemia cells and CD3 protein found on certain immune system cells. Bringing the immune cell close to the leukemia cell allows the immune cells to attack the leukemia cells better. The FDA first approved Blincyto® under accelerated approval in December 2014 for the treatment of Philadelphia chromosome (Ph)-negative relapsed or refractory positive B-cell precursor ALL. Full approval for this indication was granted in July 2017, and at that time, the indication was also expanded to include patients with Philadelphia chromosome-positive ALL.

The efficacy of Blincyto® in MRD-positive ALL was shown in a single-arm clinical trial that included 86 patients in first or second complete remission who had detectable MRD in at least 1 out of 1,000 cells in their bone marrow. Efficacy was based on achievement of undetectable MRD in an assay that could detect at least one cancer cell in 10,000 cells after one cycle of Blincyto® treatment, in addition to the length of time that the patients remained alive and in remission (hematological relapse-free survival). Overall, undetectable MRD was achieved by 70 patients. Over half of the patients remained alive and in remission for at least 22.3 months.

The side effects of Blincyto® when used to treat MRD-positive B-cell precursor ALL are consistent with those seen in other uses of the drug. Common side effects include infections (bacterial and pathogen unspecified), fever (pyrexia), headache, infusion related reactions, low levels of certain blood cells (neutropenia, anemia), febrile neutropenia (neutropenia and fever), and low levels of platelets in the blood (thrombocytopenia).

Blincyto® carries a boxed warning alerting patients and health care professionals that some clinical trial participants had problems with low blood pressure and difficulty breathing (cytokine release syndrome) at the start of the first treatment, experienced a short period of difficulty with thinking (encephalopathy) or other side effects in the nervous system. Serious risks of Blincyto® include infections, effects on the ability to drive and use machines, inflammation in the pancreas (pancreatitis), and preparation and administration errors—instructions for preparation and administration should closely be followed. There is a risk of serious adverse reactions in pediatric patients due to benzyl alcohol preservative; therefore, the drug prepared with preservative free saline should be used for patients weighing <22kg.

This new indication for Blincyto® was approved under the accelerated approval pathway, under which the FDA may approve drugs for serious conditions where there is unmet medical need and a drug is shown to have certain effects that are reasonably likely to predict a clinical benefit to patients. Further study in randomized controlled trials is required to verify that achieving undetectable MRD with Blincyto® improves survival or disease-free survival in patients with ALL.

The FDA granted this application Priority Review and it received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Blincyto® to Amgen, Inc.

Safety Announcements

FDA alerts consumers of a nationwide voluntary recall of topical drug products made by Industria Farmacéutica Andrómaco due to contamination

FDA lab confirmed high levels of microbial contamination in company's Pasta De Lassar Andromaco diaper rash treatment

[03/30/2018] The FDA is alerting consumers of a voluntary recall of a topical drug product Pasta De Lassar Andromaco zinc oxide diaper rash treatment, made by Industria Farmacéutica Andrómaco, Toluca, Mexico, and distributed by MarcasUSA LLC, El Segundo, California. FDA laboratory analysis confirmed that Pasta De Lassar Andromaco is contaminated with high levels of yeast, mold, and bacteria. This is especially concerning because Pasta De Lassar Adromoca is labeled for use to relieve diaper rash, where irritated skin can become infected. Therefore, consumers and caregivers should not use this product due to possible microbial contamination that may cause infections.

Consumers who have Pasta De Lassar Andromaco should stop using it and dispose of it immediately. Consumers also should contact their doctor or health care professional if they have concerns, or if they develop an infection following the use of topical drug products made by Industria Farmacéutica.

Pasta De Lassar Andromaco and other topical drug products made by Industria Farmacéutica are available online and in retail stores. Additionally, the company donated its Pasta De Lassar Andromaco product to a charity in California.

The FDA is not aware of reported adverse events associated with the use of these products. The FDA asks health care professionals and consumers to report any adverse reactions associated with these products to the FDA's MedWatch Adverse Event Reporting program.

Safety Announcements

FDA alerts consumers of Bayer's voluntary recall of Alka-Seltzer Plus® products due to labeling errors

[03/16/2018] The FDA is alerting consumers of a voluntary recall of Bayer's Alka-Seltzer Plus® products due to labeling errors.

Bayer is voluntarily recalling Alka-Seltzer Plus® packages that:

- Were sold only in the U.S. at Walmart, CVS, Walgreens, and Kroger (including Dillons Food Stores, Fred Meyer, Fry's Food Stores, Ralphs, King Soopers and Smith's Food and Drug) after February 9, 2018.
- Packages can be identified by checking the Bayer logo located on the lower left corner of the front of the carton. If the logo has an orange or green background, the product is included in the recall.

Consumers who purchased packages of Alka-Seltzer Plus® that are being recalled should stop using the product immediately. Consumers should contact their physician or healthcare provider if they experience any problems that may be related to using this drug product.

The affected packages are being recalled because the ingredients listed on the front sticker of the carton may be different from the ingredients listed on the back of the carton as well as the product in the carton. This may lead consumers to ingest an ingredient to which they are allergic to, or should not be taking, because of the potential for serious health consequences. Consumers can contact Bayer at (800) 986-0369 with questions, to report any issues they experienced with the product or for instructions about how to receive a refund.

The Alka-Seltzer Plus® products subject to the recall are intended to temporarily relieve symptoms associated with cold and flu, such as cough, congestion, fever and/or mucus.The FDA has not received any adverse event reports related to these recalled products.

Health care professionals and consumers should report any adverse events related to this product to FDA's MedWatch Adverse Event Reporting program.

Current Drug Shortages Index (as of April 3rd, 2018):

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

Amino Acids	***Currently in Shortage***
Aminocaproic Acid Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***

Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended Release Tablets	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Deferoxamine Mesylate for Injection, USP	***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***
Diltiazem Hydrochloride	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***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***
Fluorescein Strips	***Currently in Shortage***
Folic Acid Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tabs	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Susp	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***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***
Nitrous Oxide, Gas	***Currently in Shortage***
Pantoprazole (Protonix) Powder for Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phenytoin Sodium Injection, USP	***Currently in Shortage***
Phosphate Injection Products	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***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***
Rocuronium Bromide Injection	***Currently in Shortage***
Ropivacaine Hydrochloride injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***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***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Zolpidem Tartrate (Edluar) Sublingual Tablets	***Currently in Shortage***