Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
April 13, 2016
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – April 13, 2016

DATE: March 31, 2016

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/Chronic Medication Adherence Program Update – Appendix B

Action Item – Vote to Prior Authorize Uptravi® (Selexipag) – Appendix C

Action Item – Vote to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat) – Appendix D

Action Item – Vote to Prior Authorize Elestrin® (Estradiol Gel 0.06%) – Appendix E

Action Item – Vote to Prior Authorize Evzio® (Naloxone Auto-Injector) – Appendix F

Annual Review of SoonerCare Pharmacy Benefit – Appendix G

30-Day Notice to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir) – Appendix H

Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein], Adynovate® [Antihemophilic Factor (Recombinant), PEGylated], Alprolix® [Coagulation Factor IX (Recombinant), Fc Fusion Protein], Idelvion® [Coagulation Factor IX (Recombinant), Albumin Fusion Protein], Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence], Corifact® [Factor XIII Concentrate (Human)], Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)], and Coagadex® [Coagulation Factor X (Human)], and Establish Pharmacy Provider Standards of Care – Appendix I

Annual Review of Makena® (Hydroxyprogesterone Caproate) and 30-Day Notice to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®) – Appendix J

Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Humalog® KwikPen® U-200 (Insulin Lispro), Tresiba® (Insulin Degludec), Ryzodeg® 70/30 (Insulin Degludec/Insulin Aspart), Basaglar® (Insulin Glargine), and Synjardy® (Empagliflozin/Metformin) – Appendix K

Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Entresto™ (Sacubitril/Valsartan) – Appendix L

Annual Review of Diabetic Supplies – Appendix M

FDA and DEA Updates – Appendix N

Future Business (Upcoming Product and Class Reviews)

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – April 13, 2016 @ 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 and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

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

A. March 9, 2016 DUR Minutes – Vote
B. March 9, 2016 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – See Appendix B

A. Medication Coverage Activity for March 2016
B. Pharmacy Help Desk Activity for March 2016
C. Chronic Medication Adherence Program Update

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

5. Action Item – Vote to Prior Authorize Uptravi® (Selexipag) – See Appendix C

A. Indication and Treatment
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Elestrin® (Estradiol Gel 0.06%) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Evzio® (Naloxone Auto-Injector) – See Appendix F

A. Introduction
B. Market News and Updates
C. College of Pharmacy Recommendations

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

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

A. Pharmacy Benefit Management

B. Summary
C. Traditional Versus Specialty Pharmacy Products
D. Top 10 Therapeutic Classes by Reimbursement
E. Top 10 Medications by Reimbursement
F. Medicaid Drug Rebate Program
G. Medication Price Increases
H. Pharmacy Trend: Spending Per Member Per Year (PMPY)
I. Conclusion
J. Top 100 Reimbursed Drugs by Fiscal Year
K. Top 50 Medications by Total Number of Claims
L. Top Traditional Therapeutic Classes by Fiscal Year
M. Top Specialty Therapeutic Classes by Fiscal Year

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

10. 30-Day Notice to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir) – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Market News and Updates
D. Zepatier™ (Elbasvir/Grazoprevir) Product Summary
E. Regimen Comparison
F. College of Pharmacy Recommendations

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

11. Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein], Adynovate® [Antihemophilic Factor (Recombinant), PEGylated], Alprolix® [Coagulation Factor IX (Recombinant), Fc Fusion Protein], Idelvion® [Coagulation Factor IX (Recombinant), Albumin Fusion Protein], Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence], Corifact® [Factor XIII Concentrate (Human)], Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)], and Coagadex® [Coagulation Factor X (Human)], and Establish Pharmacy Provider Standards of Care – See Appendix I

A. Hemophilia and Other Rare Bleeding Disorders Overview
B. Complications of Hemophilia
C. Acquired Hemophilia
D. Factor X Deficiency
E. Factor XII Deficiency
F. Utilization of Factor Replacement Products
G. Product Summaries
H. Standards of Care for Pharmacy Providers for the Home Use of Factor Replacement Products for Patients with Bleeding Disorders
I. Recommendations
J. Utilization Details of Factor Replacement Products

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

12. Annual Review of Makena® (Hydroxyprogesterone Caproate) and 30-Day Notice to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Makena® (Hydroxyprogesterone Caproate)
C. Prior Authorization of Makena® (Hydroxyprogesterone Caproate)
D. Market News and Updates
E. Preterm Birth
F. Expansion of Makena® (Hydroxyprogesterone Caproate) Start Window
G. Management Guidelines for Short Cervix
H. Estimated Cost Savings
I. College of Pharmacy Recommendations
J. Utilization Details of Hydroxyprogesterone and Vaginal Progesterone

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

13. Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Humalog® KwikPen® U-200 (Insulin Lispro), Tresiba® (Insulin Degludec), Ryzodeg® 70/30 (Insulin Degludec/Insulin Aspart), Basaglar® (Insulin Glargine), and Synjardy® (Empagliflozin/Metformin) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Diabetes Medications
C. Prior Authorization of Diabetes Medications
D. Market News and Updates
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Diabetic Medications
H. Utilization Details of Insulin Medications

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

14. Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Entresto™ (Sacubitril/Valsartan) – See Appendix L

A. Utilization of Antihypertensive Medications
B. Prior Authorization of Antihypertensive Medications
C. Market News and Updates
D. Entresto™ (Sacubitril/Valsartan) Product Summary
E. College of Pharmacy Recommendations
F. Utilization Details of Antihypertensive Medications
G. Current Prior Authorization Criteria

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

15. Annual Review of Diabetic Supplies – See Appendix M

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

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

16. FDA and DEA Updates – See Appendix N

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

17. Future Business* (Upcoming Product and Class Reviews)
No Meeting Scheduled for May 2016

A. ADHD and Narcolepsy Medications
B. Atypical Antipsychotic Medications
C. Anthelmintic Medications
D. Prostate Cancer Medications
E. Cholbam™ (Cholic Acid)
F. Natpara® (Parathyroid Hormone)
G. Various Special Formulations

***Future business subject to change.**

18. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MARCH 9, 2016

BOARD MEMBERS:	PRESENT	ABSENT
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	
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
James Rhymer, D.Ph.	x	
Bruna Varalli-Claypool, MHS, PA-C	x	
Eric Winegardner, D.Ph.	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
Tammy Lambert, Ph.D.; Postdoctoral Research Fellow	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Graduate Students: Christina Bulkley, Pharm.D.		x
David George, Pharm.D.		x
Timothy Pham, Pharm.D.	x	
Visiting Pharmacy Student(s): Amy Dunaway-Knight	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	x	
Kelli Brodersen, Marketing Coordinator	x	
Nico Gomez, Chief Executive Officer		x
Ed Long, Chief Communications Officer		x
Sylvia Lopez, M.D.; FAAP; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Deputy Chief Executive Officer		x
Joseph Young, Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Bob Gustafson, Lundbeck	Don Nopper, United Therapeutics	Mai Duong, Novartis
John Schillo, Lundbeck	Rachel Gragg, Teva	Bob Atkins, Biogen
Deron Grothe, Teva	Sean Seago, Merck	Nima Nabaui, Novo Nordisk
Contessa Fincher, Teva	Toby Thompson, Pfizer	Marc Parker, Sunovion
Tari Malmgren, Actelion	Brian Maves, Pfizer	Andrea Martin, AstraZeneca
Doug Wood, ViiV Healthcare	Jim Chapman, AbbVie	Kirsten Mar, AstraZeneca
Gwendolyn Caldwell, Pharma	Josh Diesselhorst, Novo Nordisk	Charlie Collins, Genzyme
Melvin Nwamadi, Abbott	Luke Weedin, Biogen	Aaron Shaw, Boehringer

PRESENT FOR PUBLIC COMMENT:	
Kirsten Mar	AstraZeneca
Luke Weedin	Biogen
Contessa Fincher	Teva

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 NO. 8 KRISTEN MAR

2B: AGENDA NO. 10 LUKE WEEDIN

2C: AGENDA NO. 10 CONTESSA FINCHER

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: FEBRUARY 10, 2016 DUR MINUTES – VOTE

3B: FEBRUARY 10, 2016 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/FDA SAFETY ALERTS

4A: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2016

4B: PHARMACY HELP DESK ACTIVITY FOR FEBRUARY 2016

4C: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE SPRITAM® (LEVETIRACETAM), VIMPAT® (LACOSAMIDE), BANZEL® (RUFINAMIDE), AND FYCOMPA® (PERAMPANEL)

5A: INTRODUCTION

5B: MARKET NEWS AND UPDATES

5C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE SOLARAZE® (DICLOFENAC GEL)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE UCERIS® (BUDESONIDE EXTENDED-RELEASE TABLETS), UCERIS® (BUDESONIDE RECTAL FOAM), AND MISCELLANEOUS MESALAMINE PRODUCTS**

7A: INDICATION(S)

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE MITIGARE™ (COLCHICINE CAPSULES) AND ZURAMPIC® (LESINURAD)**

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE PAZEO® (OLOPATADINE OPHTHALMIC)**

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF MULTIPLE SCLEROSIS MEDICATIONS**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF MULTIPLE SCLEROSIS MEDICATIONS

10C: PRIOR AUTHORIZATION OF MULTIPLE SCLEROSIS MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: COST ANALYSIS

10F: COLLEGE OF PHARMACY RECOMMENDATIONS

10G: UTILIZATION DETAILS OF MULTIPLE SCLEROSIS MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF NALOXONE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EVZIO® (NALOXONE AUTO-INJECTOR)**

11A: CURRENT PRIOR AUTHORIZATION CRITERIA

11B: UTILIZATION OF NALOXONE MEDICATIONS

11C: NALOXONE MEDICATION UTILIZATION ANALYSIS

11D: MARKET NEWS AND UPDATES

11E: EVZIO® (NALOXONE AUTO-INJECTOR) PRODUCT SUMMARY

11F: COLLEGE OF PHARMACY RECOMMENDATIONS

11G: UTILIZATION DETAILS OF NALOXONE MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE UPTRAVI® (SELEXIPAG)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS

12C: PRIOR AUTHORIZATION OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: UPTRAVI® (SELEXIPAG) PRODUCT SUMMARY

12F: COLLEGE OF PHARMACY RECOMMENDATIONS
12G: UTILIZATION DETAILS OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE CEREZYME® (IMIGLUCERASE), ELELYSO® (TALIGLUCERASE ALFA), VPRIV® (VELAGLUCERASE ALFA), CERDELGA® (ELIGLUSTAT), AND ZAVESCA® (MIGLUSTAT)
13A: GAUCHER DISEASE (GD) OVERVIEW
13B: UTILIZATION OF GD MEDICATIONS
13C: CEREZYME® (IMIGLUCERASE) PRODUCT SUMMARY
13D: ELELYSO® (TALIGLUCERASE ALFA) PRODUCT SUMMARY
13E: VPRIV® (VELAGLUCERASE ALFA) PRODUCT SUMMARY
13F: CERDELGA® (ELIGLUSTAT) PRODUCT SUMMARY
13G: ZAVESCA® (MIGLUSTAT) PRODUCT SUMMARY
13H: COLLEGE OF PHARMACY RECOMMENDATIONS
13I: UTILIZATION DETAILS OF GD MEDICATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF VASOMOTOR SYMPTOM MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ELESTRIN® (ESTRADIOL GEL 0.06%)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF VASOMOTOR SYMPTOM MEDICATIONS
14C: PRIOR AUTHORIZATION OF VASOMOTOR SYMPTOM MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: ELESTRIN® (ESTRADIOL GEL) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF VASOMOTOR SYMPTOM MEDICATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF BOTULINUM TOXINS
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF BOTULINUM TOXIN PRODUCTS
15C: PRIOR AUTHORIZATION OF BOTULINUM TOXINS
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF BOTULINUM TOXIN PRODUCTS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF IDIOPATHIC PULMONARY FIBROSIS (IPF) MEDICATIONS
16A: INTRODUCTION
16B: CURRENT PRIOR AUTHORIZATION CRITERIA
16C: UTILIZATION OF IPF MEDICATIONS
16D: PRIOR AUTHORIZATION OF IPF MEDICATIONS
16E: MARKET NEWS AND UPDATES
16F: COLLEGE OF PHARMACY RECOMMENDATIONS
16G: UTILIZATION DETAILS OF IPF MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams (Non-presentation; questions only)
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF SYLVANT™ (SILTUXIMAB)**

17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF SYLVANT™ (SILTUXIMAB)
17D: PRIOR AUTHORIZATION OF SYLVANT™ (SILTUXIMAB)
17E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz (Non-presentation; questions only)
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: **FDA AND 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: FISCAL YEAR 2015 ANNUAL REVIEW OF SOONERCARE PHARMACY BENEFIT
19B: MAKENA® (HYDROXYPROGESTERONE CAPROATE)
19C: BOWEL PREPARATION MEDICATIONS
19D: ANTIHYPERTENSIVE MEDICATIONS
19E: HEMOPHILIA PHARMACY PROVIDERS STANDARDS OF CARE
19F: DIABETIC MEDICATIONS
19G: DIABETIC SUPPLIES
19H: HEPATITIS C MEDICATIONS

***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 5:12pm

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

Memorandum

Date: March 10, 2016

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 09, 2016

Recommendation 1: Overview of FDA Safety Alerts

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Spritam® (Levetiracetam), Vimpat® (Lacosamide), Banzel® (Rufinamide), and Fycompa® (Perampanel)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Aptiom® (eslicarbazepine) to include its new indication for monotherapy
2. The prior authorization of Spritam® (levetiracetam) with the criteria noted in red
3. The prior authorization of Vimpat® (lacosamide) with the criteria noted in red
4. The prior authorization of Banzel® (rufinamide) with the criteria noted in red
5. The prior authorization of Fycompa® (perampanel) with the criteria noted in red

New proposed criteria specific to each medication is as follows:

Aptiom® (Eslicarbazepine) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures ~~as adjunctive therapy~~; and
2. ~~Member must be on current antiepileptic drug therapy (Aptiom® is only indicated for adjunctive treatment); and~~

3. Member must not currently be taking oxcarbazepine (concurrent use is contraindicated); and
4. A patient-specific, clinically significant reason why member cannot use oxcarbazepine.
5. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (200mg and 400mg) and 60 tablets per 30 days on the higher strength tablets (600mg and 800mg).

Spritam® (Levetiracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures, myoclonic seizures, or primary generalized tonic-clonic (PGTC) seizures; and
2. A patient-specific, clinically significant reason why the member cannot use generic formulations of levetiracetam.
3. A quantity limit of 60 tablets per 30 days will apply.

Vimpat® (Lacosamide) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Vimpat® and who have a seizure diagnosis will be grandfathered.

Banzel® (Rufinamide) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut Syndrome; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Banzel® and who have a seizure diagnosis will be grandfathered.

Fycompa® (Perampanel) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of partial-onset seizures with or without secondarily generalized seizures or primary generalized tonic-clonic (PGTC) seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Fycompa® and who have a seizure diagnosis will be grandfathered.

Recommendation 3: Vote to Prior Authorize Solaraze® (Diclofenac 3% Gel)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Solaraze® (diclofenac 3% gel) with the following criteria:

Solaraze® (Diclofenac 3% Gel) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK); and
2. Patient-specific information must be documented on the prior authorization form, including all of the following:
    a. Number of AK lesions being treated; and
    b. Sizes of each lesion being treated; and
    c. Anticipated duration of treatment; and
3. Approval quantity and length will be based on patient-specific information provided, in accordance with Solaraze® prescribing information and FDA approved dosing regimen.

Recommendation 4: Vote to Prior Authorize Uceris® (Budesonide Extended-Release Tablets), Uceris® (Budesonide Rectal Foam), and Miscellaneous Mesalamine Products

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Uceris® extended-release tablets, Uceris® rectal foam, and various mesalamine products with the following criteria:

Uceris® (Budesonide) Extended-Release Tablets Approval Criteria:

1. An FDA approved diagnosis of induction of remission in patients with active, mild-to-moderate ulcerative colitis; and
2. Previous failure of at least two of the following:
    a. Oral aminosalicylates; or
    b. Topical mesalamine; or
    c. Topical steroids; or
    d. A contraindication to all preferred medications; and
3. A patient-specific, clinically significant reason why the member cannot use other oral corticosteroids available without prior authorization; and
4. Approvals will be for the duration of eight weeks in accordance with manufacturer maximum recommended duration of therapy.
5. A quantity limit of 30 tablets per 30 days will apply.

Uceris® (Budesonide) Rectal Foam Approval Criteria:

1. An FDA approved diagnosis of induction of remission in patients with active, mild-to-moderate, distal ulcerative colitis extending up to 40cm from the anal verge; and
2. A patient-specific, clinically significant reason why the member cannot use oral aminosalicylates, topical mesalamine, or other topical (rectally administered) corticosteroids available without prior authorization; and
3. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy.
4. A quantity limit of 133.6 grams per 42 days will apply.

Asacol® HD (Mesalamine) Delayed-Release Tablets Approval Criteria:

1. An FDA approved indication of the treatment of moderately active ulcerative colitis; and
2. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that do not require prior authorization; and

3. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 180 tablets per 30 days will apply.

Pentasa® (Mesalamine) 500mg Controlled-Release Capsules Approval Criteria:

1. An FDA approved indication for the induction of remission or for the treatment of patients with mildly to moderately active ulcerative colitis; and
2. A patient-specific, clinically significant reason the member cannot use Pentasa® 250mg controlled-release capsules or other available mesalamine products that do not require prior authorization; and
3. Approvals will be for the duration of eight weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 240 capsules per 30 days will apply.

Rowasa® (Mesalamine) Rectal Suspension Enema Approval Criteria:

1. The first three weeks of treatment would not require prior authorization.
2. An FDA approved indication for the treatment of active, mild-to-moderate, distal ulcerative colitis, proctosigmoiditis, or proctitis; and
3. A patient-specific, clinically significant reason the member cannot use Canasa® (mesalamine suppositories) which do not require prior authorization; and
4. Provider documentation member is still having active symptoms after three weeks of treatment; and
5. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy; and
6. A quantity limit of 30 enemas (1,800mL) per 30 days will apply.

Lialda® (Mesalamine) Delayed-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 60 capsules per 30 days will apply.
2. For quantity limit requests for greater than two capsules per day:
    a. An FDA approved indication for the induction of remission in patients with active, mild-to-moderate ulcerative colitis; and
    b. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that are indicated to induce remission that do not require prior authorization; and
    c. Approvals will be for the duration of eight weeks in accordance with manufacturer recommended duration of therapy; and
    d. A maximum approval of 120 capsules per 30 days will apply.

Colazal® (Balsalazide) Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 270 capsules per 30 days will apply.
2. The first twelve weeks of treatment would not require prior authorization.
3. After twelve weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.
4. An age restriction of five years and older will apply.

Pentasa® (Mesalamine) 250mg Controlled-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 480 capsules per 30 days will apply.
2. The first eight weeks of treatment would not require prior authorization.
3. After eight weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Canasa® (Mesalamine) Suppositories Quantity Limit Approval Criteria:

1. A quantity limit of 30 suppositories per 30 days will apply.
2. The first six weeks of treatment would not require prior authorization.
3. After six weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Apriso® (Mesalamine) Extended-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Delzicol® (Mesalamine) Delayed-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 180 capsules per 30 days will apply.

Dipentum® (Olsalazine) Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Recommendation 5: Vote to Prior Authorize Mitigare™ (Colchicine Capsules) and Zurampic™ (Lesinurad)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Mitigare™ (colchicine capsules) and Zurampic™ (lesinurad) with the following criteria:

Mitigare™ (Colchicine Capsules) and Colcrys® (Colchicine Tablets) Approval Criteria:

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

Zurampic™ (Lesinurad) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of gout in patients who have not achieved target serum uric acid (sUA) levels with a xanthine oxidase inhibitor (XOI) alone; and
3. Failure of allopurinol or febuxostat alone defined by serum urate levels greater than 6.0mg/dL; and

4. Prescriber must verify that member has a creatinine clearance greater than 45mL/min prior to initiating treatment and for continued approval; and
5. Prescriber must verify that member will take Zurampic™ concomitantly with a XOI; and
6. Prescriber must document member is not taking more than 325mg of aspirin per day and member is not taking any epoxide hydrolase inhibitors; and
7. Prescriber must document member has no contraindications for use of Zurampic™ including any of the following**:** Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl less than 30mL/min), end stage renal disease, kidney transplant recipients, or patients on dialysis.
8. A quantity limit of one tablet daily will apply.

Recommendation 6: Vote to Prior Authorize Pazeo® (Olopatadine Ophthalmic)

MOTION CARRIED by unanimous approval.

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

1. The addition of Pazeo® (olopatadine solution) to Tier-3. Current Tier-3 criteria for this category will apply.
    a. Pazeo® (olopatadine solution) is currently rebated to Tier-2, but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.
2. Move olopatadine (generic Patanol®) to Tier-2 based on state maximum allowable cost (SMAC). Current Tier-2 criteria for this category will apply.

Ocular Allergy Medications*		
Tier-1	**Tier-2**	**Tier-3**
cromolyn (Crolom®)	azelastine (Optivar®)	alcaftadine (Lastacaft™)
ketotifen (Alaway®, Zaditor® OTC)	**olopatadine (Pazeo®)**	bepotastine (Bepreve™)
	olopatadine (Patanol®)	emedastine (Emadine®)
		epinastine (Elestat®)
		lodoxamide (Alomide®)
		loteprednol (Alrex®)
		nedocromil (Alocril®)
		olopatadine (Pataday®)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications are subject to move to Tier-3.
OTC = Over-the-counter

Ocular Allergy Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of one Tier-1 product for a minimum of two weeks in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. A contraindication to all lower tiered medications.

Ocular Allergy Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and

2. Recent trials of one Tier-1 product and all available Tier-2 medications for a minimum of two weeks each that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. A contraindication to all lower tiered medications.

Recommendation 7: Annual Review of Multiple Sclerosis Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the criteria for Tysabri® (natalizumab) to reflect current indications and clinical guidelines.

Tysabri® (Natalizumab) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis (MS) or Crohn's disease; and
2. ~~Treatment with at least two different first line therapeutic categories for MS that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second line alternatives.~~ For a diagnosis of MS the following criteria will apply:
    a. Prescriber must be a neurologist or be an advanced care practitioner with a supervising prescriber that is a neurologist; and
    b. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. For a diagnosis of Crohn's disease the following criteria will apply:
    a. Treatment with at least two different first line therapeutic categories for Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second line alternatives; and
4. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

Recommendation 8: Annual Review of Naloxone Medications and 30-Day Notice to Prior Authorize Evzio® (Naloxone Auto-Injector)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Uptravi® (Selexipag)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Vasomotor Symptom Medications and 30-day Notice to Prior Authorize Elestrin® (Estradiol Gel 0.06%)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Botulinum Toxins

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Idiopathic Pulmonary Fibrosis Medications

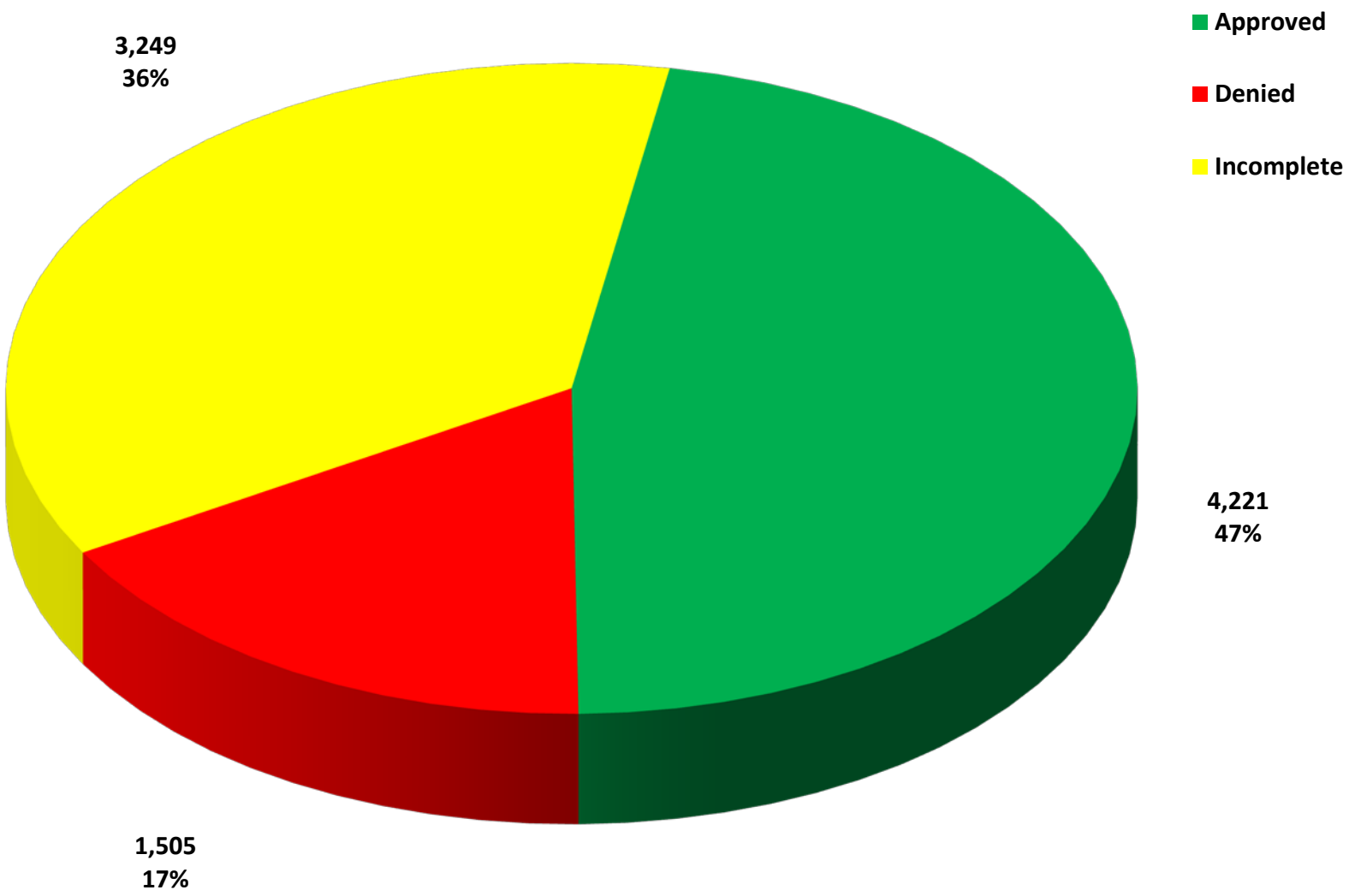
NO ACTION REQUIRED.

Recommendation 14: Annual Review of Sylvant™ (Siltuximab)

NO ACTION REQUIRED.

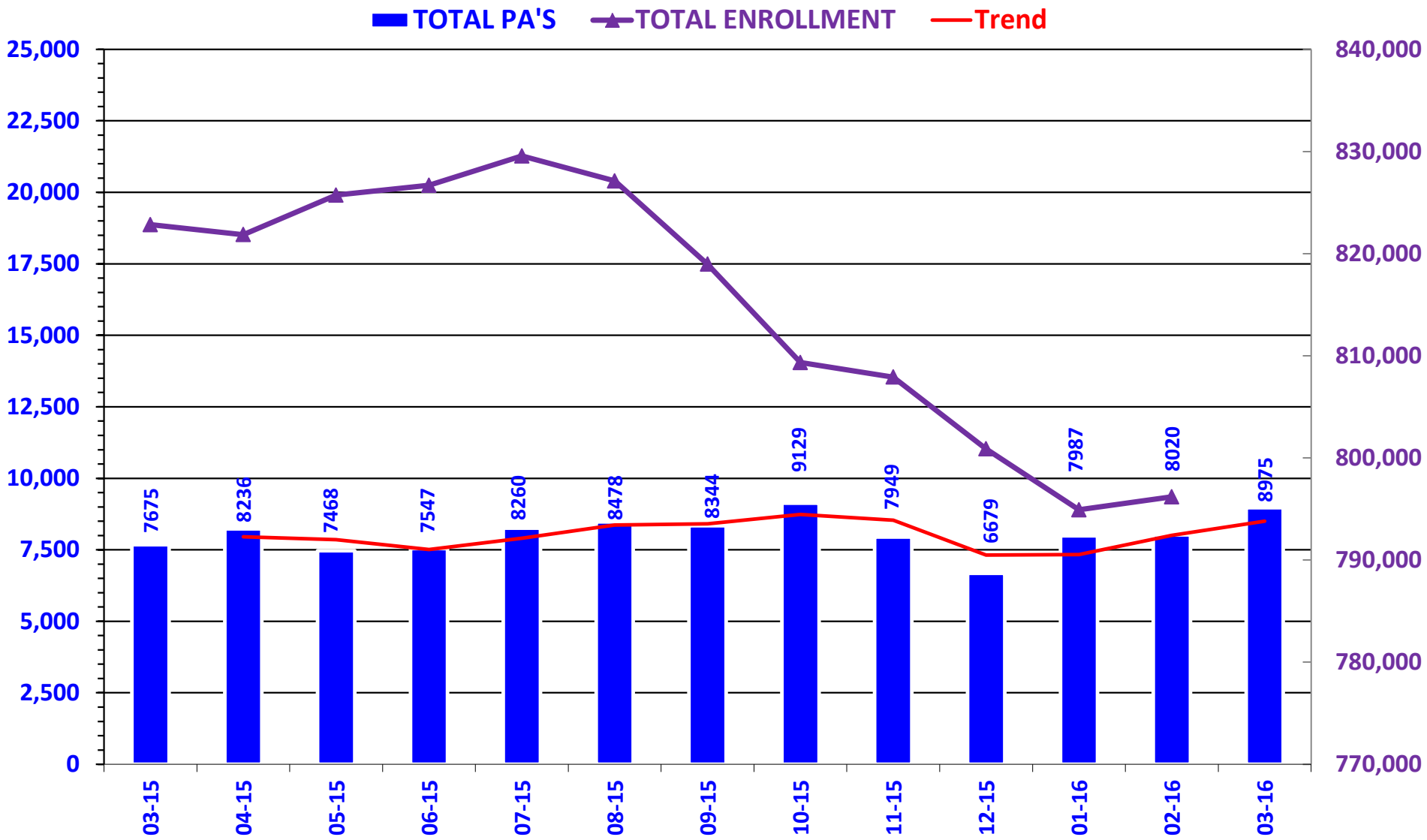
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH 2016



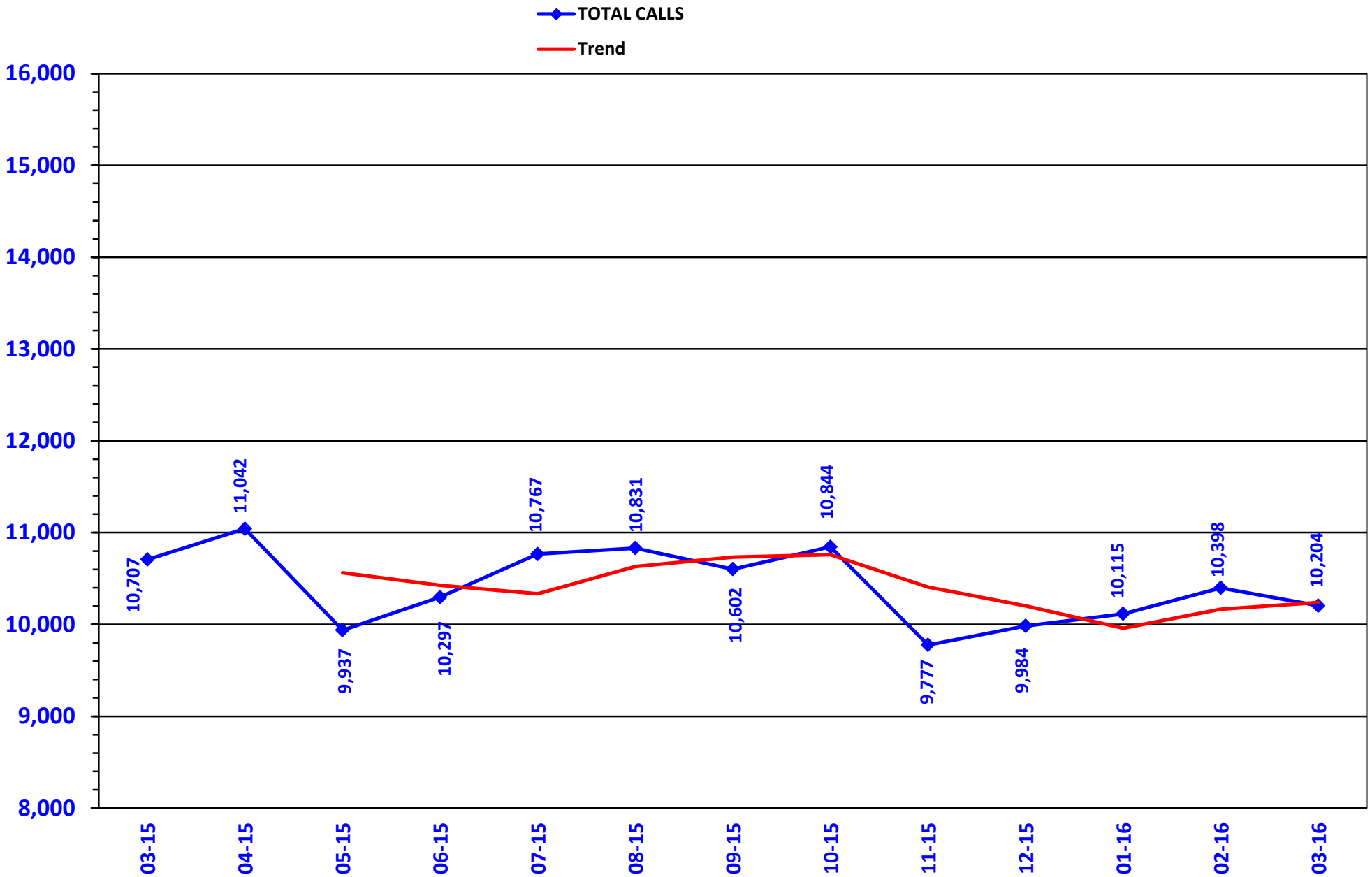
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MARCH 2015 – MARCH 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MARCH 2015 – MARCH 2016



Prior Authorization Activity

3/1/2016 Through 3/31/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	393	157	66	170	351
Analgesic - NonNarcotic	27	0	4	23	0
Analgesic - Narcotic	470	259	45	166	163
Angiotensin Receptor Antagonists	34	6	10	18	359
Antiasthma	96	28	25	43	313
Antibiotics	30	18	1	11	188
Anticonvulsants	82	31	14	37	321
Antidepressants	109	24	26	59	316
Antidiabetic	198	81	30	87	356
Antifungal	12	1	4	7	21
Antigout	14	5	4	5	357
Antihistamine	175	146	6	23	355
Antimigraine	43	12	12	19	238
Antineoplastic	43	30	4	9	184
Antiulcer	194	39	80	75	142
Anxiolytic	72	45	5	22	257
Atypical Antipsychotics	518	305	43	170	335
Biologics	117	54	25	38	305
Bladder Control	76	28	16	32	327
Blood Thinners	206	130	12	64	320
Botox	42	27	10	5	344
Buprenorphine/Naloxone	254	186	20	48	75
Calcium Channel Blockers	10	2	0	8	223
Cardiovascular	56	26	7	23	320
Cephalosporins	18	11	2	5	7
Chronic Obstructive Pulmonary Disease	75	12	16	47	334
Constipation/Diarrhea	196	21	92	83	149
Contraceptives	23	17	3	3	298
Dermatological	138	18	81	39	94
Diabetic Supplies	614	338	21	255	200
Endocrine & Metabolic Drugs	89	60	9	20	138
Erythropoietin Stimulating Agents	32	16	7	9	108
Fibromyalgia	226	41	105	80	335
Fish Oils	10	3	4	3	360
Gastrointestinal Agents	84	21	30	33	116
Genitourinary Agents	20	7	1	12	195
Growth Hormone	104	81	13	10	151
Hepatitis C	195	94	36	65	8
HFA Rescue Inhalers	48	20	7	21	301
Insomnia	56	12	15	29	169
Insulin	61	9	17	35	329
Miscellaneous Antibiotics	26	5	3	18	77
Multiple Sclerosis	49	20	9	20	189
Muscle Relaxants	61	13	21	27	28
Nasal Allergy	113	21	29	63	233
Neurological Agents	31	20	6	5	351
NSAIDs	204	20	57	127	195
Ocular Allergy	53	9	15	29	207
Ophthalmic Anti-infectives	13	1	5	7	5
Osteoporosis	19	9	4	6	313
Other*	256	59	85	112	244
Otic Antibiotics	12	2	0	10	6
Pediculicides	39	11	4	24	22
Prenatal Vitamins	10	0	0	10	0
Statins	48	15	9	24	358
Stimulants	944	449	115	380	335

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Synagis	73	24	29	20	34
Testosterone	44	8	14	22	298
Topical Antifungal	52	1	14	37	177
Topical Corticosteroids	188	1	67	120	55
Vitamins	67	22	26	19	267
Pharmacotherapy	70	64	0	6	271
Emergency PAs	0	0	0	0	
Total	**7,632**	**3,195**	**1,440**	**2,997**	
Overrides					
Brand	60	32	9	19	278
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	4	4	0	0	67
Dosage Change	330	306	3	21	11
High Dose	4	4	0	0	353
Ingredient Duplication	33	21	1	11	8
Lost/Broken Rx	99	95	1	3	11
NDC vs Age	45	41	0	4	232
Nursing Home Issue	87	85	1	1	11
Opioid Quantity	22	17	4	1	156
Other	25	23	1	1	10
Quantity vs. Days Supply	593	378	38	177	254
STBS/STBSM	20	17	1	2	72
Stolen	11	10	0	1	7
Third Brand Request	36	14	10	12	15
Overrides Total	**1,343**	**1,026**	**65**	**252**	
Total Regular PAs + Overrides	**8,975**	**4,221**	**1,505**	**3,249**	

Denial Reasons	
Unable to verify required trials.	2,828
Does not meet established criteria.	1,462
Lack required information to process request.	457

Other PA Activity	
Duplicate Requests	611
Letters	7,143
No Process	9
Changes to existing PAs	558
Helpdesk Initiated Prior Authorizations	751
PAs Missing Information	33

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
April 2016

Prescriber Mailing: Maintenance Cardiovascular Medications

The College of Pharmacy and the Oklahoma Health Care Authority are engaged in an educational quarterly mailing to prescribers with members on chronic maintenance medications for diabetes, blood pressure, or cholesterol. The purpose of these mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Each mailing includes a prescriber summary report with a "star rating" based on their overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is greater than or equal to 80%. A patient is considered non-adherent if their PDC is less than 80%. Patients must have at least two pharmacy claims for at least one medication in the drug category in the past year to be included in the calculations.

The fourth mailing was processed in August and addressed adherence to maintenance renin angiotensin system (RAS) antagonists (e.g., angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors) and HMG-CoA reductase inhibitors (i.e., statins). Prescribers with three or more patients on both classes of medications were eligible for inclusion in the mailing if their percentage of patients considered adherent was greater than or equal to 60% for either class but less than 78% for statins or 84% for RAS antagonists (1 to 4 stars). The review period was for one year and patients were assigned to prescribers if they were the last prescriber of record for a RAS antagonist and/or statin pharmacy claim.

A total of 3,108 RAS antagonist prescribers and 2,402 statin prescribers were evaluated based on the computed adherence claims. These prescribers had 3,070 statin members and 5,291 RAS antagonist members considered non-adherent based on PDC calculations. A total of 259 prescribers were included in the mailing which accounted for 4,497 patients intervened for adherence.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	259
Members	**Count**
Total Members Included	4,497

Example Star Rating[1]

Report date: 07/31/2015
Provider: <Provider Name>
NPI: <Prescriber NPI>
SoonerCare Provider ID: <Provider ID>

Percentage of patients adherent to RAS antagonists: 66.67%

1 out of 5 stars

Percentage of patients adherent to statins: 60.00%

1 out of 5 stars

Chronic Medication Adherence Star Rating

Adherence is shown in the Provider Summary Report as a percentage for RAS antagonists and as a percentage for statins, with a corresponding star rating for each category. The star ratings for the percentage of patients that are adherent to RAS antagonists or statins are based on the 2015 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. A key is shown below to illustrate the star ratings and adherence percentages for each star rating. All mailings processed in 2016 have been updated to reflect the adherence percentages in the 2016 Medicare Star Ratings.

RAS antagonists:

5 Stars: Excellent (≥ 84%)

4 Stars: Above Average (≥ 81% to < 84%)

3 Stars: Average (≥ 76% to < 81%)

2 Stars: Below Average (≥ 72% to < 76%)

1 Star: Poor (≥ 60% to < 72%)

0 Stars: Very Poor (< 60%)

Statins:

5 Stars: Excellent (≥ 78%)

4 Stars: Above Average (≥ 75% to < 78%)

3 Stars: Average (≥ 69% to < 75%)

2 Stars: Below Average (≥ 62% to < 69%)

1 Star: Poor (≥ 60% to < 62%)

0 Stars: Very Poor (< 60%)

Chronic Medication Adherence PDC by Drug Category

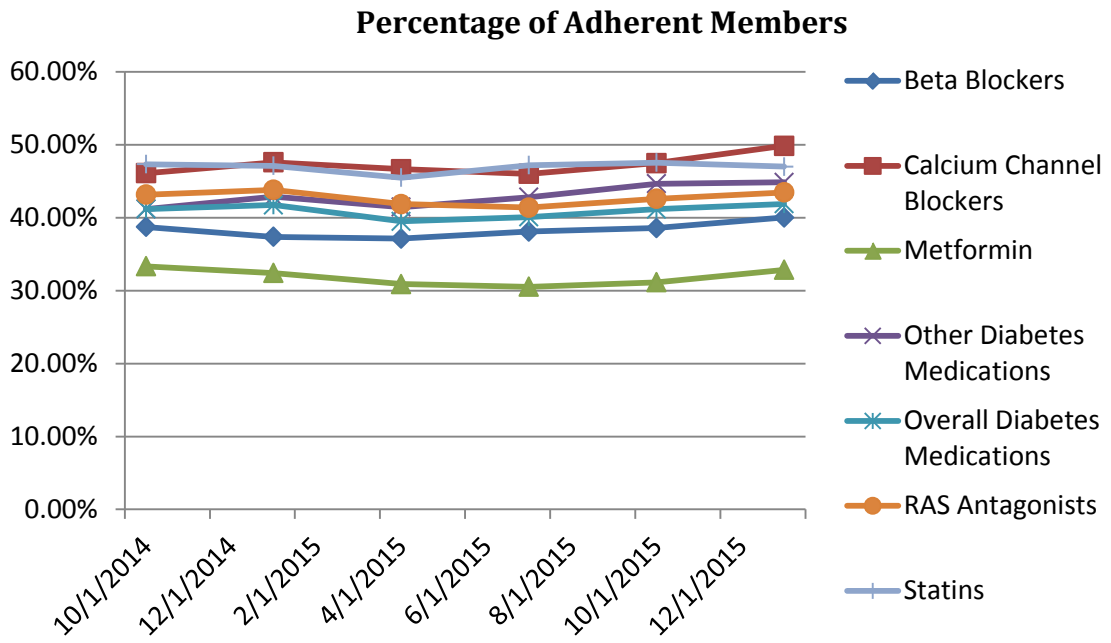
The average member PDC based on drug category is listed in the following table. Also listed is the average prescriber percentage of adherent members (PDC ≥ 80%) for each category and the average star rating for the applicable categories. Star ratings listed as N/A are either subcategories or categories that are not included in Medicare's star ratings thus far.

Drug Category	Member PDC	Prescriber % of Adherent Members	Star Rating
Beta Blockers	65.58%	38.11%	N/A
Calcium Channel Blockers	70.89%	46.03%	N/A
Metformin	60.58%	30.53%	N/A
Other Diabetes Medications	68.35%	42.83%	N/A
Overall Diabetes Medications	66.58%	40.09%	0 stars
RAS Antagonists	68.72%	41.39%	0 stars
Statins	71.46%	47.21%	0 stars

The average member PDC and the percent of adherent members is tracked for all drug categories each time a mailing is processed. The following line graph shows trends in the percentage of adherent members for each drug category since the Chronic Medication Adherence initiative commenced. The line graph depicts the percentage of adherent members for all of SoonerCare and does not differentiate those members who were included in a mailing. A promising increase can be seen in the percentage of adherent members across all categories in recent months. A review of average PDC for prescribers who received a mailing six months after the original cardiovascular chronic medication adherence mailing did not reveal increases in average PDC for any of the cardiovascular medication categories.

Of note, the beta blockers and calcium channel blockers are being monitored but have not yet been included in the mailings to prescribers. Topics and dates of previous and current mailings include the following:

- **Metformin and Other Diabetes Medications:** November 2014, May 2015, November 2015
- **RAS Antagonists and Statins:** February 2015, August 2015, February 2016



Future Mailings

The chronic medication adherence educational mailings are processed quarterly and alternate between diabetes and cardiovascular (blood pressure and cholesterol) medication adherence. Previously, prescribers were selected randomly to receive letters if they met the inclusion criteria for the mailing. Future chronic medication adherence mailings will be mailed to the same consistent prescribers. Included prescribers will receive four letters per year (two diabetes letters and two cardiovascular letters), to better inform them of their SoonerCare patients' medication adherence and to make it more convenient to track their medication adherence over time including any improvements or changes. Inclusion criteria will require the prescriber to have two or more SoonerCare patients taking diabetes, blood pressure, and cholesterol medications.

Medication Adherence Informational Page and Patient Resources[2,3,4,5,6]

Medication adherence is essential for positive therapeutic outcomes. Non-adherence may lead to false medication failure, resulting in unnecessary dose increases and/or medication changes or additions, complications associated with high blood pressure and/or high cholesterol, and increased health-care costs. Patients need to understand the importance of taking their blood pressure and/or cholesterol medications as directed to reduce the risk of serious complications, such as heart disease, stroke, kidney failure, and pre-mature death. Dosing regimens, possible adverse effects, the importance of medication compliance, and long-term serious complications associated with high blood pressure and/or high cholesterol should be discussed with the patient to address any concerns and improve medication adherence, resulting in improved blood pressure and/or cholesterol control and a decreased risk of serious complications.

Please refer to the websites below for helpful patient resources:

- *National Consumers League:* Script Your Future (videos, adherence tools for patients, medication guides)
  http://www.scriptyourfuture.org/cardiovascular/
- *FDA:* High Blood Pressure Medications and You (how hypertension medications work)
  http://www.fda.gov/downloads/Drugs/ResourcesForYou/SpecialFeatures/UCM358489.pdf
- *Million Hearts:* High Blood Pressure (patient fact sheet)
  http://millionhearts.hhs.gov/Docs/MH_PCNA_Blood_Pressure_Fact_Sheet.pdf
- *American Heart Association (AHA):* Life's Simple 7 Heart Health Factors (information and resources)
  http://mylifecheck.heart.org/Multitab.aspx?NavID=3&CultureCode=en-US
- *AHA:* Heart360® (tracks blood pressure, physical activity, cholesterol, glucose, weight, and medications)
  https://www.heart360.org/
- *Merck:* Adherence Estimator® (helps identify patients who may be at risk of medication nonadherence)
  http://www.adherenceestimator.com/

[1]Centers for Medicare & Medicaid Services: *Medicare 2015 Part C & D Star Rating Technical Notes*. Available online at http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Last updated 04/2015. Last accessed 03/17/2016.

[2] Centers for Disease Control and Prevention: *Heart Disease Facts.* Available online at: http://www.cdc.gov/heartdisease/facts.htm. Last updated 8/10/2015. Last accessed 03/17/2016.

[3] Ho PM, Bryson CL, et al. Medication Adherence: Its Importance in Cardiovascular Outcomes. *Circulation*. 2009. 119: 3028-3035.

[4] Krousel-Wood M, Thomas S, et al. Medication adherence: a key factor in achieving blood pressure control and good clinical outcomes in hypertensive patients. *Curr Opin Cardiol.* 2004. 19 (4): 357-362.

[5] Gatwood J, Bailey, JE. Improving medication adherence in hypercholesterolemia: challenges and solutions. *Vasc Health Risk Manag.* 2014. 2014 (10): 615-625.

[6] Centers for Medicare & Medicaid Services: *Medicare 2016 Part C & D Star Rating Technical Notes*. Available online at https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovgenin/performancedata.html. Last updated 09/2015. Last accessed 03/17/2016.

Appendix C

Vote to Prior Authorize Uptravi® (Selexipag)

Oklahoma Health Care Authority
April 2016

Indication and Treatment[1,2]

Uptravi® (selexipag) is a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Treatment guidelines published in *CHEST* in 2014 recommend the use of endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE-5), or soluble guanylate cyclase stimulators for treatment of PAH in low risk patients based on clinical assessment. Pharmacological treatment should be patient-specific and guided by high-level recommendations when sufficient evidence is available.

Cost Comparison:

Drug	Strength	Cost per Tablet	Cost per Month**
Uptravi® (selexipag) tablet	**200mcg**	**$164.38**	**$9,862.80**
Uptravi® (selexipag) tablet	**400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg**	**$255.55**	**$15,333.00**
Uptravi® (selexipag) titration pack	**200mcg and 800mcg**	**$115.00**	**$23,000.00**
Orenitram™ (treprostinil) tablet	0.25mg	$10.30	$618.00[+]
sildenafil tablet	20mg	$0.62*	$55.80
Tracleer® (bosentan) tablet	125mg	$162.78	$9,766.80
Adempas® (riociguat) tablet	0.5mg, 1mg, 1.5mg, 2mg, 2.5mg	$101.84	$9,165.60

Costs listed are based on estimated acquisition cost (EAC) unless otherwise noted.
*Cost based on state maximum allowed cost (SMAC).
[+]Based on 0.25mg twice daily. Dose may be titrated up based on tolerability.
**Costs do not reflect rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Uptravi® (selexipag) tablets with the following criteria:

Uptravi® (Selexipag) Tablets Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension (PAH); and
2. Member must be 18 years of age or older; and
3. Previous failed trials of at least one of each of the following categories (alone or in combination):
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    c. Adempas® (riociguat); and

   d. Orenitram™ (treprostinil); and
4. Medical supervision by a pulmonary specialist and/or cardiologist; and
5. A quantity limit of two tablets daily will apply for all strengths with an upper dose limit of 1,600mcg twice daily.

[1]Uptravi® Tablets Prescribing Information, Actelion Pharmaceutical US, Inc. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207947s000lbl.pdf . Last revised 12/2015. Last accessed 02/2016.
[2] Taichman, MD, PhD, FCCP, Darren B, et al. "Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults" *CHEST Journal*. http://journal.publications.chestnet.org/article.aspx?articleid=1881654. Issued 08/2014. Last assessed 03/2016.

Appendix D

Vote to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat)

Oklahoma Health Care Authority
April 2016

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

- **Cerezyme® (imiglucerase)** was first approved by the U.S. Food and Drug Administration (FDA) in 1994 as long-term enzyme replacement therapy (ERT) for pediatric and adult patients with a confirmed diagnosis of type-1 Gaucher disease (GD1) that results in anemia, thrombocytopenia, bone disease, and/or hepatomegaly or splenomegaly. Cerezyme® is administered as an intravenous (IV) infusion over 1 to 2 hours and the dose is individualized to each patient. The initial dosage range for which the most data is available is 2.5 units/kg of body weight three times a week to 60 units/kg every two weeks.
- **Elelyso® (taliglucerase alfa)** was FDA approved in May 2012 and is indicated for the treatment of patients 4 years of age and older with a confirmed diagnosis of GD1. Elelyso® is administered as an IV infusion over 1 to 2 hours and the recommended dosage for treatment-naïve patients is 60 units/kg of body weight every other week.
- **Vpriv® (velaglucerase alfa)** was FDA approved in February 2010 and is indicated for long-term ERT for adult and pediatric patients 4 years of age or older with GD1. Vpriv® is administered as an IV infusion and the recommended dosage for treatment-naïve patients is 60 units/kg of body weight every other week.
- **Cerdelga® (eliglustat)** was FDA approved in August 2014 and is indicated for the long-term treatment of adult patients with GD1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test. Cerdelga® is available as an 84mg oral capsule and the recommended dosing regimen is based upon patient CYP2D6 metabolizer status. The dose for CYP2D6 EMs or IMs is 84mg orally twice daily and the dose for CYP2D6 PMs is 84mg orally once daily.
- **Zavesca® (miglustat)** was FDA approved in July 2003 and is indicated as monotherapy for the treatment of adult patients with mild/moderate GD1 for whom ERT is not a therapeutic option. Zavesca® is available as oral capsules and the recommended dose is 100mg administered orally three times a day.

Recommendations

The College of Pharmacy recommends the prior authorization of Cerezyme® (imiglucerase), Elelyso® (taliglucerase alfa), Vpriv® (velaglucerase alfa), Cerdelga® (eliglustat), and Zavesca® (miglustat) with the following criteria:

Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), and Vpriv® (Velaglucerase Alfa) Approval Criteria:

1. A diagnosis of symptomatic (e.g., anemia, thrombocytopenia, bone disease, splenomegaly, or hepatomegaly) Type 1 or Type 3 Gaucher disease (GD); and
2. Member's weight (kg) must be provided and have been taken within the last four weeks to ensure accurate weight based dosing; and
3. Prescriber must verify that the member will not take requested therapy concurrently with another therapy for GD.
4. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

Cerdelga® (Eliglustat) Approval Criteria:

1. An FDA approved indication of Type 1 Gaucher disease (GD1); and
2. Member is classified as one of the following as detected by an FDA-cleared test:
    a. CYP2D6 extensive metabolizers (EMs); or
    b. CYP2D6 intermediate metabolizers (IMs); or
    c. CYP2D6 poor metabolizers (PMs); and
3. Prescriber must verify that the member will not take Cerdelga® concurrently with another therapy for GD1.
4. For CYP2D6 EMs and IMs, a quantity limit of 56 capsules per 28 days will apply. For CYP2D6 PMs, a quantity limit of 28 capsules per 28 days will apply.
5. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

Zavesca® (Miglustat) Approval Criteria:

1. An FDA approved indication of mild/moderate Type 1 Gaucher disease (GD1); and
2. A patient-specific, clinically significant reason why the member cannot use one of the following enzyme replacement therapies:
    a. Cerezyme® (imiglucerase); or
    b. Elelyso® (taliglucerase alfa); or
    c. Vpriv® (velaglucerase alfa); and
3. Prescriber must verify that the member will not take Zavesca® concurrently with another therapy for GD1.
4. A quantity limit of 90 capsules per 30 days will apply.
5. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

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[1] Cerezyme® Prescribing Information. Genzyme. Available online at: https://www.cerezyme.com/healthcare.aspx. Last revised 5/2011. Last accessed 2/2016.

[2] Elelyso™ Prescribing Information. Pfizer. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=798. Last revised 11/2015.Last accessed 2/2016

[3] Vpriv® Prescribing Information. Shire. Available online at: http://pi.shirecontent.com/PI/PDFs/Vpriv_USA_ENG.pdf. Last revised 4/2015. Last accessed 2/2016.

[4] Cerdelga™ Prescribing Information. Genzyme. Available online at: http://www.cerdelga.com/pdf/cerdelga_prescribing_information.pdf. Last revised 8/2014. Last accessed 2/2016.

[5] Zavesca® Prescribing Information. Actelion. Available online at: https://www.zavesca.com/pdf/ZAVESCA-Full-Prescribing-Information.pdf. Last revised 7/2015. Last accessed 2/2016.

Appendix E

Vote to Prior Authorize Elestrin® (Estradiol Gel 0.06%)

Oklahoma Health Care Authority
April 2016

Introduction[1]

Elestrin® (estradiol gel 0.06%) is indicated for the treatment of moderate-to-severe vasomotor symptoms due to menopause. It acts through binding to nuclear receptors in estrogen-responsive tissues. These vary in proportion from tissue to tissue. Circulating estrogens modulate the pituitary secretion of the gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), through a negative feedback mechanism. Estrogens act to reduce the elevated levels of these hormones seen in postmenopausal women. Elestrin® is designed with the unique and patented Advanced Transdermal Delivery (ATD™) system. This system increases the absorption rate of low-dose estrogen into the skin. Elestrin® is available in a metered dose pump which delivers 0.52mg of estradiol in 0.87g of gel per pump actuation. Patients should be started with the lowest effective dose, which is one pump per day (0.87g per day, which contains 0.52mg of estradiol). Subsequent dosage adjustments may be made based upon individual patient response.

Recommendations

The College of Pharmacy recommends sending an educational mailing to prescribers of members who are 65 years of age or older receiving hormone therapy. The purpose of the mailing would be to ensure appropriate use of hormone therapy for vasomotor symptoms in members over the age of 65 years. The letter will address the need for regular monitoring of these members, and to ensure members are receiving the lowest effective dose of hormone therapy for the shortest duration of time.

The College of Pharmacy recommends the prior authorization of Elestrin® (estradiol gel 0.06%) with the following criteria:

Elestrin® (Estradiol Gel 0.06%) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe vasomotor symptoms due to menopause; and
2. Member must not have any contraindications for use of Elestrin®; and
3. A patient-specific, clinically significant reason why other topical estradiol formulations (e.g., Divigel®) are not appropriate for the member; and
4. Members greater than 65 years of age will generally not be approved without supporting information; and
5. Approvals will be for the duration of six months to ensure the need for continued therapy is reassessed periodically and the medication is being used for the shortest duration possible; and
6. A quantity limit of 52 grams per 30 days will apply.

[1] Elestrin® Product Information. Meda Pharmaceuticals®. Available online at http://www.elestrin.com/pdf/Elestrin_Full_Prescribing_Information.pdf. Last revised 2/1/2014. Last accessed 2/24/2016.

Appendix F

Vote to Prior Authorize Evzio® (Naloxone Auto-Injector)

Oklahoma Health Care Authority
April 2016

Introduction[1,2,3]

Evzio® (naloxone auto-injector) is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and central nervous system depression. Evzio® is supplied in a carton containing two pre-filled 0.4mg/0.4mL naloxone hydrochloride auto-injectors and a speaker that provides voice instructions to guide the user through each step of the injection. Each auto-injector contains a single dose of naloxone. Generic naloxone injection and naloxone nasal spray (Narcan®) are also indicated for emergency treatment of opioid overdose; both are available without prior authorization.

Cost Comparison:

Medication	Cost/mL	Package Size	Cost/Package
Evzio® (naloxone auto-injector)	**$4,950.00**	**0.8mL (two 0.4mL syringes)**	**$3,960.00**
Narcan® (naloxone nasal spray)	$66.00[+]	8mg (two 4mg blister packages)	$132.00
naloxone 0.4mg/mL syringe	$16.30*	1mL	$16.30

*Cost/mL based on state maximum allowable costs (SMAC); all other costs not denoted with an asterisk are based on estimated acquisition cost (EAC).
[+]Cost per blister package. Each carton contains two blister packages each with a single dose of naloxone nasal spray.
Costs listed in the table do not take into account federal or supplemental rebate participation and do not reflect net costs.

Market News and Updates[4]

A recent news article reported that Representative Elijah Cummings (Democrat-Maryland) denounced Amphastar Pharmaceuticals Incorporated at a United States House Committee on Oversight and Government Reform hearing for raising prices on naloxone as the demand has increased. Cummings accused the pharmaceutical company of profiting off of the heroin epidemic crisis. Since 2012 the estimated acquisition cost (EAC) of naloxone 0.4mg/mL has risen by more than 300%.

Recommendations

The College of Pharmacy recommends the prior authorization of Evzio® (naloxone auto-injector) with the following criteria:

Evzio® (Naloxone Auto-Injector) Approval Criteria:

1. An FDA approved diagnosis of potential or risk for opioid overdose; and
2. A patient-specific, clinically significant reason why the member cannot use other formulations of naloxone.

Additionally, the College of Pharmacy recommends further education via letter or newsletter for prescribers and pharmacies who have patients utilizing high-dose opioid analgesics. Education should include the available naloxone medications reimbursable by SoonerCare and the importance of training and access to these medications.

[1] Evzio® Prescribing Information. Kaléo, Inc. Available online at: http://www.evzio.com/pdfs/Evzio%20PI.PDF. Last revised 04/2014. Last accessed 03/2016.
[2] Narcan® Prescribing Information. Adapt Pharma Operations Limited. Available online at: http://www.narcannasalspray.com/pdf/NARCAN-Prescribing-Information.pdf. Last revised 11/2015. Last accessed 03/2016.
[3] Naloxone Hydrochloride Injection Solution Prescribing Information. Hospira, Inc. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b598c237-032d-4bb5-0e92-50eabd863dac. Last revised 09/2015. Last accessed 03/2016.
[4] Cherkis Jason. *Huffington Post.* "Rep Cummings Rips Pharma Company For Price Gouging on Heroin Overdose Drug". Available online at: http://www.huffingtonpost.com/entry/pharmaceutical-companies-profit-heroin-epidemic_us_56f1eafae4b02c402f65b30d. Issued 03/22/2016. Last accessed 03/24/2016.

Appendix G

Fiscal Year 2015 Annual Review of SoonerCare Pharmacy Benefit

Oklahoma Health Care Authority
April 2016

Pharmacy Benefit Management[1*]

Oklahoma has a fee-for-service pharmacy benefit for the SoonerCare program. In contrast, many states have contracted out the management of their Medicaid programs, including pharmacy, under capitated payment arrangements. Most of the Medicaid managed care organizations subcontract the pharmacy benefit to a separate pharmacy benefit manager (PBM). Some states use a PBM for their fee-for-service pharmacy programs as well, contracting out services such as claims processing and payment, prior authorization processing, drug utilization review, and formulary management. For over 20 years, the Oklahoma Health Care Authority (OHCA) has chosen to contract 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, we compared Oklahoma's statistics to those of a national PBM. For several years, Express Scripts (ESI) has published a Drug Trend Report detailing their results for managing millions of patients' pharmacy benefits. ESI is the largest PBM in the United States. In recent years, they have published a separate report on their Medicaid covered lives. These include the same case mix as covered by OHCA: Temporary Assistance for Needy Families (TANF) children and their parents, Aged, Blind and Disabled adults and children, and Children's Health Insurance Program (CHIP) children.

Compared to ESI, OHCA and PMC manage a tighter program with a lower Per Member Per Year (PMPY) cost of care. For calendar year 2014, ESI's Medicaid PMPY was $883.43 – 35% higher than OHCA's $653.26. If OHCA had experienced the same PMPY as ESI for calendar year 2014, it would have cost over $165 million more than the $472 million spent. Similarly, for calendar year 2015, ESI's Medicaid PMPY was $969.56 – 40% higher than OHCA's $690.71. At the ESI PMPY rate, it would have cost over $202 million more than the $501 million spent during calendar year 2015 for pharmacy reimbursement.

Comparing the trend of the PMPY from 2014 to 2015, ESI experienced a 9.87% increase, while OHCA saw a 5.73% increase. OHCA believes our prior authorization policies, coupled with quantity limits and monthly prescription limits yield these better than average results while still providing a comprehensive pharmacy benefit for 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 partners, PMC, spent about $4 million of their $4.4 million contract both years. As a return on investment, using the overage generated by the ESI PMPY rate, for 2014 the return on investment (ROI) is $33 to $1 and for 2015 it is $40 to $1.

*SoonerCare PMPY cost estimates differ from PMPY estimates contained at the end of this report. These differences can be accounted for by the time-frame of analysis (calendar year versus fiscal year), values calculated using average monthly enrollment instead of annual unduplicated members, and the removal of dual eligible members.

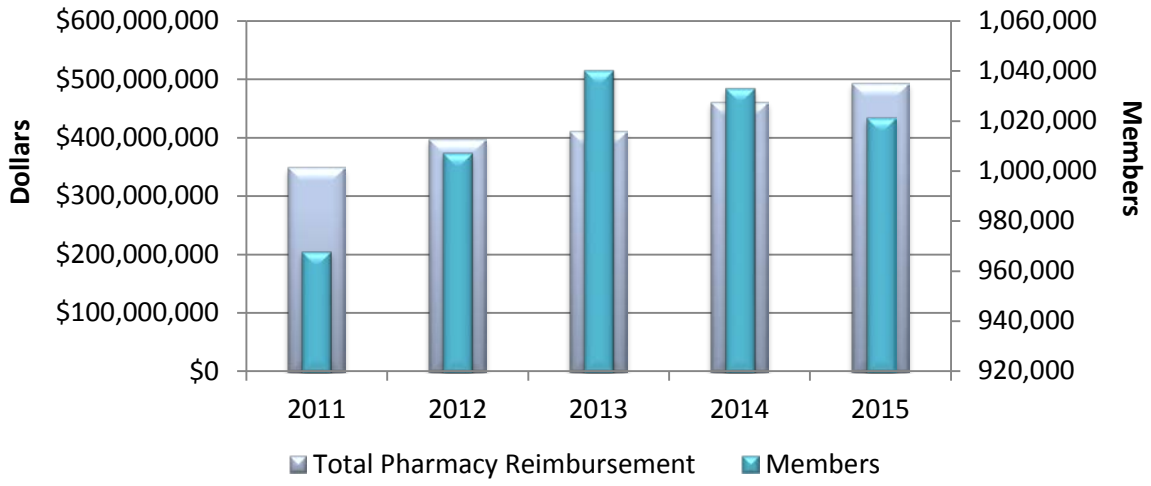
Pharmacy Benefit Management (PBM) Comparison			
	CY2014	CY2015	Comments
Adjusted Enrollment	722,620	725,744	(Remove Duals)
SoonerCare Spend	$472,061,461	$501,281,206	
SoonerCare PMPY	$653.26	$690.71	**Percentage Increase:** 5.73%
ESI PMPY	$882.43	$969.56	**Percentage Increase:** 9.87%
Percentage Difference in PMPY	35.08%	40.37%	
ESI Spend	$637,661,860	$703,652,110	
Additional Spend for ESI	**$165,600,398**	**$202,370,904**	
ROI	**$33.12**	**$40.47**	

Summary[2]

Pharmacy benefits are optional for Medicaid programs; however, all fifty states and the District of Columbia have chosen to include pharmacy coverage for their members. During State Fiscal Year (SFY) 2015, prescription drugs accounted for $485 million of over $5 billion spent in the SoonerCare program. Over the past four fiscal years, SoonerCare has served over one million members each year. In terms of costs, total pharmacy reimbursement has increased, and subsequently cost per claim and cost per day. The rate of change for pharmacy reimbursement can be attributed to overall healthcare cost increases, new emerging and breakthrough therapies, and unfortunate drug shortages that drive use of other, more costly therapeutic alternatives. There has been a small decline in the number of members and utilizers in the last two years which may correlate with new health care reforms and laws such as the Affordable Care Act.

SFY	Members	Utilizers	Claims	Reimbursement	Days	Cost/Claim	Cost/Day
2011	968,296	553,200	5,782,249	$349,029,291	137,444,282	$60.36	$2.54
2012	1,007,356	579,892	6,334,413	$397,692,844	153,973,718	$62.78	$2.58
2013	1,040,332	600,950	6,479,131	$410,385,880	158,274,398	$63.34	$2.59
2014	1,033,114	576,526	6,423,750	$464,592,748	158,213,899	$72.32	$2.94
2015	1,021,359	568,219	6,291,640	$485,828,513	154,985,336	$77.22	$3.13

Total Pharmacy Reimbursement and Member Enrollment Comparison



Traditional Versus Specialty Pharmacy Products

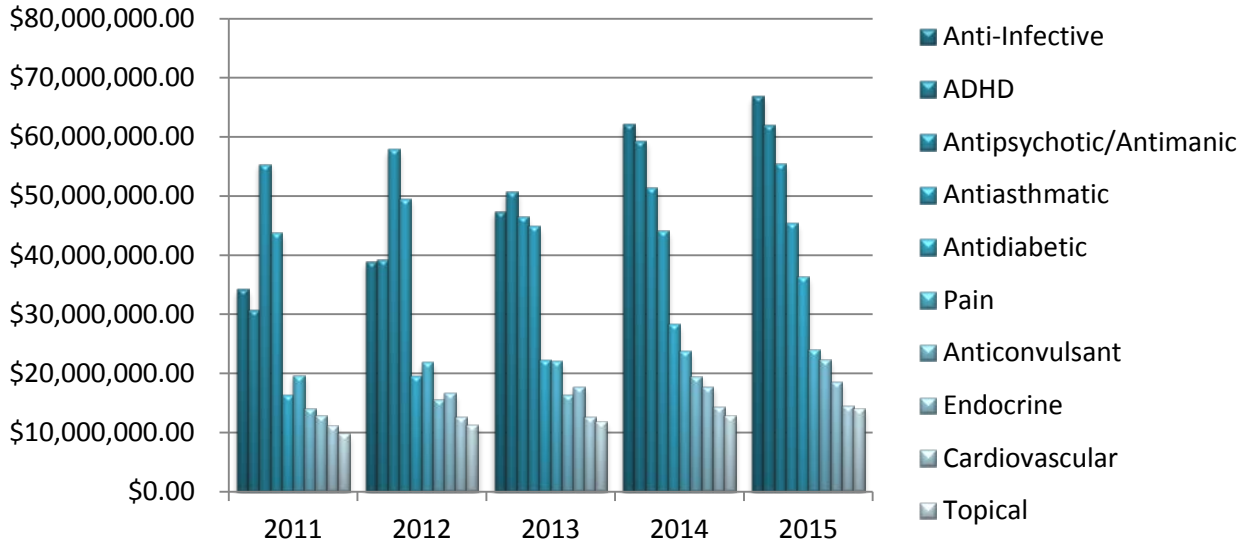
Traditional pharmaceuticals include products which are typically non-injectable and do not require special transportation, storage, or administration. These products treat many common chronic diseases such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). During SFY2015 the traditional pharmaceutical products comprised 85% of the total pharmacy reimbursement costs and were utilized by 99.4% of members. Specialty products, in contrast, are typically injectable, require special handling such as refrigerated transport, and special administration techniques provided by dedicated facilities or personnel. These products include treatments for hemophilia, rheumatoid arthritis, and genetic deficiencies, for example. During SFY15 the specialty pharmaceutical products comprised 15% and 0.6% of total pharmacy reimbursement costs and member utilization, respectively.

Top 10 Therapeutic Classes by Reimbursement: Fiscal Year 2015

Traditional therapeutic class reimbursement ranking has not changed from the previous fiscal year and differs slightly from SFY2013. The reimbursement increase is minimal and more than likely due to expected yearly price increases by product manufacturers. Notable changes include the anti-infective class becoming the highest ranking class, along with anticonvulsant reimbursement increasing over endocrine therapies. Hepatitis C treatments are included in the anti-infective class and implementation of a hepatitis C medication therapy management program has assisted with keeping costs as low as possible while still making the therapies available to members in need. The anti-diabetic class increase can be attributed to new products, use of new insulin options, and a trend toward multiple agents used concurrently for this disease state. The anticonvulsant class is reviewed annually to avoid over expenditure for off-label utilization. The continual influx of generically available products for attention deficit hyperactivity disorder (ADHD) agents and antipsychotic/anti-manic classes has minimized cost increases for those categories. Agents used to treat pain have seen a decrease in reimbursement despite the increased cost of new abuse deterrent formulations, thus indicating implementation of quantity restrictions on immediate-release opioid medications and class management of nonsteroidal anti-inflammatory drugs (NSAIDs) and anti-migraine medications were cost effective.

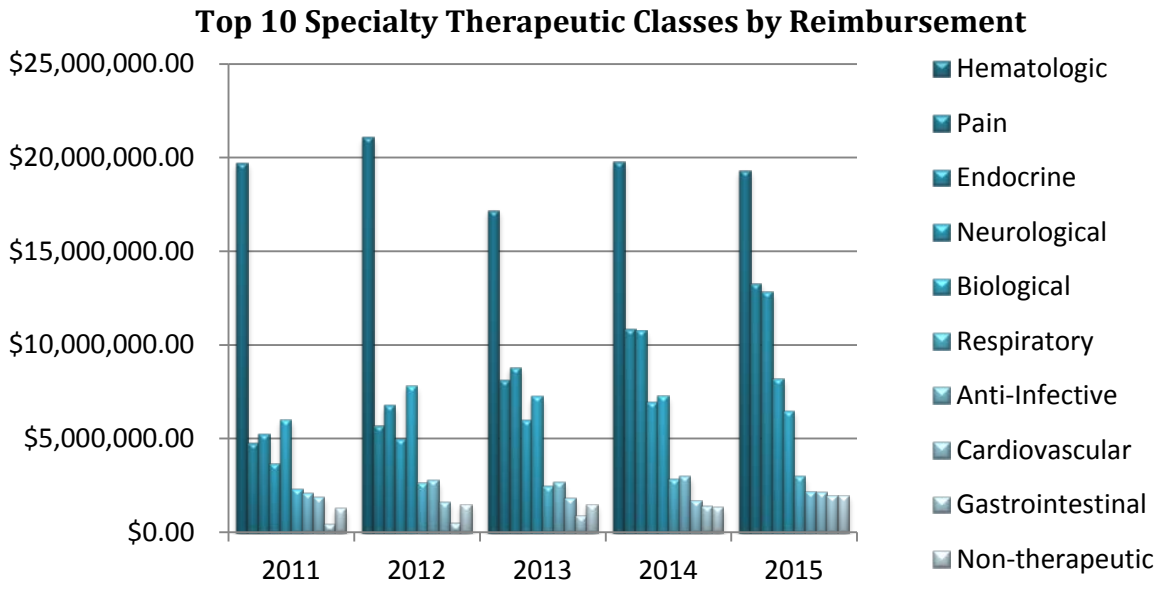
Traditional Top 10 Classes by Reimbursement					
	2011	2012	2013	2014	2015
Anti-Infectives	$34,156,254	$39,001,643	$47,491,962	$62,318,150	$65,368,288
ADHD Agents	$30,672,084	$39,264,858	$50,747,046	$59,700,076	$61,096,535
Antipsychotics/Antimanics	$55,452,246	$57,938,004	$46,596,337	$51,639,215	$54,567,459
Antiasthmatics	$43,783,923	$49,538,833	$44,950,083	$44,465,237	$44,690,081
Antidiabetes	$16,365,995	$19,474,144	$22,219,365	$28,333,483	$35,900,969
Pain Agents	$19,737,070	$21,844,293	$22,064,126	$23,750,036	$23,707,634
Anticonvulsants	$14,086,343	$15,591,403	$16,396,098	$19,599,529	$22,018,892
Endocrine Agents	$13,030,446	$16,661,513	$17,683,908	$17,780,593	$18,318,324
Cardiovascular Agents	$11,276,679	$12,533,620	$12,500,403	$14,278,301	$14,210,475
Topical Agents	$9,844,837	$11,225,286	$11,983,191	$12,941,687	$13,909,470

Top 10 Traditional Therapeutic Classes by Reimbursement



On the specialty side, hematological agents remained the highest cost category in 2015 despite a slight decrease in reimbursement. Tumor necrosis factor alpha (TNFα) medications such as Enbrel® (etanercept) and Humira® (adalimumab) are indicated for the treatment of rheumatoid arthritis among other autoimmune disorders and are included in the pain agents' specialty class. Several of these products are in waning patent stages and will soon face biosimilar competition. Additionally, the majority of utilization among this class was seen in Tier-2 medications which are supplemental rebated products. Increased reimbursement for the endocrine specialty agents can be attributed to increased utilization of injectable progestins such as Makena® to prevent preterm births. The addition of new products for the treatment of multiple sclerosis account for the reimbursement increase in the neurological agents. The decrease in reimbursement for biological agents can be attributed to the adoption of updated guidance for Synagis® (palivizumab). The implementation of a prior authorization to avoid off-label utilization for inhaled aminoglycosides including Tobi® (tobramycin) contributed to the decrease in reimbursement in the anti-infective class. Continuous review and management of respiratory agents, cardiovascular agents, and gastrointestinal agents has promoted minimal reimbursement increases other than expected yearly price increases by product manufacturers.

Specialty Top 10 Classes by Reimbursement					
	2011	**2012**	**2013**	**2014**	**2015**
Hematological Agents	$19,737,663	$21,094,430	$17,218,955	$20,047,687	$19,056,730
Pain Agents	$4,762,275	$5,743,446	$8,087,586	$10,862,638	$13,164,383
Endocrine Agents	$5,225,651	$6,792,319	$8,806,490	$10,787,827	$12,611,515
Neurological Agents	$3,695,513	$4,964,755	$5,985,823	$6,944,096	$8,060,038
Biological Agents	$6,026,595	$7,849,145	$7,274,995	$7,388,848	$6,458,154
Respiratory Agents	$2,282,523	$2,670,374	$2,438,662	$2,862,695	$2,935,359
Anti-Infectives	$2,107,395	$2,761,979	$2,645,237	$3,035,845	$2,211,393
Cardiovascular Agents	$1,880,002	$1,621,252	$1,829,626	$1,703,702	$2,133,289
Gastrointestinal Agents	$438,726	$462,307	$886,903	$1,390,862	$1,981,029
Non-Therapeutics Agents	$1,270,198	$1,510,148	$1,510,762	$1,348,122	$1,936,560



Top 10 Medications by Reimbursement: Fiscal Year 2015

The top 10 medications ranked by reimbursement remains similar to SFY2014 with Abilify® (aripiprazole) ranked first followed by the hepatitis C medications Sovaldi® (sofosbuvir) and Harvoni® (ledipasvir/sofosbuvir). Other drugs in the top 10 include highly utilized medications such as albuterol inhalers and insulin. Tamiflu® (oseltamivir) is new to the top 10, but will soon face generic competition due to expiring exclusivity patents. Similar to the past five fiscal years, ADHD medications and atypical antipsychotics comprise the majority of the top 10 medications by reimbursement.

Top 10 Medications by Reimbursement*					
Rank	**2011**	**2012**	**2013**	**2014**	**2015**
1	aripiprazole	aripiprazole	aripiprazole	aripiprazole	aripiprazole
2	quetiapine	quetiapine	methylphenidate	sofosbuvir	sofosbuvir/ ledipasvir
3	methylphenidate	montelukast	albuterol	albuterol	lisdexamphetamine
4	montelukast	methylphenidate	amphetamine	methylphenidate	albuterol
5	albuterol	albuterol	dexmethylphenidate	lisdexamphetamine	methylphenidate
6	olanzapine	amphetamine	guanfacine	guanfacine	oseltamivir
7	lisdexamphetamine	olanzapine	budesonide	amphetamine	insulin glargine
8	budesonide	budesonide	lisdexamphetamine	insulin glargine	guanfacine
9	oxycodone	lisdexamphetamine	paliperidone palmitate inj	dexmethylphenidate	atomoxetine
10	fluticasone/ salmeterol	palivizumab	fluticasone inh	paliperidone palmitate inj	paliperidone palmitate inj

*Includes brand and generic where applicable.
inj = injection
inh = inhalation

Medicaid Drug Rebate Program[3,4]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). 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 payer. Best prices are reported to the Centers for Medicare & Medicaid Services (CMS) by the manufacturer, but are not publicly available.

If a branded 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 for branded drugs despite increases in branded drug prices. The cost increases found in this report do not reflect net cost increases.

Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. In SFY2015 the Oklahoma Health Care Authority (OHCA) collected almost $237 million in federal rebates and over $13 million in state supplemental rebates. These rebates are collected after reimbursement for the medication and are not reflected in this report.

Medication Price Increases[5,6,7]

A white paper published by Elsevier Clinical Solutions highlighted the rising cost of generic medications. In their analysis of 4,421 generic medications over a one year period (2013-2014), the authors found that more than 222 drug groups had increased in price by more than 100%, 90 by more than 200%, 25 by more than 500%, and 17 by more than 1,000%. The authors attributed the rising costs of generic medications to industry consolidation, drug shortages, raw material shortages, manufacturing difficulties, regulations, and business decisions.

Fiscal Year	Percent of Rx Spending on Generic Medications	Cost per Generic Claim	Cost per Brand Claim
2011	24%	$18.36	$213.30
2012	25%	$19.36	$236.18
2013	26%	$20.12	$253.66
2014	24%	$21.38	$310.61
2015	23%	$21.09	$340.13

It is important to note that while some individual products have increased in price the overall cost per generic claim decreased from SFY2014 to SFY2015; this implies that while some products increased in price others decreased. The rising cost of both brand and generic medications have contributed to a total increase in prescription drug expenditures. Generic medication cost increases are particularly difficult to manage because they are often still more cost effective than their brand counterpart making non-preferred drug status a less appropriate option.

Generic Price Increase Examples			
Medication	**2012 Price***	**2016 Price***	**% Increase**
amitriptyline 100mg tablet	$0.14	$1.09	679%
neomycin/polymyxin B/hydrocortisone otic	$1.76	$8.46	381%
naloxone 0.4mg/mL syringe	$3.96	$16.30	312%
tetracycline 500mg tablet	$0.11	$10.67	9,600%

*State maximum allowable cost per unit.

A national analysis conducted by Truveris, a healthcare data company, found that prescription drug costs rose by 10% in 2015. The 10% cost increase was found across almost every drug class and exceeds the United States inflation rate of 1.6% considerably. Additionally, Truveris discovered that in 2015, the price of branded drugs rose 14.77%, specialty drugs rose 9.21%, and generic drugs rose 2.93%. The analysis revealed that the price increases in 2015 were similar to 2014 which had increases of 10.9%. A recent report from the federal government revealed an increase in prescription drug spending in 2014 of almost 13% which is the most substantial annual increase in more than a decade.

The SoonerCare cost per claim of branded medications rose by 9.50% in SFY2015 in comparison to SFY2014, while the cost per generic claim declined slightly. Where appropriate, generic price increases were managed by moving the more costly medications to non-preferred status when there was a suitable, cost-effective alternative. Branded medication cost increases are minimized through the CPI penalty of the federal rebate as well as prior authorization or non-preferred status.

Pharmacy Trend: Spending Per Member Per Year (PMPY)

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. While SFY2012 and SFY2013 were similar, SFY2014 and SFY2015 saw increases. When broken down by age group, the traditional PMPY saw the greatest increase from 2014 to 2015 in the 46 to 64 year old age group; this large increase can be attributed to increased utilization of the costly hepatitis C medications. Ages 0 to 4 years traditional PMPY values for SFY2015 decreased from SFY2014 as a result of the prior authorization of the more costly cephalosporin antibiotics such as Suprax® (cefixime), Cedax® (ceftibuten), and Spectracef® (cefditoren).

Overall PMPY	2011	2012	2013	2014	2015
Overall PMPY	$360.46	$394.79	$394.48	$449.70	$475.67

An evaluation of the overall pharmacy trend for SFY2015 in comparison to SYF2014 can be seen below. Fewer members utilized the pharmacy benefit corresponding with a decrease in the number of claims. Both the PMPY spend and the cost per claim increased in comparison to SFY2014. As previously mentioned the price increases are likely due to increased utilization of the costly hepatitis C medications and price increases by product manufacturers.

Overall Pharmacy Trend SFY2015 Comparison*				
	Trend			
Drug Class	PMPY Spend	Utilizers	Claims	Cost/Claim
Traditional	5.35%	-1.43%	-2.06%	6.35%
Specialty	8.22%	-1.23%	1.06%	5.87%
Overall Numeric Change from SFY2014	**$25.97**	**-8,307**	**-132,110**	**$4.90**
Overall Percentage Change from SFY2014	**5.77%**	**-1.44%**	**-2.06%**	**6.78%**

*Percentage changes are in comparison to SFY2014.

Conclusion

Over the past five years, reimbursement to pharmacies by SoonerCare increased annually after SFY2011. This is expected as price inflation and new products came to market after the corrections made in SFY2010 in response to the economic recession. Even though costs have risen, they have not risen in direct proportion to the increase in membership, indicating cost-effective management measures were successful. 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 prescriber 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 the citizens it serves.

Top 100 Reimbursed Drugs by Fiscal Year

Top 100 Reimbursed Drugs By Fiscal Year		2015		2014	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Aripiprazole	Abilify*	1	$25,791,508.63	1	$24,932,424.50
Sofosbuvir/Ledipasvir	Sovaldi/Harvoni	2	$20,020,926.28	2	$14,483,538.83
Lisdexamfetamine Dimesylate	Vyvanse	3	$16,250,901.36	5	$11,124,688.48
Albuterol Sulfate	Multiple Products	4	$13,962,042.21	3	$13,496,493.67
Methylphenidate	Multiple Products	5	$12,393,741.88	4	$12,635,052.96
Oseltamivir Phosphate	Tamiflu	6	$10,904,773.05	25	$4,113,319.01
Insulin Glargine	Lantus	7	$9,603,115.46	8	$7,780,239.38
Guanfacine	Intuniv*	8	$9,453,047.93	6	$10,377,855.09
Atomoxetine	Strattera	9	$9,031,118.91	12	$6,719,331.05
Paliperidone Palmitate Injection	Invega Sustenna	10	$8,512,873.88	10	$7,594,081.18
Fluticasone Inhalation	Flovent	11	$7,476,717.74	11	$6,870,389.74
Adalimumab Injection	Humira	12	$7,411,660.44	15	$5,923,690.86
Amphetamine-Dextroamphetamine	Multiple Products	13	$6,936,399.76	7	$9,509,024.80
Insulin Aspart	Novolog	14	$6,765,609.66	18	$5,132,639.18
Somatropin Injection	Genotropin	15	$6,362,557.89	16	$5,715,563.56
Antihemophilic Factor (Recombinant)	Multiple Products	16	$6,192,908.56	19	$5,113,963.57
Oxycodone	Multiple Products	17	$6,187,971.68	14	$5,925,104.33
Insulin Detemir	Levemir	18	$5,972,176.08	26	$3,851,652.73
Dexmethylphenidate	Focalin*	19	$5,961,650.94	9	$7,714,991.35
Lurasidone	Latuda	20	$5,325,003.23	31	$3,418,905.77
Budesonide Inhalation	Pulmicort*	21	$5,305,011.05	13	$6,053,890.33
Palivizumab	Synagis	22	$4,846,408.76	17	$5,454,280.96
Fluticasone-Salmeterol	Advair	23	$4,644,543.08	20	$4,836,017.28
Epinephrine	Multiple Products	24	$4,527,754.72	30	$3,470,438.28
Pregabalin	Lyrica	25	$4,226,517.26	32	$3,229,251.65
Etanercept Injection	Enbrel	26	$3,894,682.87	29	$3,596,300.31

Top 100 Reimbursed Drugs By Fiscal Year		2015		2014	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Hydrocodone-Acetaminophen	Multiple Products	27	$3,877,520.86	23	$4,351,307.53
Hydroxyprogesterone Caproate	Makena	28	$3,714,755.36	35	$2,864,118.32
Quetiapine	Seroquel*	29	$3,536,297.74	24	$4,278,038.72
Insulin Lispro	Humalog	30	$3,488,082.23	36	$2,748,149.02
Cefdinir	Omnicef*	31	$3,221,433.55	33	$3,006,609.89
Tiotropium	Spiriva	32	$3,189,373.66	34	$2,973,457.96
Paliperidone	Invega	33	$2,927,754.57	40	$2,573,390.70
Glatiramer Acetate	Copaxone	34	$2,913,283.12	43	$2,481,847.06
Oxycodone-Acetaminophen	Multiple Products	35	$2,873,247.84	45	$2,256,034.66
Buprenorphine-Naloxone	Multiple Products	36	$2,832,905.44	39	$2,611,131.00
Prednisolone Sodium Phosphate	Multiple Products	37	$2,829,817.93	48	$2,213,287.82
Lacosamide	Vimpat	38	$2,673,475.39	46	$2,244,486.69
Anti-inhibitor Coagulant Complex Inj.	Feiba	39	$2,604,598.72	28	$3,638,809.35
Dornase Alfa Inhalation	Pulmozyme	40	$2,530,956.63	37	$2,716,604.62
Azithromycin	Zithromax*	41	$2,495,105.57	38	$2,645,597.31
Antihemophilic Factor rAHD-PFM Inj.	Advate	42	$2,465,073.85	27	$3,682,862.47
Divalproex Sodium	Depakote*	43	$2,283,068.17	44	$2,415,662.19
Amoxicillin	Amoxil*	44	$2,039,230.41	47	$2,236,265.38
Pancrelipase	Multiple Products	45	$1,941,693.25	59	$1,618,694.62
Ipratropium-Albuterol Inhalation	Multiple Products	46	$1,935,457.14	49	$1,996,014.92
Sitagliptin	Januvia	47	$1,881,363.08	56	$1,643,390.24
Efavirenz-Emtricitabine-Tenofovir	Atripla	48	$1,874,552.49	42	$2,509,366.78
Deferasirox	Jadenu	49	$1,871,071.02	73	$1,335,611.04
Montelukast	Singulair*	50	$1,810,553.89	51	$1,852,290.62
Amoxicillin-K-Clavulanate	Augmentin*	51	$1,781,286.59	52	$1,847,902.33
Tobramycin Inhalation	Multiple Products	52	$1,781,119.72	41	$2,515,218.88
Clozapine	Versacloz*	53	$1,777,279.81	50	$1,929,019.73
Clobazam	Onfi	54	$1,771,991.61	77	$1,257,429.07
Eculizumab Injection	Soliris	55	$1,721,852.82	61	$1,580,192.48
Memantine	Namenda	56	$1,662,667.64	62	$1,534,265.77
Beclomethasone Inhalation	QVAR	57	$1,624,282.87	74	$1,310,985.20
Cetirizine	Multiple Products	58	$1,616,902.95	54	$1,671,237.44
Interferon Beta-1a	Multiple Products	59	$1,606,991.73	55	$1,654,427.22
Rifaximin	Xifaxan	60	$1,550,238.59	92	$1,018,410.04
Gabapentin	Neurontin*	61	$1,527,367.54	63	$1,529,889.83
Morphine Sulfate	Multiple Products	62	$1,497,975.82	70	$1,370,908.30
Emtricitabine-Tenofovir-Disoproxil	Truvada	63	$1,460,183.67	53	$1,748,623.54
Everolimus	Afinitor	64	$1,451,077.34	106	$877,887.65
Dimethyl Fumarate	Tecfidera	65	$1,444,917.60	85	$1,105,730.34
Permethrin	Multiple Products	66	$1,440,493.03	71	$1,353,801.21
Oxcarbazepine	Multiple Products	67	$1,423,308.17	65	$1,518,832.69
Budesonide-Formoterol Inhalation	Symbicort	68	$1,395,825.30	81	$1,183,187.36
Spacer/Aerosol-Holding Chambers	Multiple Products	69	$1,385,962.88	75	$1,276,083.68

Top 100 Reimbursed Drugs By Fiscal Year		2015		2014	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Iloperidone	Fanapt	70	$1,362,416.57	66	$1,499,003.18
Sulfamethoxazole-Trimethoprim	Bactrim*	71	$1,348,956.48	133	$676,937.56
Duloxetine	Cymbalta*	72	$1,344,990.17	22	$4,441,110.25
Vigabatrin	Sabril	73	$1,343,679.54	117	$788,565.22
Imatinib Mesylate	Gleevec	74	$1,290,020.45	72	$1,348,594.71
Liraglutide Injection	Victoza	75	$1,288,881.27	87	$1,073,805.90
Enoxaparin Sodium	Lovenox*	76	$1,284,992.26	60	$1,611,242.55
Fingolimod	Gilenya	77	$1,234,458.33	94	$996,679.56
Certolizumab	Cimzia	78	$1,211,313.05	102	$887,686.07
Etonogestrel-Ethinyl Estradiol Ring	Nuvaring	79	$1,188,793.64	69	$1,382,816.94
Linezolid	Zyvox*	80	$1,182,622.78	83	$1,162,369.86
Levothyroxine Soduim	Multiple Products	81	$1,170,415.73	98	$928,739.54
Risperidone Microspheres Injection	Risperdal Consta	82	$1,119,130.36	82	$1,165,842.54
Fluticasone Propionate Nasal	Flonase*	83	$1,101,786.95	64	$1,524,580.59
Levetiracetam	Keppra*	84	$1,085,508.22	78	$1,244,219.99
Rufinamide	Banzel	85	$1,060,408.62	105	$878,939.70
Sapropterin Dihydrochloride	Kuvan	86	$1,049,919.64	97	$943,170.72
Tazarotene	Tazorac	87	$1,014,749.49	112	$850,720.73
Insulin Aspart Protamine Mix	Novolog Mix	88	$1,007,485.07	104	$880,818.67
Fentanyl	Multiple Products	89	$996,347.39	67	$1,471,643.88
Tetrabenazine	Xenazine	90	$989,297.96	134	$673,015.19
Darunavir Ethanolate	Prezista	91	$980,550.95	89	$1,047,336.85
Norgestimate-Ethinyl Estradiol	Multiple Products	92	$979,279.44	80	$1,191,875.82
Insulin Regular (Human)	Multiple Products	93	$975,355.98	119	$769,466.25
Idursulfase Injection	Elaprase	94	$961,355.16	132	$687,471.93
Acyclovir Topical	Zovirax*	95	$956,143.34	93	$1,018,118.36
Sevelamer Carbonate	Renvela*	96	$952,902.49	122	$743,752.61
C1 Esterase Inhibitor (Human)	Multiple Products	97	$950,336.41	88	$1,066,966.55
Elvitegrav-Cobicis-Emtricitab-Tenofov	Stribild	98	$948,402.14	128	$708,384.48
Lamotrigine	Lamictal*	99	$944,911.98	86	$1,098,948.89
Simeprevir	Olysio	100	$934,412.25	100	$911,006.36

*Includes brand and generic where applicable.

Top 50 Medications by Total Number of Claims

Top 50 Medications by Total Number of Claims										
Rank	Generic Name	Brand Name	Claims	Members	Cost	Units/ Day	Cost/ Claim	Claims/ Client	Cost/ Day	% Cost
1	Albuterol	Multiple	263,711	112,026	$13,962,042.21	2.45	$52.94	2.35	$2.44	10.48%
2	Hydrocodone-Acetaminophen	Multiple	248,940	86,101	$3,877,520.86	4.04	$15.58	2.89	$0.89	2.91%
3	Amoxicillin	Amoxil*	234,583	167,365	$2,039,230.41	11.82	$8.69	1.4	$0.90	1.53%
4	Cetirizine	Multiple	211,588	91,599	$1,616,902.95	2.97	$7.64	2.31	$0.25	1.21%
5	Azithromycin	Zithromax*	148,191	109,969	$2,495,105.57	3.06	$16.84	1.35	$3.38	1.87%
6	Montelukast	Singulair*	113,669	32,030	$1,810,553.89	1	$15.93	3.55	$0.53	1.36%
7	Fluticasone Propionate Nasal	Flonase*	97,098	54,156	$1,101,786.95	0.47	$11.35	1.79	$0.33	0.83%
8	Ibuprofen	Multiple	92,922	63,323	$646,572.06	4.14	$6.96	1.47	$0.43	0.49%
9	Omeprazole	Prilosec*	92,484	26,228	$634,861.12	1.25	$6.86	3.53	$0.20	0.48%
10	Clonidine	Catapres*	83,141	14,883	$558,321.03	1.46	$6.72	5.59	$0.22	0.42%
11	Methylphenidate	Multiple	82,331	12,731	$12,393,741.88	1.35	$150.54	6.47	$5.05	9.30%
12	Gabapentin	Neurontin*	78,266	17,712	$1,527,367.54	3.12	$19.52	4.42	$0.62	1.15%
13	Lisdexamfetamine Dimesylate	Vyvanse	77,316	14,700	$16,250,901.36	1	$210.19	5.26	$7.08	12.20%
14	Alprazolam	Xanax*	76,913	12,844	$437,629.40	2.35	$5.69	5.99	$0.20	0.33%
15	Loratadine	Multiple	75,609	34,097	$633,209.31	2.52	$8.37	2.22	$0.27	0.48%
16	Sertraline	Zoloft*	69,803	17,372	$494,715.50	1.17	$7.09	4.02	$0.22	0.37%
17	Amoxicillin-K-Clavulanate	Augmentin*	67,241	55,278	$1,781,286.59	8.59	$26.49	1.22	$2.66	1.34%
18	Ondansetron	Zofran*	65,220	50,717	$740,945.18	1.7	$11.36	1.29	$1.50	0.56%
19	Cefdinir	Omnicef*	64,518	49,526	$3,221,433.55	6.78	$49.93	1.3	$4.98	2.42%
20	Lisinopril	Multiple	63,106	16,234	$261,388.31	1.09	$4.14	3.89	$0.10	0.20%
21	Sulfamethoxazole-Trimethoprim	Multiple	62,621	49,339	$1,348,956.48	7.51	$21.54	1.27	$2.02	1.01%
22	Oseltamivir	Tamiflu	62,336	58,776	$10,904,773.05	10.81	$174.94	1.06	$29.06	8.18%
23	Trazodone	Desyrel*	62,288	15,391	$434,264.16	1.24	$6.97	4.05	$0.22	0.33%
24	Fluoxetine	Prozac*	60,873	14,614	$505,768.66	1.27	$8.31	4.17	$0.26	0.38%
25	Prednisolone Sodium Phosphate	Multiple	60,035	43,798	$2,829,817.93	7.23	$47.14	1.37	$8.67	2.12%
26	Oxycodone-Acetaminophen	Multiple	59,200	27,440	$2,873,247.84	4.05	$48.53	2.16	$3.03	2.16%
27	Amphetamine-Dextroamphetamine	Multiple	59,187	9,200	$6,936,399.76	1.35	$117.19	6.43	$3.94	5.21%
28	Prednisone	Multiple	57,987	42,045	$340,674.02	1.99	$5.88	1.38	$0.63	0.26%
29	Risperidone	Risperdal*	56,420	10,359	$725,258.27	1.5	$12.85	5.45	$0.42	0.54%
30	Tramadol	Ultram*	56,310	22,394	$314,500.45	3.84	$5.59	2.51	$0.29	0.24%
31	Levothyroxine	Multiple	56,286	11,318	$1,170,415.73	1	$20.79	4.97	$0.51	0.88%

Top 50 Medications by Total Number of Claims										
Rank	Generic Name	Brand Name	Claims	Members	Cost	Units/ Day	Cost/ Claim	Claims/ Client	Cost/ Day	% Cost
32	Cephalexin	Keflex*	53,730	45,700	$917,332.29	9.29	$17.07	1.18	$1.87	0.69%
33	Triamcinolone Acetonide Topical	Multiple	51,080	35,581	$721,450.78	5.12	$14.12	1.44	$0.93	0.54%
34	Cyclobenzaprine	Multiple	48,929	22,854	$274,867.06	2.4	$5.62	2.14	$0.25	0.21%
35	Citalopram	Celexa*	47,325	13,012	$212,726.48	1	$4.50	3.64	$0.13	0.16%
36	Clonazepam	Klonopin*	45,984	9,509	$288,591.50	2.1	$6.28	4.84	$0.22	0.22%
37	Metformin	Multiple	44,938	10,954	$213,143.39	2.04	$4.74	4.1	$0.15	0.16%
38	Quetiapine	Seroquel*	43,700	8,237	$3,536,297.74	1.46	$80.92	5.31	$2.60	2.65%
39	Promethazine	Multiple	41,000	26,095	$375,774.34	5.33	$9.17	1.57	$1.11	0.28%
40	Fluticasone Propionate Inhalation	Flovent	40,684	17,339	$7,476,717.74	0.36	$183.78	2.35	$5.74	5.61%
41	Ranitidine	Zantac*	40,670	16,933	$322,203.24	3.21	$7.92	2.4	$0.27	0.24%
42	Acetaminophen-Codeine	Multiple	39,999	28,070	$312,510.46	6.24	$7.81	1.42	$0.81	0.23%
43	Dexmethylphenidate	Focalin*	38,807	5,263	$5,961,650.94	1.14	$153.62	7.37	$5.16	4.47%
44	Mupirocin Topical	Bactroban*	38,793	32,119	$486,282.47	2.09	$12.54	1.21	$1.14	0.36%
45	Oxycodone	Multiple	34,972	5,791	$6,187,971.68	3.54	$176.94	6.04	$6.50	4.64%
46	Guanfacine Extended-Release	Intuniv*	33,614	5,409	$9,453,047.93	1	$281.22	6.21	$9.49	7.09%
47	Meloxicam	Mobic*	32,830	15,171	$126,555.88	1.11	$3.85	2.16	$0.11	0.09%
48	Zolpidem	Multiple	32,333	7,366	$190,451.27	0.99	$5.89	4.39	$0.20	0.14%
49	Hydroxyzine HCl	Atarax*	32,187	16,949	$374,187.78	4.91	$11.63	1.9	$0.57	0.28%
50	Lamotrigine	Lamictal*	31,498	5,628	$944,911.98	1.93	$30.00	5.6	$0.98	0.71%

*Includes brand and generic where applicable.

Top Traditional Therapeutic Classes by Fiscal Year*

Anti-Infective Agents	2015		2014	
	Total Claims	Total Paid	Total Claims	Total Paid
Antiviral	85,826	$43,056,341.33	54,628	$35,570,048.62
Anti-Infectives	108,481	$6,274,149.86	117,824	$5,187,572.52
Cephalosporins	131,113	$4,904,505.64	139,333	$10,296,761.23
Penicillins	315,776	$4,162,690.63	303,736	$4,396,277.02
Macrolide Antibiotics	152,749	$3,194,695.00	158,506	$3,174,479.26
Tetracyclines	23,044	$1,157,064.87	24,123	$1,399,387.50
Antifungals	28,623	$1,075,274.81	30,698	$1,216,800.74
Anthelmintic	2,790	$914,863.74	2,692	$570,260.01
Antimalarial	3,970	$313,117.45	3,895	$62,134.83
Fluoroquinolones	27,587	$259,487.42	28,920	$384,037.14
Antimycobacterial Agents	497	$33,108.24	506	$28,707.69
Aminoglycosides	421	$18,705.08	511	$29,926.18
Sulfonamides	9	$4,284.29	5	$1,757.75
Amebicides	0	$0.00	0	$0.00
Total:	**880,886**	**$65,368,288.36**	**865,377**	**$62,318,150.49**

ADHD Agents	2015		2014	
	Total Claims	Total Paid	Total Claims	Total Paid
ADHD/Anti-Narcolepsy	325,127	$61,096,535.96	331,007	$59,700,076.02
Total:	**325,127**	**$61,096,535.96**	**331,007**	**$59,700,076.02**

Antipsychotics	2015		2014	
	Total Claims	Total Paid	Total Claims	Total Paid
Antipsychotics	202,344	$54,567,459.04	205,868	$51,639,215.31
Total:	**202,344**	**$54,567,459.04**	**205,868**	**$51,639,215.31**

Antiasthmatic and Bronchodilator Agents	2015		2014	
	Total Claims	Total Paid	Total Claims	Total Paid
Antiasthmatic and Bronchodilator Agents	510,000	$44,690,081.55	502,663	$44,465,237.93
Total:	**510,000**	**$44,690,081.55**	**502,663**	**$44,465,237.93**

Anti-Diabetic Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Anti-Diabetic Agents		144,446	$35,900,969.13	149,675	$28,333,483.21
	Total:	**144,446**	**$35,900,969.13**	**149,675**	**$28,333,483.21**
Pain Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Analgesics - Narcotic		493,941	$20,965,636.78	546,955	$20,434,596.72
Analgesics - Anti-Inflammatory		178,746	$1,762,148.26	196,053	$2,293,981.97
Analgesics - Non-Narcotic		23,174	$501,100.30	25,879	$335,617.78
Migraine Agents		12,086	$332,356.67	12,412	$563,419.95
Gout		6,441	$134,880.47	5,310	$110,851.35
Local Anesthetics - Parenteral		1,388	$7,511.26	1,277	$7,175.24
General Anesthetics		187	$4,001.14	205	$4,393.64
	Total:	**715,963**	**$23,707,634.88**	**788,091**	**$23,750,036.65**
Anticonvulsant Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticonvulsant Agents		327,884	$22,018,892.35	320,685	$19,599,529.38
	Total:	**327,884**	**$22,018,892.35**	**320,685**	**$19,599,529.38**
Endocrine Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Contraceptives		116,377	$7,351,778.58	138,563	$8,711,225.20
Corticosteroids		184,580	$4,237,792.75	176,945	$3,669,160.85
Other Endocrine Agents		20,629	$4,028,053.23	21,397	$2,719,113.76
Thyroid		59,397	$1,243,238.03	60,105	$999,291.54
Estrogens		12,157	$970,563.11	14,989	$1,064,173.92
Progestins		5,128	$283,840.12	5,895	$313,166.11
Androgen - Anabolic		616	$153,153.26	879	$250,042.19
Oxytocics		349	$49,905.25	539	$54,419.98
	Total:	**399,233**	**$18,318,324.33**	**419,312**	**$17,780,593.55**
Cardiovascular Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Vasopressors		11,089	$4,563,331.32	11,384	$3,505,263.50

Antihyperlipidemics		81,634	$3,276,673.87	91,144	$3,596,945.44
Antihypertensives		234,812	$2,402,471.64	233,426	$2,817,161.67
Beta Blockers		84,053	$1,797,208.25	91,505	$1,956,508.29
Antianginal Agents		9,323	$727,892.95	9,523	$726,375.97
Diuretics		60,138	$569,205.55	66,000	$638,777.77
Calcium Channel Blockers		40,444	$467,085.04	43,355	$670,228.23
Cardiotonics		4,109	$219,706.99	4,556	$173,527.70
Antiarrhythmic Agents		2,236	$99,538.44	2,299	$100,569.68
Other Cardiovascular Agents		286	$87,360.99	346	$92,943.17
	Total:	**528,124**	**$14,210,475.04**	**553,538**	**$14,278,301.42**
Topical Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological Agents		215,139	$9,823,113.94	216,839	$9,355,046.21
Ophthalmic Agents		64,373	$2,058,616.52	63,313	$2,057,283.51
Otic Agents		50,010	$1,608,082.45	49,278	$1,035,014.74
Mouth/Throat/Dental Agents		26,665	$343,175.75	28,562	$429,798.28
Anorectal Agents		1,460	$76,482.13	1,620	$64,544.32
	Total:	**357,647**	**$13,909,470.79**	**359,612**	**$12,941,687.06**
Gastrointestinal Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Ulcer Agents		205,008	$3,535,749.61	218,325	$4,204,629.78
Other Gastrointestinal Agents		14,438	$2,569,433.86	15,906	$2,055,484.21
Digestive Aids		1,735	$1,941,693.25	1,638	$1,618,694.62
Antiemetics		96,581	$1,465,224.69	91,058	$1,450,611.01
Laxatives		41,139	$912,288.05	40,528	$1,024,973.41
Antidiarrheals		3,207	$39,891.24	3,523	$40,385.79
Antacids		508	$2,651.56	473	$3,003.06
	Total:	**362,616**	**$10,466,932.26**	**371,451**	**$10,397,781.88**
Antineoplastic Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antineoplastic Agents		13,089	$8,940,560.56	13,754	$8,646,509.64
	Total:	**13,089**	**$8,940,560.56**	**13,754**	**$8,646,509.64**

Antidepressants		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Antidepressants		413,852	$6,491,839.84	414,112	$9,650,310.15
	Total:	**413,852**	**$6,491,839.84**	**414,112**	**$9,650,310.15**
Allergy Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antihistamines		336,450	$2,863,779.98	339,214	$3,180,148.33
Systemic & Topical Nasal Agents		106,086	$1,651,874.40	98,849	$1,976,440.47
Cough/Cold/Allergy		1,595	$35,143.16	2,021	$55,878.48
	Total:	**444,131**	**$4,550,797.54**	**440,084**	**$5,212,467.28**
Non-Therapeutic Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Assorted Classes		6,165	$2,026,529.41	6,142	$2,137,232.50
Medical Devices		30,608	$1,449,011.66	23,412	$1,277,283.18
Diagnostic Agents		5,845	$848,686.91	117	$19,493.60
Chemicals		12,240	$222,894.24	15,015	$488,665.16
Antidotes		1,604	$103,283.24	1,199	$71,945.69
Pharmaceutical Adjuvants		1,284	$60,026.22	1,528	$46,509.07
Antiseptics & Disinfectants		7	$185.44	62	$2,469.53
Alternative Medicines		3	$20.57	0	$0.00
	Total:	**57,756**	**$4,710,637.69**	**47,475**	**$4,043,598.73**
Psychotherapeutic/Neurologic Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Psychotherapeutic & Neurological Agents		17,886	$4,609,891.32	17,255	$3,826,648.52
	Total:	**17,886**	**$4,609,891.32**	**17,255**	**$3,826,648.52**
Hematological Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticoagulants		14,752	$2,473,239.47	14,647	$2,582,313.24
Other Hematological Agents		14,453	$702,738.08	15,425	$709,919.21
Hematopoietic Agents		16,239	$180,377.85	17,331	$370,125.53
Hemostatics		225	$57,127.93	221	$46,553.73
	Total:	**45,669**	**$3,413,483.33**	**47,624**	**$3,708,911.71**

Genitourinary Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Urinary Anti-Infectives		19,400	$872,765.86	19,517	$1,026,724.31
Urinary Antispasmodics		13,652	$801,793.71	13,641	$928,965.09
Other Genitourinary Agents		12,047	$576,928.71	14,913	$474,928.74
Vaginal Agents		5,815	$540,888.57	7,137	$582,534.65
	Total:	**50,914**	**$2,792,376.85**	**55,208**	**$3,013,152.79**
Neuromuscular Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Musculoskeletal Therapy Agents		113,333	$1,862,023.99	123,379	$1,842,638.21
Antiparkinsonian Agents		25,759	$752,160.60	25,882	$692,797.47
Antimyasthenic Agents		191	$59,799.09	147	$19,189.46
Neuromuscular Agents		2	$338.29	14	$2,817.05
	Total:	**139,285**	**$2,674,321.97**	**149,422**	**$2,557,442.19**
Nutritional Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Multivitamins		43,239	$1,355,379.71	47,408	$1,236,599.86
Minerals & Electrolytes		26,214	$561,002.74	30,422	$715,541.68
Vitamins		615	$238,162.78	612	$138,239.71
Dietary Products		86	$38,342.08	111	$50,660.19
Nutrients		193	$5,839.44	360	$13,586.34
	Total:	**70,347**	**$2,198,726.75**	**78,913**	**$2,154,627.78**
Antianxiety Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antianxiety Agents		203,758	$1,642,314.24	209,060	$2,124,947.32
	Total:	**203,758**	**$1,642,314.24**	**209,060**	**$2,124,947.32**
Hypnotics		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Hypnotics		50,229	$506,876.23	57,501	$826,443.01
	Total:	**50,229**	**$506,876.23**	**57,501**	**$826,443.01**

Biological Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Vaccines		5,823	$182,036.00	5,716	$179,878.84
Passive Immunizing Agents		37	$99,095.43	20	$86,354.72
Toxoids		568	$23,385.06	282	$11,524.96
	Total:	**6,428**	**$304,516.49**	**6,018**	**$277,758.52**

Top Specialty Therapeutic Classes by Fiscal Year*

Hematological Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Other Hematological Agents		713	$16,716,192.26	824	$18,194,585.62
Hematopoietic Agents		710	$2,340,537.88	599	$1,853,102.16
	Total:	**1,423**	**$19,056,730.14**	**1,423**	**$20,047,687.78**

Pain Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Analgesics - Anti-Inflammatory		3,828	$13,163,265.83	3,607	$10,860,111.15
Local Anesthetics - Parenteral		46	$1,118.12	147	$2,527.50
	Total:	**3,874**	**$13,164,383.95**	**3,754**	**$10,862,638.65**

Endocrine Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Other Endocrine Agents		2,798	$8,896,760.39	2,785	$7,923,709.60
Progestins		1,027	$3,714,755.36	788	$2,864,118.32
	Total:	**3,825**	**$12,611,515.75**	**3,573**	**$10,787,827.92**

Psychotherapeutic/Neurologic Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Psychotherapeutic & Neurological Agents		1,615	$8,060,038.03	1,514	$6,944,096.69
	Total:	**1,615**	**$8,060,038.03**	**1,514**	**$6,944,096.69**

Biological Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Passive Immunizing Agents		3,146	$6,056,480.25	3,408	$6,926,433.46
Other Biological Agents		12	$401,673.78	14	$462,414.99
	Total:	**3,158**	**$6,458,154.03**	**3,422**	**$7,388,848.45**

Specialized Respiratory Agents		2015		2014	
		Total Claims	Total Paid	Total Claims	Total Paid
Specialized Respiratory Agents		921	$2,935,359.32	987	$2,862,695.66
	Total:	**921**	**$2,935,359.32**	**987**	**$2,862,695.66**
Anti-Infective Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Aminoglycosides		299	$1,781,119.72	405	$2,515,218.88
Other Anti-Infective Agents		69	$395,177.86	79	$472,473.03
Antivirals		11	$35,096.03	16	$48,153.26
	Total:	**379**	**$2,211,393.61**	**500**	**$3,035,845.17**
Cardiovascular Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Cardiovascular Agents		847	$2,133,289.84	893	$1,703,702.25
	Total:	**847**	**$2,133,289.84**	**893**	**$1,703,702.25**
Gastrointestinal Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Gastrointestinal Agents		478	$1,981,029.51	339	$1,390,862.30
	Total:	**478**	**$1,981,029.51**	**339**	**$1,390,862.30**
Non-Therapeutic Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidotes		303	$1,936,560.45	290	$1,348,122.97
	Total:	**303**	**$1,936,560.45**	**290**	**$1,348,122.97**
Antiasthmatic and Bronchodilator Agents		**2015**		**2014**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antiasthmatic and Bronchodilator Agents		81	$269,672.99	72	$203,305.20
	Total:	**81**	**$269,672.99**	**72**	**$203,305.20**

Total	2015		2014	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Top Traditional and Specialty Therapeutic Classes	**6,284,518**	**$477,909,534.12**	**6,420,472**	**$457,822,543.58**

*Table contains top traditional and specialty therapeutic classes and is not an all-inclusive list.

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[2] Centers for Medicare & Medicaid Services. "National Health Expenditure Projections 2014-2024, Forecast Summary". Available online at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/proj2014.pdf. Last revised 05/2014. Last accessed 03/17/2016.
[3] Peters CP. National Health Policy Forum. "The Basics: The Medicaid Drug Rebate Program". Available Online at: https://www.nhpf.org/library/the-basics/Basics_MedicaidDrugRebate_04-13-09.pdf. Issued 04/13/2009. Last accessed 03/16/2016.
[4] Office of Inspector General. Department of Health and Human Services. "States' Collection of Offset and Supplemental Medicaid Rebates". Available online at: http://oig.hhs.gov/oei/reports/oei-03-12-00520.pdf. Last revised 12/2014. Last accessed 03/17/2016.
[5] Elsevier Clinical Solutions. "Generic Drug Price Increases: Causes and Impact". Available online at: http://elscsforms.com/risinggenericdrugprices/?campid=16N13694&utm_campaign=gsdd_risingdrugprice_em_16n13694&mm=lombardol®=na&prod=gsdd&utm_medium=email&utm_source=list_provided&utm_content=3rd_party. Issued 2015. Last accessed 03/17/2016.
[6] Dennis B. *Washington Post*. "Prescription Drug Prices Jumped more than 10 Percent in 2015, Analysis Finds". Available online at: https://www.washingtonpost.com/news/to-your-health/wp/2016/01/11/prescription-drug-prices-jumped-more-than-10-percent-in-2015/. Issued 01/11/2016. Last accessed 03/18/2016.
[7] The World Bank. "Inflation, Consumer Prices (Annual %). Available online at: http://data.worldbank.org/indicator/FP.CPI.TOTL.ZG. Last revised 2016. Last accessed 03/18/2016.

Appendix H

30-Day Notice to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir)

Oklahoma Health Care Authority
April 2016

Introduction

The annual review of hepatitis C medications was conducted in December 2015. Refer to the December 2015 drug utilization review (DUR) packet for a detailed claims analysis and regimen comparison.

Current Prior Authorization Criteria

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Harvoni® (sofosbuvir/ledipasvir), and Sovaldi® (sofosbuvir) are the preferred direct-acting antivirals (DAAs) for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination or Olysio® (simeprevir) alone for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira Pak™, Harvoni®, or Sovaldi® with peginterferon and ribavirin are not appropriate for the member. Detailed prior authorization criteria for hepatitis C products with criteria changes can be found at the end of this report in the recommendations section. Detailed criteria for medications with no changes to the coverage criteria are not included in this DUR packet (please refer to the December DUR packet).

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

Anticipated Patent Expiration(s):

- Olysio® (simeprevir): September 2029
- Sovaldi® (sofosbuvir): December 2030
- Harvoni® (ledipasvir/sofosbuvir): December 2030
- Daklinza™ (daclatasvir): June 2031
- Technivie™ (ombitasvir/paritaprevir/ritonavir): April 2032
- Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir): September 2032

Removal(s) from Market:

- **September 2015:** Merck announced a voluntarily discontinuation of the manufacture and distribution of Pegintron® Redipen® (peginterferon alfa-2b) and Rebetrol® (ribavirin capsules) in the United States by February 2016. The discontinuations were a business decision by Merck, and were not based on any safety or efficacy findings.

New Indication(s):

- **February 2016:** Bristol-Myers Squibb announced that the U.S. Food and Drug Administration (FDA) approved Daklinza™ (daclatasvir) in combination with sofosbuvir to treat hepatitis C virus (HCV) genotype-1 infections. Daklinza™ was previously approved to treat patients with HCV genotype-3 in July 2015. The expanded indication includes data in three additional patient populations: chronic HCV patients with human

immunodeficiency virus (HIV-1) co-infection, advanced cirrhosis, and post-liver transplant recurrence of HCV.

- **February 2016:** The FDA approved additional indications for Gilead's Harvoni® (ledipasvir/sofosbuvir) to treat chronic HCV genotype-1 or -4 liver transplant recipients without cirrhosis or with compensated cirrhosis. Harvoni® was also approved for genotype-1 infected patients with decompensated cirrhosis including those who have undergone liver transplantation. Harvoni® was previously approved in October 2014 for the treatment of chronic HCV genotype-1 infection and again in November 2015 for genotypes 4, 5, and 6 and in patients co-infected with HIV.

New FDA Approval(s):

- **January 2016:** Merck announced the FDA approval of Zepatier™ (elbasvir/grazoprevir) for the treatment of chronic HCV genotype-1 or -4 infection with or without ribavirin. Zepatier™ is a once-daily, oral tablet containing elbasvir, a NS5A inhibitor, and grazoprevir, a NS3/4A protease inhibitor. Zepatier™ was granted two Breakthrough Therapy designations by the FDA, for the treatment of HCV genotype-1 infected in patients with end-stage renal disease on hemodialysis, and for the treatment of patients with HCV genotype-4 infection. Breakthrough Therapy designation is given to investigational medicines for serious or life-threatening conditions that may offer substantial improvement over existing therapies.

Safety Update(s):

- **March 2016:** A study presented at the International Conference on Viral Hepatitis found that despite being highly effective, direct-acting antivirals (DAAs) may increase the risk of adverse reactions in older patients. Additionally older adults were found to frequently require adjustments of other medications (95.1% of the patients achieved a sustained virologic response; however, 43.8% experienced adverse events).
- **March 2016:** The European Medicines Agency (EMA) has launched a review of six DAAs approved for the treatment of HCV. The review was initiated following cases of hepatitis B re-activation in patients who were co-infected with hepatitis B and C and who were treated with DAAs for hepatitis C.

Pipeline:

- **January 2016:** Gilead Sciences announced that the FDA granted priority review for sofosbuvir/velpatasvir, an oral combination of a nucleotide analog polymerase inhibitor, sofosbuvir, and an investigational pan-genotypic NS5A inhibitor, velpatasvir. The priority review was granted for the treatment of HCV genotypes 1 through 6. The FDA has set a target date of June 28, 2016. The FDA has assigned sofosbuvir/velpatasvir a Breakthrough Therapy designation.

News:

- **March 2016:** A study presented at the International Conference on Viral Hepatitis found that across six studies, five of which were considered real-world, eight weeks of treatment with Harvoni® (ledipasvir/sofosbuvir) achieved high sustained virologic responses (97%) in patients who met the FDA approved criteria for eight weeks of

treatment (treatment-naïve, non-cirrhotic, and a viral load ≤6 million IU/mL) and in some patients who did not meet the FDA approved criteria.

- **March 2016:** Merck won a jury verdict allowing the company to seek royalties from Gilead Sciences based on claims that Merck's scientists were responsible for early breakthroughs that led to the development of Gilead's hepatitis C drugs, Harvoni® (ledipasvir/sofosbuvir) and Sovaldi® (sofosbuvir). Gilead is expected to appeal.

Guideline Update(s):

- **February 2016:** The American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) updated the guidelines on when and in whom to initiate HCV therapy. The updated guidelines include the addition of Daklinza™ and Sovaldi® combination regimens for genotype-1 as well as the addition of Zepatier™ for genotypes 1 and 4 following FDA approval of both regimens in February 2016.

Zepatier™ (Elbasvir/Grazoprevir) Product Summary[14]

FDA Approval: January 2016

Indications: Zepatier™ (elbasvir/grazoprevir) is a fixed-dose combination product containing elbasvir, a HCV NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, indicated with or without ribavirin for the treatment of chronic HCV genotypes 1 or 4 infection in adults.

Dosing:

- Zepatier™ is available as combination oral tablets containing 50mg elbasvir and 100mg grazoprevir.
- The recommended dosing of elbasvir/grazoprevir is one 50mg/100mg tablet by mouth once daily with or without food. The regimen and duration of therapy is dependent on host and viral factors including: genotype, prior treatment experience, and NS5A polymorphisms. The following table contains the recommended regimens and treatment durations:

Dosage Regimens for Zepatier™ in Patients With Genotype-1 or -4 HCV With or Without Cirrhosis		
Patient Population	**Treatment**	**Duration**
Genotype-1a: Treatment-naïve or PEG IFN/RBV experienced without baseline NS5A polymorphisms*	Zepatier™	12 weeks
Genotype-1a: Treatment-naïve or PEG IFN/RBV experienced with baseline NS5A polymorphisms*	Zepatier™ + RBV	16 weeks
Genotype-1b: Treatment-naïve or PEG IFN/RBV experienced	Zepatier™	12 weeks
Genotype-1a[+] or -1b: PEG IFN/RBV/PI experienced	Zepatier™ + RBV	12 weeks
Genotype-4: Treatment-naïve	Zepatier™	12 weeks
Genotype-4: PEG IFN/RBV experienced	Zepatier™ + RBV	16 weeks

*Polymorphisms at amino acid positions 28, 30, 31, or 93.

[+]The optimal elbasvir/grazoprevir-based treatment regimen and duration of therapy for PEG IFN/RBV/PI-experienced genotype-1a infected patients with baseline NS5A resistance-associated polymorphisms has not been established.

PEG IFN = Peginterferon Alfa, RBV = Ribavirin, PI = NS3/4A Protease Inhibitor

RBV dosing is weight-based, and administered orally in two divided doses with food.

- Testing patients with HCV genotype-1a infection for the presence of virus with NS5A resistance-associated polymorphisms is recommended prior to initiation of treatment with elbasvir/grazoprevir to determine dosage regimen and duration. In clinical studies of subjects who received elbasvir/grazoprevir for 12 weeks, sustained virologic response (SVR) rates were lower in genotype-1a infected patients with one or more NS5A resistance-associated polymorphism(s).
- HCV/HIV-1 Coinfection: Patients should follow the dosage recommendations in the previous regimens table.
- Renal Impairment: No dosage adjustment of elbasvir/grazoprevir is recommended in patients with any degree of renal impairment including patients on hemodialysis. Dosing modifications may be required for ribavirin in this population.

Mechanism of Action: Elbasvir/grazoprevir combines two direct-acting antiviral agents with distinct mechanisms of action and non-overlapping resistance profiles to target HCV at multiple steps in the viral lifecycle.

- Elbasvir is an inhibitor of NS5A, which is essential for viral RNA replication and virion assembly.
- Grazoprevir is an inhibitor of HCV NS3/4A protease which is necessary for the proteolytic cleavage of the HCV encoded polyprotein and is essential for viral replication.

Contraindications:

- Elbasvir/grazoprevir is contraindicated in patients with moderate or severe hepatic impairment (Child Pugh B or C) due to increased grazoprevir concentrations resulting in increased risk of alanine transaminase (ALT) elevations.
- Elbasvir/grazoprevir is contraindicated when taken in combination with drugs that strongly induce cytochrome P450 3A (CYP3A) and, thus, may lead to lower exposure and loss of efficacy of elbasvir/grazoprevir *(see drug interactions section)*.
- Elbasvir/grazoprevir is contraindicated when taken in combination with drugs that inhibit organic anion-transporting polypeptides 1B1/3 (OATP1B1/3) and, thus, may lead to significant increases in grazoprevir plasma concentrations resulting in increased risk of ALT elevations *(see drug interactions section)*.
- When elbasvir/grazoprevir is administered with ribavirin, the contraindications for ribavirin also apply to the combination regimen.

Warnings and Precautions:

- Increased Risk of ALT Elevations: During clinical trials with elbasvir/grazoprevir with or without ribavirin, 1% of subjects experienced elevations of ALT from normal levels to greater than five times the upper limit of normal (ULN) generally at or after treatment week 8. ALT elevations were typically asymptomatic and most resolved with ongoing or completion of therapy. Higher rates of late ALT elevations occurred in the following subpopulations: female sex (2%), Asian race (2%), and age 65 years or older (2%).
    - Hepatic laboratory testing should be performed prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, additional hepatic laboratory testing should be performed at treatment week 12.

- Risks Associated with Ribavirin Combination Treatment: If elbasvir/grazoprevir is administered with ribavirin, the warnings and precautions for ribavirin, including the pregnancy avoidance warning, also apply to this combination regimen.
- Risk of Adverse Reactions or Reduced Therapeutic Effect Due to Drug Interactions: The concomitant use of elbasvir/grazoprevir and certain drugs may result in significant drug interactions (*see drug interactions section*), some of which may lead to:
    - Adverse reactions from greater exposure of concomitant drugs or components of elbasvir/grazoprevir.
    - Significant decreases of elbasvir or grazoprevir plasma concentrations which may lead to reduced therapeutic effect of elbasvir/grazoprevir and possible development of resistance.

Adverse Reactions: The most common adverse reactions (≥5%) reported during elbasvir/grazoprevir clinical trials include the following:

- Headache
- Fatigue
- Insomnia
- Nausea
- Diarrhea

Use in Special Populations:

- Pregnancy: No adequate human data are available to establish whether or not elbasvir/grazoprevir poses a risk to pregnancy outcomes. In animal reproduction studies, no evidence of adverse developmental outcomes was observed with elbasvir/grazoprevir at exposures greater than the recommended human dose. If elbasvir/grazoprevir is administered with ribavirin, the combination regimen is contraindicated in pregnant women and in men whose female partners are pregnant.
- Nursing Mothers: It is not known whether elbasvir/grazoprevir is present in human breast milk, affects human milk production, or has effects on the breastfed infant. When administered to lactating rats, the components of elbasvir/grazoprevir were present in milk without effects on growth and development observed in nursing pups.
- Females and Males of Reproductive Potential: If elbasvir/grazoprevir is administered with ribavirin, the warnings and precautions for ribavirin with regard to pregnancy testing, contraception, and infertility also applies to this combination regimen.
- Pediatric Use: The safety and effectiveness of elbasvir/grazoprevir in pediatric patients younger than 18 years of age have not been established.
- Geriatric Use: A higher rate of ALT elevations was observed in subjects aged 65 years and older in clinical trials. However, no dosage adjustment of elbasvir/grazoprevir is recommended in geriatric patients.
- Gender: Higher elbasvir and grazoprevir plasma concentrations were observed in females compared to males. Females experienced a higher rate of late ALT elevations in clinical trials. However, no dosage adjustment of elbasvir/grazoprevir is recommended based on gender.
- Race: Higher elbasvir and grazoprevir plasma concentrations were observed in Asians compared to Caucasians. Asians experienced a higher rate of late ALT elevations in clinical trials. However, no dosage adjustment of elbasvir/grazoprevir is recommended based on race.

- Renal Impairment: No dosage adjustment of elbasvir/grazoprevir is recommended in patients with any degree of renal impairment including patients receiving hemodialysis. Dosing modifications may be required for ribavirin in this population.
- Hepatic Impairment: No dosage adjustment is required for patients with mild hepatic impairment. Elbasvir/grazoprevir is contraindicated in patients with moderate hepatic impairment (Child Pugh B) due to the lack of clinical safety and efficacy experience in HCV-infected Child Pugh B patients, and in patients with severe hepatic impairment (Child Pugh C) due to a 12-fold increase in grazoprevir exposure.
- Liver Transplant Patients: The safety and efficacy of elbasvir/grazoprevir have not been established in patients awaiting liver transplant or in liver transplant patients.

Drug Interactions: Grazoprevir is a substrate of OATP1B1/3 transporters. Co-administration of elbasvir/grazoprevir with drugs that inhibit OATP1B1/3 transporters may result in a significant increase in the plasma concentrations of grazoprevir. Elbasvir and grazoprevir are substrates of CYP3A. Co-administration of elbasvir/grazoprevir with drugs that moderately or strongly induce CYP3A may result in decreased plasma concentrations of elbasvir/grazoprevir leading to reduced therapeutic effect. Co-administration of elbasvir/grazoprevir with strong CYP3A inducers or efavirenz is contraindicated. Co-administration of elbasvir/grazoprevir with moderate CYP3A inducers is not recommended. Co-administration of elbasvir/grazoprevir with strong CYP3A inhibitors may increase elbasvir/grazoprevir concentrations, and co-administration with certain strong CYP3A inhibitors is not recommended.

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comment(s)**
Strong CYP3A Inducers phenytoin, carbamazepine, rifampin, St. John's wort, efavirenz	Decreased elbasvir/grazoprevir	May lead to reduced therapeutic effect of elbasvir/grazoprevir. Co-administration is contraindicated.
OATP1B1/3 Inhibitors atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine	Increased grazoprevir	May increase the risk of ALT elevations.
Antibiotics nafcillin	Decreased elbasvir/grazoprevir	May lead to reduced therapeutic effect of elbasvir/grazoprevir. Co-administration is not recommended.
Antifungals ketoconazole	Increased elbasvir/grazoprevir	May increase grazoprevir exposure and risk of hepatotoxicity. Co-administration is not recommended.
Endothelin Antagonists bosentan	Decreased elbasvir/grazoprevir	May lead to reduced therapeutic effect of elbasvir/grazoprevir. Co-administration is not recommended.
HIV Medications etravirine, elvitegravir/cobicistat/ emtricitabine/tenofovir	etravirine: decreased elbasvir/ grazoprevir elvitegravir/cobicistat/ emtricitabine/tenofovir: increased elbasvir/grazoprevir	etravirine: May lead to reduced therapeutic effect of elbasvir/ grazoprevir. Co-administration is not recommended. elvitegravir/cobicistat/ emtricitabine/tenofovir: Co-administration is not recommended.
Wakefulness-Promoting Agents modafinil	Decreased elbasvir/grazoprevir	May lead to reduced therapeutic effect of elbasvir/grazoprevir. Co-administration is not recommended.

Table modified from: Zepatier™ Product Information. Merck & Co., INC. Refer to the prescribing information for a complete list of drug interactions.

Regimen Comparison[12,14,15,16,17,18,19,20]

The following table shows the current FDA approved or AASLD/IDSA recommended regimens of DAAs for the treatment of HCV infection in treatment-naïve patients with or without cirrhosis in genotypes 1 or 4. Specific regimens are used in particular patient populations depending on pre-treatment viral load, prior hepatitis C treatment experience, fibrosis stage, cirrhosis status, and baseline viral polymorphisms. Regimens marked with a star are not currently FDA approved, but are recommended by the AASLD/IDSA guidance. Most non-FDA approved regimens were studied in very small populations with limited sustained virologic response (SVR) or "cure" data. SVR rates found in clinical studies can be used as a measure of clinical efficacy for each regimen. SVR rates were obtained from studies cited in the AASLD/IDSA guidance or from an individual product's package labeling. Some SVR percentages in the following table may contain treatment experienced patients if the study did not differentiate. Overall SVR percentages for genotypic subtypes may be reported together if the study did not differentiate.

Genotype	Host Factors	Treatment Regimen	Total Cost	SVR**
Genotype-1a	Treatment-naïve, Non-cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	98% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	$57,657.60-$77,400.96	92%-100%[+]
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	93% or 96%
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	97%
		SIM + **SOF** 12 wks	$158,780.16	95% (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	$99,605.04	92%[¥]
	Treatment-naïve, Cirrhotic	**DAC** + **SOF** 12 weeks	$155,232.00	91% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	$57,657.60-$77,400.96	92%-100%[+]
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 24 wks	$176,756.16	95%
		SIM + **SOF** +/- RBV 24 wks	$317,560.32-$318,346.56	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-92%[¥] (1a & 1b)
Genotype-1b	Treatment-naïve, Non-cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	98% (1a & 1b)
		EBR/GZR 12 wks	$57,657.60	98%
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	98%
		PAR/RIT/OMB/DAS 12 wks	$87,984.96	100%
		SIM + **SOF** 12 wks	$158,780.16	95% (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	$99,605.04	83%[¥]
	Treatment-naïve, Cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	91% (1a & 1b)
		EBR/GZR 12 wks	$57,657.60	98%
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	100%
		SIM + **SOF** +/- RBV 24 wks	$317,560.32-$318,346.56	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-83%[¥] (1a & 1b)
Genotype-4	Treatment-naïve, Non-cirrhotic	**EBR/GZR** 12 wks	$57,657.60	97%
		LED/SOF 12 wks	$99,792.00	93%-100%
		PAR/RIT/OMB + RBV 12 wks	$81,338.88	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	96%[¥]
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$57,657.60	97%
		LED/SOF 12 wks	$99,792.00	93%
		***PAR/RIT/OMB** + RBV 12 wks	$81,338.88	96%-97%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-96%[¥]

*Not an FDA approved regimen, **SVR = Sustained virologic response 12 weeks after therapy completion in clinical studies
[¥]Percentage includes some cirrhotic and some non-cirrhotic patients. Lower percentage may include genotype-4 and both -1a and -1b subtypes.
[+]Lower percentage accounts for those with baseline RAVs and some cirrhotic patients; lower percentage shown is for 12 weeks without RBV.
Costs based on estimated acquisition cost (EAC).
Some SVR percentages may contain treatment-experienced or cirrhotic patients if the study did not differentiate.
If genotypic subtype not indicated then both GT1a and GT1b were included in the SVR results.
SIM = simeprevir SOF = sofosbuvir LED = ledipasvir PAR = paritaprevir RIT = ritonavir OMB = ombitasvir GT = Genotype
DAS = dasabuvir DAC = daclatasvir EBR = elbasvir GZR = grazoprevir RBV = Ribavirin PEG IFN = peginterferon alfa
RBV Dosing based on >75kg patient (1200mg).

Recommendations

The College of Pharmacy recommends the prior authorization of Zepatier™ (elbasvir/ grazoprevir) with criteria similar to the other prior authorized hepatitis C medications (see criteria noted in red). Additionally, the College of Pharmacy recommends the changes noted in red to the individual Hepatitis C medications prior authorization criteria. The following table highlights the preferred regimens for each genotype in treatment naïve and PEG-IFN and RBV-experienced members (listed in alphabetical order). Additional regimens other than those listed may be considered based on patient-specific clinical situations.

Genotype	Patient Factors	Preferred Regimen(s)
Genotype-1		
1	Treatment-naïve, non-cirrhotic	Harvoni® for 8 or 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-naïve, cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 24 weeks 1b: Viekira Pak™ + RBV for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-experienced, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks 1a: Zepatier™ + RBV for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ + RBV for 12 weeks
1	Treatment-experienced, cirrhotic	Harvoni® + RBV for 12 weeks Harvoni® for 24 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 24 weeks 1b: Viekira Pak™ + RBV for 12 weeks 1a: Zepatier™ + RBV for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ + RBV for 12 weeks
Genotype-2		
2	Treatment-naïve, non-cirrhotic	Sovaldi® + RBV for 12 weeks Sovaldi® + Daklinza™ for 12 weeks (if RBV intolerant)
2	Treatment-naïve, cirrhotic	Sovaldi® + RBV for 12 or 16 weeks Sovaldi® + Daklinza™ for 16 weeks (if RBV intolerant)
2	Treatment-experienced, non-cirrhotic	Sovaldi® + RBV for 12 weeks Sovaldi® + Daklinza™ for 12 weeks

Genotype	Patient Factors	Preferred Regimen(s)
2	Treatment-experienced, cirrhotic	Sovaldi® + RBV for 16 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + Daklinza™ for 16 weeks
Genotype-3		
3	Treatment-naïve, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
3	Treatment-naïve, cirrhotic	Daklinza™ + Sovaldi® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
3	Treatment-experienced, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
3	Treatment-experienced, cirrhotic	Daklinza™ + Sovaldi® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
Genotype-4		
4	Treatment-naïve, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-naïve, cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-experienced, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
4	Treatment-experienced, cirrhotic	Harvoni® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
Genotype-5 or Genotype-6		
5 or 6	Treatment-naïve or -experienced, non-cirrhotic or cirrhotic	Harvoni® for 12 weeks

Not all regimens included are FDA approved.
All regimens are either FDA approved or recommended in AASLD/IDSA treatment guidance.
If not specified, regimen applies to all genotypic subtypes.
RBV = Ribavirin PEG IFN = Peginterferon Alfa RAV = Resistance-Associated Polymorphisms

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), and Zepatier™ (elbasvir/grazoprevir) are the preferred direct-acting antivirals for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (Daclatasvir) in combination for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira Pak™, Harvoni®, Sovaldi® with peginterferon

and ribavirin, or Zepatier™ (elbasvir/grazoprevir) are not appropriate for the member. Detailed criteria for medications with no changes to the coverage criteria are not included in the criteria on the following pages. The criteria for each medication may include FDA approved regimens or AASLD guideline recommended regimens that are not included in the SoonerCare preferred regimens table. Preferred regimens for each genotype can be found in the preferred regimens table. Additional regimens other than those listed in the preferred regimens table may be considered based on patient-specific clinical situations.

Zepatier™ (Elbasvir/Grazoprevir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1** or **genotype-4**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Zepatier™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. If the member has genotype-1a, testing results for the presence of virus with NS5A resistance-associated polymorphisms must be indicated on the prior authorization request; and
7. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
8. The following regimens and requirements based on genotype, polymorphisms, and prior treatment status will apply (all regimens apply to patients with and without cirrhosis, HIV/HCV co-infected patients, and patients with or without renal impairment):
    a. **Genotype-1a, treatment-naïve or peginterferon alfa + ribavirin experienced without baseline NS5A polymorphisms:**
        i. Zepatier™ for 12 weeks
    b. **Genotype-1a, treatment-naïve or peginterferon alfa + ribavirin experienced with baseline NS5A polymorphisms:**
        i. Zepatier™ with weight-based ribavirin for 16 weeks
    c. **Genotype-1b, treatment-naïve or peginterferon alfa + ribavirin experienced:**
        i. Zepatier™ for 12 weeks
    d. **Genotype-1a or -1b, peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor (e.g., boceprevir, simeprevir, teleprevir) experienced:**
        i. Zepatier™ with weight-based ribavirin for 12 weeks
    e. **Genotype-4, treatment-naïve:**
        i. Zepatier™ for 12 weeks
    f. **Genotype-4, treatment-experienced:**
        i. Zepatier™ with weight-based ribavirin for 16 weeks
    g. New regimens will apply as approved by the FDA
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and

10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
16. The prescriber must verify that the member's ALT levels will be monitored prior to treatment initiation, at treatment week eight, and as clinically indicated thereafter (patients receiving 16 weeks of therapy should receive additional ALT levels at treatment week 12); and
17. Member must not be taking the following medications: phenytoin, carbamazepine, rifampin, St. John's wort, efavirenz, atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine, nafcillin, ketoconazole, bosentan, etravirine, elvitegravir/cobicstat/ emtricitabine/tenofovir, or modafinil; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 or 16 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Daklinza™ (Daclatasvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-3**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Daklinza™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and

5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype and concomitant drug therapy will apply:
    a. **Genotype-1, treatment-naïve or treatment-experienced, without cirrhosis or with compensated cirrhosis:**
        i. Daklinza™ 60mg with Sovaldi® for 12 weeks
    b. **Genotype-1, treatment-naïve or treatment-experienced, with decompensated cirrhosis, or post-transplant:**
        i. Daklinza™ 60mg with Sovaldi® and weight-based ribavirin for 12 weeks
    c. **Genotype-2, treatment-naïve or treatment-experienced, without cirrhosis, RBV intolerant:**
        i. Daklinza™ 60mg with Sovaldi® for 12 weeks
    d. **Genotype-2, treatment-naïve or treatment-experienced, with cirrhosis, RBV intolerant:**
        i. Daklinza™ 60mg with Sovaldi® for 16 weeks
    e. **Genotype-3, treatment-naïve or treatment-experienced, without cirrhosis:**
        i. Daklinza™ 60mg with Sovaldi® for 12 weeks
    f. **Genotype-3, treatment-naïve or treatment-experienced, with compensated or decompensated cirrhosis, or post-transplant:**
        i. Daklinza™ 60mg with Sovaldi® and weight-based ribavirin for 12 weeks
    g. **Concomitant use of moderate CYP3A inducer(s):**
        i. Daklinza™ 90mg (all other regimen criteria applies)
        ii. Moderate Inducers: bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, and rifapentine
    h. **Concomitant use of strong CYP3A inhibitors:**
        i. Daklinza™ 30mg (all other regimen criteria applies)
        ii. Strong CYP3A inhibitors include the following: atazanavir/ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, and voriconazole
    i. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~13. Member must not have decompensated cirrhosis; and~~

14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: carbamazepine, phenytoin, phenobarbital, rifampin, amiodarone, or St. John's wort; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
19. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-4**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Technivie™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype, cirrhosis status, and prior treatment status will apply:
    a. **Genotype-4, treatment-naïve or treatment-experienced, non-cirrhotic or compensated cirrhotic:**
        i. Technivie™ in combination with weight-based ribavirin for 12 weeks
    b. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and

11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have cirrhosis, decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
16. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and
17. Member must not be taking the following medications: alfuzosin, carbamazepine, phenytoin, phenobarbital, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol containing medications (combined oral contraceptives), St. John's wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil, triazolam, orally administered midazolam, atazanavir/ritonavir, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine, salmeterol, or voriconazole; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Harvoni® (Ledipasvir/Sofosbuvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1, genotype-4, genotype-5, or genotype-6**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and

5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **Genotype-1:**
        i. **Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA less than 6 million IU/mL:**
            1. Harvoni® for 8 weeks
        ii. **Treatment-naïve with or without compensated cirrhosis:**
            1. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA greater than 6 million IU/mL
            2. Harvoni® for 12 weeks
        iii. **Treatment-experienced without cirrhosis:**
            1. Harvoni® for 12 weeks
        iv. **Treatment-experienced with compensated cirrhosis:**
            1. Harvoni® for 24 weeks
        v. **Treatment-naïve or treatment-experienced with decompensated cirrhosis:**
            1. Harvoni® with weight-based ribavirin for 12 weeks
    b. **Genotype-1 or Genotype-4:**
        i. **Treatment-naïve or treatment-experienced liver transplant recipients with or without compensated cirrhosis:**
            1. Harvoni® with weight-based ribavirin for 12 weeks
    c. **Genotype-4, Genotype-5, or Genotype-6:**
        i. **Treatment-naïve or treatment-experienced with or without compensated cirrhosis:**
            1. Harvoni® for 12 weeks
    d. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. ~~Member must not have decompensated cirrhosis; and~~
14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of

non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and

16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/ emtricitabine in combination with tenofovir disoproxil fumarate; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

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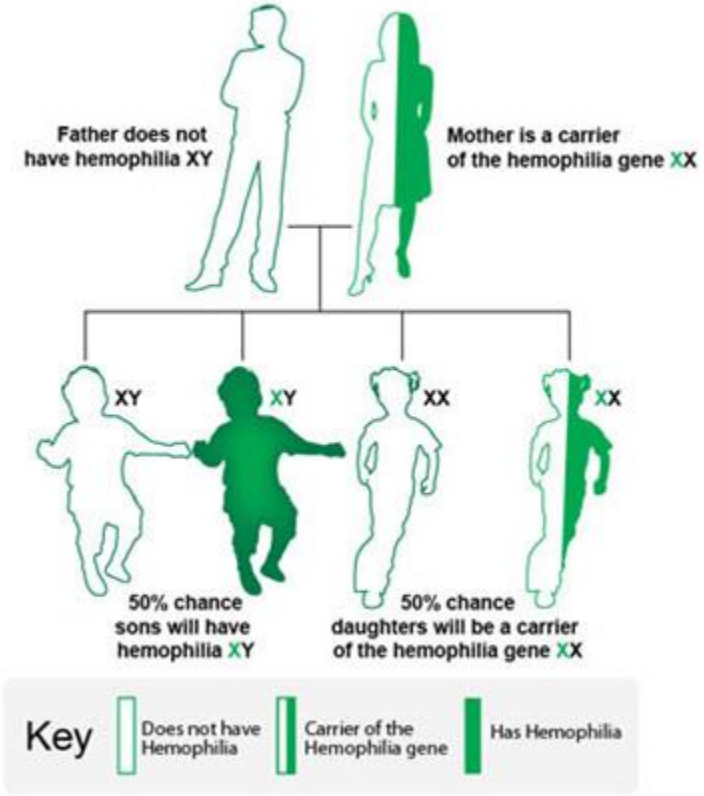
Appendix I

Calendar Year 2015 Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein], Adynovate® [Antihemophilic Factor (Recombinant), PEGylated], Alprolix® [Coagulation Factor IX (Recombinant), Fc Fusion Protein], Idelvion® [Coagulation Factor IX (Recombinant), Albumin Fusion Protein], Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence], Corifact® [Factor XIII Concentrate (Human)], Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)], and Coagadex® [Coagulation Factor X (Human)], and Establish Pharmacy Provider Standards of Care

Oklahoma Health Care Authority
April 2016

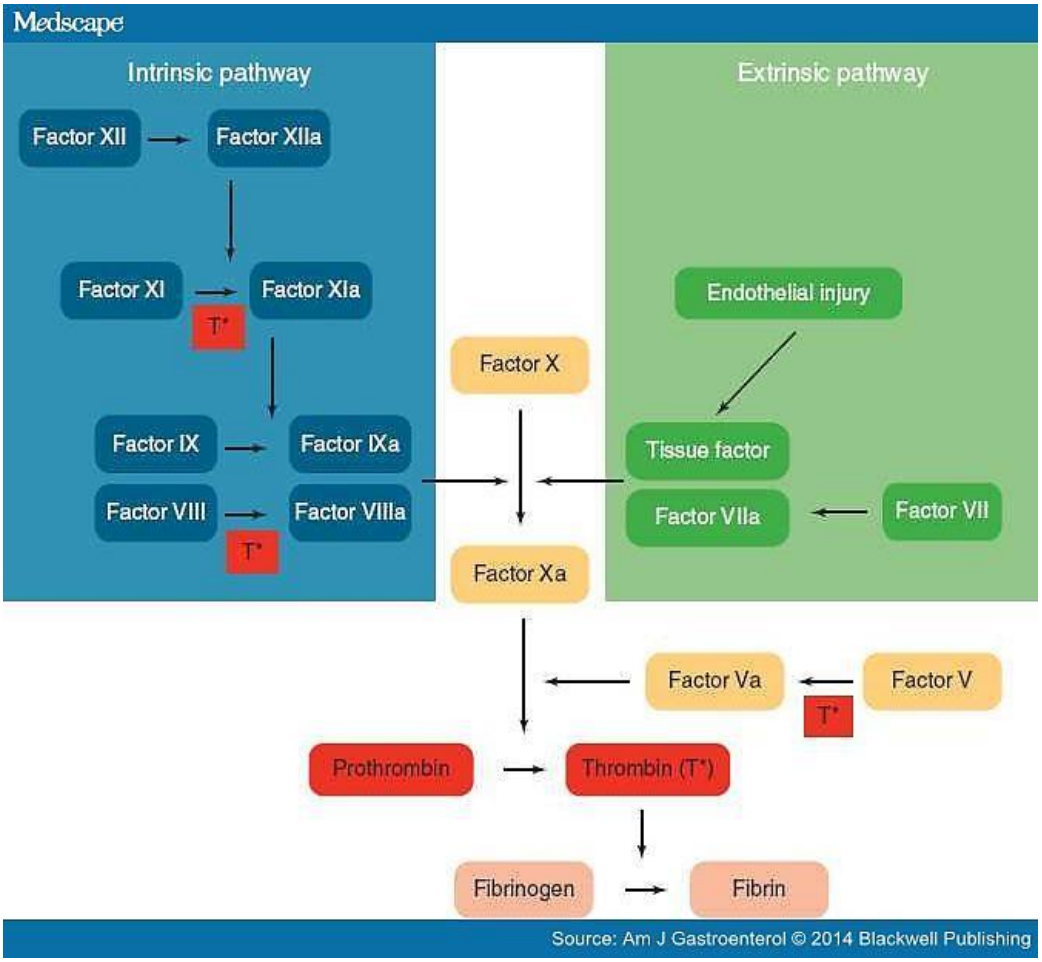
Hemophilia and Other Rare Bleeding Disorders Overview[1,2,3,4]

Hemophilia is a rare bleeding disorder in which the blood does not clot properly due to a lack of one or more clotting factors. It is an inherited genetic mutation most often, but it occurs through a random gene mutation in approximately one-third of patients. It is X-linked; therefore, a son can inherit from his mother who is a carrier of the gene.



Hemophilia occurs in about 1 in 5,000 male births with approximately 20,000 males in the United States living with the disorder currently. There are different types of hemophilia. Approximately 80% of patients with hemophilia have factor VIII deficiency. This is called Classic Hemophilia or Hemophilia A. Approximately 20% of patients are factor IX deficient which is called Christmas Disease, named after Stephen Christmas who was the first patient described with this disease. Factor IX deficiency is also referred to as Hemophilia B. There are other clotting factor deficiencies, but they are more rare.

The severity of hemophilia is determined by the amount of circulating clotting factor. Patients with mild hemophilia have a circulating factor level of 6% to 30% of the normally expected level and make up 25% of cases. Moderate hemophilia patients have factor levels of 1% to 5% and make up 15% of cases, while severe hemophilia patients have less than 1% of expected circulating factor and make up 60% of cases.



Due to a low or absent factor level, these patients typically have internal bleeds including joint, muscle, soft tissue, brain, and organ. These bleeds can be either spontaneous or due to an injury. The frequency of bleeding episodes is determined by the amount of circulating factor in the body. If the factor level is low, the likelihood of bleeding is increased and vice versa. The aim of treatment is to raise the factor level to stop a bleeding episode or prevent bleeding from occurring. This is achieved by giving the patient the factor they are missing, or in mild hemophilia A cases, desmopressin can be given to release factor VIII stored in the endothelial

cells and platelets. Additionally, antifibrinolytics such as aminocaproic acid and tranexamic acid are used to slow the degradation of a formed clot.

There are two main types of treatment, episodic and prophylactic. Episodic treatment refers to treating only when there is a bleeding episode. Prophylactic treatment occurs on a regular basis to prevent bleeding episodes from occurring. The purpose of prophylactic treatment is to prevent the damage of bleeding episodes over time by having at least some factor in the body at all times. Patients with hemophilia keep factor replacement products in the home for infusion.

Complications of Hemophilia[1]

One of the major complications of hemophilia is the development of an antibody against the clotting factor. This is called an inhibitor. Inhibitors occur in 15% to 20% of patients with hemophilia. The development of an inhibitor makes treatment more difficult and more expensive. Depending on the severity of the inhibitor, a patient can be given large doses of factor to overcome the inhibitor, given a bypassing agent, such as recombinant factor VIIa or anti-inhibitor coagulant complex, or undergo immune tolerance induction therapy.

Another complication of hemophilia is damage to the joints where bleeding has occurred. Once a bleed has occurred in a specific joint, there is an increased risk for future bleeds occurring in the same joint. Over time the bleeding and recovery cycle causes degradation of the synovium and eventually the joint itself. This decreases the range of motion of the joint and causes pain. Eventually, the patient may need a radiosynovectomy, joint fusion, or joint replacement.

Also, the transmission of blood borne infections such as HIV and hepatitis has been a serious problem for patients with hemophilia. In the 1970's and 1980's treatment was plasma derived. There were not methods for testing for blood borne diseases. Many patients with hemophilia were infected with HIV and hepatitis. In the 1980's methods for blood donor screening and removing blood borne pathogens were developed, such as heat treatments and nanofiltration, which made plasma derived factor much safer. However, the risk of transmission of an unknown virus or disease remains a possibility. In the early 1990's recombinant technology was used to develop recombinant factor. The first generation of recombinant factor was still stabilized with human albumin making it not completely risk free. Since then there have been improvements in manufacturing and currently there are recombinant factor products available which have never been in contact with any human blood products. The development of vaccines has decreased the transmission of some diseases.

Acquired Hemophilia[5]

Acquired Hemophilia (AH) is a rare autoimmune disorder caused by the development of autoantibodies which inactivate factor VIII (FVIII) but not factor IX. AH is rarer than congenital hemophilia affecting approximately two per one million of population. The median age of onset is 78 years with less than 15% under 65 years of age. Men and women are equally affected except during the age span of 20 to 40 years in women due to pregnancy. Around 50% of AH can be attributed to an underlying disease/cause such as pregnancy, malignancy, other autoimmune disorders, and certain medications such as penicillin, ciprofloxacin, phenytoin, and fludarabine to name a few. Patients with AH usually present with extensive cutaneous purpura

and internal bleeding, while joint bleeds are not a prominent feature as it is with congenital hemophilia. Due to the high risk of significant bleeding episodes patients with acquired hemophilia should be under the care of a specialist in hemophilia. The first step of treatment should be to control bleeding by using bypassing agents which is the same as with congenital hemophilia inhibitor development or using porcine FVIII. Immunosuppression to control and stop antibody production is the second part of AH treatment. Drugs that have been used for immunosuppression are corticosteroids, rituximab, cyclosporin, cyclophosphamide, azathioprine, vincristine, and mycophenolate mofetil. Some are used as monotherapy, but most of the time a combination of drugs are used.

Factor X Deficiency[6,7]

Factor X deficiency is a disorder wherein the body does not produce enough factor X (FX), or the FX produced does not function properly. It is an autosomal recessive disorder; therefore, both parents must be carriers of the gene. Both males and females are equally affected. FX deficiency occurs in around 1 per million of population worldwide. FX deficiency commonly causes nose and mouth bleeding, easy bruising, soft tissue bleeds, prolonged bleeding after surgery, heavy and prolonged menstruation, prolonged bleeding after childbirth, miscarriages, bleeding into joints, and central nervous system bleeding. The treatment for FX deficiency is replacement of factor X. Antifibrinolytics are useful to slow the breakdown of a clot.

Factor XIII Deficiency[8]

Factor XIII deficiency is an autosomal recessive disorder in which the body does not produce any or enough factor XIII (FXIII). Both parents must carry the gene in order to pass it on to offspring. It is the rarest of all the factor deficiencies occurring in 1 per 5 million births. The disorder affects males and females equally. FXIII is a fibrin stabilizer. Most patients with FXIII deficiency experience symptoms from birth such as bleeding from the umbilical cord stump which occurs in up to 80% of patients. The leading cause of mortality is intracranial hemorrhage which can occur in up to 30% of patients. Other symptoms include easy bruising, nose and mouth bleeds, prolonged and heavy menstruation, repeated miscarriages, muscle bleeding, and prolonged bleeding after surgery. Factor replacement is the primary treatment for patients with FXIII deficiency. Antifibrinolytics are used to slow the clot degradation process.

Utilization of Factor Replacement Products: Calendar Year 2015

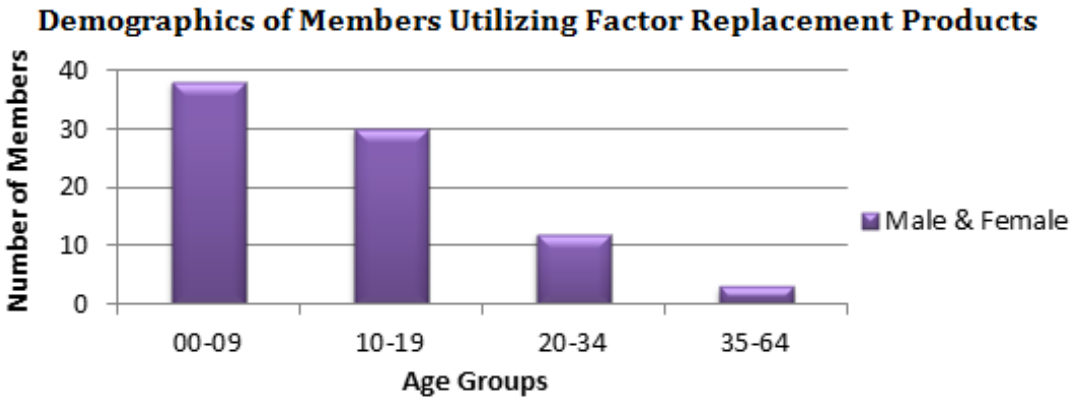
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Total Units (IU)	Cost PUPY[Ŧ]
2014	88	636	$13,936,576.69	11,506,998	$158,370.18
2015	83	594	$14,853,256.91	11,613,793	$178,954.90
% Change	**-5.68%**	**-6.60%**	**6.58%**	**0.93%**	**13.00%**
Change	**5**	**42**	**$916,680.22**	**106,795**	**$20,584.72**

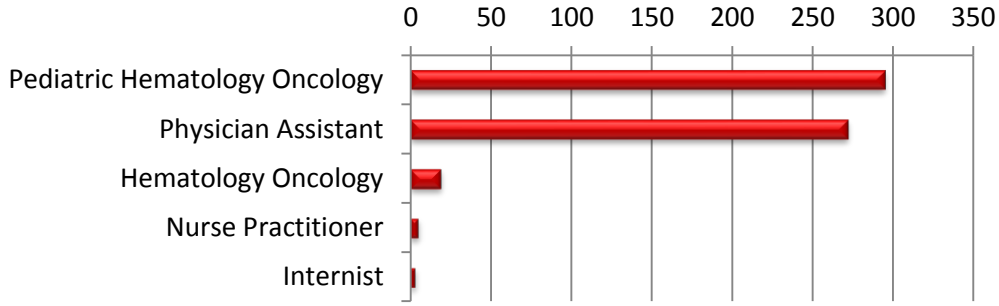
*Total number of unduplicated members.

[Ŧ]PUPY = Cost Per Utilizer Per Year

Costs do not reflect rebated prices or net costs.



Top Prescriber Specialties of Factor Replacement Products by Number of Claims



Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein] Summary[9,10]

FDA Approval: June 2014

Indication: Eloctate™ [antihemophilic factor (recombinant), Fc fusion protein] is a recombinant DNA derived, antihemophilic factor indicated in adults and children with Hemophilia A (congenital Factor VIII deficiency) for:

- Control and prevention of bleeding episodes
- Perioperative management
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes

Dosing: One international unit (IU) of Eloctate™ per kilogram (kg) of body weight is expected to increase the circulating level of factor VIII by 2% [IU/dL]; therefore the recommended dose is calculated by the following equation:

- Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL)
    - Example: 50kg x 40 IU/dl (%) x 0.5 IU/kg per IU/dL = 1000 IU per dose
- <u>Bleeding Episodes:</u>
    - Minor-to-Moderate: the desired factor VIII level is 40% to 60% of normal; repeat every 24 to 48 hours until bleeding is resolved
    - Major: the desired factor VIII level is 80% to 100% of normal; repeat every 12 to 24 hours until bleeding is resolved

- Perioperative Management:
    - Minor Surgery: the desired factor VIII level is 50% to 80% of normal; repeat every 24 hours as needed to control bleeding
    - Major Surgery: the desired factor VIII level is 80% to 120% of normal; initial preoperative dose of 40 to 60 IU/kg followed by a repeat dose of 40 to 50 IU/kg after 8 to 24 hours and then every 24 hours to maintain FVIII activity within the target range
- Routine Prophylaxis:
    - For individualized prophylaxis, the recommended regimen is 50 IU/kg every 4 days. The dose may be adjusted based on patient response in the range of 25 to 65 IU/kg at 3 to 5 day intervals.
    - For children under 6 years of age, the recommended starting regimen is 50 IU/kg twice weekly. The dose may be adjusted on patient response with dosing in the range of 25 to 65 IU/kg at 3 to 5 day intervals. More frequent or higher doses up to 80 IU/kg may be required.

Prolonged Half-life: Eloctate™ contains the Fc region of human immunoglobulin G1 (IgG1), which binds to the neonatal Fc receptor (FcRn). FcRn is part of a naturally occurring pathway that delays lysosomal degradation of immunoglobulins by cycling them back into circulation and prolonging their plasma half-life. Eloctate™ has an extended half-life (t ½) of 12.7 to 19.7 hours which may decrease the frequency of infusions needed. Plasma derived factor VIII has an average half-life of 12 hours.

Cost Comparison:

Factor Replacement Product	Cost per Unit*	Cost for 1 Week of Prophylaxis Therapy
Eloctate™ [antihemophilic factor (recombinant), Fc fusion protein]**	**$1.899**	**$9,495**
Advate® [antihemophilic factor (recombinant)]+	$1.181	$7,086

*Average sales price (ASP) + 6%
**Eloctate™ dosing using 50 u/kg twice a week for a 50kg patient.
+Advate® dosing using 40 u/kg three times a week for a 50kg patient.

Adynovate® [Antihemophilic Factor (Recombinant), PEGylated] Summary[10,11]

FDA Approval: November 2015

Indication: Adynovate® [antihemophilic factor (recombinant), PEGylated] is a human antihemophilic factor indicated in adolescent and adult patients (12 years and older) with hemophilia A (congenital factor VIII deficiency) for:

- On-demand treatment and control of bleeding episodes
- Routine prophylaxis to reduce the frequency of bleeding episodes

Dosing: One IU of Adynovate® per kg of body weight increases the plasma factor VIII level by 2 IU per dL of plasma; therefore the recommended dose is calculated by the following equation:

- Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL)
    - Example: 50kg x 40 IU/dl (%) x 0.5 IU/kg per IU/dL = 1000 IU per dose

- Bleeding Episodes:
    - Minor: the desired factor VIII level is 20% to 40% of normal; repeat every 12 to 24 hours until bleeding is resolved
    - Moderate: the desired factor VIII level is 30% to 60% of normal; repeat every 12 to 24 hours until bleeding is resolved
    - Major: the desired factor VIII level is 60% to 100% of normal; repeat every 8 to 24 hours until bleeding is resolved
- Routine Prophylaxis:
    - 40 to 50 IU per kg of body weight twice per week

Prolonged Half-life: Adynovate® exhibits an extended terminal t½ through pegylation of the parent molecule, Advate®, which reduces binding to the physiological factor VIII clearance receptor (LRP1). Adynovate® has an extended t½ of 13.43 to 14.69 hours which may decrease the frequency of infusions needed. Plasma derived factor VIII has an average t½ of 12 hours.

Cost Comparison:

Factor Replacement Product	Cost per Unit	Cost for 1 Week of Prophylaxis Therapy
Adynovate® [antihemophilic factor (recombinant), PEGylated]ŦŦ	**$2.09***	**$10,450**
Advate® [antihemophilic factor (recombinant)]+	$1.181**	$7,086

*EAC = estimated acquisition cost.
**Average sales price (ASP) + 6%
ŦŦAdynovate® dosing using 50 u/kg twice a week for a 50kg patient.
+Advate® dosing using 40 u/kg three times a week for a 50kg patient.

Alprolix® [Coagulation Factor IX (Recombinant), Fc Fusion Protein] Summary[12,13]

FDA Approval: March 2014

Indication: Alprolix® [coagulation factor IX (recombinant), Fc fusion protein] is a recombinant DNA derived, coagulation Factor IX concentrate indicated in adults and children with hemophilia B for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

Dosing: One IU of Alprolix® per kg of body weight increases the circulating level of Factor IX by 1% [IU/dL]; therefore the recommended dose is calculated by the following equation:

- Dose (IU) = body weight (kg) x desired factor IX rise (IU/dL or, % of normal) x reciprocal of recovery (IU/kg per IU/dL)
    - Example: 70kg x 30 IU/dL (%) x 1 IU/kg per IU/dL = 2100 IU per dose
- Bleeding Episodes:
    - Minor-to-Moderate: the desired circulating factor IX level is 30% to 60%; repeat every 48 hours if there is further evidence of bleeding
    - Major: the desired factor circulating IX level is 80% to 100%; consider a repeat dose after 6 to 10 hours and then every 24 hours for the first three days and then every 48 hours or longer until bleeding resolves and healing is achieved

- Perioperative Management:
    - Minor Surgery: the desired circulating factor IX level is 50% to 80%; repeat every 24 to 48 hours until bleeding resolves and healing is achieved
    - Major Surgery: the desired circulating factor IX level is 60% to 100%; consider a repeat dose after 6 to 10 hours and then every 24 hours for the first three days and then every 48 hours or longer until bleeding resolves and healing is achieved
- Routine Prophylaxis:
    - The recommended starting regimens are either 50 IU/kg once weekly or 100 IU/kg once every ten days.

Prolonged Half-life: Alprolix® contains the Fc region of human IgG1, which binds FcRn. FcRn is part of a naturally occurring pathway that delays lysosomal degradation of immunoglobulins by cycling them back into circulation, and prolonging their plasma t½. Alprolix® has an extended t½ of 66.40 to 86.25 hours which may decrease the frequency of infusions needed. Plasma derived factor IX has a t½ of 18 to 24 hours.

Cost Comparison:

Factor Replacement Product	Cost per Unit*	Cost for 1 Week of Prophylaxis Therapy
Alprolix® [coagulation factor IX (recombinant), Fc fusion protein]Ŧ	**$2.815**	**$9,852.50**
Benefix® [coagulation factor IX (recombinant)]+	$1.448	$7,906.08

*Average Sales Price (ASP) + 6%
ŦAlprolix® dosing using 50 u/kg once a week for a 70kg patient.
+Benefix® dosing using 30 u/kg twice a week for a 70kg patient.

Idelvion® [Coagulation Factor IX (Recombinant), Albumin Fusion Protein] Summary[13,14]

FDA Approval: March 2016

Indication: Idelvion® [coagulation factor IX (recombinant), albumin fusion protein (rIX-FP)] is a recombinant human blood coagulation factor indicated in children and adults with hemophilia B (congenital Factor IX deficiency) for:

- On demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes

Dosing: One IU of Idelvion® per kg body weight is expected to increase the circulating level of factor IX by 1.3 IU/dL in patients ≥12 years of age and by 1 IU/dL in patients <12 years of age; therefore, the required units are calculated based on the following equation:

- Required Units (IU) = body weight (kg) x desired factor IX rise (% of normal or IU/dL) x [reciprocal of recovery (IU/dL per IU/kg)]
    - Example (18 year old): 70kg x 30 IU/dL (%) x 1.3 IU/dL per IU/kg = 2,730 IU per dose
- Bleeding Episodes:
    - Minor-to-Moderate: the desired circulating factor IX level is 30% to 60%; repeat every 48 to 72 hours until bleeding is resolved

- Major: the desired factor circulating IX level is 60% to 100%; repeat every 48 to 72 hours until bleeding is resolved and healing is achieved

- Perioperative Management:
  - Minor Surgery: the desired circulating factor IX level is 50% to 80%; repeat every 48 to 72 hours as needed to control bleeding
  - Major Surgery: the desired circulating factor IX level is 60% to 100%; repeat every 48 to 72 hours for the first week then administer a maintenance dose one to two times per week until bleeding is resolved and healing is achieved
- Routine Prophylaxis:
  - For patients greater than or equal to 12 years of age, the recommended dose is 25 to 40 IU Idelvion® per kg of body weight every seven days. Patients who are well-controlled on this regimen may be switched to a 14-day interval at 50 to 75 IU Idelvion® per kg of body weight.
  - For patients less than 12 years of age, the recommended dose is 40 to 55 IU per kg of body weight every seven days.

Prolonged Half-life: Idelvion® is comprised of genetically fused recombinant coagulation factor IX and recombinant albumin. Fusion with recombinant albumin extends the t½ of factor IX. Idelvion® has an extended t½ of 87 to 118 hours which may decrease the frequency of infusions needed. Plasma derived factor IX has a t½ of 18 to 24 hours.

Cost Comparison:

Factor Replacement Product	Cost per Unit	Cost for 1 Week of Prophylaxis Therapy
Idelvion® [coagulation factor IX (recombinant), albumin fusion protein]ǂ	**$4.488***	**$12,566.40**
Benefix® [coagulation factor IX (recombinant)]+	$1.448**	$7,906.08

*EAC = Estimated acquisition cost
**Average Sales Price (ASP) + 6%
ǂIdelvion® dosing using 40 u/kg once a week for a 70kg patient.
+Benefix® dosing using 30 u/kg twice a week for a 70kg patient.

Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence] Summary[15]

FDA Approval: October 2014

Indication: Obizur® [antihemophilic factor (recombinant), porcine sequence] is an antihemophilic factor indicated for the treatment of bleeding episodes in adults with acquired hemophilia A.

Dosing:

- Bleeding Episodes: The initial dose for all bleeding episodes is 200 units per kg.
  - Minor-to-Moderate: the desired factor VIII level is 50% to 100%; repeat every 4 to 12 hours until bleeding is resolved
  - Major: the desired factor VIII level is 100% to 200%; repeat every 4 to 12 hours until acute bleeding is controlled; then 50% to 100% if required for further healing
- Dosing after the initial dose should be determined based on t½ study results.

Cost Comparison:

Factor Replacement Product	Cost per Unit	Cost for 1 Day of Treatment
Obizur® [antihemophilic factor (recombinant), porcine sequence][Ŧ]	**$5.448***	**$228,816**
Feiba® (anti-inhibitor coagulant complex)[+]	$1.901**	$26,614
NovoSeven® RT [coagulation factor VIIa (recombinant)][¥]	$1.900**	$71,820

*EAC = Estimated acquisition cost

**Average Sales Price (ASP) + 6%

[Ŧ]Obizur® dosing at 200 u/kg for a 70kg patient based on median number of doses in 24 hours in a clinical study as reported in prescribing information.

[+]Feiba® dosing at 100 u/kg for a 70kg patient based on a maximum of 200 u/kg in 24 hours.

[¥]NovoSeven® dosing at 90 mcg/kg for a 70kg patient based on median number of doses in 24 hours in a clinical study as reported in prescribing information.

Corifact® [Factor XIII Concentrate (Human)] Summary[16]

FDA Approval: February 2011

Indication: Corifact® [factor XIII concentrate (human)] is indicated for adult and pediatric patients with congenital Factor XIII deficiency for:

- Routine prophylactic treatment
- Peri-operative management of surgical bleeding

Dosing: The recommended dose is 40 IU per kg of body weight every 28 days. Additional dosing peri-operatively may be given based on FXIII activity level. Half-life studies should be performed to determine appropriate dose and interval.

Cost:

Factor Replacement Product	Cost per Unit*	Cost per Dose
Corifact® [factor XIII concentrate (human)][Ŧ]	**$7.774**	**$21,767.20**

*Average Sales Price (ASP) + 6%

[Ŧ]Prescribing Information used to determine dosing information for a 70kg patient

Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)] Summary[17]

FDA Approval: December 2013

Indication: Tretten® [coagulation factor XIII A-subunit (recombinant)] is indicated for routine prophylaxis for bleeding in patients with congenital factor XIII A-subunit deficiency.

Dosing: The recommended dosing of Tretten® is 35 IU per kg of body weight monthly. Half-life studies should be performed to determine appropriate dose and interval.

Cost:

Factor Replacement Product	Cost per Unit*	Cost per Dose
Tretten® [coagulation factor XIII A-subunit (recombinant)][Ŧ]	**$14.836**	**$36,348.20**

*EAC = estimated acquisition cost

[Ŧ]Prescribing information used to determine dosing information for a 70kg patient.

Coagadex® [Coagulation Factor X (Human)] Summary[18]

FDA Approval: October 2015

Indication: Coagadex® [coagulation factor X (human)] is a plasma-derived human blood coagulation factor indicated in adults and children (aged 12 years and older) with hereditary Factor X deficiency for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding in patients with mild hereditary factor X deficiency

Dosing: One IU of Coagadex® per kg of body weight increases the plasma factor VIII level by two IU per dL of plasma; therefore the recommended dose is calculated by the following equation:

- Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL)
    - Example: 50kg x 40 IU/dl (%) x 0.5 IU/kg per IU/dL = 1000 IU per dose
- Bleeding Episodes:
    - The recommended dose is 25 IU per kg at the first sign of bleeding; repeat every 24 hours until bleeding is resolved
- Perioperative Management:
    - Pre-surgery: 70 to 90 IU/dL
    - Post-surgery: maintain factor X levels at a minimum of 50 IU/dL until the patient is no longer at risk of bleeding due to surgery

Cost:

Factor Replacement Product	Cost per Unit*	Cost per Dose
Coagadex® [coagulation factor X (human)]Ŧ	**$8.173**	**$14,302.75**

*EAC = Estimated acquisition cost

Ŧ Prescribing information used to determine dosing information for a 70kg patient.

Standards of Care for Pharmacy Providers for the Home Use of Factor Replacement Products for Patients with Bleeding Disorders[19]

The National Hemophilia Foundation developed the Medical and Scientific Advisory Council (MASAC) to establish quality of care guidelines, promote hemophilia research, and advance clinical care for the treatment of hemophilia and other bleeding disorders. The MASAC committee consists of scientists, hematologists, other treating professionals, US government agencies, and patient representatives.

The MASAC committee developed recommendations as minimum standards of care for pharmacies providing factor replacement products for use in patients' homes. These recommendations were developed to help ensure patients with bleeding disorders receive optimal service. When quality care is not provided there is a potential for adverse events leading to poor outcomes and increased cost. These standards of care for pharmacy providers were developed in collaboration with the Oklahoma Center for Bleeding and Clotting Disorders and other pharmacies providing factor replacement products.

Recommendations

The Oklahoma Health Care Authority Recommends prior authorize Eloctate™ [antihemophilic factor (recombinant), Fc fusion protein], Adynovate® [antihemophilic factor (recombinant), PEGylated], Alprolix® [coagulation factor IX (recombinant), Fc fusion protein], Idelvion® [coagulation factor IX (recombinant), albumin fusion protein], Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence], Corifact® [Factor XIII Concentrate (Human)], Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)], and Coagadex® [Coagulation Factor X (Human)] with the following criteria:

Eloctate™, Adynovate®, Alprolix®, and Idelvion® Approval Criteria:

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

Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence] Approval Criteria:

1. An FDA Approved Indication; and
2. Obizur® must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use Feiba® (anti-inhibitor coagulant complex) or NovoSeven® RT [coagulation factor VIIa (recombinant)]; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval.
5. Initial approval will be for the duration of the half-life study. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Corifact® [Factor XIII Concentrate (Human)] and Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)] Approval Criteria:

1. An FDA approved indication; and
2. Corifact® or Tretten® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval.

4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Coagadex® (Coagulation Factor X, Human) Approval Criteria:

1. An FDA approved indication; and
2. Coagadex® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval.
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Additionally, the following standards of care are recommended for pharmacies providing factor replacement products:

1. The Blood Clotting Factor Provider must be licensed as a pharmacy by the Oklahoma State Board of Pharmacy. The Pharmacist-in-Charge must be licensed as a pharmacist in Oklahoma.
2. Blood Clotting Factor provider services:
    a. The pharmacy must be able to provide a full range of factor products including all available vial sizes.
    b. The pharmacy must have 24 hours per day, 7 days per week support in the event of an after-hours emergency.
    c. Pharmacy staff must deliver within 24 hours (with a target of 4 hours) of notification of a need due to current bleeding episode. If the member is not having an emergency/current bleeding episode the pharmacy must deliver factor within 3 days of notification of need.
    d. The pharmacy must provide all necessary supplies for appropriate preparation and administration of the factor product as well as appropriate sharps and bio-hazardous disposal unit which includes retrieval and destruction of disposal unit. If the items are SoonerCare compensable, they must be billed as durable medical equipment (DME) via a DME contract.
    e. Pharmacy must provide access to multilingual interpreters for those patients and families where English is not the primary language. The interpreters must be available 24/7 in the event of an emergency.
    f. Case Management:
        i. Case Management can be performed by a pharmacist, nurse, social worker, or case manager.
        ii. An in-home patient assessment must be performed upon initiation of services and at least yearly thereafter:
            1. In-home assessments will include but not be limited to the following:
                a. Verification of appropriate and adequate storage
                b. Current inventory of factor product and supplies
                c. Verification of bio-hazardous waste disposal unit

d. Current treatment records/logs
e. Educational opportunities to be performed by appropriately trained staff (please refer to 3 b ii below)
f. Check for adverse events

2. In the event a patient refuses entry to home, the pharmacy must keep a document stating refusal signed by the patient or caregiver. A yearly attempt must be made for an in-home assessment. If refusal continues, a yearly signed document must be obtained and kept.

iii. Regular follow up with the patient either via telephone, video call, or in-person. This contact should be quarterly and should include but not be limited to the following:

1. All recent bleed episodes reported should be forwarded to the prescribing practitioner immediately.
2. Current inventory
   a. Number of factor doses on hand
   b. Expiration dates of vials on hand
3. Confirmation of factor storage
4. Adverse events
   a. If adverse events are reported to a non-clinical case manager, a clinician should become involved immediately.

iv. Coordination of care including nursing, DME, treating practitioner, and all medications, regardless of source.

3. Educational requirements:
   a. Staff Education:
      i. Staff having contact with the patient via telephone, video calling, or in-person, must be knowledgeable about hemophilia and other bleeding disorders.
      ii. Two hours of Continuing Education (CE) on hemophilia or other related bleeding disorders must be completed each year. Licensed staff must use accredited CE based on their license type. Non-licensed staff may use non-accredited CE performed by a licensed professional.
         1. Staff members, whether employed or contracted by the pharmacy, required to complete CE include but are not limited to the following:
            a. Pharmacist in Charge
            b. Nurse manager
            c. Nurse performing direct patient care
            d. Social worker
            e. Case Manager (including customer service representatives)
         2. Documentation of educational activity completed must be kept at the pharmacy and must include the CE certificate or date of activity, staff in attendance, and name and license of professional providing activity.
   b. Member and Caregiver Education:
      i. Pharmacy staff must encourage engagement with the Oklahoma Comprehensive Hemophilia Treatment Center. Studies have shown better clinical outcomes for those patients engaged with a comprehensive hemophilia treatment center.

ii. Pharmacy staff must discuss educational needs of the patient with the treating practitioner. Once educational opportunities are identified, the pharmacy staff must provide training for the patients and family members in accordance with the treating physician or mid-level practitioner. All patient efforts must be documented. Areas of education may include but are not limited to the following:
    1. Proper storage for factor products and ancillary supplies
    2. Proper disposal of bio-hazardous waste
    3. Preparation of factor and supplies
    4. Training on self-infusion
        a. Prescriber to provide order
            i. Professional licensed nurse (LPN or RN) to train patients or caregivers for peripheral venous access.
            ii. Licensed RN to train patients or caregivers on central line care (e.g. PICC line, InfusaPort, etc.) which includes but is not limited to access, flushing, infusions, and dressing changes.
        b. Training must be in accordance with the MASAC guidelines.
    5. Treatment record keeping
    6. Factor and supply management

4. Factor Product Dispensing and Delivery:
    a. Prescriptions cannot be filled without an expressed need from the patient, caregiver or prescribing practitioner. Auto-filling is not allowed.
    b. Factor products must be packaged in such a way that a patient or caregiver can easily determine what is to be used for each dose.
        i. If the factor dose to be infused only consists of one vial/box then the vial/box should be labeled as such.
        ii. If the factor dose to be infused consists of two or more vials/boxes then each dose should be packaged as a group of appropriate vials/boxes and labeled as an individual dose.
    c. Factor dose must be within 5% of the prescribed dose
        i. If unable to provide factor dosing within 5% of prescribed dose, then pharmacy must provide proof of all available vial sizes from the manufacturer at the time dispensing occurred.
        ii. Any dose requiring more than 3 vials/boxes to be used must be approved by the prescribing practitioner and documented.
        iii. Monthly, pharmacy staff must fax or email to the Oklahoma Health Care Authority a copy of the prescription, units per vial dispensed, quantity of each vial size, how the doses were packaged if more than one vial was to be used per dose, and delivery confirmation with member or caregivers signature.
    d. Any factor product which is short-dated (expiring within 6 months) may only be dispensed after approval from the prescribing practitioner and must be documented.

e. The pharmacy staff must assure appropriate storage of the factor products and supplies including cold chain supply shipping and delivery. The pharmacy must be able to trace the supply chain from manufacturer to patient delivery.
f. The pharmacy must keep records of all lots of factor products dispensed to each patient and notify patient and treating practitioner of any recalls of dispensed factor products. The pharmacy must participate in the National Patient Notification System for clotting factor recalls.
g. The pharmacy provider must have a plan in place for delivery of factor products to the patient in the event of a natural disaster.

5. Blood Clotting Factor Providers must originally attest to the Oklahoma Health Care Authority these standards of care will be followed and must re-attest yearly.
6. Oklahoma Health Care Authority (OHCA) Auditing:
    a. The OHCA has the right to audit records of the blood clotting factor providers to assure all requirements are being met. The OHCA will audit these records which include but is not limited to the following:
        i. In-home assessment records
        ii. Educational information and training provided
        iii. Adverse Event records including reports to other state and federal agencies
        iv. Sharps and bio-hazardous waste disposal units delivery proof and education on proper disposal in patient record.
        v. Patient records
            1. Original Prescriptions
            2. Dispensing records (including lot numbers and expiration dates)
    b. The pharmacy will be excluded from providing blood factor products if OHCA finds that the pharmacy is out of compliance with the requirements as outlined.

Utilization Details of Factor Replacement Products: Calendar Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Advate Products					
ADVATE INJ 1000UNIT	69	14	$1,162,350.65	$851.54	$16,845.66
ADVATE INJ 500UNIT	60	13	$871,207.00	$811.94	$14,520.12
ADVATE INJ 3000UNIT	12	3	$522,930.00	$1,815.73	$43,577.50
ADVATE INJ 1500UNIT	10	5	$337,142.60	$1,311.84	$33,714.26
ADVATE INJ 2000UNIT	8	3	$271,702.93	$1,306.26	$33,962.87
ADVATE INJ 250UNIT	4	2	$25,328.88	$291.14	$6,332.22
Subtotal	**163**	**21**	**$3,190,662.06**	**$973.36**	**$19,574.61**
Kogenate Products					
KOGENATE FS INJ 2000UNIT	48	11	$1,862,791.36	$1,760.67	$38,808.15
KOGENATE FS INJ 500UNIT	40	9	$508,646.91	$514.82	$12,716.17
KOGENATE FS INJ 1000UNIT	37	9	$766,948.96	$856.93	$20,728.35
KOGENATE FS INJ 3000UNIT	25	6	$1,459,872.23	$2,470.17	$14,939.50
KOGENATE FS INJ 250UNIT	16	3	$85,806.89	$199.09	$58,394.89
KOGENATE FS INJ 500/BS	7	4	$118,622.38	$685.68	$18,210.74
KOGENATE FS INJ 2000/BS	1	1	$45,123.07	$1,804.92	$5,362.93
Subtotal	**174**	**31**	**$4,847,811.80**	**$1,165.06**	**$27,860.99**
Feiba Products					
FEIBA INJ	29	6	$2,099,534.28	$3,528.63	$72,397.73
FEIBA NF INJ	1	1	$251,324.00	$12,566.20	$251,324.00
Subtotal	**30**	**6**	**$2,350,858.28**	**$3,822.53**	**$78,361.94**
Helixate Products					
HELIXATE FS INJ 1000UNIT	27	9	$403,366.63	$1,172.58	$14,939.50
HELIXATE FS INJ 2000UNIT	19	5	$346,004.11	$2,453.93	$18,210.74
HELIXATE FS INJ 500UNIT	9	4	$76,184.56	$1,190.38	$8,464.95
HELIXATE FS INJ 3000UNIT	5	4	$25,735.71	$2,573.57	$5,147.14
HELIXATE FS INJ 250UNIT	2	2	$5,053.87	$297.29	$2,526.94
Subtotal	**62**	**24**	**$856,344.88**	**$1,486.71**	**$13,812.01**
Wilate Products					
WILATE INJ	17	4	$670,596.42	$1,989.90	$39,446.85
WILATE INJ	1	1	$4,166.00	$416.60	$4,166.00
Subtotal	**18**	**4**	**$674,762.42**	**$1,944.56**	**$37,486.80**
Alphanate Products					
ALPHANATE INJ VWF/HUM	14	2	$36,049.26	$99.31	$2,574.95
ALPHANATE INJ VWF/HUM	12	2	$78,084.56	$278.87	$6,507.05
ALPHANATE INJ VWF/HUM	4	2	$36,849.93	$433.53	$9,212.48
ALPHANATE INJ VWF/HUM	1	1	$17,020.71	$1,702.07	$17,020.71
Subtotal	**31**	**4**	**$168,004.46**	**$227.65**	**$5,419.50**
NovoSeven Products					
NOVOSEVEN RT INJ 5MG	12	3	$801,239.81	$12,718.09	$66,769.98
NOVOSEVEN RT INJ 2MG	5	2	$76,934.95	$1,972.69	$15,386.99
NOVOSEVEN RT INJ 1MG	1	1	$12,094.91	$4,031.64	$12,094.91
Subtotal	**18**	**4**	**$890,269.67**	**$8,478.76**	**$49,459.43**
Alprolix Products					
ALPROLIX INJ 2000UNIT	11	1	$668,810.05	$2,354.96	$60,800.91
ALPROLIX INJ 1000UNIT	8	2	$50,044.69	$1,191.54	$6,255.59
ALPROLIX INJ 3000UNIT	2	1	$73,194.87	$1,219.91	$36,597.44

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
ALPROLIX INJ 500UNIT	1	1	$6,552.60	$3,276.30	$6,552.60
Subtotal	**22**	**3**	**$798,602.21**	**$2,058.25**	**$36,300.10**
Eloctate Products					
ELOCTATE INJ 500UNIT	8	2	$46,774.34	$233.87	$5,846.79
ELOCTATE INJ 1000UNIT	5	2	$118,836.19	$1,042.42	$23,767.24
ELOCTATE INJ 750UNIT	5	1	$53,060.27	$457.42	$10,612.05
ELOCTATE INJ 1500UNIT	4	1	$124,580.72	$1,112.33	$31,145.18
ELOCTATE INJ 250UNIT	3	2	$30,259.84	$432.28	$10,086.61
Subtotal	**25**	**4**	**$373,511.36**	**$610.31**	**$14,940.45**
Xyntha Products					
XYNTHA SOLOF INJ 2000UNIT	8	1	$225,703.40	$1,187.91	$28,212.93
XYNTHA SOLOF INJ 500UNIT	3	1	$2,675.04	$535.01	$891.68
XYNTHA INJ 500UNIT	1	1	$1,085.00	$542.50	$1,085.00
XYNTHA SOLOF INJ 1000UNIT	1	1	$16,731.72	$2,788.62	$16,731.72
Subtotal	**13**	**1**	**$246,195.16**	**$1,212.78**	**$18,938.09**
Monoclate Products					
MONOCLATE-P INJ 1500UNIT	7	1	$103,216.87	$1,495.90	$14,745.27
MONOCLATE-P INJ 1000UNIT	1	1	$18,935.41	$1,893.54	$18,935.41
Subtotal	**8**	**2**	**$122,152.28**	**$1,546.23**	**$15,269.04**
Humate Products					
HUMATE-P SOL 2400UNIT	5	2	$91,552.36	$2,692.72	$18,310.47
HUMATE-P SOL 500-1200	3	3	$29,663.40	$1,977.56	$9,887.80
HUMATE-P SOL 250-600	3	2	$12,660.00	$744.71	$4,220.00
Subtotal	**11**	**5**	**$133,875.76**	**$2,028.42**	**$12,170.52**
Rixubis Products					
RIXUBIS INJ 500UNIT	4	3	$8,486.96	$1,212.42	$2,121.74
RIXUBIS INJ 3000UNIT	1	1	$3,405.56	$3,405.56	$3,405.56
Subtotal	**5**	**4**	**$11,892.52**	**$1,486.57**	**$2,378.50**
Benefix Products					
BENEFIX INJ 1000UNIT	3	2	$9,281.71	$1,160.21	$3,093.90
BENEFIX INJ 2000UNIT	2	1	$9,765.41	$1,953.08	$4,882.71
BENEFIX INJ 3000UNIT	1	1	$4,186.66	$1,395.55	$4,186.66
BENEFIX INJ 500UNIT	1	1	$684.28	$228.09	$684.28
Subtotal	**7**	**5**	**$23,918.06**	**$1,258.85**	**$3,416.87**
Recombinate Products					
RECOMBINATE INJ	3	1	$114,243.93	$1,936.34	$38,081.31
RECOMBINATE INJ 801-1240	2	1	$36,114.62	$737.03	$18,057.31
RECOMBINATE INJ 401-800	2	1	$14,037.44	$250.67	$7,018.72
Subtotal	**7**	**2**	**$164,395.99**	**$1,002.41**	**$23,485.14**
Total	**594**	**83***	**$14,853,256.91**	**$1,307.62**	**$25,005.48**

*Total number of unduplicated members.

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[19] National Hemophilia Foundation. MASAC document #188. Available online at: https://www.hemophilia.org/Advocacy-Healthcare-Coverage/Payer-Education/MASAC. Last accessed 03/2016.

Appendix J

Fiscal Year 2015 Annual Review of Makena® (Hydroxyprogesterone Caproate) and 30-Day Notice to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®)

Oklahoma Health Care Authority
April 2016

Current Prior Authorization Criteria

Makena® (hydroxyprogesterone caproate) was approved by the U.S. Food and Drug Administration (FDA) in February 2011 and is currently covered through SoonerCare as a pharmacy-only benefit with the following criteria:

Makena® (Hydroxyprogesterone Caproate) Approval Criteria:

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and
3. Gestational age between 16 weeks, 0 days and 20 weeks, 6 days of gestation.
4. Authorizations will be for once a week administration by a healthcare professional through 36 weeks, 6 days of gestation.

When it is determined to be appropriate to use the compounded generic hydroxyprogesterone caproate product, this product is covered through SoonerCare as a medical-only benefit without a prior authorization requirement.

Utilization of Makena® (Hydroxyprogesterone Caproate): Fiscal Year 2015

Comparison of Fiscal Years: Makena® (Pharmacy)

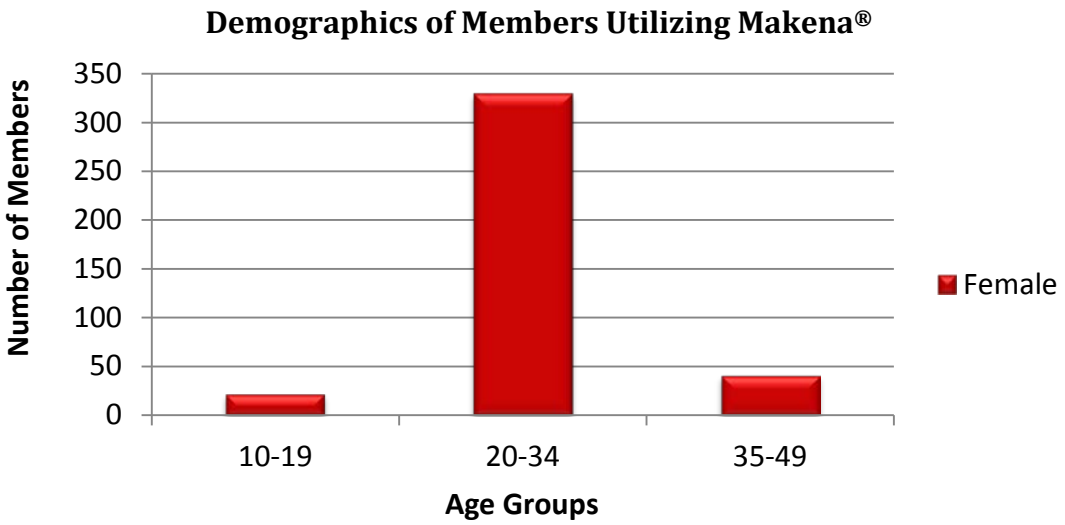
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	297	788	$2,864,118.32	$3,634.67	$120.91	3,940	23,688
2015	393	1,027	$3,714,755.36	$3,617.09	$110.14	5,135	33,729
% Change	**32.30%**	**30.30%**	**29.70%**	**-0.50%**	**-8.90%**	**30.30%**	**42.40%**
Change	**96**	**239**	**$850,637.04**	**-$17.58**	**-$10.77**	**1,195**	**10,041**

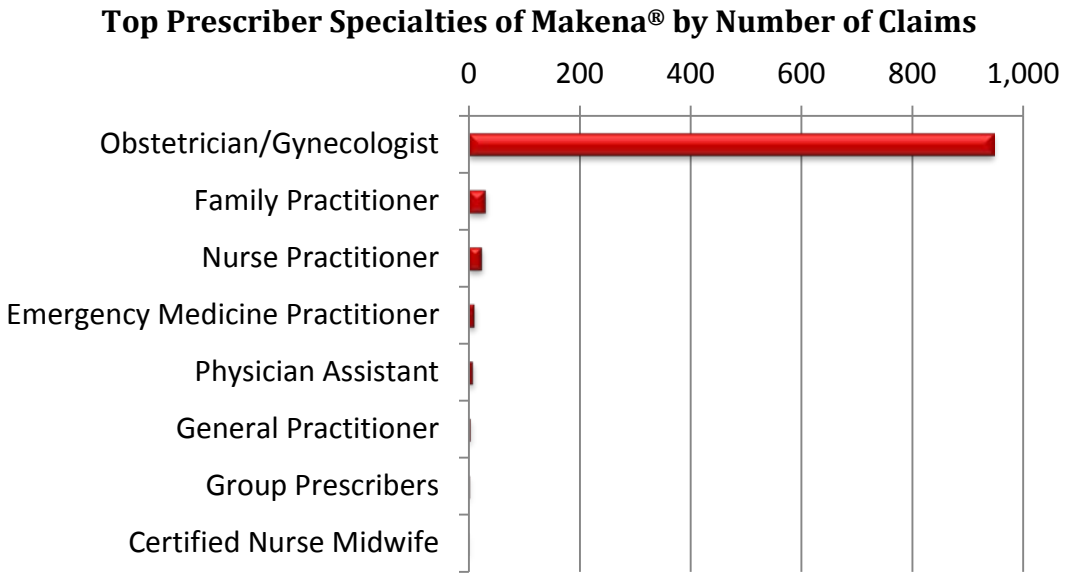
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Fiscal Years: Generic Hydroxyprogesterone Caproate (Medical)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2014	153	1,173	$13,472.50	$11.49	7.67
2015	69	374	$3,968.14	$10.61	5.42
% Change	**-54.90%**	**-68.12%**	**-70.55%**	**-7.66%**	**-29.30%**
Change	**-84**	**-799**	**-$9,504.36**	**-$0.88**	**-2.25**

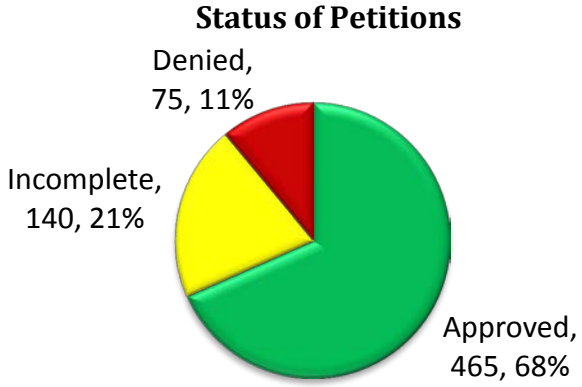
*Total number of unduplicated members.





Prior Authorization of Makena® (Hydroxyprogesterone Caproate)

There were 680 prior authorization requests submitted for Makena® during fiscal year 2015. The following chart shows the status of the submitted petitions.



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

Anticipated Exclusivity Expiration:

- Makena® (hydroxyprogesterone caproate): February 2018

New FDA Approval(s):

- **February 2016:** The FDA approved a single-dose, preservative-free formulation of Makena® (hydroxyprogesterone caproate). Makena® was previously available only in a multi-dose vial, which contains five weekly injections. The new single-dose formulation provides the convenience of a single-use vial for once-weekly dosing, without the need for storage or the possibility of waste of a multi-dose vial. The new single-dose formulation is also preservative-free, for patients and healthcare providers who prefer this option.

Compounded Generic Hydroxyprogesterone Caproate:

- The FDA released a statement in June 2012 regarding the compounding of hydroxyprogesterone caproate when a commercially available product (Makena®) is accessible. The FDA emphasized that the compounding of any drug should not exceed the scope of traditional pharmacy compounding, and the FDA generally prioritizes enforcement actions related to compounded drugs using a risk-based approach, giving the highest priority to pharmacies that compound products that are causing harm or that amount to health fraud.
- The Oklahoma State Board of Pharmacy has ruled that "*compounding a drug preparation that is commercially available in the marketplace or that is essentially a copy of an available FDA-approved drug product is generally prohibited unless patient therapy is compromised*" (Oklahoma Pharmacy Law Book, 2015, section 535:15-10-53).
- There have not been any updates from the FDA regarding compounding of generic hydroxyprogesterone caproate since the 2012 statement and the compounding of generic hydroxyprogesterone caproate has not been specifically addressed by the

Oklahoma State Board of Pharmacy; however, SoonerCare pharmacy compounding of the generic product has continually decreased over the past few years.

Preterm Birth[5,6]

Preterm birth, or birth at less than 37 completed weeks of gestation, is the leading cause of neonatal mortality in the United States. Spontaneous preterm birth includes birth that follows preterm labor, preterm spontaneous rupture of membranes, and cervical insufficiency, but does not include indicated preterm delivery for maternal or fetal conditions. Infants born prematurely have increased risks of mortality and morbidity throughout childhood, especially during the first year of life, and often are admitted to the neonatal intensive care unit (NICU) shortly following birth. The associated emotional and economic costs to families and the economic burden to hospitals and payers are overwhelming.

The American College of Obstetricians and Gynecologists (ACOG) published an updated practice bulletin in 2012 on the prediction and prevention of preterm birth. The ACOG practice bulletin addresses risk factors and screening modalities, and then provides clinical considerations and recommendations regarding the prediction and prevention of preterm birth. The Oklahoma Perinatal Quality Improvement Collaborative (OPQIC) is engaged in the Oklahoma Preterm Birth Initiative, which includes working with perinatal care providers and birthing hospitals to ensure that all hospitals practice a standardized evaluation of women who present with signs and symptoms of preterm labor. The OPQIC Oklahoma Preterm Birth Initiative is also working to increase the number of women at risk for preterm birth who receive progesterone.

Expansion of Makena® (Hydroxyprogesterone Caproate) Start Window[7]

Makena® (hydroxyprogesterone caproate) is FDA approved to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. One of the strongest clinical risk factors for preterm birth is a prior preterm birth. Maternal history of preterm birth is commonly reported to confer a 1.5-fold to 2-fold increased risk in a subsequent pregnancy. Also, the number of prior preterm births and the gestational age at the prior delivery significantly affect the recurrence risk of preterm birth.

Makena® is indicated to begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation, and continue once weekly administration until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first. The indicated start window for Makena® (between 16 weeks, 0 days and 20 weeks, 6 days of gestation) is based on the clinical trials that were completed for FDA approval. The majority of SoonerCare Makena® prior authorization request denials in fiscal year 2015 were due to the start date being outside of the approved start window (greater than 20 weeks, 6 days of gestation). Revising the existing SoonerCare criteria for Makena® (hydroxyprogesterone caproate injection) to expand the start window to a gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation could result in a significant annual savings (*see estimated cost savings section*) and reduce the risk of preterm births among pregnant SoonerCare women.

Management Guidelines for Short Cervix[8,9]

Short cervical length as measured by transvaginal ultrasonography has been associated with an increased risk of preterm birth. Short cervical length is most commonly defined as less than 25mm, usually before 24 weeks of gestation, but up to 28 weeks of gestation in some series. Clinically, the shorter the cervical length, the greater the risk of preterm birth. Cerclage and progesterone are the two interventions that have been evaluated in randomized trials for effectiveness in preventing preterm birth in women with singleton gestations without a prior preterm birth. Vaginal progesterone is recommended by the ACOG practice bulletin as a management option to reduce the risk of preterm birth in asymptomatic women with a short cervix identified with transvaginal ultrasonography (cervical length of 20mm or less before or at 24 weeks of gestation), singleton gestation, and no prior spontaneous preterm birth.

Crinone® is available as a 4% (45mg) and 8% (90mg) progesterone vaginal gel in single-use, prefilled applicators, and the recommended dosing is 90mg daily to reduce the risk of preterm birth in women with a short cervix. Endometrin® is available as 100mg progesterone vaginal inserts, and the recommended dosing is 200mg daily to reduce the risk of preterm birth in women with a short cervix. After taking into account federal and supplemental rebate participation, the net cost of the management of short cervix using Endometrin® is significantly less costly than using Crinone®.

Estimated Cost Savings

Based on fiscal year 2015 data, the Oklahoma Health Care Authority (OHCA) Finance Department has estimated the combined total annual savings in NICU costs of extending the start window for Makena® to 26 weeks, 6 days of gestation and of covering Endometrin® for pregnant women with a short cervix to be approximately $1 million. This estimated cost savings does not take into account federal or supplemental rebate participation, which could contribute to even more savings.

Recommendations

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Makena® (hydroxyprogesterone caproate injection) to expand the start window to a gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation
2. The prior authorization of Crinone® (progesterone vaginal gel) with the criteria noted in red
3. The prior authorization of Endometrin® (progesterone vaginal insert) with the criteria noted in red

New proposed criteria specific to each medication is as follows:

Makena® (Hydroxyprogesterone Caproate) Approval Criteria:

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and

3. Gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation.
4. Authorizations will be for once a week administration by a healthcare professional through 36 weeks, 6 days of gestation.

Crinone® (Progesterone Vaginal Gel) Approval Criteria:

1. Current singleton pregnancy; and
2. Member must not have history of previous singleton spontaneous preterm delivery (SPTD); and
3. Cervical length of ≤ 20mm; and
4. Gestational age between 20 weeks, 0 days and 26 weeks, 6 days of gestation; and
5. A patient-specific, clinically significant reason why the member cannot use Endometrin® (progesterone vaginal insert).
6. Authorizations will be given for treatment through 36 weeks, 6 days of gestation.
7. Crinone® will not be covered for use with assisted reproductive technology (ART) for female infertility.

Endometrin® (Progesterone Vaginal Insert) Approval Criteria:

1. Current singleton pregnancy; and
2. Member must not have history of previous singleton spontaneous preterm delivery (SPTD); and
3. Cervical length of ≤ 20mm; and
4. Gestational age between 20 weeks, 0 days and 26 weeks, 6 days of gestation.
5. Authorizations will be given for treatment through 36 weeks, 6 days of gestation.
6. Endometrin® will not be covered for use with assisted reproductive technology (ART) for female infertility.

Utilization Details of Hydroxyprogesterone and Vaginal Progesterone: Fiscal Year 2015

Utilization Details of Makena® (Hydroxyprogesterone Caproate): Pharmacy

Medication Name	Claims	Members*	Cost	Cost/ Claim	Claims/ Member
Makena®	1,027	393	$3,714,755.36	$3,617.09	2.61

Utilization Details of Generic Hydroxyprogesterone Caproate: Medical

Medication Name	Claims	Members*	Cost	Cost/ Claim	Claims/ Member
hydroxyprogesterone caproate	374	69	$3,968.14	$10.61	5.42

Utilization Details of Crinone® (Progesterone Vaginal Gel): Pharmacy

Medication Name	Claims	Members*	Cost	Cost/ Claim	Claims/ Member
Crinone® 8%	14	6	$4,498.68	$321.33	2.33
Crinone® 4%	3	1	$219.69	$73.23	3.00
Total	**17**	**7**	**$4,718.37**	**$277.55**	**2.43**

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 03/10/2016. Last accessed 03/11/2016.
[2] AMAG Pharmaceuticals Press Release: AMAG Pharmaceuticals Announces FDA Approval of New Single-Dose, Preservative-Free Makena® (hydroxyprogesterone caproate injection). Available online at: http://ir.amagpharma.com/phoenix.zhtml?c=61596&p=irol-newsArticle&id=2142283. Issued 02/23/2016. Last accessed 03/17/2016.
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[4] Oklahoma State Board of Pharmacy: 2015 Oklahoma Pharmacy Law Book. Available online at: http://ok.gov/pharmacy/documents/2015%20LAW%20BOOK.pdf. Last revised 11/01/2015. Last accessed 03/30/2016.
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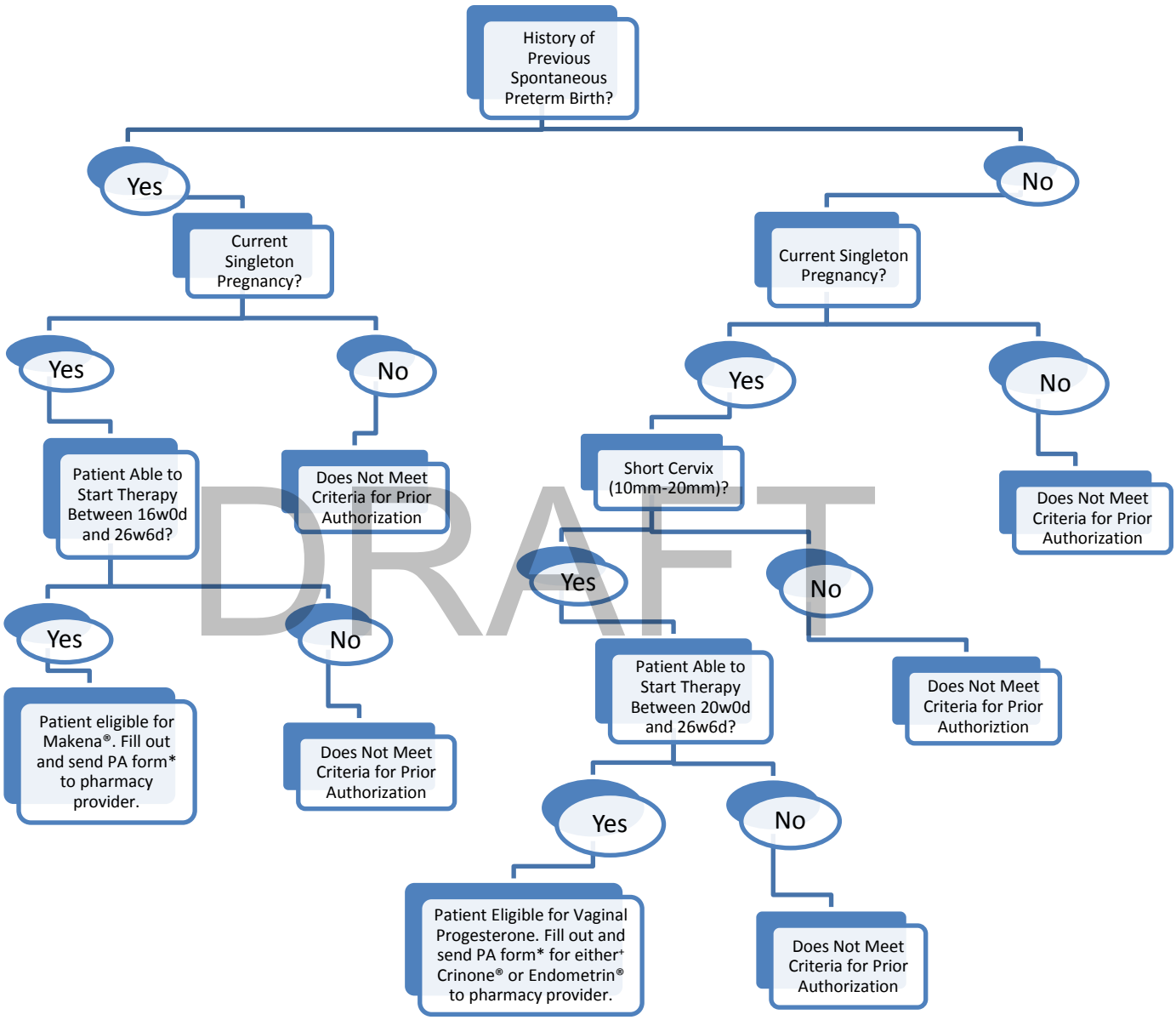
SoonerCare Coverage of Makena®, Crinone®, and Endometrin® for the Prevention of Spontaneous Preterm Birth



*Makena® PA form (**PHARM-23**) and Endometrin®/Crinone® PA form (**PHARM-04**) for SoonerCare can be found at www.okhca.org/forms.

+Endometrin® is the SoonerCare preferred vaginal progesterone product, authorization of Crinone® requires a patient-specific, clinically significant reason the member cannot use Endometrin®.

This information may be subject to change and is accurate as of 9/16/2015.

SoonerCare
Oklahoma Health Care Authority

SoonerCare Coverage of Progesterone Products for the Prevention of Spontaneous Preterm Birth (SPTB)

Product	SoonerCare Coverage	PA required	Prior Authorization requirements*# and Comments
Makena®	Pharmacy Benefit	Y	**1**. Documented history of previous singleton SPTB prior to 37 weeks gestation **2**. Current singleton pregnancy **3**. Gestational age at start of therapy between 16w0d and 26w6d **4.** Weekly injections via healthcare professional through 36w6d **5.** Use PA form specific for Makena (PHARM-23)
Compounded 17 alpha-hydroxprogesterone caproate	Medical Benefit (S5000)	N	In June 2012 the FDA issued a statement on compounded versions of hydroxyprogesterone caproate.[Ŧ] Also, the Oklahoma State Board of Pharmacy rules prohibit compounding medications that are essentially a copy of an available FDA approved product.
Progesterone oral	Pharmacy Benefit	N	
Progesterone vaginal gel (Crinone® only)	Pharmacy Benefit	Y	**1.** No history of previous singleton SPTB **2.** Current singleton pregnancy **3.** Gestational age at start of therapy between 20w0d and 26w6d **4.** Short Cervix (10mm-20mm) **5.** Reason why member cannot use Endometrin® **6.** Daily dosing through week 36w6d **7.** Use universal PA form (PHARM-04)
Progesterone vaginal insert (Endometrin® only)	Pharmacy Benefit	Y	**1.** No history of previous singleton SPTB **2.** Current singleton pregnancy **3.** Gestational age at start of therapy between 20w0d and 26w6d 4. Short Cervix (10mm-20mm) **5.** Daily dosing through week 36w6d **6.** Use universal PA form (PHARM-04)
Compounded Progesterone	Pharmacy Benefit	N	The Oklahoma State Board of Pharmacy rules prohibit compounding medications that are essentially a copy of an available FDA approved product.

* PA criteria can be found in the Endocrine Therapeutic Category at www.okhca.org/pa

PA forms can be found at www.okhca.org/forms

Ŧ The FDA statement can be found at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308546.htm

This information is subject to change and is accurate as of 9/16/2015

SoonerCare
Oklahoma Health Care Authority

Appendix K

Calendar Year 2015 Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Humalog® KwikPen® U-200 (Insulin Lispro), Tresiba® (Insulin Degludec), Ryzodeg® 70/30 (Insulin Degludec/Insulin Aspart), Basaglar® (Insulin Glargine), and Synjardy® (Empagliflozin/Metformin)

Oklahoma Health Care Authority
April 2016

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 can be approved based on current American Association of Clinical Endocrinologists (AACE) or American Diabetes Association (ADA) guidelines.

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 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.

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Biguanides metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®) **Sulfonylureas** chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide Micronized (Micronase®) tolbutamide **Alpha-Glucosidase Inhibitors** acarbose (Precose®) **Glinides** repaglinide (Prandin®) **Thiazolidinedione** pioglitazone (Actos®)	**DPP-4 Inhibitors** linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto™) 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 (Bydureon®) liraglutide (Victoza®)	**DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) **Thiazolidinediones** pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®) **Alpha-Glucosidase Inhibitors** miglitol (Glyset®) **SGLT 2 Inhibitor** canagliflozin (Invokana™) canagliflozin/metformin (Invokamet™) dapagliflozin (Farxiga™) dapagliflozin/metformin (Xigduo™ XR) empagliflozin (Jardiance®) **Dopamine Agonist** bromocriptine (Cycloset®) **SGLT-2/DPP-4 Inhibitor** empagliflozin/linagliptin (Glyxambi®) **GLP-1 Agonists** albiglutide (Tanzeum™) dulaglutide (Trulicity™)	**Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®) **Amylinomimetic** pramlintide (Symlin®)

*Tier structure based on supplemental rebate participation and state maximum allowable cost (SMAC).
DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT2 = sodium-glucose cotransporter-2

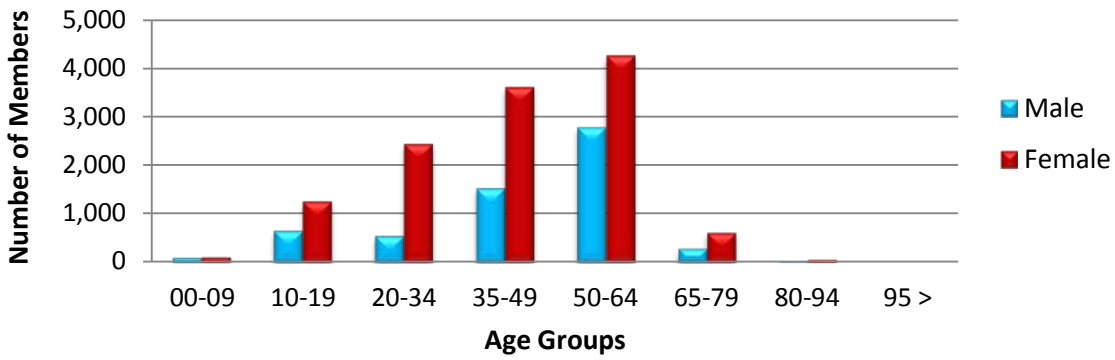
Utilization of Diabetes Medications: Calendar Year 2015

Comparison of Calendar Years

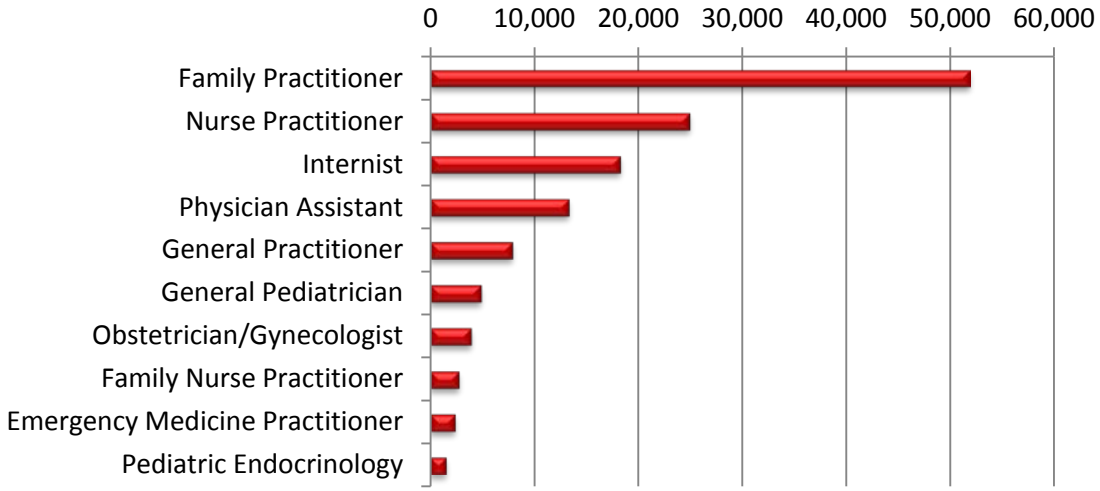
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	18,465	145,812	$31,915,632.75	$218.88	$6.51	6,177,139	4,898,919
2015	18,328	140,098	$37,873,266.95	$270.33	$7.94	5,870,233	4,772,164
% Change	**-0.70%**	**-3.90%**	**18.70%**	**23.50%**	**22.00%**	**-5.00%**	**-2.60%**
Change	**-137**	**-5,714**	**$5,957,634.20**	**$51.45**	**$1.43**	**-306,906**	**-126,755**

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

Demographics of Members Utilizing Diabetes Medications



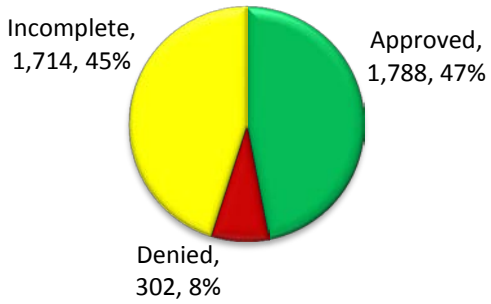
Top Prescriber Specialties of Diabetes Medications by Number of Claims



Prior Authorization of Diabetes Medications

There were 3,804 prior authorization requests submitted for diabetes medications during calendar year 2015. Of the 3,804 total prior authorizations submitted, 2,461 petitions were for oral diabetic medications and 1,343 were submitted for insulin requests. Computer edits are in place to detect Tier-1 medications in members' recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expirations:

- Byetta® (exenatide): January 2020
- Victoza® (liraglutide): August 2025
- Januvia® (sitagliptin): November 2026
- Toujeo® (insulin glargine): March 2028
- Invokana™ (canagliflozin): February 2029
- Invokamet™ (canagliflozin/metformin): February 2029
- Jardiance® (empagliflozin): October 2029
- Farxiga™ (dapagliflozin): May 2030
- Xigduo™ XR (dapagliflozin/metformin extended-release): May 2030
- Glyxambi® (empagliflozin/linagliptin): June 2030
- Tradjenta® (linagliptin): March 2031
- Cycloset® (bromocriptine): April 2032
- Afrezza® (insulin human inhalation powder): July 2032

New FDA Approvals:

- Humalog® KwikPen® U-200 (insulin lispro 200 units/mL): May 2015
- Synjardy® (empagliflozin/metformin): August 2015
- Tresiba® (insulin degludec): September 2015
- Ryzodeg® 70/30 (insulin degludec/insulin aspart): September 2015
- Basaglar® (insulin glargine): December 2015

Pipeline:

- Semaglutide is a glucagon-like peptide-1 (GLP-1) analogue by Novo Nordisk, the makers of Victoza®. Semaglutide is in Phase 3 trials for an injectable formulation and currently recruiting for a Phase 3 oral formulation as of February 2016.
- Lixisenatide (known as Lyxumia® in Europe) is a once-daily, prandial GLP-1 receptor agonist for the treatment of adults with Type-2 Diabetes Mellitus (T2DM). Sanofi filed for review of lixisenatide by the U.S. Food and Drug Administration (FDA) in September 2015 and a ruling by the FDA is expected late May of 2016.
- Lixisenatide/insulin glargine (LixiLan™) is a once-daily, single injection combination product of a GLP-1 receptor agonist and long-acting basal insulin currently in Phase 3 of development. The FDA accepted the New Drug Application from Sanofi in February 2016 and the FDA's decision is expected by August 2016.

New Clinical Data:

- **August 2015:** Jardiance® (empagliflozin) reduced the risk of cardiovascular (CV) events in adults with T2DM who are at high risk for such events, making it the only glucose-lowering agent to demonstrate this benefit in a dedicated trial. The EMPA-REG OUTCOME® trial met its primary endpoint (defined as time to first occurrence of either CV death, or non-fatal myocardial infarction (MI), or non-fatal stroke) and demonstrated superiority of Jardiance® when added to standard of care, in CV risk reduction.
- **December 2015:** An FDA safety review of the FDA Adverse Event Reporting System (FAERS) database from March 2013 to May 2015 identified 73 cases of ketoacidosis in Type-1 Diabetes Mellitus (T1DM) and T2DM patients treated with sodium-glucose cotransporter-2 (SGLT-2) inhibitors. The FDA also identified 19 cases of life-threating blood infections and kidney infections that started as urinary tract infections with SGLT-2 inhibitors. As a result, the FDA has added new Warnings and Precautions to SGLT-2 drug labels regarding risks of ketoacidosis and serious urinary tract infections. The FDA is also requiring manufactures of SGLT-2 inhibitors to conduct a post-marketing study.
- **December 2015:** The FDA is eliminating the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone-containing T2DM medications which include: Avandia®, Avandamet®, Avandaryl®, and generics. The FDA determined that data did not demonstrate an increased risk of heart attack with rosiglitazone medications compared to the standard T2DM medications, metformin and a sulfonylurea.
- **February 2016:** *The New England Journal of Medicine* published a study that found in patients without diabetes who had insulin resistance along with a recent history of ischemic stroke or transient ischemic attack (TIA), the risk of stroke or MI was lower among patients receiving pioglitazone versus placebo.
- **March 2016:** Liraglutide (Victoza®) was shown to significantly reduce the risk of major adverse CV events in the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results - a Long Term Evaluation (LEADER®) trial. The LEADER® trial investigated the CV safety of Victoza® over a period of up to five years in more than 9,000 adults with T2DM at high risk of major adverse CV events. The trial compared the addition of Victoza® or placebo to standard of care and met the primary endpoint showing non-inferiority as well as demonstrating superiority, with a statistically

significant reduction in CV risk. The detailed results are planned to be presented in June 2016 at the 76th Scientific Session of the American Diabetes Association.

Humalog® KwikPen® U-200 (Insulin Lispro 200 units/mL) Product Summary[15,16]

Indications: Humalog® (insulin lispro) is a rapid-acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.

Dosing:

- Humalog® (insulin lispro) is available as 100 units/mL (U-100) and 200 units/mL (U-200).
  - Humalog® U-100 is available as: 10mL vial, 3mL vial, 3mL Humalog® KwikPen® (prefilled), and 3mL cartridge
  - Humalog® U-200 is available as: 3mL Humalog® KwikPen® (prefilled)
- The dosage of Humalog® (insulin lispro) should be individualized and adjusted based on route of administration, the individual's metabolic needs, blood glucose monitoring results, and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function, or during acute illness.
- Dose conversions should not be performed when using either the Humalog® U-100 or U-200 KwikPens®. The dose window shows the number of insulin units to be delivered and no conversion is needed.
- Humalog® U-200 should not be transferred from the KwikPen® to a syringe for administration.
- Humalog® U-200 should not be mixed with any other insulins.
- Humalog® U-200 should not be administered using a continuous subcutaneous infusion pump (i.e., insulin pump).
- Humalog® U-200 should not be administered intravenously.
- The dose of Humalog® U-100 or Humalog® U-200 should be administered within fifteen minutes before a meal or immediately after a meal by injection into the subcutaneous tissue of the abdominal wall, thigh, upper arm, or buttocks. To reduce the risk of lipodystrophy, the injection site should be rotated within the same region from one injection to the next.
- Humalog® administered by subcutaneous injection should generally be used in regimens with intermediate-acting or long-acting insulin.

Mechanism of Action:

- Regulation of glucose metabolism is the primary activity of insulins and insulin analogs, including insulin lispro. Insulins lower blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulins inhibit lipolysis and proteolysis, and enhance protein synthesis.

Contraindications:

- Use during episodes of hypoglycemia or in patients who are hypersensitive to Humalog® or to any of its excipients.

Safety:

- Sharing Devices: Humalog® KwikPen® cartridges, reusable pens, or syringes should never be shared between patients, even if the needle is changed.
- Hyper- or Hypoglycemia with Changes in Insulin Regimen: Changes in insulin regimen should be carried out under close medical supervision and increased frequency of blood glucose monitoring should be implemented.
- Hypoglycemia: Hypoglycemia may be life-threatening. Blood glucose should be monitored and monitoring frequency should be increased with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity, in patients with renal or hepatic impairment, and in patients with hypoglycemia unawareness.
- Hypoglycemia Due to Medication Errors: Accidental mix-ups between insulin products can occur. Patients should be instructed to check insulin labels before injection. Patients should not transfer Humalog® U-200 from the Humalog® KwikPen® to a syringe as overdosage and severe hypoglycemia can result.
- Hypersensitivity Reactions: Hypersensitivity reactions may be life-threatening. Humalog® should be discontinued and the patient should be monitored and treated if indicated.
- Hypokalemia: Hypokalemia may be life-threatening. Potassium levels should be monitored in patients at risk of hypokalemia and treated if indicated.
- Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Patients should be observed for signs and symptoms of heart failure; dosage reduction or discontinuation should be considered if heart failure occurs.
- Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction: Patients should monitor glucose and administer Humalog® U-100 by subcutaneous injection if pump malfunction occurs.

Adverse Reactions: Adverse reactions associated with Humalog® include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, and rash.

Efficacy: The safety and efficacy of Humalog® U-200 KwikPen® was based on demonstration of the bioequivalence of Humalog® 200 units/mL relative to Humalog® 100 units/mL in a pharmacokinetic/pharmacodynamics study.

Cost Comparison:

Drug (Rapid-Acting Insulins)	Package Size	Cost per mL**	Cost per Month+
Humalog® U-200 KwikPen® (insulin lispro)	**3mL syringe**	**$64.44**	**$257.76**
Humalog® U-100 KwikPen® (insulin lispro)	3mL syringe	$32.11	$256.88
Humalog® U-100 (insulin lispro)	3mL vial	$25.03	$200.24
Novolog® U-100 FlexPen® (insulin aspart)	3mL syringe	$32.18	$257.44
Apidra® Solostar® U-100 (insulin glulisine)	3mL syringe	$32.13	$257.04

Costs listed are based on estimated acquisition cost (EAC) unless otherwise noted.
+Monthly cost based on 1 unit/kg/day in an 80kg patient.
**Costs do not reflect rebated prices or net costs.

Tresiba® (Insulin Degludec) Product Summary[17,18]

Indications:

- Tresiba® (insulin degludec) is a long-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus.
- Limitation of use: Tresiba® is not recommended for treating diabetic ketoacidosis.

Dosing:

- Tresiba® is available in the following package sizes:
  - 100 units/mL (U-100): 3mL FlexTouch®
  - 200 units/mL (U-200): 3mL FlexTouch®
- The dose should be individualized based on type of diabetes, metabolic needs, blood glucose monitoring results, and glycemic control goal.
- Injection sites should be rotated to reduce the risk of lipodystrophy.
- Tresiba® should not be diluted or mixed with any other insulin or solution.
- Tresiba® can be administered subcutaneously once daily at any time of day.
- Dose conversion should not be performed when using the Tresiba® U-100 or U-200 FlexTouch® pens. The Tresiba® U-100 and U-200 FlexTouch® pens dose window shows the number of insulin units to be delivered and no conversion is needed.
- In-use Tresiba® FlexTouch® pen should not be refrigerated. The in-use Tresiba® FlexTouch® pen may be used for up to 56 days (8 weeks) after being opened, if it is kept at room temperature.

Mechanism of Action: The primary activity of insulin, including Tresiba®, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin also inhibits lipolysis and proteolysis, and enhances protein synthesis. Tresiba® forms multi-hexamers when injected into the subcutaneous tissue resulting in a subcutaneous insulin degludec depot. The protracted time action profile of Tresiba® is predominantly due to delayed absorption of insulin degludec from the subcutaneous tissue to the systemic circulation and to a lesser extent due to binding of insulin degludec to circulating albumin.

Contraindications:

- Tresiba® should not be used during episodes of hypoglycemia or in patients with hypersensitivity to Tresiba® or one of its excipients.

Safety:

- Sharing Devices: Tresiba® FlexTouch® pen should never be shared between patients, even if the needle is changed.
- Hyper- or Hypoglycemia with Changes in Insulin Regimen: Changes in insulin regimen should be carried out under close medical supervision with an increase in the frequency of blood glucose monitoring.
- Hypoglycemia: Hypoglycemia may be life-threatening. Monitoring should be increased with changes to: insulin dosage, co-administered glucose lowering medications, meal

pattern, physical activity, in patients with renal impairment or hepatic impairment, or in patients with hypoglycemia unawareness.

- Hypoglycemia Due to Medication Errors: Accidental mix-ups between insulin products can occur. Patients should be instructed to check insulin labels before injection. Tresiba® should not be transferred into a syringe for administration as over dosage and severe hypoglycemia can result.
- Hypersensitivity Reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Tresiba® should be discontinued and the patient should be monitored and treated if indicated.
- Hypokalemia: Hypokalemia may be life-threatening. Potassium levels should be monitored in patients at risk for hypokalemia and treated if indicated.
- Fluid Retention and Heart Failure with Concomitant use of Thiazolidinediones (TZDs): Patients should be observed for signs and symptoms of heart failure; consideration should be given to dosage reductions or discontinuation if heart failure occurs.

Adverse Reactions: Adverse reactions commonly associated with Tresiba® are hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain.

Efficacy: The efficacy and safety of Tresiba® was evaluated in nine randomized, active-controlled trials in patients with type-1 and type-2 DM. In type-2 DM, Tresiba® was evaluated in combination with mealtime insulin or as add-on to background oral antidiabetic drugs.

- In type-1 and type-2 DM, Tresiba® provided reductions in HbA1c in line with reductions achieved with other, previously approved long-acting insulin. At week 26 in a type-1 DM study, the difference in HbA1c reduction from baseline between Tresiba® and insulin detemir was -0.09% with a 95% CI of [-0.23%; 0.05%]. At week 52 in a type-2 DM study, the difference in HbA1c reduction from baseline between Tresiba® and insulin glargine U-100 was 0.09% with a 95% CI of [-0.04%; 0.22%].
- Patients treated with Tresiba® achieved levels of glycemic control similar to those achieved with Lantus® (insulin glargine 100 U/mL) and Levemir® (insulin detemir) and achieved statistically significant improvements compared to sitagliptin (-0.43%, 95% CI [-0.61;-0.24]).

Cost Comparison:

Drug (Long-Acting Insulins)	Package Size	Cost per mL**	Cost per Month+
Tresiba® (insulin degludec) U-100 FlexTouch®	**3mL syringe**	**$31.25**	**$250.00**
Tresiba® (insulin degludec) U-200 FlexTouch®	**3mL syringe**	**$62.49**	**$249.96**
Lantus® (insulin glargine) Solostar® U-100	3mL syringe	$26.24	$209.92
Levemir® (insulin detemir) FlexTouch® U-100	3mL syringe	$28.41	$227.28
Toujeo® (insulin glargine) Solostar® U-300	1.5mL syringe	$78.73	$472.38

Costs listed are based on estimated acquisition cost (EAC) unless otherwise noted.
+Monthly cost based on 1 unit/kg/day in an 80kg patient.
**Costs do not reflect rebated prices or net costs.

Ryzodeg® 70/30 (Insulin Degludec/Insulin Aspart) Product Summary[19,20]

Indications:

- Ryzodeg® 70/30 mix (insulin degludec/insulin aspart) is an insulin analog indicated to improve glycemic control in adults with diabetes mellitus.
- Limitation of use: Ryzodeg® is not recommended for treating diabetic ketoacidosis.

Dosing:

- Ryzodeg® 70/30 is available in a 3mL FlexTouch® as 100 units/mL (U-100).
- Ryzodeg® 70/30 should not be diluted or mixed with any other insulin products or solutions.
- Injection sites should be rotated to reduce the risk of lipodystrophy.
- The dose should be individualized based on type of diabetes, metabolic needs, blood glucose monitoring results, and glycemic control goal.
- Ryzodeg® 70/30 is administered subcutaneously once or twice daily with any main meal(s).
- A rapid- or short-acting insulin should be administered at other meals if needed.
- Patients with type-1 diabetes will generally require a rapid- or short-acting insulin at meals when Ryzodeg® 70/30 is not administered.
- The dose should be adjusted according to fasting blood glucose measurements.
- The recommended time between dose increases is three to four days.
- Converting from other insulin therapies may require adjustment of timing and dose of Ryzodeg® 70/30.
- In-use Ryzodeg® 70/30 Flextouch® pen should not be refrigerated. The in-use Ryzodeg® 70/30 Flextouch® pen may be used for up to 28 days (4 weeks) after being opened, if it is kept at room temperature.

Mechanism of Action: The primary activity of insulin, including Ryzodeg®, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin also inhibits lipolysis and proteolysis, and enhances protein synthesis. The insulin degludec component in Ryzodeg® 70/30 forms multi-hexamers when injected into the subcutaneous tissue resulting in a subcutaneous insulin degludec depot. The protracted time action profile of Ryzodeg® is predominantly due to delayed absorption of insulin degludec from the subcutaneous tissue to the systemic circulation and to a lesser extent due to binding of insulin-degludec to circulating albumin. Insulin aspart monomers are released rapidly into circulation.

Contraindications:

- Ryzodeg® 70/30 should not be used during episodes of hypoglycemia or in patients with hypersensitivity to Ryzodeg® or one of its excipients.

Safety:

- Sharing Devices: Ryzodeg® 70/30 FlexTouch® pen should not be shared between patients, even if the needle is changed.

- Hyper- or Hypoglycemia with Changes in Insulin Regimen: Changes in insulin regimen should be carried out under close medical supervision with an increase in the frequency of blood glucose monitoring.
- Hypoglycemia: Hypoglycemia may be life-threatening. Monitoring should be increased with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity, in patients with renal impairment or hepatic impairment, or in patients with hypoglycemia unawareness.
- Hypoglycemia Due to Medication Errors: Accidental mix-ups between insulin products can occur. Patients should be instructed to check insulin labels before injection. Ryzodeg® should not be transferred into a syringe for administration as overdosage and severe hypoglycemia can result.
- Hypersensitivity Reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Ryzodeg® should be discontinued, and patients should be monitored and treated if indicated.
- Hypokalemia: Hypokalemia may be life-threatening. Potassium levels in patients at risk for hypokalemia should be monitored and treated if indicated.
- Fluid retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Patients should be observed for signs and symptoms of heart failure; consideration should be given to dosage reductions or discontinuation if heart failure occurs.

Adverse Reactions: Adverse reactions commonly associated with Ryzodeg® are hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain.

Efficacy: The efficacy and safety of Ryzodeg® 70/30 was evaluated in five randomized, active-controlled trials in patients with type-1 and type-2 DM.

- In participants with type-1 and 2 diabetes who had inadequate blood sugar control at trial entry, treatment with Ryzodeg® 70/30 provided reductions in HbA1c equivalent to reductions achieved with other, previously approved long-acting or pre-mixed insulin. In the T1DM study, the difference in HbA1c reduction from baseline at week 26 between Ryzodeg® 70/30 and insulin detemir was -0.05% (95% CI [-0.18, 0.08%]).

Cost and Launch information: Ryzodeg® cost information is not currently available but is expected to be launched approximately one year after Tresiba®, in the respective markets.

Basaglar® (Insulin Glargine) Product Summary[21,22,23,24]

Indications:

- Basaglar® (insulin glargine) is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type-1 diabetes mellitus and in adults with type-2 diabetes mellitus.
- Limitation of use: Basaglar® is not recommended for treating diabetic ketoacidosis.

Dosing:

- Basaglar® is available as 100 units/mL (U-100) in a 3mL prefilled Basaglar® KwikPen® delivery device.

- The dosage should be individualized based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, and prior insulin use.
- Basaglar® is administered subcutaneously once daily at any time of day, but at the same time every day.
- Injection sites should be rotated to reduce the risk of lipodystrophy.
- Glucose should be closely monitored when converting to Basaglar® and during initial weeks thereafter.
- Basaglar® should not be diluted or mixed with any other insulin or solution.

Mechanism of Action: The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analog lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis and enhances protein synthesis.

Contraindications:

- Basaglar® should not be used during episodes of hypoglycemia or in patients who with hypersensitivity to Basaglar® or one of its excipients.

Safety:

- Sharing Devices: Basaglar® KwikPen® should not be shared between patients, even if the needle is changed.
- Hyper- or Hypoglycemia with Changes in Insulin Regimen: Changes in the insulin regimen should be carried out under close medical supervision.
- Hypoglycemia: Hypoglycemia may be life-threatening. Frequency of glucose monitoring should be increased with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity, in patients with renal or hepatic impairment, or in patients with hypoglycemia unawareness.
- Medication Errors: Accidental mix-ups between insulin products can occur. Patients should be instructed to check insulin labels before injection.
- Hypersensitivity Reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Basaglar® should be discontinued, and the patient should be monitored and treated if indicated.
- Hypokalemia: Hypokalemia may be life-threatening. Potassium levels should be monitored in patients at risk of hypokalemia and treated if indicated.
- Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Patients should be observed for signs and symptoms of heart failure; consideration should be given to dosage reductions or discontinuation if heart failure occurs.

Adverse Reactions: Adverse reactions commonly associated with insulin glargine products in clinical trials (5% or greater incidence) were hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain.

Efficacy: Basaglar® was approved based on the safety and effectiveness of Lantus® and on two trials comparing Basaglar® to a comparator insulin glargine product in T1DM and T2DM

patients. The data demonstrated that Basaglar® was sufficiently similar to Lantus® to scientifically justify reliance and to establish the safety and efficacy of Basaglar® for its approved uses.

Cost and Launch information: Basaglar® is expected to be launched in the United States starting on December 15, 2016. Basaglar® cost information is not available but is anticipated to be less expensive than Lantus® (insulin glargine). Basaglar® is approved as a biosimilar to Lantus® in the European Union. Due to Lantus® being FDA approved through the New Drug Application pathway, Basaglar® had to be filed through the 505(b)(2) regulatory pathway versus the 351(k) biosimilar pathway and is not considered to be a biosimilar in the United States.

Synjardy® (Empagliflozin/Metformin) Product Summary[25]

Indications:

- Synjardy® (empagliflozin/metformin) is a combination of empagliflozin, a sodium-glucose co-transporter-2 (SGLT2) inhibitor, and metformin, a biguanide, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes mellitus who are not adequately controlled on a regimen containing empagliflozin or metformin, or in patients already being treated with both empagliflozin and metformin.
- Limitation of use: Empagliflozin/metformin is not for the treatment of type-1 diabetes mellitus or diabetic ketoacidosis.

Dosing:

- Synjardy® (empagliflozin/metformin) is available as an oral tablet in four strengths: 5mg/500mg, 5mg/1000mg, 12.5mg/500mg, and 12.5mg/1000mg.
- The starting dose of Synjardy® should be individualized based on the patient's current regimen.
- The maximum recommended dose is 12.5mg empagliflozin/1000mg metformin twice daily.
- Synjardy® should be taken by mouth twice daily with meals, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin.
- Renal function should be assessed before initiating Synjardy®. Synjardy® should not be initiated or continued if creatinine levels are greater than or equal to 1.5 mg/dL for males or 1.4 mg/dL for females, or if eGFR is below 45 mL/min/1.73 m^2.

Mechanism of Action:

- Synjardy® combines two antihyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type-2 diabetes: empagliflozin, a sodium-glucose co-transporter-2 (SGLT2) inhibitor, and metformin, a member of the biguanide class.
- Empagliflozin: Sodium-glucose co-transporter-2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Empagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

- Metformin Hydrochloride: Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type-2 diabetes mellitus, lowering both basal and postprandial plasma glucose. It is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike sulfonylureas (SUs), metformin does not produce hypoglycemia in either patients with type-2 diabetes mellitus or normal subjects (except in special circumstances) and does not cause hyperinsulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

Contraindications:

- Patients with renal Impairment, end-stage renal disease (ESRD), or who are on dialysis
- Patients with metabolic acidosis, including diabetic ketoacidosis
- Patients with a history of serious hypersensitivity reaction to empagliflozin or metformin

Safety:

- Lactic acidosis: Patients should be warned against excessive alcohol use. Synjardy® is not recommended in hepatic impairment or hypoxic states and is contraindicated in renal impairment. Normal renal function should be assured before initiating and at least annually thereafter.
- Hypotension: Before initiating Synjardy® in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics volume status should be assessed and corrected. Patients should be monitored for signs and symptoms during therapy.
- Ketoacidosis: Patients who present with signs and symptoms of metabolic acidosis or ketoacidosis should be assessed, regardless of blood glucose level. If suspected, Synjardy® should be discontinued, and the patient should be evaluated and treated promptly. Before initiating Synjardy®, prescribers should consider risk factors for ketoacidosis. Patients on Synjardy® may require monitoring and temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis.
- Impairment in Renal Function: Renal function should be monitored during therapy.
- Radiological Studies and Surgical Procedures: Synjardy® should be temporarily discontinued in patients undergoing radiologic studies with intravascular administration of iodinated contrast materials or any surgical procedures necessitating restricted intake of food and fluids.
- Urosepsis and Pyelonephritis: Patients should be evaluated for signs and symptoms of urinary tract infections and treated promptly, if indicated.
- Hypoglycemia: Consideration should be given to lowering the dose of insulin secretagogues or insulin to reduce the risk of hypoglycemia when initiating Synjardy®.
- Genital Mycotic Infections: Patients should be monitored and treated as appropriate.
- Vitamin B12 Deficiency: Metformin may lower vitamin B12 levels. Hematologic parameters should be monitored annually.
- Increased LDL-C: Patients should be monitored and treated as appropriate.

- Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Synjardy®.

Adverse Reactions:

- The most common adverse reactions associated with empagliflozin (5% or greater incidence) during clinical trials were urinary tract infection and female genital mycotic infections.
- The most common adverse reactions associated with metformin (>5%) during clinical trials were diarrhea, nausea/vomiting, flatulence, abdominal discomfort, indigestion, asthenia, and headache.

Efficacy: Synjardy® approval was based on results from multiple clinical trials examining the co-administration of empagliflozin and metformin, with or without a sulfonylurea, versus placebo in patients with type-2 diabetes mellitus.

- There have been no clinical efficacy studies conducted with Synjardy®; however, bioequivalence of Synjardy® to empagliflozin and metformin coadministered as individual tablets was demonstrated in healthy subjects.
- In patients with type-2 diabetes, treatment with empagliflozin and metformin produced clinically and statistically significant improvements in HbA1c (-0.7, -0.8 vs -0.1; p-value <0.0001) compared to placebo. Reductions in hemoglobin A1c (HbA1c) were observed across subgroups including age, gender, race, and baseline body mass index (BMI).

Cost Comparison:

Drug	Strength	Cost per Tablet	Cost per Month**
Synjardy® (empagliflozin/metformin)	**All strengths**	**$6.39**	**$383.40**
metformin HCL tablet	1,000mg	$0.05*	$3.00
Jardiance® (empagliflozin)	10mg, 25mg	$12.79	$383.70
Invokamet® (canagliflozin/metformin)	All strengths	$6.39	$383.40

Costs listed are based on estimated acquisition cost (EAC) unless otherwise noted.
*SMAC = state maximum allowable cost
** Costs do not reflect rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Humalog® Kwikpen® U-200 (insulin lispro 200 units/mL), Tresiba® (insulin degludec), Ryzodeg® (insulin degludec/insulin aspart), and Basaglar® (insulin glargine) with the following criteria:

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

1. A patient-specific, clinically significant reason the member cannot use the 100 unit/mL strength is required for authorization of the 200 unit/mL strength.

Tresiba® (Insulin Degludec Injection) Approval Criteria:

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

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

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

Basaglar® (Insulin Glargine) Approval Criteria:

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

Additionally, the College of Pharmacy recommends the placement of Synjardy® (empagliflozin/metformin) into Tier-3 of the diabetes medications Product Based Prior Authorization (PBPA) category. The existing Tier-3 criteria for this category will apply.

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Biguanides metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®) **Sulfonylureas** chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide Micronized (Micronase®) tolbutamide **Alpha-Glucosidase Inhibitors** acarbose (Precose®) **Glinides** repaglinide (Prandin®) **Thiazolidinedione** pioglitazone (Actos®)	**DPP-4 Inhibitors** linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto™) 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 (Bydureon®) liraglutide (Victoza®)	**DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) **Thiazolidinediones** pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®) **Alpha-Glucosidase Inhibitors** miglitol (Glyset®) **SGLT 2 Inhibitor** canagliflozin (Invokana™) canagliflozin/metformin (Invokamet™) dapagliflozin (Farxiga™) dapagliflozin/metformin (Xigduo™ XR) empagliflozin (Jardiance®) **empagliflozin/metformin (Synjardy®)** **Dopamine Agonist** bromocriptine (Cycloset®) **SGLT-2/DPP-4 Inhibitor** empagliflozin/linagliptin (Glyxambi®) **GLP-1 Agonists** albiglutide (Tanzeum™) dulaglutide (Trulicity™)	**Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®) **Amylinomimetic** pramlintide (Symlin®)

*Tier structure based on supplemental rebate participation and state maximum allowable cost (SMAC).
DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT2 = sodium-glucose cotransporter-2

Utilization Details of Diabetic Medications: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 PRODUCTS						
METFORMIN PRODUCTS						
METFORMIN TAB 500MG	21,100	5,934	$93,400.21	$0.14	$4.43	1.45%
METFORMIN TAB 1000MG	16,521	4,078	$61,372.22	$0.12	$3.71	0.95%
METFORMIN TAB 500MG ER	4,219	1,365	$23,896.41	$0.17	$5.66	0.37%
METFORMIN TAB 850MG	1,630	398	$6,712.43	$0.13	$4.12	0.10%
METFORMIN TAB 750MG ER	431	144	$3,518.11	$0.21	$8.16	0.05%
METFORMIN ER TAB 1000MG	9	3	$3,482.92	$8.93	$386.99	0.05%
GLUCOPHAGE TAB 500MG	4	4	$28.53	$0.24	$7.13	0.00%
SUBTOTAL	**43,914**	**11,926**	**$192,410.83**	**$1.42**	**$60.03**	**2.97%**
GLIMEPIRIDE PRODUCTS						
GLIMEPIRIDE TAB 4MG	1,621	381	$12,322.50	$0.20	$7.60	0.19%
GLIMEPIRIDE TAB 2MG	993	282	$6,018.23	$0.15	$6.06	0.09%
GLIMEPIRIDE TAB 1MG	354	115	$1,691.94	$0.11	$4.78	0.03%
SUBTOTAL	**2,968**	**778**	**$20,032.67**	**$0.15**	**$6.15**	**0.31%**
GLIPIZIDE PRODUCTS						
GLIPIZIDE TAB 5MG	2,835	793	$10,398.29	$0.10	$3.67	0.16%
GLIPIZIDE TAB 10MG	2,622	674	$10,470.05	$0.11	$3.99	0.16%
GLIPIZIDE ER TAB 10MG	1,093	312	$20,069.97	$0.50	$18.36	0.31%
GLIPIZIDE ER TAB 5MG	921	259	$10,214.37	$0.30	$11.09	0.16%
GLIPIZIDE XL TAB 10MG	583	170	$10,809.73	$0.53	$18.54	0.17%
GLIPIZIDE ER TAB 2.5MG	265	87	$3,154.28	$0.29	$11.90	0.05%
GLIPIZIDE XL TAB 5MG	255	68	$3,060.99	$0.33	$12.00	0.05%
GLIPIZIDE XL TAB 2.5MG	187	49	$2,432.56	$0.36	$13.01	0.04%
GLUCOTROL TAB 5MG	2	2	$13.05	$0.22	$6.53	0.00%
GLUCOTROL TAB 10MG	1	1	$5.86	$0.20	$5.86	0.00%
SUBTOTAL	**8,764**	**2415**	**$70,629.15**	**$0.29**	**$10.50**	**1.10%**
GLYBURIDE PRODUCTS						
GLYBURIDE TAB 5MG	4,115	1,050	$52,602.73	$0.38	$12.78	0.81%
GLYBURIDE TAB 2.5MG	1,101	502	$8,926.09	$0.24	$8.11	0.14%
GLYBURIDE TAB 1.25MG	116	57	$870.71	$0.22	$7.51	0.01%
GLYBURID MCR TAB 3MG	65	15	$295.70	$0.12	$4.55	0.00%
GLYBURID MCR TAB 6MG	36	13	$203.27	$0.16	$5.65	0.00%
GLYBURID MCR TAB 1.5MG	7	4	$41.30	$0.20	$5.90	0.00%
SUBTOTAL	**5,440**	**1,641**	**$62,939.80**	**$0.22**	**$7.42**	**0.96%**
GLIPIZIDE/METFORMIN PRODUCTS						
GLIP/METFORM TAB 5-500MG	152	33	$6,409.39	$1.29	$42.17	0.10%
GLIP/METFORM TAB 2.5-500M	93	26	$3,791.57	$1.17	$40.77	0.06%
GLIP/METFORM TAB 2.5-250M	18	6	$595.13	$1.10	$33.06	0.01%
SUBTOTAL	**263**	**65**	**$10,796.09**	**$1.19**	**$38.67**	**0.17%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
GLYBURIDE/METFORMIN PRODUCTS						
GLYB/METFORM TAB 5-500MG	631	120	$6,789.28	$0.34	$10.76	0.11%
GLYB/METFORM TAB 2.5-500	234	43	$2,191.45	$0.30	$9.37	0.03%
GLYB/METFORM TAB 1.25-250	18	4	$140.59	$0.26	$7.81	0.00%
SUBTOTAL	**883**	**167**	**$9,121.32**	**$0.30**	**$9.31**	**0.14%**
ACARBOSE PRODUCTS						
ACARBOSE TAB 50MG	59	10	$1,787.02	$1.01	$30.29	0.03%
ACARBOSE TAB 25MG	56	15	$1,531.56	$0.91	$27.35	0.02%
ACARBOSE TAB 100MG	2	2	$96.88	$1.47	$48.44	0.00%
PRECOSE TAB 50MG	2	1	$29.29	$0.49	$14.65	0.00%
SUBTOTAL	**119**	**28**	**$3,444.75**	**$0.97**	**$30.18**	**0.05%**
REPAGLINIDE PRODUCTS						
REPAGLINIDE TAB 1MG	26	7	$1,493.41	$1.86	$57.44	0.02%
REPAGLINIDE TAB 2MG	23	7	$1,364.71	$1.91	$59.34	0.02%
REPAGLINIDE TAB 0.5MG	18	7	$672.75	$1.13	$37.38	0.01%
SUBTOTAL	**67**	**21**	**$3,530.87**	**$1.63**	**$51.39**	**0.05%**
PIOGLITAZONE PRODUCTS						
PIOGLITAZONE TAB 30MG	882	232	$10,809.87	$0.31	$12.26	0.17%
PIOGLITAZONE TAB 15MG	585	161	$6,185.93	$0.25	$10.57	0.10%
PIOGLITAZONE TAB 45MG	445	120	$6,785.43	$0.34	$15.25	0.11%
ACTOS TAB 30MG	2	1	$22.16	$0.37	$11.08	0.00%
SUBTOTAL	**1,914**	**514**	**$23,803.39**	**$0.32**	**$12.29**	**0.38%**
TIER-1 SUBTOTAL	**64,332**	**17,555**	**$396,708.87**	**$0.72**	**$25.10**	**6.13%**
TIER-2 PRODUCTS						
SAXAGLIPTIN PRODUCTS						
ONGLYZA TAB 5MG	1,222	279	$465,618.09	$11.58	$381.03	7.21%
ONGLYZA TAB 2.5MG	188	48	$70,490.95	$11.25	$374.95	1.09%
SUBTOTAL	**1,410**	**327**	**$536,109.04**	**$11.42**	**$377.99**	**8.30%**
SITAGLIPTIN PRODUCTS						
JANUVIA TAB 100MG	3,350	731	$1,601,143.58	$11.69	$477.95	24.78%
JANUVIA TAB 50MG	920	205	$418,844.93	$13.22	$455.27	6.48%
JANUVIA TAB 25MG	205	44	$88,329.93	$12.26	$430.88	1.37%
SUBTOTAL	**4,475**	**980**	**$2,108,318.44**	**$12.39**	**$454.70**	**32.63%**
SAXAGLIPTIN/METFORMIN PRODUCTS						
KOMBIGLYZE TAB 2.5-1000	124	37	$40,080.05	$10.40	$323.23	0.62%
KOMBIGLYZE TAB 5-1000MG	71	22	$31,923.92	$11.20	$449.63	0.49%
KOMBIGLYZE TAB 5-500MG	35	6	$9,970.82	$11.47	$284.88	0.15%
SUBTOTAL	**230**	**65**	**$81,974.79**	**$11.02**	**$352.58**	**1.26%**
SITAGLIPTIN/METFORMIN PRODUCTS						
JANUMET TAB 50-1000	1,303	231	$451,910.22	$11.20	$346.82	6.99%
JANUMET TAB 50-500MG	282	67	$105,468.16	$11.12	$374.00	1.63%
JANUMET XR TAB 100-1000	236	39	$82,982.06	$11.72	$351.62	1.28%
JANUMET XR TAB 50-1000	229	49	$71,707.55	$10.54	$313.13	1.11%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
JANUMET XR TAB 50-500MG	8	2	$1,374.40	$5.73	$171.80	0.02%
SUBTOTAL	**2,058**	**388**	**$713,442.39**	**$10.06**	**$311.47**	**11.03%**
LINAGLIPTIN PRODUCTS						
TRADJENTA TAB 5MG	939	147	$323,964.03	$11.55	$345.01	5.01%
SUBTOTAL	**939**	**147**	**$323,964.03**	**$11.55**	**$345.01**	**5.01%**
LINAGLIPTIN/METFORMIN PRODUCTS						
JENTADUETO TAB 2.5-1000	191	48	$76,005.44	$11.62	$397.93	1.18%
JENTADUETO TAB 2.5-500	60	14	$20,277.52	$11.41	$337.96	0.31%
JENTADUETO TAB 2.5-850	7	1	$1,921.96	$9.15	$274.57	0.03%
SUBTOTAL	**258**	**63**	**$98,204.92**	**$10.73**	**$336.82**	**1.52%**
EXENATIDE PRODUCTS						
BYDUREON INJ	255	63	$128,733.80	$17.72	$504.84	1.99%
BYDUREON INJ	237	68	$123,374.70	$18.21	$520.57	1.91%
BYETTA INJ 5MCG	65	24	$33,100.06	$16.47	$509.23	0.51%
BYETTA INJ 10MCG	56	16	$35,012.99	$17.16	$625.23	0.54%
SUBTOTAL	**613**	**171**	**$320,221.55**	**$17.39**	**$539.97**	**4.95%**
LIRAGLUTIDE PRODUCTS						
VICTOZA INJ 18MG/3ML	2,398	523	$1,395,470.43	$18.71	$581.93	21.59%
SUBTOTAL	**2,398**	**523**	**$1,395,470.43**	**$18.71**	**$581.93**	**21.59%**
NATEGLINIDE PRODUCTS						
NATEGLINIDE TAB 120MG	53	16	$3,866.82	$2.37	$72.96	0.06%
NATEGLINIDE TAB 60MG	38	8	$2,952.43	$2.71	$77.70	0.05%
SUBTOTAL	**91**	**24**	**$6,819.25**	**$2.54**	**$75.33**	**0.11%**
TIER-2 SUBTOTAL	**12,472**	**2,688**	**$5,584,524.84**	**$11.76**	**$375.09**	**86.40%**
TIER-3 PRODUCTS						
ALOGLIPTIN PRODUCTS						
NESINA TAB 25MG	59	11	$25,403.97	$11.29	$430.58	0.39%
NESINA TAB 6.25MG	1	1	$329.15	$10.97	$329.15	0.01%
SUBTOTAL	**60**	**12**	**$25,733.12**	**$11.13**	**$379.87**	**0.40%**
ALOGLIPTIN/PIOGLITAZONE PRODUCTS						
OSENI TAB 25-15MG	14	2	$4,815.82	$11.47	$343.99	0.07%
OSENI TAB 25-30MG	12	3	$8,761.05	$11.23	$730.09	0.14%
SUBTOTAL	**26**	**5**	**$13,576.87**	**$11.35**	**$537.04**	**0.21%**
ALOGLIPTIN/METFORMIN PRODUCTS						
KAZANO 12.5- TAB 1000MG	16	2	$5,379.20	$11.21	$336.20	0.08%
SUBTOTAL	**16**	**2**	**$5,379.20**	**$11.21**	**$336.20**	**0.08%**
EMPAGLIFLOZIN/LINAGLIPTIN PRODUCTS						
GLYXAMBI TAB 25-5 MG	10	3	$3,037.38	$10.12	$303.74	0.05%
GLYXAMBI TAB 10-5 MG	7	4	$3,673.73	$17.49	$524.82	0.06%
SUBTOTAL	**17**	**7**	**$6,711.11**	**$13.81**	**$414.28**	**0.11%**
EMPAGLIFLOZIN PRODUCTS						
JARDIANCE TAB 25MG	72	22	$26,412.55	$12.23	$366.84	0.41%
JARDIANCE TAB 10MG	40	12	$14,461.10	$12.05	$361.53	0.22%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SUBTOTAL	**112**	**34**	**$40,873.65**	**$12.14**	**$364.19**	**0.63%**
ALBIGLUTIDE PRODUCTS						
TANZEUM INJ 30MG	22	9	$8,703.05	$13.43	$395.59	0.13%
TANZEUM INJ 50MG	13	3	$5,290.63	$14.22	$406.97	0.08%
SUBTOTAL	**35**	**12**	**$13,993.68**	**$13.83**	**$401.28**	**0.21%**
DULAGLUTIDE PRODUCTS						
TRULICITY INJ 1.5/0.5	22	7	$12,348.38	$19.73	$561.29	0.19%
TRULICITY INJ 0.75/0.5	18	7	$9,960.46	$19.15	$553.36	0.15%
SUBTOTAL	**40**	**14**	**$22,308.84**	**$19.44**	**$557.33**	**0.34%**
PIOGLITAZONE/METFORMIN PRODUCTS						
PIOGLITA/MET TAB 15-500MG	50	7	$7,251.97	$4.65	$145.04	0.11%
PIOGLITA/MET TAB 15-850MG	48	6	$6,604.55	$3.71	$137.59	0.10%
SUBTOTAL	**98**	**13**	**$13,856.52**	**$4.18**	**$141.32**	**0.21%**
CANAGLIFLOZIN PRODUCTS						
INVOKANA TAB 300MG	445	85	$156,861.74	$12.09	$352.50	2.43%
INVOKANA TAB 100MG	246	67	$89,432.02	$12.14	$363.54	1.38%
SUBTOTAL	**691**	**152**	**$246,293.76**	**$12.12**	**$358.02**	**3.81%**
CANAGLIFLOZIN/METFORMIN PRODUCTS						
INVOKAMET TAB 150-1000	17	2	$6,206.00	$12.17	$365.06	0.10%
INVOKAMET TAB 50-1000	13	4	$4,711.28	$12.08	$362.41	0.07%
INVOKAMET TAB 50-500MG	3	1	$1,137.30	$12.64	$379.10	0.02%
INVOKAMET TAB 150-500	2	1	$774.20	$12.90	$387.10	0.01%
SUBTOTAL	**35**	**8**	**$12,828.78**	**$12.45**	**$373.42**	**0.20%**
DAPAGLIFLOZIN PRODUCTS						
FARXIGA TAB 10MG	111	19	$34,464.02	$12.21	$310.49	0.53%
FARXIGA TAB 5MG	100	23	$34,269.98	$11.42	$342.70	0.53%
SUBTOTAL	**211**	**42**	**$68,734.00**	**$11.82**	**$326.60**	**1.06%**
DAPAGLIFLOZIN/METFORMIN PRODUCTS						
XIGDUO XR TAB 5-1000MG	5	1	$820.45	$6.31	$164.09	0.01%
XIGDUO XR TAB 5-500MG	2	1	$752.96	$12.55	$376.48	0.01%
XIGDUO XR TAB 10-1000	1	1	$379.11	$12.64	$379.11	0.01%
SUBTOTAL	**8**	**3**	**$1,952.52**	**$10.50**	**$306.56**	**0.03%**
TIER-3 SUBTOTAL	**1,349**	**304**	**$472,242.05**	**$12.00**	**$374.68**	**7.29%**
SPECIAL PRIOR AUTHORIZATION PRODUCTS						
PRAMLINTIDE PRODUCTS						
SYMLNPEN 120 INJ 1000MCG	5	1	$7,593.79	$50.63	$1,518.76	0.12%
SUBTOTAL	**5**	**1**	**$7,593.79**	**$50.63**	**$1,518.76**	**0.12%**
METFORMIN PRODUCTS						
RIOMET SOL	3	1	$1,193.97	$12.98	$397.99	0.02%
SUBTOTAL	**3**	**1**	**$1,193.97**	**$12.98**	**$397.99**	**0.02%**
SPECIAL PA SUBTOTAL	**8**	**2**	**$8,787.76**	**$31.81**	**$958.38**	**0.14%**
TOTAL	**78,161**	**13,796***	**$6,462,263.52**	**$2.46**	**$228.06**	**100%**

* 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.

Utilization Details of Insulin Medications: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ CLIENT	COST/ CLAIM
NO PRIOR AUTHORIZATION REQUIRED PRODUCTS						
RAPID-ACTING INSULIN LISPRO PRODUCTS						
HUMALOG KWIK INJ 100/ML	3,904	1,074	$2,304,237.48	0.58	3.64	$590.22
HUMALOG INJ 100/ML	3,260	767	$1,506,946.86	0.71	4.25	$462.25
HUMALOG INJ 100/ML	296	71	$131,416.27	0.52	4.17	$443.97
HUMALOG KWIK INJ 200/ML	2	2	$3,097.11	1.26	1	$1,548.56
SUBTOTAL	**7,462**	**1,914**	**$3,945,697.72**	**0.7675**	**3.265**	**$761.25**
RAPID-ACTING INSULIN ASPART PRODUCTS						
NOVOLOG INJ FLEXPEN	8,336	2,185	$4,978,089.48	0.59	3.82	$597.18
NOVOLOG INJ 100/ML	5,429	1,192	$2,299,991.25	0.71	4.55	$423.65
NOVOLOG INJ PENFILL	355	94	$157,957.34	0.46	3.78	$444.95
SUBTOTAL	**14,120**	**3,471**	**$7,436,038.07**	**0.586667**	**4.05**	**$488.59**
RAPID-ACTING INSULIN GLULISINE PRODUCTS						
APIDRA INJ SOLOSTAR	495	151	$273,979.11	0.53	3.28	$553.49
APIDRA INJ U-100	371	88	$131,413.17	0.61	4.22	$354.21
SUBTOTAL	**866**	**239**	**$405,392.28**	**0.57**	**3.75**	**$453.85**
SHORT-ACTING REGULAR INSULIN (R) PRODUCTS						
HUMULIN R INJ U-100	1,352	366	$234,086.55	0.53	3.69	$173.14
NOVOLIN R INJ U-100	1,061	284	$173,101.77	0.54	3.74	$163.15
HUMULIN INJ 70/30	751	150	$229,150.32	0.79	5.01	$305.13
NOVOLIN R INJ RELION	358	121	$16,400.28	0.51	2.96	$45.81
HUMULIN R INJ U-500	314	60	$460,779.52	0.72	5.23	$1,467.45
HUMULIN INJ 70/30KWP	207	53	$132,108.85	0.74	3.91	$638.21
SUBTOTAL	**4,043**	**1034**	**$1,245,627.29**	**0.638333**	**4.09**	**$465.48**
INTERMEDIATE-ACTING INSULIN NPH (N) PRODUCTS						
NOVOLIN N INJ U-100	568	157	$131,414.16	0.59	3.62	$231.36
HUMULIN N INJ U-100	560	172	$133,378.27	0.56	3.26	$238.18
NOVOLIN N INJ RELION	362	106	$16,969.13	0.59	3.42	$46.88
HUMULIN N INJ U-100KWP	303	136	$141,341.58	0.49	2.23	$466.47
HUMULIN N PN INJ U-100	9	5	$2,770.35	0.43	1.8	$307.82
SUBTOTAL	**1802**	**576**	**$425,873.49**	**0.532**	**2.866**	**$258.14**
PRE-MIXED INSULIN REGULAR AND INSULIN NPH PRODUCTS						
NOVOLIN INJ 70/30	553	142	$180,268.23	0.82	3.89	$325.98
NOVOLIN 70/30 INJ RELION	326	85	$17,050.16	0.73	3.84	$52.30
HUMULIN PEN INJ 70/30	4	4	$1,810.04	0.82	1	$452.51
SUBTOTAL	**883**	**231**	**$199,128.43**	**0.79**	**2.91**	**$276.93**
PRE-MIXED INSULIN ASPART PROTAMINE (INTERMEDIATE) AND INSULIN ASPART (RAPID) PRODUCTS						
NOVOLOG MIX INJ FLEXPEN	1,109	266	$858,511.19	0.78	4.17	$774.13
NOVOLOG MIX INJ 70/30	359	93	$202,995.59	0.76	3.86	$565.45
SUBTOTAL	**1,468**	**359**	**$1,061,506.78**	**0.77**	**4.015**	**$669.79**
PRE-MIXED INSULIN LISPRO PROTAMINE (INTERMEDIATE) AND INSULIN LISPRO (RAPID) PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ CLIENT	COST/ CLAIM
HUMALOG MIX INJ 75/25KWP	344	77	$240,534.88	0.79	4.47	$699.23
HUMALOG MIX SUS 75/25	159	35	$96,097.55	0.73	4.54	$604.39
HUMALOG MIX INJ 50/50KWP	48	15	$39,082.53	0.84	3.2	$814.22
HUMALOG MIX INJ 50/50	39	6	$30,651.66	1.06	6.5	$785.94
SUBTOTAL	**590**	**133**	**$406,366.62**	**0.855**	**4.6775**	**$725.95**
LONG-ACTING PRODUCTS						
LANTUS INJ SOLOSTAR	10,926	2,870	$5,749,467.09	0.49	3.81	$526.22
LANTUS INJ 100/ML	8,441	1,782	$4,021,498.98	0.59	4.74	$476.42
LEVEMIR INJ FLEXTOUC	7,361	1,895	$4,251,731.39	0.54	3.88	$577.60
LEVEMIR INJ	3,788	893	$2,165,589.10	0.69	4.24	$571.70
LEVEMIR INJ FLEXPEN	67	50	$34,072.18	0.62	1.34	$508.54
SUBTOTAL	**30,583**	**7,490**	**$16,222,358.74**	**0.586**	**3.602**	**$532.10**
SUBTOTAL	**61,817**	**15,447**	**$31,347,989.42**	**0.677278**	**3.691722**	**$514.68**
PRIOR AUTHORIZATION REQUIRED PRODUCTS						
INHALED INSULIN PRODUCTS						
AFREZZA POW 4UNIT	3	1	$703.29	3	3	$234.43
SUBTOTAL	**3**	**1**	**$703.29**	**3**	**3**	**$234.43**
LONG-ACTING PRODUCTS						
TOUJEO SOLO INJ 300IU/ML	117	44	$62,310.72	0.22	2.66	$532.57
SUBTOTAL	**117**	**44**	**$62,310.72**	**0.22**	**2.66**	**$532.57**
SUBTOTAL	**120**	**45**	**$63,014.01**	**1.61**	**2.83**	**$383.50**
TOTAL	**61,937**	**8,286***	**$31,411,003.43**	**0.59**	**7.47**	**$500.10**

*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 L

Fiscal Year 2015 Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Entresto™ (Sacubitril/Valsartan)

Oklahoma Health Care Authority
April 2016

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. Calcium Channel Blockers (CCBs)
2. Angiotensin I Converting Enzyme Inhibitors (ACEIs)
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 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 medications; 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 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 ACEI (or an 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 in either monotherapy or combination therapy.

The following restrictions also apply for each individual product based on FDA approval information, special formulations, or individualized Drug Utilization Review Board criteria:

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

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

Epaned™ (Enalapril Powder for 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 swallow the oral tablet formulation even when crushed.

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

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

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.

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, etc; and
3. Prescriber must verify member does not have any of the following contraindications:
    a. Coronary insufficiency
    b. Recent myocardial infarction
    c. Rising or elevated BUN, or known renal insufficiency
    d. Uremia
    e. Glaucoma
    f. Organic pyloric stenosis
    g. Currently receiving sulfonamides or antibiotics
    h. Known sensitivity to Vecamyl™ (mecamylamine)

Hemangeol™ (Propranolol Hydrochloride Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of 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.

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.

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.

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 form criteria applies where applicable.

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

Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Hydrochlorothiazide (HCTZ)Combinations		
Tier-1	**Tier-2**	**Tier-3**
benazepril/HCTZ (Lotensin® HCT)		fosinopril/HCTZ (Monopril-HCT®)
captopril/HCTZ (Capozide®)		
enalapril/HCTZ (Vasoretic®)		
lisinopril/HCTZ (Prinzide®, Zestoretic®)		
moexipril/HCTZ (Uniretic®)		
quinapril/HCTZ (Accuretic®)		

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
ACE Inhibitor:	amlodipine/olmesartan (Azor™)	amlodipine/valsartan/HCTZ (Exforge® HCT)
benazepril (Lotensin®)	amlodipine/valsartan (Exforge®)	azilsartan (Edarbi®)
captopril (Capoten®)	olmesartan (Benicar®)	azilsartan/chlorthalidone (Edarbyclor®)
enalapril (Vasotec®)	olmesartan/HCTZ (Benicar HCT®)	candesartan (Atacand®)
enalaprilat (Vasotec® IV)	olmesartan/ amlodipine/HCTZ (Tribenzor®)	candesartan/HCTZ (Atacand® HCT)
fosinopril (Monopril®)	valsartan (Diovan®)	eprosartan (Teveten®)
lisinopril (Prinivil®, Zestril®)		eprosartan/HCTZ (Teveten® HCT)
moexipril (Univasc®)		telmisartan (Micardis®)
quinapril (Accupril®)		telmisartan/HCTZ (Micardis® HCT)
ramipril (Altace®)		telmisartan/amlodipine (Twynsta®)
trandolapril (Mavik®)		
ARB:		
irbesartan (Avapro®)		
irbesartan/HCTZ (Avalide®)		
losartan (Cozaar®)		
losartan/HCTZ (Hyzaar®)		
valsartan/HCTZ (Diovan HCT®)		

Calcium Channel Blockers (CCB)		
Tier-1	**Tier-2**	**Tier-3**
amlodipine (Norvasc®)	amlodipine/atorvastatin (Caduet®)	diltiazem CD 360mg (Cardizem® CD)
diltiazem (Cardizem®)	diltiazem LA (Cardizem® LA, Matzim® LA)	nimodipine solution (Nymalize®)
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 CC (Adalat® CC)		
nifedipine ER		
nifedipine XL (Nifedical XL®, Procardia XL®)		
nimodipine (Nimotop®)		
verapamil (Calan®, Isoptin®, Verelan®)		
verapamil SR (Calan® SR, Isoptin® SR)		

*All strengths other than the 360mg.

Angiotensin Converting Enzyme(ACE) Inhibitor/ Calcium Channel Blocker (CCB) Combinations*		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACEI + Tier-1 CCB		benazepril/amlodipine (Lotrel®)
		enalapril/felodipine (Lexxel®)
		perindopril/amlodipine (Prestalia®)
		trandolapril/verapamil (Tarka®)

*Tier-2 criterion applies for Tier-3 medications when there are no Tier-2 medications available.

Direct Renin Inhibitors		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	aliskiren (Tekturna®)
		aliskiren/HCTZ (Tekturna HCT®)
		aliskiren/valsartan (Valturna®)
		aliskiren/amlodipine (Tekamlo®)

ACE = Angiotensin Converting Enzyme, HCTZ = Hydrochlorothiazide

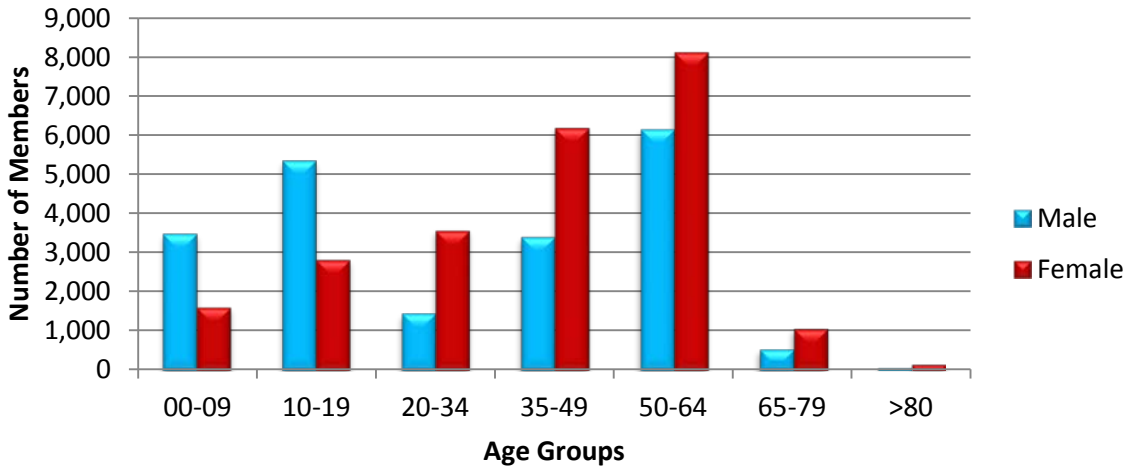
Utilization of Antihypertensive Medications: Fiscal Year 2015

Comparison of Fiscal Years

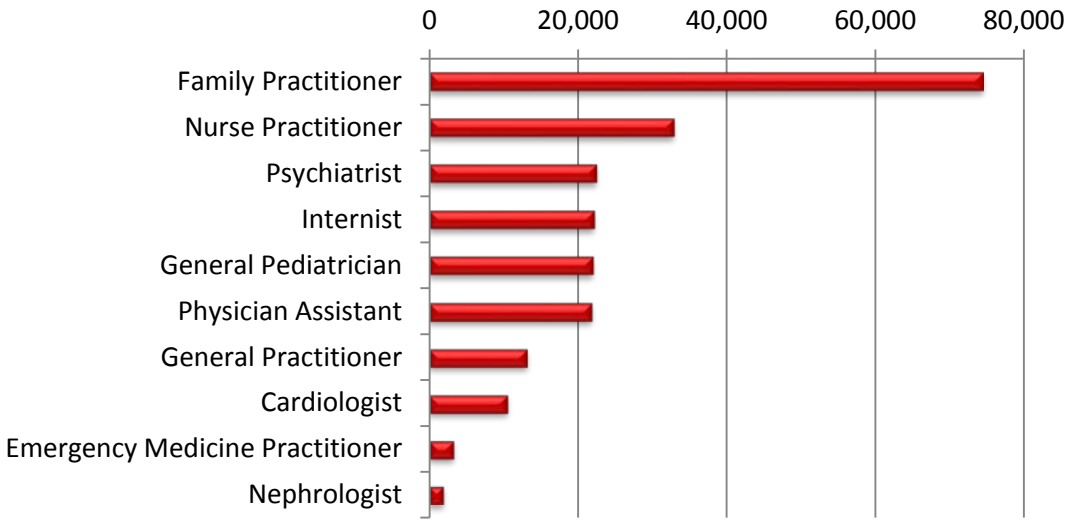
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	46,543	246,638	$3,179,871.71	$12.89	$0.34	11,383,700	9,267,420
2015	44,086	238,318	$2,478,669.17	$10.40	$0.28	11,068,401	9,006,317
% Change	**-5.30%**	**-3.40%**	**-22.10%**	**-19.30%**	**-17.60%**	**-2.80%**	**-2.80%**
Change	**-2,457**	**-8,320**	**-$701,202.54**	**-$2.49**	**-$0.06**	**-315,299**	**-261,103**

*Total number of unduplicated members.

Demographics of Members Utilizing Antihypertensive Medications



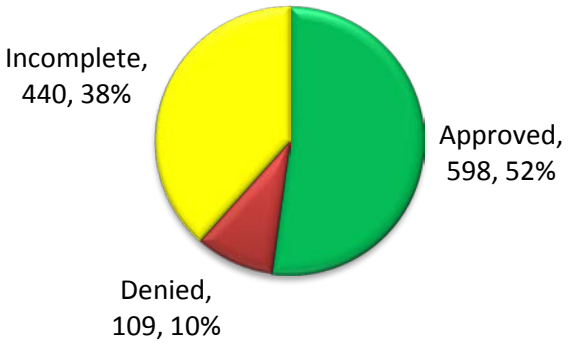
Top Prescriber Specialties of Antihypertensive Medications by Number of Claims



Prior Authorization of Antihypertensive Medications

There were 1,147 petitions submitted for antihypertensive medications during fiscal year 2015. Computer edits are in place to detect Tier-1 medications in members' recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Benicar® (olmesartan), Benicar HCT® (olmesartan/HCTZ), Azor® (amlodipine/olmesartan), Tribenzor® (amlodipine/HCTZ/olmesartan): April 2016
- Tekturna® (aliskiren) and Tekturna HCT® (aliskiren/HCTZ): July 2018
- Edarbi® (azilsartan) and Edarbyclor® (azilsartan/chlorthalidone): January 2025
- Hemangeol™ (propranolol hydrochloride oral solution): October 2028
- Prestalia® (perindopril arginine/amlodipine): October 2029
- Entresto™ (sacubitril/valsartan): May 2027
- Epaned® (enalapril powder): November 2032

New Generic Approval(s):

- **January 2014**: The generic for Micardis® (telmisartan tablets) and Twynsta® (telmisartan/amlodipine tablets) is currently available through multiple generic manufacturers.
- **February 2014**: The generic for Micardis® HCT (telmisartan/hydrochlorothiazide tablets) is currently available through multiple generic manufacturers.

FDA Approval(s):

- **July 2015**: The U.S. Food and Drug Administration (FDA) approved Entresto™ (sacubitril/valsartan) for the treatment of heart failure. The drug has been shown to reduce the rate of cardiovascular death and hospitalization related to heart failure. Entresto™ was reviewed under the FDA's priority review program, which provides expedited review of drugs that are intended to treat a serious disease or condition and may provide a significant improvement over available therapy. It was also granted fast track designation, which supports the FDA's efforts to facilitate the development and expedite the review of drugs to treat serious or life threatening conditions and fill an unmet medical need.

FDA Safety Update:

- **June 2015:** The FDA approved a new update to the Cardura® XL (doxazosin mesylate) Warning and Precautions section of the drug label to include priapism. Alpha-1 antagonists, including doxazosin, have rarely been associated with priapism.

Medication(s) in the Pipeline:

- **Ixmyelocel-T**: Vericel Corp's experimental drug, ixmyelocel-T, showed reduced death, hospitalizations, and emergency visits in patients with advanced heart failure due to ischemic dilated cardiomyopathy in a Phase 2b trial. The drug, which has orphan drug status in the United States, is derived from the patient's bone marrow using the company's cell therapy. The full data from the trial is expected to be reported at the American College of Cardiology's Annual Scientific Session and Expo in April 2016.

Guideline Update(s):

- **December 2013:** Eighth Joint National Committee (JNC 8) hypertension guidelines were published in the *Journal of the American Medical Association*. The new guidelines emphasize control of systolic and diastolic blood pressure with age- and comorbidity-specific treatment cutoffs. Important changes from the JNC 7 guidelines include:
    - Goal blood pressure level of <150/90mmHG in patients 60 years of age or older who do not have diabetes or chronic kidney disease (CKD)
    - Goal blood pressure level of <140/90mmHG in patients 18 to 59 years of age without comorbidities, and in patients 60 years of age or older who have diabetes, CKD, or both

Entresto™ (Sacubitril/Valsartan) Product Summary[8,9]

Indications: Entresto™ (sacubitril/valsartan) is a combination of a neprilysin inhibitor and an angiotensin II receptor blocker indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with reduced ejection fraction and chronic heart failure (NYHA Class II-IV).

Dosing:

- Entresto™ (sacubitril/valsartan) is available as an oral tablet in the following strengths: 24/26mg, 49/51mg, and 97/103mg.
- The recommended starting dose is 49/51mg twice daily. After two to four weeks, the dose should be doubled to the target maintenance dose of 97/103mg twice daily, as tolerated by the patient.
- The starting dose should be reduced to 24/26mg twice daily for:
  - Patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2)
  - Patients with moderate hepatic impairment (Child Pugh B classification)
  - Patients not currently taking an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents

Mechanism of Action: Entresto™ contains a neprilysin inhibitor, sacubitril, and an angiotensin receptor blocker, valsartan. Sacubitril inhibits neprilysin via LBQ657, the active metabolite of the prodrug sacubitril, and valsartan blocks the angiotensin II type-1 receptor (AT_1). Sacubitril/ valsartan cardiovascular and renal effects in heart failure patients are attributed to the increased levels of peptides that are degraded by neprilysin by LBQ657 and the simultaneous inhibition of the effects of angiotensin II by valsartan.

Contraindications:

- Hypersensitivity to any component
- History of angioedema related to previous ACE inhibitor or ARB therapy
- Concomitant use with ACE inhibitors
- Concomitant use with aliskiren in patients with diabetes

Warnings and Precautions:

- Fetal Toxicity: Sacubitril/valsartan can cause fetal harm when administered to a pregnant woman. Drugs that act on the renin-angiotensin system during the second and third trimesters reduce fetal renal function and increase fetal and neonatal morbidity and death. Alternative drug treatment should be considered when pregnancy is detected. If there is no appropriate alternative to therapy, and if the drug is considered lifesaving for the mother, the potential risk to the fetus should be discussed with the pregnant woman.
- Angioedema: Sacubitril/valsartan may cause angioedema. If angioedema occurs, sacubitril/valsartan should be immediately discontinued, appropriate therapy should be provided and the patient should be monitored for airway compromise. Sacubitril/ valsartan should not be re-administered. Patients with a prior history of angioedema may be at increased risk of angioedema with sacubitril/valsartan.
- Hypotension: Sacubitril/valsartan lowers blood pressure and may cause symptomatic hypotension. Patients with an activated renin-angiotensin system, such as salt or volume-depleted patients are at greater risk. Volume or salt depletion should be corrected prior to administration of sacubitril/valsartan or the patient should be started on a lower dose.
- Impaired Renal Function: Decreases in renal function may be anticipated in susceptible individuals treated with sacubitril/valsartan, due to the inhibition of the renin-angiotensin-aldosterone system (RAAS).

- Hyperkalemia: Hyperkalemia may occur with sacubitril/valsartan due to its action on the RAAS. Serum potassium should be periodically monitored and treated appropriately, especially in patients with risk factors for hyperkalemia such as severe renal impairment, diabetes, hypoaldosteronism, or a high potassium diet.

Adverse Reactions: The most common adverse reactions experienced during clinical trials with sacubitril/valsartan (occurring ≥ 5% of patients) were:

- Hypotension
- Hyperkalemia
- Cough
- Dizziness
- Renal failure

Clinical Studies: The safety and efficacy of sacubitril/valsartan was evaluated in the PARADIGM-HF trial. The trial looked at 8,442 patients with symptomatic chronic heart failure (NYHA class II-IV) and reduced ejection fraction (≤40%). Patients had to have been on an ACE inhibitor or ARB for at least four weeks and on maximally tolerated doses of beta-blockers. Patients were randomized to one of two groups, sacubitril/valsartan 97/103mg tablet twice daily or enalapril 10mg twice daily. Most patients were also on recommended heart failure therapy. The primary outcome was the first event in the composite of death from cardiovascular causes or hospitalization from HF. At follow-up at 27 months, more patients on enalapril died or were hospitalized versus sacubitril/valsartan (26.5% vs. 21.8%, respectively; HR 0.80; 95% CI [0.73, 0.87], p<0.001).

Utilization: Sacubitril/valsartan has been utilized by 18 members in the SoonerCare population since its approval on July 7, 2015.

Cost Comparison:

Medication Name	Strength	Cost/ Tablet	Cost/ Month	Cost/ Year
Entresto™ (sacubitril/valsartan)	**24/26mg, 49/51mg, 97/103mg**	**$6.60***	**$396.00**	**$4,752.00**
enalapril	10mg	$0.35[+]	$21.00	$252.00
valsartan	160mg[◊]	$0.37[+]	$22.20	$266.40

*Estimated acquisition cost.

[+]Cost based on state maximum allowable cost (SMAC).

[◊]103mg of valsartan in Entresto™ (sacubitril/valsartan) is equivalent to 160mg of valsartan in Diovan® due to the fact that they are different salts

Recommendations

The College of Pharmacy recommends the prior authorization of Entresto™ (sacubitril/valsartan) with the following criteria:

Entresto™ (Sacubitril/Valsartan) Approval Criteria:

1. An FDA approved diagnosis of chronic heart failure (NYHA Class II, III, or IV); and
2. The prescriber must verify that the member has a left ventricular ejection fraction ≤ 40%; and
3. The member must be on a maximally tolerated dose of a beta-blocker or have a contraindication to beta-blocker therapy; and

4. The prescriber must verify the member has been on an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) for at least four weeks; and
5. The member must not take an ACE inhibitor while taking Entresto™ as concomitant use is contraindicated; and
6. Members with a diagnosis of diabetes must not be taking aliskiren while taking Entresto™ as concomitant use is contraindicated; and
7. A quantity limit of 60 tablets per 30 days will apply.

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

1. Move Aceon® (perindopril) to Tier-1 of the ACE Inhibitor category based on state maximum allowable cost (SMAC).
2. Move Lotrel® (amlodipine/benazepril) to Tier-1 of the ACE Inhibitor/CCB combination category based on SMAC.
3. Remove Lexxel® (enalapril/felodipine) from the ACE Inhibitor/CCB Combination category and remove Valturna® (aliskiren/valsartan) from the Direct Renin Inhibitors category due to product discontinuations.
4. Move Diovan® (valsartan) to Tier-1 based on SMAC.
5. Move Micardis® (telmisartan) to Tier-2 based on SMAC. Current Tier-2 criteria for this category will apply.

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

Angiotensin Converting Enzyme(ACE) Inhibitor/ Calcium Channel Blocker (CCB) Combinations*		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACEI + Tier-1 CCB		~~**enalapril/felodipine (Lexxel®)**~~
benazepril/amlodipine (Lotrel®)		perindopril/amlodipine (Prestalia®)
		trandolapril/verapamil (Tarka®)

*Tier-2 criterion applies for Tier-3 medications when there are no Tier-2 medications available.

Direct Renin inhibitors		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	aliskiren (Tekturna®)
		aliskiren/HCTZ (Tekturna HCT®)
		~~aliskiren/valsartan (Valturna®)~~
		aliskiren/amlodipine (Tekamlo®)

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
ACE Inhibitor:	amlodipine/olmesartan (Azor™)	amlodipine/valsartan/HCTZ (Exforge® HCT)
benazepril (Lotensin®)	amlodipine/valsartan (Exforge®)	azilsartan (Edarbi®)
captopril (Capoten®)	olmesartan (Benicar®)	azilsartan/chlorthalidone (Edarbyclor®)
enalapril (Vasotec®)	olmesartan/HCTZ (Benicar HCT®)	candesartan (Atacand®)
enalaprilat (Vasotec® IV)	olmesartan/ amlodipine/HCTZ (Tribenzor®)	candesartan/HCTZ (Atacand® HCT)
fosinopril (Monopril®)	**telmisartan (Micardis®)**	eprosartan (Teveten®)
lisinopril (Prinivil®, Zestril®)		eprosartan/HCTZ (Teveten® HCT)
moexipril (Univasc®)		telmisartan/HCTZ (Micardis® HCT)
quinapril (Accupril®)		telmisartan/amlodipine (Twynsta®)
perindopril erbumine (Aceon®)		
ramipril (Altace®)		
trandolapril (Mavik®)		
ARB:		
irbesartan (Avapro®)		
irbesartan/HCTZ (Avalide®)		
losartan (Cozaar®)		
losartan/HCTZ (Hyzaar®)		
valsartan/HCTZ (Diovan HCT®)		
valsartan (Diovan®)		

ACE = Angiotensin Converting Enzyme, HCTZ = Hydrochlorothiazide

Utilization Details of Antihypertensive Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
CALCIUM CHANNEL BLOCKERS						
TIER-1 UTILIZATION						
AMLODIPINE TAB 10MG	15,594	4,025	$61,855.66	$0.09	$3.97	2.50%
AMLODIPINE TAB 5MG	11,417	3,333	$38,943.90	$0.08	$3.41	1.57%
AMLODIPINE TAB 2.5MG	1,315	386	$5,649.66	$0.11	$4.30	0.23%
NIFEDIPINE CAP 10MG	949	727	$47,261.30	$2.73	$49.80	1.91%
VERAPAMIL TAB 240MG ER	811	191	$10,054.20	$0.29	$12.40	0.41%
NIFEDICAL XL TAB 60MG	663	168	$17,374.86	$0.73	$26.21	0.70%
NIFEDICAL XL TAB 30MG	656	261	$11,384.20	$0.51	$17.35	0.46%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
NIFEDIPINE TAB 30MG ER	626	272	$10,421.74	$0.47	$16.65	0.42%
NIFEDIPINE TAB 60MG ER	477	160	$12,500.87	$0.71	$26.21	0.50%
NIFEDIPINE TAB 90MG ER	464	123	$17,693.99	$0.90	$38.13	0.71%
DILTIAZEM CAP 240MG CD	454	103	$10,327.94	$0.56	$22.75	0.42%
DILTIAZEM CAP 180MG CD	403	119	$9,279.77	$0.62	$23.03	0.37%
VERAPAMIL TAB 120MG ER	383	117	$5,094.80	$0.35	$13.30	0.21%
VERAPAMIL TAB 180MG ER	368	97	$4,455.39	$0.29	$12.11	0.18%
DILTIAZEM CAP 120MG CD	330	108	$6,324.59	$0.47	$19.17	0.26%
DILTIAZEM TAB 120MG	327	82	$4,619.16	$0.42	$14.13	0.19%
NIFEDIPINE TAB 30MG ER	324	128	$6,224.31	$0.47	$19.21	0.25%
VERAPAMIL TAB 120MG	312	87	$2,086.99	$0.18	$6.69	0.08%
VERAPAMIL TAB 80MG	312	93	$2,013.37	$0.18	$6.45	0.08%
DILTIAZEM TAB 60MG	292	74	$2,928.94	$0.32	$10.03	0.12%
NIFEDIPINE TAB 60MG ER	243	85	$9,884.73	$1.10	$40.68	0.40%
DILTIAZEM CAP 240MG ER	236	64	$6,356.68	$0.67	$26.94	0.26%
NIFEDIPINE CAP 20MG	191	154	$19,929.66	$5.42	$104.34	0.80%
DILTIAZEM TAB 30MG	185	63	$1,380.56	$0.25	$7.46	0.06%
CARTIA XT CAP 120/24HR	183	56	$3,117.64	$0.46	$17.04	0.13%
DILTIAZEM TAB 90MG	178	37	$2,800.64	$0.50	$15.73	0.11%
DILTIAZEM CAP 180MG ER	172	65	$4,308.31	$0.58	$25.05	0.17%
NIFEDIPINE TAB 90MG ER	168	45	$13,578.91	$1.73	$80.83	0.55%
DILTIAZEM CAP 180MG ER	166	43	$4,468.15	$0.71	$26.92	0.18%
AFEDITAB TAB 30MG CR	158	38	$3,117.31	$0.54	$19.73	0.13%
DILTIAZEM CAP 120MG ER	157	70	$3,111.90	$0.45	$19.82	0.13%
CARTIA XT CAP 240/24HR	156	49	$3,677.27	$0.55	$23.57	0.15%
DILTIAZEM CAP 120MG/24	147	29	$4,164.02	$0.93	$28.33	0.17%
DILTIAZEM CAP 240MG ER	139	60	$3,625.98	$0.55	$26.09	0.15%
VERAPAMIL TAB 40MG	120	36	$2,126.47	$0.57	$17.72	0.09%
DILTIAZEM CAP 120MG ER	115	42	$2,834.66	$0.58	$24.65	0.11%
CARTIA XT CAP 180/24HR	104	36	$2,413.19	$0.54	$23.20	0.10%
VERAPAMIL CAP 240MG SR	104	33	$4,186.39	$0.81	$40.25	0.17%
TAZTIA XT CAP 360MG/24	95	23	$3,998.26	$0.82	$42.09	0.16%
VERAPAMIL CAP 240MG ER	87	28	$3,422.55	$0.87	$39.34	0.14%
VERAPAMIL CAP 360MG SR	87	21	$7,201.44	$1.63	$82.78	0.29%
DILTIAZEM CAP 240MG/24	85	22	$2,987.28	$1.05	$35.14	0.12%
DILTIAZEM CAP 180MG/24	84	19	$3,203.92	$1.19	$38.14	0.13%
VERAPAMIL CAP 120MG ER	78	34	$3,169.53	$0.93	$40.64	0.13%
AFEDITAB TAB 60MG CR	75	12	$2,241.01	$1.00	$29.88	0.09%
FELODIPINE TAB 10MG ER	69	21	$2,544.70	$0.70	$36.88	0.10%
DILTIAZEM CAP 300MG CD	66	19	$2,614.40	$0.77	$39.61	0.11%
DILTIAZEM CAP 360MG/24	62	18	$2,242.84	$0.91	$36.17	0.09%
DILT-XR CAP 180MG	59	19	$1,837.27	$0.71	$31.14	0.07%
DILT-XR CAP 240MG	59	20	$1,593.51	$0.67	$27.01	0.06%
DILTIAZEM CAP 60MG ER	54	16	$5,125.63	$2.68	$94.92	0.21%
DILTIAZEM CAP 90MG ER	48	11	$4,679.41	$2.67	$97.49	0.19%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
VERAPAMIL CAP 180MG SR	48	15	$1,696.58	$0.75	$35.35	0.07%
VERAPAMIL CAP 180MG ER	43	21	$1,410.26	$0.72	$32.80	0.06%
TAZTIA XT CAP 120MG/24	43	20	$1,307.09	$0.76	$30.40	0.05%
FELODIPINE TAB 5MG ER	40	12	$1,091.95	$0.58	$27.30	0.04%
TAZTIA XT CAP 240MG/24	36	15	$1,541.94	$0.88	$42.83	0.06%
TAZTIA XT CAP 180MG/24	35	11	$1,155.55	$0.84	$33.02	0.05%
VERAPAMIL CAP 120MG SR	34	15	$1,071.71	$0.81	$31.52	0.04%
DILTIAZEM CAP 360MG ER	29	10	$1,127.78	$0.96	$38.89	0.05%
DILTIAZEM CAP 120MG ER	26	8	$2,248.61	$2.43	$86.49	0.09%
DILTIAZEM CAP 300MG ER	26	7	$1,014.93	$0.94	$39.04	0.04%
DILT-XR CAP 120MG	25	17	$781.31	$0.61	$31.25	0.03%
VERAPAMIL CAP 100MG ER	25	7	$2,146.84	$1.59	$85.87	0.09%
CARDIZEM CD CAP 180MG/24	20	7	$380.66	$0.63	$19.03	0.02%
DILTIAZEM CAP 300MG/24	19	6	$707.62	$1.24	$37.24	0.03%
TAZTIA XT CAP 300MG/24	19	4	$1,000.51	$1.08	$52.66	0.04%
CARTIA XT CAP 300/24HR	19	10	$901.45	$0.73	$47.44	0.04%
VERAPAMIL POW	18	3	$360.39	$0.69	$20.02	0.01%
DILTIAZEM CAP 420MG/24	17	5	$1,003.36	$1.29	$59.02	0.04%
ADALAT CC TAB 90MG ER	14	2	$801.96	$1.91	$57.28	0.03%
NORVASC TAB 2.5MG	13	4	$74.36	$0.19	$5.72	0.00%
CARDIZEM CD CAP 240MG/24	12	4	$228.95	$0.64	$19.08	0.01%
NICARDIPINE CAP 20MG	12	1	$839.52	$2.33	$69.96	0.03%
FELODIPINE TAB 2.5MG ER	10	3	$287.43	$0.68	$28.74	0.01%
CARDIZEM CD CAP 120MG/24	10	1	$267.27	$0.89	$26.73	0.01%
NIFEDIPINE POW	7	6	$74.83	$0.48	$10.69	0.00%
NICARDIPINE CAP 30MG	7	2	$684.83	$1.76	$97.83	0.03%
DILTIAZEM ER TAB 300MG	6	1	$596.76	$3.32	$99.46	0.02%
DILTIAZEM ER TAB 420MG	6	2	$953.93	$3.97	$158.99	0.04%
PROCARDIA CAP 10MG	4	2	$78.71	$0.86	$19.68	0.00%
DILTIAZEM ER TAB 180MG	3	1	$362.92	$2.42	$120.97	0.01%
TIAZAC CAP 120MG/24	1	1	$35.92	$1.20	$35.92	0.00%
TIAZAC CAP 180MG/24	1	1	$30.42	$1.01	$30.42	0.00%
TIER-1 SUBTOTAL	**41,035**	**12,166**	**$454,706.21**	**$0.28**	**$11.08**	**18.34%**
TIER-2 UTILIZATION						
AMLODIPINE/ATORVASTATIN TAB 10-20MG	54	13	$22,933.40	$6.09	$424.69	0.93%
AMLODIPINE/ATORVASTATIN TAB 10-40MG	47	11	$15,233.03	$6.04	$324.11	0.61%
AMLODIPINE/ATORVASTATIN TAB 10-10MG	29	6	$7,264.88	$4.60	$250.51	0.29%
MATZIM LA TAB 240MG/24	22	7	$2,551.94	$2.58	$116.00	0.10%
ISRADIPINE CAP 2.5MG	20	2	$1,476.62	$2.00	$73.83	0.06%
AMLODIPINE/ATORVASTATIN TAB 5-40MG	18	5	$6,447.14	$6.82	$358.17	0.26%
MATZIM LA TAB 360MG/24	17	4	$3,039.10	$3.75	$178.77	0.12%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AMLODIPINE/ATORVASTATIN TAB 5-20MG	14	3	$4,989.19	$5.94	$356.37	0.20%
CARDIZEM LA TAB 120MG	13	4	$2,045.88	$4.01	$157.38	0.08%
VERAPAMIL CAP 300MG ER	12	1	$750.23	$2.08	$62.52	0.03%
ISRADIPINE CAP 5MG	11	1	$1,918.88	$5.81	$174.44	0.08%
AMLODIPINE/ATORVASTATIN TAB 10-80MG	11	3	$4,375.40	$5.83	$397.76	0.18%
AMLODIPINE/ATORVASTATIN TAB 5-10MG	9	1	$1,206.18	$4.47	$134.02	0.05%
VERELAN CAP 240MG SR	9	1	$2,261.03	$6.35	$251.23	0.09%
MATZIM LA TAB 180MG/24	6	6	$753.16	$2.17	$125.53	0.03%
MATZIM LA TAB 420MG/24	5	3	$854.98	$4.07	$171.00	0.03%
VERAPAMIL CAP 200MG ER	5	1	$532.17	$1.36	$106.43	0.02%
TIER-2 SUBTOTAL	**302**	**72**	**$78,633.21**	**$5.00**	**$260.37**	**3.17%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
NIMODIPINE CAP 30MG	6	4	$3,665.66	$34.91	$610.94	0.15%
SPECIAL PA SUBTOTAL	**6**	**4**	**$3,665.66**	**$34.91**	**$610.94**	**0.15%**
TOTAL	**41,343**	**12,242**	**$537,005.08**	**$0.32**	**$12.99**	**21.67%**
ANGIOTENSIN RECEPTOR BLOCKERS (ARB) AND COMBINATION PRODUCTS						
TIER-1 UTILIZATION						
LOSARTAN POT TAB 50MG	4,011	1,124	$24,348.30	$0.15	$6.07	0.98%
LOSARTAN POT TAB 100MG	3,476	888	$29,158.69	$0.19	$8.39	1.18%
LOSARTAN POT TAB 25MG	1,928	548	$10,733.14	$0.13	$5.57	0.43%
LOSARTAN/HCT TAB 100-25	1,489	369	$12,325.05	$0.18	$8.28	0.50%
LOSARTAN/HCT TAB 50-12.5	1,038	301	$7,666.78	$0.17	$7.39	0.31%
LOSARTAN/HCT TAB 100-12.5	515	148	$4,705.61	$0.20	$9.14	0.19%
VALSARTAN/HCTZ TAB 160-	405	86	$5,856.94	$0.35	$14.46	0.24%
IRBESARTAN TAB 150MG	271	64	$3,583.80	$0.30	$13.22	0.14%
IRBESARTAN TAB 300MG	249	56	$3,815.84	$0.40	$15.32	0.15%
VALSARTAN /HCTZ TAB 160-25MG	235	60	$4,435.57	$0.37	$18.87	0.18%
VALSARTAN /HCTZ TAB 80-12.5	225	56	$3,394.64	$0.35	$15.09	0.14%
VALSARTAN /HCTZ TAB 320-25MG	183	48	$4,542.69	$0.48	$24.82	0.18%
IRBESARTAN/HCTZ TAB 150-	101	24	$1,942.34	$0.42	$19.23	0.08%
VALSARTAN /HCTZ TAB 320-	84	20	$1,458.55	$0.44	$17.36	0.06%
IRBESARTAN TAB 75MG	68	17	$687.04	$0.24	$10.10	0.03%
IRBESARTAN /HCTZ TAB 300-	49	14	$1,009.05	$0.47	$20.59	0.04%
COZAAR TAB 25MG	6	3	$42.60	$0.24	$7.10	0.00%
AVAPRO TAB 150MG	2	1	$24.94	$0.42	$12.47	0.00%
COZAAR TAB 50MG	1	1	$143.90	$4.80	$143.90	0.01%
TIER-1 SUBTOTAL	**14,336**	**3,828**	**$119,875.47**	**$0.20**	**$8.36**	**4.84%**
TIER-2 UTILIZATION						
VALSARTAN TAB 320MG	217	59	$32,774.39	$3.37	$151.03	1.32%
VALSARTAN TAB 160MG	213	50	$28,112.29	$3.13	$131.98	1.13%
VALSARTAN TAB 80MG	199	42	$23,324.80	$2.52	$117.21	0.94%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
BENICAR TAB 20MG	180	40	$39,161.30	$4.67	$217.56	1.58%
BENICAR TAB 40MG	173	33	$49,553.97	$6.12	$286.44	2.00%
BENICAR HCT TAB 20-12.5	100	21	$24,758.41	$4.77	$247.58	1.00%
BENICAR HCT TAB 40-12.5	99	16	$28,322.81	$6.14	$286.09	1.14%
BENICAR HCT TAB 40-25MG	96	19	$29,793.31	$6.04	$310.35	1.20%
EXFORGE TAB 10-320MG	75	17	$17,474.17	$7.77	$232.99	0.70%
AMLODIPINE/VALSARTAN TAB 10-320MG	75	18	$10,860.81	$4.83	$144.81	0.44%
EXFORGE TAB 5-160MG	49	7	$7,282.51	$4.95	$148.62	0.29%
DIOVAN TAB 160MG	47	17	$9,277.73	$6.06	$197.40	0.37%
AZOR TAB 5-40MG	46	8	$14,445.59	$6.98	$314.03	0.58%
VALSARTAN TAB 40MG	43	14	$2,576.64	$2.05	$59.92	0.10%
DIOVAN TAB 320MG	42	23	$14,583.68	$6.58	$347.23	0.59%
AZOR TAB 10-40MG	40	7	$8,855.87	$7.03	$221.40	0.36%
DIOVAN TAB 80MG	38	19	$7,096.91	$5.00	$186.76	0.29%
TRIBENZOR40- TAB 10-25MG	25	8	$10,201.46	$6.94	$408.06	0.41%
AMLODIPINE/VALSARTAN TAB 5-160MG	22	6	$1,443.82	$2.19	$65.63	0.06%
TRIBENZOR40- TAB 5-12.5MG	20	5	$7,150.50	$7.01	$357.53	0.29%
BENICAR TAB 5MG	17	3	$2,290.31	$2.83	$134.72	0.09%
AMLODIPINE/VALSARTAN TAB 10-160MG	14	4	$1,525.32	$3.63	$108.95	0.06%
AZOR TAB 5-20MG	13	3	$3,541.25	$5.62	$272.40	0.14%
DIOVAN TAB 40MG	12	6	$2,986.16	$4.67	$248.85	0.12%
EXFORGE TAB 10-160MG	10	3	$1,818.50	$6.06	$181.85	0.07%
EXFORGE TAB 5-320MG	6	2	$1,206.84	$6.70	$201.14	0.05%
TRIBENZOR40- TAB 5-25MG	5	2	$3,099.86	$6.89	$619.97	0.13%
AMLODIPINE/VALSARTAN TAB 5-320MG	2	1	$325.90	$5.43	$162.95	0.01%
TRIBENZOR20- TAB 5-12.5MG	2	1	$324.46	$5.41	$162.23	0.01%
TIER-2 SUBTOTAL	**1,880**	**454**	**$384,169.57**	**$4.71**	**$204.35**	**15.50%**
TIER-3 UTILIZATION						
TELMISARTAN TAB 80MG	146	16	$17,119.23	$3.71	$117.26	0.69%
TELMISARTAN TAB 40MG	110	20	$15,420.45	$2.95	$140.19	0.62%
EDARBYCLOR TAB 40-12.5	42	8	$7,093.77	$4.35	$168.90	0.29%
EXFORGE HCT TAB 160-12.5	38	7	$6,052.28	$5.31	$159.27	0.24%
TELMISARTAN/HCTZ TAB 80-	38	8	$8,000.70	$4.94	$210.54	0.32%
TELMISA/HCTZ TAB 40-12.5	37	6	$4,634.35	$3.96	$125.25	0.19%
EXFORGE HCT TAB 320-25	37	9	$8,537.03	$7.69	$230.73	0.34%
CANDESARTAN TAB 32MG	36	6	$6,301.17	$3.94	$175.03	0.25%
EDARBI TAB 80MG	35	6	$5,585.42	$4.77	$159.58	0.23%
TELMISA/HCTZ TAB 80-25MG	34	8	$6,076.83	$4.02	$178.73	0.25%
AMLOD/VALSAR TAB /HCTZ	29	8	$4,641.73	$4.99	$160.06	0.19%
CANDESARTAN TAB 8MG	27	5	$2,327.23	$2.20	$86.19	0.09%
TELMISARTAN TAB 20MG	25	5	$2,706.42	$3.87	$108.26	0.11%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AMLOD/VALSAR TAB /HCTZ	24	5	$2,818.00	$3.91	$117.42	0.11%
CANDESA/HCTZ TAB 32-12.5	24	5	$2,017.73	$1.60	$84.07	0.08%
MICARDIS TAB 80MG	18	3	$1,725.48	$3.20	$95.86	0.07%
AMLOD/VALSAR TAB /HCTZ	15	4	$2,161.60	$4.80	$144.11	0.09%
EXFORGE HCT 160-25	10	3	$1,825.12	$6.08	$182.51	0.07%
CANDESARTAN TAB 16MG	8	2	$1,188.64	$2.48	$148.58	0.05%
MICARDIS HCT TAB 80-25MG	7	1	$1,101.58	$5.25	$157.37	0.04%
EDARBI TAB 40MG	7	2	$1,627.79	$7.75	$232.54	0.07%
MICARDIS TAB 20MG	6	1	$1,257.64	$5.24	$209.61	0.05%
CANDESA/HCTZ TAB 16-12.5	5	2	$350.49	$2.34	$70.10	0.01%
CANDESARTAN TAB 4MG	4	3	$390.25	$2.37	$97.56	0.02%
TEVETEN HCT TAB 600-12.5	4	1	$494.38	$4.94	$123.60	0.02%
MICARDIS HCT TAB 80/12.5	4	2	$1,599.61	$5.33	$399.90	0.06%
TEVETEN TAB 600MG	4	2	$1,271.61	$4.62	$317.90	0.05%
EXFORGE HCT TAB 160-12.5	3	2	$544.95	$6.06	$181.65	0.02%
MICARDIS TAB 40MG	2	1	$1,032.52	$5.74	$516.26	0.04%
EDARBYCLOR TAB 40-25MG	1	1	$445.86	$4.95	$445.86	0.02%
EPROSART MES TAB 600MG	1	1	$260.18	$2.89	$260.18	0.01%
TIER-3 SUBTOTAL	**781**	**153**	**$116,610.04**	**$3.97**	**$149.31**	**4.70%**
TOTAL	**16,997**	**4,435**	**$620,655.08**	**$0.86**	**$36.52**	**25.04%**
ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIs) AND COMBINATION PRODUCTS						
TIER-1 UTILIZATION						
LISINOPRIL TAB 20MG	21,070	5,999	$89,908.39	$0.10	$4.27	3.63%
LISINOPRIL TAB 10MG	19,319	5,746	$68,304.68	$0.09	$3.54	2.76%
LISINOPRIL TAB 40MG	10,571	2,657	$60,791.53	$0.13	$5.75	2.45%
LISINOPRIL TAB 5MG	8,585	2,567	$29,220.09	$0.08	$3.40	1.18%
LISINOP/HCTZ TAB 20-25MG	6,336	1,905	$29,157.04	$0.09	$4.60	1.18%
LISINOP/HCTZ TAB 20-12.5	6,325	1,854	$25,027.45	$0.09	$3.96	1.01%
LISINOPRIL TAB 2.5MG	3,478	988	$11,770.90	$0.08	$3.38	0.47%
LISINOP/HCTZ TAB 10-12.5	3,288	1,113	$11,880.94	$0.08	$3.61	0.48%
ENALAPRIL TAB 10MG	2,028	468	$24,878.92	$0.33	$12.27	1.00%
ENALAPRIL TAB 20MG	1,933	431	$36,326.39	$0.48	$18.79	1.47%
ENALAPRIL TAB 5MG	1,839	387	$24,927.31	$0.39	$13.55	1.01%
LISINOPRIL TAB 30MG	1,267	321	$6,662.80	$0.14	$5.26	0.27%
ENALAPRIL TAB 2.5MG	993	194	$12,108.72	$0.36	$12.19	0.49%
BENAZEPRIL TAB 20MG	713	178	$3,980.56	$0.13	$5.58	0.16%
BENAZEPRIL TAB 40MG	481	119	$2,980.10	$0.13	$6.20	0.12%
FOSINOPRIL TAB 40MG	437	73	$4,699.54	$0.32	$10.75	0.19%
RAMIPRIL CAP 10MG	348	66	$3,386.77	$0.21	$9.73	0.14%
BENAZEPRIL TAB 10MG	309	102	$1,777.91	$0.13	$5.75	0.07%
CAPTOPRIL TAB 25MG	287	51	$14,891.86	$1.71	$51.89	0.60%
ENALAPR/HCTZ TAB 10-25MG	280	62	$2,290.64	$0.19	$8.18	0.09%
FOSINOPRIL TAB 20MG	246	45	$2,141.65	$0.24	$8.71	0.09%
QUINAPRIL TAB 40MG	238	45	$2,300.20	$0.23	$9.66	0.09%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
CAPTOPRIL TAB 50MG	204	32	$16,410.19	$2.64	$80.44	0.66%
QUINAPRIL TAB 20MG	194	41	$2,168.19	$0.26	$11.18	0.09%
FOSINOPRIL TAB 10MG	141	25	$1,314.23	$0.24	$9.32	0.05%
CAPTOPRIL TAB 12.5MG	137	32	$5,910.90	$1.16	$43.15	0.24%
RAMIPRIL CAP 2.5MG	134	33	$1,284.55	$0.20	$9.59	0.05%
RAMIPRIL CAP 5MG	121	35	$1,267.40	$0.21	$10.47	0.05%
BENAZEP/HCTZ TAB 20-25MG	112	22	$6,875.83	$1.44	$61.39	0.28%
ENALAPR/HCTZ TAB 5-12.5MG	99	20	$571.75	$0.15	$5.78	0.02%
BENAZEPRIL TAB 5MG	97	22	$616.23	$0.13	$6.35	0.02%
BENAZEP/HCTZ TAB 20-12.5	80	19	$4,860.57	$1.57	$60.76	0.20%
RAMIPRIL CAP 1.25MG	76	21	$837.70	$0.26	$11.02	0.03%
QUINAPRIL TAB 10MG	57	22	$639.08	$0.19	$11.21	0.03%
BENAZEP/HCTZ TAB 10-12.5	55	13	$4,695.21	$1.71	$85.37	0.19%
CAPTOPR/HCTZ TAB 50-25MG	46	7	$3,747.34	$2.19	$81.46	0.15%
QUINAPRIL/HCTZ TAB 20-25MG	38	8	$1,030.06	$0.66	$27.11	0.04%
QUINAPRIL TAB 5MG	34	6	$208.00	$0.15	$6.12	0.01%
TRANDOLAPRIL TAB 4MG	21	3	$267.76	$0.43	$12.75	0.01%
TRANDOLAPRIL TAB 1MG	20	2	$228.96	$0.35	$11.45	0.01%
CAPTOPR/HCTZ TAB 25-15MG	18	3	$1,390.15	$1.48	$77.23	0.06%
QNAPRIL/HCTZ TAB 20-12.5	14	4	$452.69	$0.69	$32.34	0.02%
TRANDOLAPRIL TAB 2MG	13	2	$108.18	$0.28	$8.32	0.00%
CAPTOPRIL TAB 100MG	11	1	$747.07	$2.26	$67.92	0.03%
MOEXIPRIL TAB 15MG	10	1	$152.37	$0.51	$15.24	0.01%
CAPTOPR/HCTZ TAB 25-25MG	8	4	$264.87	$0.49	$33.11	0.01%
QNAPRIL/HCTZ TAB 10-12.5	5	1	$261.30	$0.67	$52.26	0.01%
MOEXIPR/HCTZ TAB 15-25MG	4	1	$276.67	$0.77	$69.17	0.01%
ACCURETIC TAB 20-25MG	4	1	$999.28	$2.78	$249.82	0.04%
TIER-1 SUBTOTAL	**92,124**	**25,752**	**$527,000.92**	**$0.14**	**$5.72**	**21.26%**
TIER-2 UTILIZATION						
PERINDOPRIL TAB 4MG	11	1	$293.96	$0.65	$26.72	0.01%
TIER-2 SUBTOTAL	**11**	**1**	**$293.96**	**$0.65**	**$26.72**	**0.01%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
EPANED SOL 1MG/ML	440	134	$131,685.30	$6.32	$299.28	5.31%
SPECIAL PA SUBTOTAL	**440**	**134**	**$131,685.30**	**$6.32**	**$299.28**	**5.31%**
TOTAL	**92,575**	**25,887**	**$658,980.18**	**$0.17**	**$7.12**	**26.59%**
ACE INHIBITOR/CALCIUM CHANNEL BLOCKER COMBINATIONS						
TIER-3 UTILIZATION						
AMLOD/BENAZP CAP 10-20MG	206	35	$5,787.52	$0.56	$28.09	0.23%
AMLOD/BENAZP CAP 10-40MG	184	38	$6,057.38	$0.66	$32.92	0.24%
AMLOD/BENAZP CAP 5-	145	27	$3,204.38	$0.52	$22.10	0.13%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
20MG						
AMLOD/BENAZP CAP 5-10MG	66	12	$1,726.26	$0.67	$26.16	0.07%
AMLOD/BENAZP CAP 5-40MG	31	7	$922.63	$0.63	$29.76	0.04%
TARKA TAB 2-240 CR	13	1	$1,915.71	$4.91	$147.36	0.08%
TARKA TAB 4-240 CR	9	2	$4,227.66	$7.42	$469.74	0.17%
AMLOD/BENAZP CAP 2.5-10MG	8	1	$164.98	$0.69	$20.62	0.01%
TRANDO/VERAP TAB 4-240 ER	1	1	$401.94	$4.47	$401.94	0.02%
TIER-3 SUBTOTAL	**663**	**124**	**$24,408.46**	**$0.79**	**$36.82**	**0.98%**
TOTAL	**663**	**124**	**$24,408.46**	**$0.79**	**$36.82**	**0.98%**
DIRECT RENIN INHIBITORS (ALISKIREN)						
TIER-3 UTILIZATION						
TEKTURNA TAB 300MG	19	6	$4,669.24	$5.76	$245.75	0.19%
TEKTURNA TAB 150MG	11	4	$2,576.42	$5.05	$234.22	0.10%
TEKTURNA HCT TAB 300-25MG	7	2	$1,744.32	$5.29	$249.19	0.07%
TEKTURNA HCT TAB 300-12.5	2	1	$980.72	$5.45	$490.36	0.04%
AMTURNIDE 300 TAB -5-12.5	1	1	$138.23	$4.61	$138.23	0.01%
TIER-3 SUBTOTAL	**40**	**14**	**$10,108.93**	**$5.43**	**$252.72**	**0.41%**
TOTAL	**40**	**14**	**$10,108.93**	**$5.43**	**$252.72**	**0.41%**
CLONIDINE PRODUCTS						
NO PRIOR AUTHORIZATION REQUIRED						
CLONIDINE TAB 0.1MG	57,918	11,924	$357,529.10	$0.20	$6.17	14.42%
CLONIDINE TAB 0.2MG	21,860	3,865	$135,647.00	$0.20	$6.21	5.47%
CLONIDINE TAB 0.3MG	4,654	770	$32,942.59	$0.22	$7.08	1.33%
CLONIDINE POW	82	32	$15,558.64	$6.27	$189.74	0.63%
CATAPRES TAB 0.2MG	12	4	$120.06	$0.33	$10.01	0.00%
CATAPRES TAB 0.1MG	3	2	$19.71	$0.22	$6.57	0.00%
SUBTOTAL	**84,529**	**16,597**	**$541,817.10**	**$0.21**	**$6.41**	**21.86%**
SPECIAL PRIOR AUTHORIZATION (CLONIDINE TRANSDERMAL PATCH)						
CLONIDINE DIS 0.2/24HR	108	31	$12,173.35	$4.21	$112.72	0.49%
CLONIDINE DIS 0.1/24HR	88	23	$6,158.83	$2.46	$69.99	0.25%
CLONIDINE DIS 0.3/24HR	63	19	$11,985.56	$6.81	$190.25	0.48%
SPECIAL PA SUBTOTAL	**259**	**73**	**$30,317.74**	**$4.24**	**$117.06**	**1.22%**
TOTAL	**84,788**	**16,670**	**$572,134.84**	**$0.22**	**$6.75**	**23.08%**
SOTALOL PRODUCTS						
NO PRIOR AUTHORIZATION REQUIRED						
SOTALOL HCL TAB 80MG	242	54	$2,545.74	$0.32	$10.52	0.10%
SOTALOL HCL TAB 120MG	79	17	$985.08	$0.42	$12.47	0.04%
SOTALOL AF TAB 80MG	40	9	$393.34	$0.31	$9.83	0.02%
SOTALOL HCL TAB 160MG	38	8	$592.53	$0.50	$15.59	0.02%
SOTALOL AF TAB 120MG	12	1	$140.40	$0.39	$11.70	0.01%
TOTAL	**411**	**89**	**$4,657.09**	**$0.36**	**$11.33**	**0.19%**
MISCELLANEOUS COMBINATION PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
NO PRIOR AUTHORIZATION REQUIRED						
ATENOL/CHLOR TAB 50-25MG	376	111	$4,203.69	$0.23	$11.18	0.17%
BISOPRL/HCTZ TAB 5-6.25MG	322	72	$2,018.20	$0.14	$6.27	0.08%
ATENOL/CHLOR TAB 100-25MG	158	50	$2,548.10	$0.34	$16.13	0.10%
BISOPRL/HCTZ TAB 10/6.25	146	42	$906.17	$0.13	$6.21	0.04%
METOPRL/HCTZ TAB 50-25MG	132	26	$6,877.13	$1.25	$52.10	0.28%
BISOPRL/HCTZ TAB 2.5/6.25	102	27	$721.88	$0.15	$7.08	0.03%
BIDIL TAB	80	19	$19,149.84	$7.92	$239.37	0.77%
METOPRL/HCTZ TAB 100-25MG	78	23	$5,163.50	$1.41	$66.20	0.21%
DUTOPROL TAB 50-12.5	22	4	$2,241.91	$3.40	$101.91	0.09%
PROPRAN/HCTZ TAB 40/25	21	5	$867.90	$1.38	$41.33	0.04%
PROPRAN/HCTZ TAB 80/25	18	3	$1,281.61	$1.64	$71.20	0.05%
METOPRL/HCTZ TAB 100-50MG	16	2	$1,111.42	$1.54	$69.46	0.04%
DUTOPROL TAB 25-12.5	15	4	$1,298.11	$2.88	$86.54	0.05%
DUTOPROL TAB 100-12.5	12	6	$1,395.41	$3.32	$116.28	0.06%
HEMANGEOL SOL 4.28/ML	2	1	$839.02	$12.91	$419.51	0.03%
METHYLD/HCTZ TAB 250/25	1	1	$95.62	$3.19	$95.62	0.00%
TOTAL	**1,501**	**396**	**$50,719.51**	**$0.77**	**$33.79**	**2.05%**
GRAND TOTAL	**238,318**	**44,086***	**$2,478,669.17**	**$0.28**	**$10.40**	**100.00%**

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 03/2016. Last accessed 03/2016.

[2] Drugs@FDA: FDA Approved Drug Products. Available online at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.MonthlyApprovalsAll. Last accessed 03/2016.

[3] FDA News Release: FDA Approves New Drug to Treat Heart Failure. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm453845.htm. Issued 07/08/2015. Last accessed 03/22/2016.

[4] Novartis' New Heart Failure Medicine LCZ696, Now Called Entresto, Approved by FDA to Reduce Risk of Cardiovascular Death and Heart Failure Hospitalization. Novartis Pharmaceuticals. Available online at: https://www.novartis.com/news/media-releases/novartis-new-heart-failure-medicine-lcz696-now-called-entrestotm-approved-fda. Issued 07/07/2015. Last accessed 03/22/2016.

[5] Safety Labeling Changes Approved by FDA Center for Drug Evaluation and Research: Cardura XL (doxazosin mesylate) extended release tablets. Available online at: http://www.fda.gov/safety/medwatch/safetyinformation/ucm208679.htm. Issued 07/14/2015. Last accessed 03/22/2016.

[6] Positive Results Reported for Ixymyelocel-T in Heart Failure Trial. Managed Care. Available online at: http://www.managedcaremag.com/news/positive-results-reported-ixmyelocel-t-heart-failure-trial. Issued 03/10/2016. Last accessed 03/22/2016.

[7] The JNC 8 Hypertension Guidelines: An In-Depth Guide. Pharmacy Times. Available online at: http://www.pharmacytimes.com/news/the-jnc-8-hypertension-guidelines-an-in-depth-guide. Last revised 01/06/2014. Last accessed 03/2016.

[8] Entresto™ Product Information. Novartis Pharmaceuticals. Available online at: https://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf. Last revised 08/2015. Last accessed 03/2016.

[9] PL Detail-Document, New Drug: *Entresto* (Sacubitril/Valsartan). Pharmacist's Letter/Prescriber's Letter. September 2015.

Appendix M

Calendar Year 2015 Annual Review of Diabetic Supplies

Oklahoma Health Care Authority
April 2016

Current Prior Authorization Criteria

- As of April 1, 2015 pharmacies began submitting claims for diabetic testing supplies through the pharmacy point of sale (POS) system. Prior to April 1, 2015 claims were processed as durable medical equipment (DME).
- The preferred brands for SoonerCare members are OneTouch®, FreeStyle™, and Precision™ test strips and meters. Other brands of test strips and meters are not covered.
- In addition to test strips and meters, lancets, syringes, pen needles, and control solution are also covered in the pharmacy claims system. Supplies for insulin pumps remain DME claims.
- Meters are limited to one per member per year. Test strips are limited to 100 strips per 30 days for members using insulin and 100 strips per 90 days for members using oral medications. Members diagnosed with gestational diabetes are limited to 150 strips per 30 days.
- Diabetic supplies have a zero copay and do not count against the monthly prescription limit.
- An automated prior authorization process looks for insulin and other diabetic medications in the member's claims history. If the medication is not found in claims history or if the quantity submitted exceeds the maximum allowed, the claim will deny for prior authorization.
- Automated refills of diabetic supplies are not allowed. Refills should be ordered by the member or the member's representative.

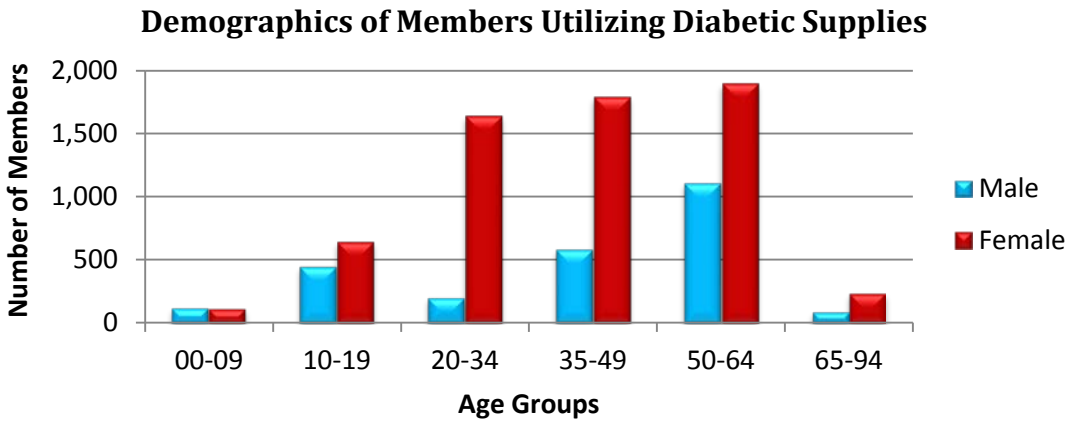
Utilization of Diabetic Supplies: Calendar Year 2015

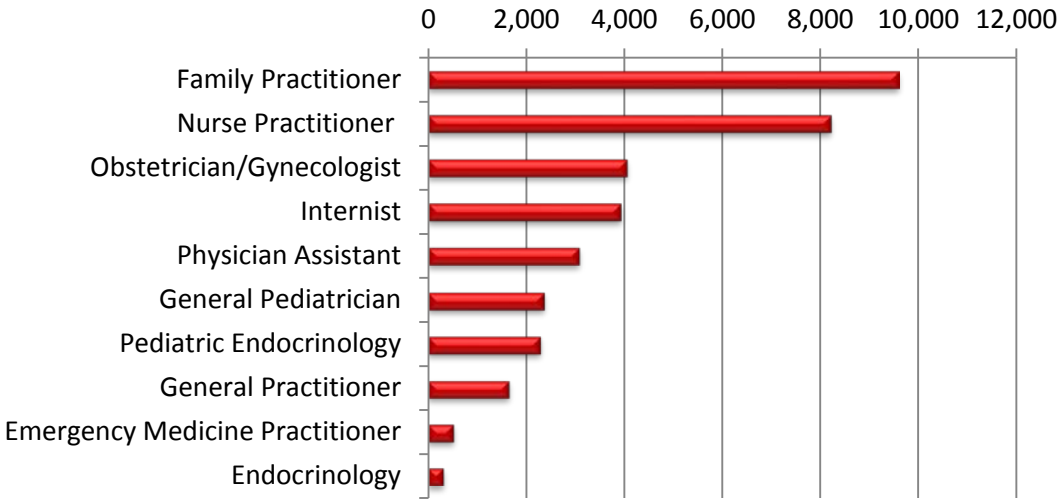
Diabetic Supplies: Calendar Year 2015

Diabetic supplies began processing as pharmacy claims on April 1, 2015. Therefore, there are no claims for 2014 and a comparison of calendar years is not available.

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	18,711	37,251	$3,137,452.63	$84.22	$2.27	3,846,365	1,384,140

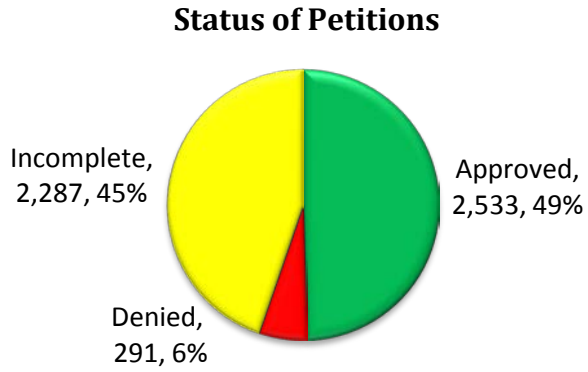
*Total number of members is not unduplicated.





Prior Authorization of Diabetic Supplies

There were 5,111 prior authorization requests submitted for diabetic supplies during calendar year 2015. Computer edits are in place to detect claims for diabetic medications and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



Market News and Updates[1]

The American Diabetes Association Standards of Medical Care in Diabetes 2016 was published in the January 2016 supplemental issue of *Diabetes Care*. As the publication indicates, diabetes is a complex, chronic illness that requires continuous medical care. Further, the publication states that two primary techniques are available for health providers and patients to assess the effectiveness of the management plan on glycemic control: patient self-monitoring of blood glucose (SMBG) and A1C. Major clinical trials of insulin-treated patients have included SMBG as part of the multifactorial interventions to demonstrate the benefit of intensive glycemic control on diabetes complications. SMBG is, therefore, a vital component of effective therapy. SMBG allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being achieved. Integrating SMBG results into diabetes management can be a useful tool for guiding medical nutrition therapy and physical activity, preventing hypoglycemia, and adjusting medications (particularly prandial insulin doses). Among patients with type-1 diabetes, there is a correlation between greater SMBG frequency and lower A1C. The patient's specific needs and goals should dictate SMBG frequency and timing. Additionally, the ongoing need for and frequency of SMBG should be reevaluated at each routine visit to avoid overuse. SMBG is especially important for insulin-treated patients to monitor for and prevent asymptomatic hypoglycemia and hyperglycemia.

Recommendations

The College of Pharmacy does not recommend any changes to the diabetic supplies coverage criteria at this time.

Utilization Details of Diabetic Supplies: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER	UNITS/ MEMBER
DIABETIC TEST STRIPS							
FREESTYLE LITE 100CT	8,980	3,424	$1,679,483.95	$5.16	$187.02	2.62	350.22
ONETOUCH ULTRA BLUE	8,124	3,117	$1,064,133.27	$3.26	$130.99	2.61	283.45
BAYER CONTOR NEXT	1,026	327	$30,961.22	$0.89	$30.18	3.14	486.54
PRECISION XTRA	664	207	$45,486.83	$2.18	$68.50	3.21	298.55
FREESTYLE	395	175	$64,820.73	$4.65	$164.10	2.26	291.71
FREESTYLE INSULINX 100CT	181	77	$35,132.58	$5.53	$194.10	2.35	306.49
EASYMAX	19	8	$520.50	$0.91	$27.39	2.38	312.50
FREESTYLE LITE 50CT	1,128	401	$25,027.51	$0.76	$22.19	2.81	297.43
FREESTYLE INSULINX 50CT	108	48	$18,294.41	$5.27	$169.39	2.25	258.33
SUBTOTAL	**20,625**	**7,784**	**$2,963,861.00**	**$3.87**	**$143.70**	**2.65**	**305.85**
GLUCOMETERS							
FREESTYLE LITE	1,858	1,850	$27,730.34	$0.52	$14.92	1.00	1.01
ONETOUCH ULTRA 2	1,493	1,486	$23,714.19	$0.46	$15.88	1.00	1.07
ONETOUCH ULTRA MINI	940	935	$15,105.48	$0.52	$16.07	1.01	1.17
PRECISION XTRA	90	83	$2,147.16	$0.74	$23.86	1.08	1.73
EASYMAX V SYSTEM	2	2	$75.00	$0.58	$37.50	1.00	1.00
FREEDOM FREESTYLE LITE	310	309	$4,596.47	$0.48	$14.83	1.00	1.01
FREESTYLE INSULINX	56	56	$2,116.00	$1.10	$37.79	1.00	1.00
SUBTOTAL	**4,749**	**4,721**	**$75,484.64**	**$0.51**	**$15.89**	**1.01**	**1.07**
LANCETS & LANCING DEVICES							
FREESTYLE LANCETS	3,227	1,715	$6,689.58	$0.05	$2.07	1.88	241.14
ONETOUCH LANCETS	1,727	1,019	$3,006.10	$0.04	$1.74	1.69	185.81
EASY TOUCH LANCETS	1,093	549	$1,821.54	$0.04	$1.67	1.99	209.11
TRUPLUS LANCETS 28G	541	327	$950.55	$0.04	$1.76	1.65	176.76
ONETOUCH US LANCETS	336	217	$614.37	$0.04	$1.83	1.55	178.82
TRUPLUS LANCETS 33G	325	192	$577.41	$0.04	$1.78	1.69	182.81
ONETOUCH LANCETS 30G	310	182	$530.17	$0.04	$1.71	1.7	182.97
TRUPLUS LANCENTS 30G	212	150	$367.63	$0.04	$1.73	1.41	149.87
MICROLET LANCETS	196	100	$428.81	$0.06	$2.19	1.96	270.00
FASTCLIX LANCETS	74	33	$184.99	$0.09	$2.50	2.24	342.73
ASSURE COMFORT 30G	73	45	$122.12	$0.04	$1.67	1.62	166.69
LANCING DEVICE	72	58	$673.88	$0.21	$9.36	1.24	4.66
BAYER MICROLET LANCETS	57	39	$72.90	$0.03	$1.28	1.46	128.64
UNILET GP LANCETS	46	23	$85.80	$0.03	$1.87	2	239.13
PRODIGY TWIST TOP	44	32	$77.55	$0.03	$1.76	1.38	146.88
TECHLITE LANCETS	21	10	$49.50	$0.04	$2.36	2.1	300.00
SOFTCLIX LANCETS	18	13	$34.65	$0.05	$1.93	1.38	161.54
TRUPLUS LANCETS 26G	16	11	$26.06	$0.04	$1.63	1.45	145.45
ACCU-CHEK MULTICLIX	11	6	$32.00	$0.10	$2.91	1.83	323.00
ONETOUCH LANCING DEV	9	9	$22.68	$0.08	$2.52	1	1.00
SURE COMFORT LANCETS	4	4	$8.25	$0.05	$2.06	1	125.00
ULTILET LANCETS	4	1	$6.60	$0.03	$1.65	4	400.00
LANCETS 28G	4	3	$5.12	$0.04	$1.28	1.33	243.33
BAYER MICRLT LANC DEV	2	2	$5.04	$0.16	$2.52	1	1.00
ONETOUCH LANC DEV	2	1	$3.30	$0.06	$1.65	2	200.00

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER	UNITS/ MEMBER
ULTRA THIN LANCET S 28G	2	2	$3.30	$0.07	$1.65	1	100.00
ULTRA THIN LANC ETS 30G	2	2	$3.30	$0.03	$1.65	1	100.00
SAFE-T-PRO MIS LANCETS	1	1	$3.30	$0.11	$3.30	1	200.00
ADV LANCING DEVICE	1	1	$2.52	$0.08	$2.52	1	1.00
ACCU-CHEK KIT FASTCLIX	1	1	$2.52	$0.08	$2.52	1	1.00
GLUCOLET 2 LANCING DEV	1	1	$2.52	$0.08	$2.52	1	1.00
ULTILET 26G	1	1	$1.65	$0.06	$1.65	1	100.00
ULTILET 28G	1	1	$1.65	$0.03	$1.65	1	100.00
LANCET SUPER 30G	1	1	$1.65	$0.07	$1.65	1	100.00
SUBTOTAL	**8,435**	**4,752**	**$16,419.01**	**$0.05**	**$1.95**	**1.96**	**205.78**
PEN NEEDLES							
NOVOFINE 30GX8MM	1,279	417	$36,223.68	$0.90	$28.32	3.07	334.53
NOVOFINE 32GX6MM	841	307	$27,065.02	$0.97	$32.18	2.74	350.42
PEN NEEDLES 31GX1/4"	69	24	$1,304.39	$0.63	$18.90	2.88	326.25
PEN NEEDLES 31GX5/16	62	25	$1,054.47	$0.50	$17.01	2.48	248.00
NOVOTWIST 32GX5MM	45	20	$1,544.46	$1.02	$34.32	2.25	310.00
NOVOFINE AUT 30GX8MM	24	14	$569.40	$0.58	$23.73	1.71	156.43
NOVOFINE PLS 32GX4MM	21	13	$701.16	$0.55	$33.39	1.62	206.92
PEN NEEDLES 31GX3/16	16	7	$442.00	$0.49	$27.63	2.29	242.86
PEN NEEDLES 31GX6MM	7	1	$130.13	$0.67	$18.59	7	700.00
PEN NEEDLES 29GX1/2"	6	3	$100.26	$0.84	$16.71	2	200.00
NOVOTWIST 30GX8MM	3	2	$130.00	$1.35	$43.33	1.5	250.00
PEN NEEDLE 29GX1/2"	1	1	$26.00	$0.87	$26.00	1	100.00
SUBTOTAL	**2,374**	**834**	**$69,290.97**	**$0.90**	**$29.19**	**2.85**	**330.68**
INSULIN SYRINGES							
INSULIN SYRG 0.5/31G	61	28	$1,107.91	$0.53	$18.16	2.18	188.93
INSULIN SYRG 1ML/31G	58	22	$1,282.60	$0.64	$22.11	2.64	280.00
INSULIN SYRG 0.3/31G	43	24	$1,048.89	$0.66	$24.39	1.79	205.42
INSULIN SYRG 0.5/30G	20	10	$464.28	$0.57	$23.21	2	210.00
INSULIN SYRG 1ML/30G	19	10	$534.03	$0.76	$28.11	1.9	247.00
INSULIN SYRG 0.3/30G	8	4	$194.04	$0.66	$24.26	2	225.00
INSULIN SYRG 1ML/28G	8	4	$141.52	$0.32	$17.69	2	200.00
INSULIN SYRG 0.5/29G	4	3	$48.00	$0.19	$12.00	1.33	133.33
ULTICARE SYG 0.5CC/29G	4	2	$36.76	$0.26	$9.19	2	200.00
INSULIN SYRG 0.5/28G	3	2	$64.68	$0.72	$21.56	1.5	150.00
INSULIN SYRG 0.3/29G	3	1	$63.36	$0.42	$21.12	3	300.00
ULTICARE SYG 1CC/29G	2	2	$18.38	$0.23	$9.19	1	100.00
INSULIN SYRG 0.3/29G	1	1	$14.46	$0.43	$14.46	1	100.00
SUBTOTAL	**234**	**113**	**$5,018.91**	**$0.58**	**$21.45**	**2.07**	**215.49**
GLUCOMETER CONTROL SOLUTION							
FREESTYLE LIQ NORMAL	45	43	$236.00	$0.16	$5.24	1.05	1.37
ONETOUCH SOL ULT CONT	40	40	$188.00	$0.15	$4.70	1	1.20
SUBTOTAL	**85**	**83**	**$424.00**	**$0.15**	**$4.99**	**1.02**	**1.29**
KETONE STRIPS							
KETOSTIX TEST STRIP	585	324	$4,589.78	$0.25	$7.85	1.81	123.30
KETOCARE TEST	132	79	$973.78	$0.24	$7.38	1.67	120.25
PRECISION XTRA (BLOOD)	17	8	$1,260.96	$5.48	$74.17	2.13	31.25
KETONE TEST STRIP	15	13	$129.58	$0.24	$8.64	1.15	84.62

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER	UNITS/ MEMBER
SUBTOTAL	749	424	$6,954.10	$0.30	$9.28	1.77	119.81
TOTAL	37,251	18,711	$3,137,452.63	$2.27	$84.22	1.99	205.57

*Total number of members is not unduplicated.
Costs do not reflect rebated prices or net costs.
Cost per claim may correspond to a member receiving several months of therapy in one claim.

[1] American Diabetes Association. Standards of Medical Care in Diabetes—2016. *Diabetes Care*. 2016; 39(suppl 1):S1-S106. Available online at: http://care.diabetesjournals.org/content/suppl/2015/12/21/39.Supplement_1.DC2/2016-Standards-of-Care.pdf. Last revised 1/2016. Last accessed 3/29/2016.

Appendix N

FDA & DEA Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: March 11th, 2016

FDA expands use of Xalkori to treat rare form of advanced non-small cell lung cancer

The U.S. Food and Drug Administration approved Xalkori (crizotinib) to treat people with advanced (metastatic) non-small cell lung cancer (NSCLC) whose tumors have an ROS-1 gene alteration. Xalkori is the first and only FDA approved treatment for patients with ROS-1 positive NSCLC.

Lung cancer is the leading cause of cancer-related deaths in the United States, with an estimated 221,200 new diagnoses and 158,040 deaths in 2015, according to the National Cancer Institute. ROS-1 gene alterations, thought to lead to abnormal cells, have been identified in various cancers, including NSCLC. ROS-1 gene alterations are present in approximately 1 percent of patients with NSCLC. The overall patient and disease characteristics of NSCLC with ROS-1 gene alterations appear similar to NSCLC with anaplastic lymphoma kinase (ALK) gene alterations, for which crizotinib use was previously approved. Xalkori was approved to treat certain patients with late-stage NSCLC that expresses an abnormal ALK gene in 2011. Xalkori is an oral medication that blocks the activity of the ROS-1 protein in tumors that have ROS-1 gene alterations. This effect on ROS-1 may prevent NSCLC from growing and spreading.

The safety and efficacy of Xalkori for the treatment of patients with ROS-1 positive tumors were evaluated in a multi-center, single-arm study of 50 patients with ROS-1 positive metastatic NSCLC. Patients received Xalkori twice daily to measure the drug's effect on their lung cancer tumors. The studies were designed to measure overall response rate, the percentage of patients who experienced complete or partial shrinkage of their tumors. Results showed 66 percent of participants experienced a complete or partial shrinkage of their NSCLC tumors, an effect that lasted a median of 18.3 months.

The safety results of this study were generally consistent with the safety profile of Xalkori evaluated in 1,669 patients with ALK-positive metastatic NSCLC.

The most common side effects of Xalkori are vision disorders, nausea, diarrhea, vomiting, swelling (edema), constipation, liver problems (elevated transaminases), fatigue, decreased appetite, upper respiratory infection, and dizziness and numbness or tingling in the hands or feet (neuropathy). Xalkori may cause serious side effects, including liver problems, life-threatening or fatal inflammation of the lungs, abnormal heartbeats and partial or complete loss of vision in one or both eyes.

The FDA granted the Xalkori expanded use application breakthrough therapy designation and priority review status. These are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions. Xalkori also received orphan drug designation, which provides incentives such as tax credits, user fee waivers and eligibility for exclusivity to assist and encourage the development of drugs for rare diseases.

Xalkori is marketed by Pfizer, based in New York, New York.

FDA NEWS RELEASE

For Immediate Release: March 21st, 2016

FDA approves new treatment for inhalation anthrax

On March 18, the U.S. Food and Drug Administration approved Anthim (obiltoxaximab) injection to treat inhalational anthrax in combination with appropriate antibacterial drugs. Anthim is also approved to prevent inhalational anthrax when alternative therapies are not available or not appropriate.

Inhalational anthrax is a rare disease that can occur after exposure to infected animals or contaminated animal products, or as a result of an intentional release of anthrax spores. It is caused by breathing in the spores of the bacterium Bacillus anthracis. When inhaled, the anthrax bacteria replicate in the body and produce toxins that can cause massive and irreversible tissue injury and death. Anthrax is a potential bioterrorism threat because the spores are resistant to destruction and can be spread by release in the air.

Anthim is a monoclonal antibody that neutralizes toxins produced by B. anthracis. Anthim was approved under the FDA's Animal Rule, which allows efficacy findings from adequate and well-controlled animal studies to support FDA approval when it is not feasible or ethical to conduct efficacy trials in humans. Anthim's effectiveness for treatment and prophylaxis of inhalational anthrax was demonstrated in studies conducted in animals based on survival at the end of the studies. More animals treated with Anthim lived

compared to animals treated with placebo. Anthim administered in combination with antibacterial drugs resulted in higher survival outcomes than antibacterial therapy alone.
The safety of Anthim was evaluated in 320 healthy human volunteers. The most frequently reported side effects were headache, itching (pruritus), upper respiratory tract infections, cough, nasal congestion, hives, and bruising, swelling and pain at the infusion site.
Anthim carries a Boxed Warning alerting patients and health care providers that the drug can cause allergic reactions (hypersensitivity), including a severe reaction called anaphylaxis. Anthim should be administered in settings where patients can be monitored and treated for anaphylaxis. However, given that anthrax is a very serious and often deadly condition, the benefit of Anthim for treating anthrax is expected to outweigh this risk.
Anthim was developed by Elusys Therapeutics, Inc. of Pine Brook, New Jersey, in conjunction with the U.S. Department of Health and Human Services' Biomedical Advanced Research and Development Authority.

FDA NEWS RELEASE

For Immediate Release: March 27th, 2016

FDA approves new psoriasis drug Taltz

The U.S. Food and Drug Administration approved Taltz (ixekizumab) to treat adults with moderate-to-severe plaque psoriasis.
Psoriasis is a skin condition that causes patches of skin redness and flaking. Psoriasis is an autoimmune disorder that occurs more commonly in patients with a family history of the disease, and most often begins in people between the ages of 15 and 35. The most common form of psoriasis is plaque psoriasis, in which patients develop thick, red skin with flaky, silver-white scales.
Taltz's active ingredient is an antibody (ixekizumab) that binds to a protein (interleukin (IL)-17A) that causes inflammation. By binding to the protein, ixekizumab is able to inhibit the inflammatory response that plays a role in the development of plaque psoriasis.
Taltz is administered as an injection. It is intended for patients who are candidates for systemic therapy, phototherapy or a combination of both.
Taltz's safety and efficacy were established in three randomized, placebo-controlled clinical trials with a total of 3,866 participants with plaque psoriasis who were candidates for systemic or phototherapy therapy. The results showed that Taltz achieved greater clinical response than placebo, with skin that was clear or almost clear, as assessed by scoring of the extent, nature and severity of psoriatic changes of the skin.
Because Taltz is a medicine that affects the immune system, it is being approved with a Medication Guide to inform patients that they may have a greater risk of an infection, or an allergic or autoimmune condition. Serious allergic reactions and development or worsening of inflammatory bowel disease have been reported with the use of Taltz. Monitor patients closely for these conditions. The most common side effects include upper respiratory infections, injection site reactions and fungal (tinea) infections.
Taltz is marketed by Indanapolis, Indiana-based Eli Lilly and Company.

FDA NEWS RELEASE

For Immediate Release: March 23rd, 2016

FDA approves Cinqair to treat severe asthma

The U.S. Food and Drug Administration approved Cinqair (reslizumab) for use with other asthma medicines for the maintenance treatment of severe asthma in patients aged 18 years and older. Cinqair is approved for patients who have a history of severe asthma attacksdespite receiving their current asthma medicines.
Asthma is a chronic disease that causes inflammation in the airways of the lungs. During an asthma attack, airways become narrow making it hard to breathe. Severe asthma attacks can lead to asthma-related hospitalizations because these attacks can be serious and even life-threatening. According to the Centers for Disease Control and Prevention, as of 2013, more than 22 million people in the U.S. have asthma, and there are more than 400,000 asthma-related hospitalizations each year.
Cinqair is administered once every four weeks via intravenous infusion by a health care professional in a clinical setting prepared to manage anaphylaxis. Cinqair is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in murine myeloma non-secreting 0 (NS0) cells. Cinqair reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.
The safety and efficacy of Cinqair were established in four double-blind, randomized, placebo-controlled trials in patients with severe asthma on currently available therapies. Cinqair or a placebo was administered to patients every four weeks as an add-on asthma treatment. Compared with placebo, patients with severe

asthma receiving Cinqair had fewer asthma attacks, and a longer time to the first attack. In addition, treatment with Cinqair resulted in a significant improvement in lung function, as measured by the volume of air exhaled by patients in one second.
Cinqair can cause serious side effects including allergic (hypersensitivity) reactions. These reactions can be life-threatening. The most common side effects in clinical trials for Cinqair included anaphylaxis, cancer, and muscle pain.
Cinqair is made by Teva Pharmaceuticals in Frazer, Pennsylvania.

Safety Announcements

FDA Drug Safety Communication: Sagent Pharmaceuticals Initiates a Nationwide Voluntary Recall of Fluconazole Injection, USP, (in 0.9% Sodium Chloride) 200mg per 100ml Due to the Discovery of an Out of Specification Impurity Result Detected During Routine Quality Testing of Stability Samples at the 18-Month Interval

[3-7-2016] SCHAUMBURG, IL – Sagent Pharmaceuticals, Inc. announced the voluntary nationwide recall of one lot of Fluconazole Injection, USP, (in 0.9% Sodium Chloride) 200mg per 100mL flexible container bag (NDC 25021-113-82) Lot 40608 manufactured by ACS Dobfar INFO S.A. and distributed by Sagent. Sagent has initiated this voluntary recall of Fluconazole Injection, USP, 200mg per 100mL to the user level due to the discovery of an out of specification impurity result detected during routine quality testing of stability samples at the 18-month interval. This impurity has been identified as Metronidazole. An elevated impurity has the potential to decrease effectiveness of the product in patients. Patients on the product and on concomitant medication of Metronidazole may receive an increased dose of Metronidazole.
Sagent is not aware of any adverse patient events resulting from the use of the subject product lot.
The lot number being recalled is Lot 40608 which was distributed to hospitals, wholesalers and distributors nationwide from November 2014 through December 2014. Fluconazole Injection, USP, 200mg per 100mL is indicated, for the treatment of Oropharyngeal and esophageal candidiasis, cryptococcal meningitis, and is supplied in 100mL and 200mL flexible container bags.
Customers are being notified by fax, email, FedEx, and/or certified mail that includes arrangements for return of all recalled product. Customers have been instructed to examine their inventory immediately and to quarantine, discontinue distribution of and return the recalled lot of product. Customers who may have further distributed this product have been requested to identify their customers and notify them at once of this product recall. The necessary form by which to document this information as well as other information regarding this recall is available at www.Sagentpharma.com.
Any questions about returning unused product should be directed to the customer call center at (866) 625-1618 M-F 8am-7pm CST. Healthcare workers who have medical questions about Fluconazole Injection, USP may contact Sagent Medical Affairs (866-625-1618, Option 3) M-F 8am-5pm CST.
Consumers should contact their physician or healthcare provider if they have experienced any problems that may be related to taking or using this product.
Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.
Complete and submit the report **Online:** www.fda.gov/medwatch/report.htm
Regular Mail or Fax: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178
This recall is being conducted with the knowledge of the U.S. Food and Drug Administration.
About Sagent Pharmaceuticals, Inc.
Sagent Pharmaceuticals, Inc., founded in 2006, is a specialty pharmaceutical company focused on developing, manufacturing, sourcing and marketing pharmaceutical products, with a specific emphasis on injectables.

Safety Announcements

FDA Drug Safety Communication: FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes

[3-22-2016] The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. We are requiring changes to the labels of all opioid drugs to warn about these risks.

- Opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity (see List of Serotonergic Medicines).
- Taking opioids may lead to a rare, but serious condition in which the adrenal glands do not produce adequate amounts of the hormone cortisol. Cortisol helps the body respond to stress.
- Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as reduced interest in sex, impotence, or infertility.

Opioids are a class of powerful narcotic pain medicines that are used to treat moderate to severe pain that may not respond well to other pain medicines (see List of Opioids). They can help manage pain when other treatments and medicines are not able to provide enough pain relief, but they also have serious risks including misuse and abuse, addiction, overdose, and death.

Safety Announcements

FDA Drug Safety Communication: FDA Alerts Healthcare Professionals About Clinical Trials with Zydelig (idelalisib) in Combination with other Cancer Medicines

[3-14-2016] The U.S. Food and Drug Administration is alerting health care professionals about reports of an increased rate of adverse events, including deaths, in clinical trials with the cancer medicine Zydelig (idelalisib) in combination with other cancer medicines.

Gilead Sciences, Inc. has confirmed that they are stopping six clinical trials in patients with chronic lymphocytic leukemia, small lymphocytic lymphoma and indolent non-Hodgkin lymphomas. The FDA is reviewing the findings of the clinical trials and will communicate new information as necessary.

Health care professionals should be aware that Zydelig is not approved for previously untreated chronic lymphocytic leukemia.

Zydelig is currently approved by the FDA for the treatment of:

- Relapsed chronic lymphocytic leukemia, in combination with rituximab, in patients for whom rituximab alone would be considered appropriate 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 small lymphocytic lymphoma in patients who have received at least two prior systemic therapies.

Patients should talk to their doctor if they have questions or concerns about Zydelig. The FDA urges health care professionals and patients to report adverse events involving Zydelig to the FDA MedWatch program.

Current Drug Shortages Index (as of April 5th, 2016):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Desmopressin Acetate Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***

Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Eptifibatide (Integrilin) Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigotindisulfonate Sodium (Indigo Carmine) Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
LifeCare PCA™ Sterile Empty Vial and Injector	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP, CII, (Preservative-Free)(For PCA Use Only)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***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***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sumatriptan (Imitrex) Nasal Spray	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tigecycline (Tygacil) Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Tretinoin Capsules	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***