Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
April 12, 2017
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 Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – April 12, 2017

DATE: April 1, 2017

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

State Fiscal Year (SFY) 2018 Appropriation Scenarios and Access to Care

Update on Medication Coverage Authorization Unit/Nonsteroidal Anti-Inflammatory Drug (NSAID) Safety Mailing Update – Appendix B

Action Item – Vote to Prior Authorize Spinraza™ (Nusinersen) – Appendix C

Action Item – Vote to Prior Authorize Zinbryta™ (Daclizumab) – Appendix D

Action Item – Vote to Prior Authorize Zinplava™ (Bezlotoxumab) – Appendix E

Action Item – Vote to Prior Authorize Hydroxyprogesterone Caproate Injection (Generic Delalutin®) – Appendix F

Action Item – Vote to Update Adempas® (Riociguat) Approval Criteria – Appendix G

Fiscal Year 2016 Annual Review of SoonerCare Pharmacy Benefit – Appendix H

Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Invokamet® XR (Canagliflozin/Metformin Extended-Release), Jentadueto® XR (Linagliptin/Metformin Extended-Release), Adlyxin® (Lixisenatide), Xultophy® 100/3.6 (Insulin Degludec/Liraglutide), Soliqua™ 100/33 (Insulin Glargine/Lixisenatide), Synjardy® XR (Empagliflozin/Metformin Extended-Release), and Qtern® (Dapagliflozin/Saxagliptin) – Appendix I

Annual Review of Ulcerative Colitis (UC) Medications and 30-Day Notice to Prior Authorize Giazo® (Balsalazide Disodium Tablets) – Appendix J

Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Byvalson™ (Nebivolol/Valsartan) and Qbrelis™ (Lisinopril Oral Solution) – Appendix K

Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Fosamax® (Alendronate 40mg Tablets) – Appendix L

Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) – Appendix M

Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications – Appendix N

Annual Review of Strensiq® (Asfotase Alfa) – Appendix O

FDA and DEA Updates – Appendix P

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – April 12, 2017 @ 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. Acknowledgement of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. March 8, 2017 DUR Minutes – Vote
B. March 8, 2017 DUR Recommendations Memorandum
C. Correspondence

Items to be presented by Carrie Evans, Tywanda Cox, Dr. Muchmore, Chairman:

4. State Fiscal Year (SFY) 2018 Appropriation Scenarios and Access to Care

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

5. Update on Medication Coverage Authorization Unit/Nonsteroidal Anti-Inflammatory Drug (NSAID) Safety Mailing Update – See Appendix B

A. Medication Coverage Activity for March 2017
B. Pharmacy Help Desk Activity for March 2017
C. Nonsteroidal Anti-Inflammatory Drug (NSAID) Safety Mailing Update

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

6. Action Item – Vote to Prior Authorize Spinraza™ (Nusinersen) – See Appendix C

A. Introduction
B. Motor Function Tests Used in Nusinersen Clinical Trials
C. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Zinbryta™ (Daclizumab) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Zinplava™ (Bezlotoxumab) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Hydroxyprogesterone Caproate Injection (Generic Delalutin®) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Update Adempas® (Riociguat) Approval Criteria – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

11. Fiscal Year 2016 Annual Review of SoonerCare Pharmacy Benefit – See Appendix H

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

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

12. Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Invokamet® XR (Canagliflozin/Metformin Extended-Release), Jentadueto® XR (Linagliptin/Metformin Extended-Release), Adlyxin® (Lixisenatide), Xultophy® 100/3.6 (Insulin Degludec/Liraglutide), Soliqua™ 100/33 (Insulin Glargine/Lixisenatide), Synjardy® XR (Empagliflozin/Metformin Extended-Release), and Qtern® (Dapagliflozin/Saxagliptin) – See Appendix I

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 Non-Insulin Diabetes Medications
H. Utilization Details of Insulin Medications

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

13. Annual Review of Ulcerative Colitis (UC) Medications and 30-Day Notice to Prior Authorize Giazo® (Balsalazide Disodium Tablets) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of UC Medications
C. Prior Authorization of UC Medications
D. Market News and Updates
E. Giazo® (Balsalazide) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of UC Medications

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

14. Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Byvalson™ (Nebivolol/Valsartan) and Qbrelis™ (Lisinopril Oral Solution) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Antihypertensive Medications
C. Prior Authorization of Antihypertensive Medications
D. Market News and Updates
E. Byvalson™ (Nebivolol/Valsartan) Product Summary
F. Qbrelis™ (Lisinopril Oral Solution) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Antihypertensive Medications

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

15. Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Fosamax® (Alendronate 40mg Tablets) – See Appendix L

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

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

16. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) – See Appendix M

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

Non-presentation; questions only:

17. Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications – See Appendix N

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

Non-presentation; questions only:

18. Annual Review of Strensiq® (Asfotase Alfa) – See Appendix O

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Strensiq® (Asfotase Alfa)
D. Prior Authorization of Strensiq® (Asfotase Alfa)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

19. FDA and DEA Updates – See Appendix P

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

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

A. Bowel Preparation Medications
B. Lung Cancer Medications
C. Gauchers Disease Medications
D. Alpha-1 Proteinase Inhibitors
E. Botulinum Toxins
F. Gonadotropin Releasing Hormone Medications
G. Elaprase® (Idursulfase)
H. Antiparasitic Medications
I. Lumizyme® (Alglucosidase Alfa)

**Future business subject to change.*

21. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MARCH 8, 2017

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	
Lee Munoz, Pharm.D.		x
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
Bruna Varalli-Claypool, MHS, PA-C	x	
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	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow	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
Corby Thompson, Pharm.D.	x	
Visiting Pharmacy Student(s):		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Deputy State Medicaid Director	x	
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	x	
Kelli Brodersen, Marketing Coordinator	x	
Michael Herndon, D.O.; 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; CEO	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:		
Pam Sardo, Avanir	Matt Forney, Merck	Denise Hill, Astellas
Deron Grothe, Teva	Quynhchau Doan, AbbVie	Bob Atkins, Biogen
Tony Locke, Tris Pharma	Jim Dunlap, PhRMA	Scott Sabrsula, ZS Pharma
Kari Suttee, Novartis	Mai Duong, Novartis	Monique Lambring, Intersect ENT
Charlie Collins, Genzyme	Doug Wood, ViiV Healthcare	Stacie Cadle, Acorda
Mark DeClark, Lilly	Kelli Fancher, Acorda	Shelby Foral, Acorda
Brandon Ross, Merck	Maria Agapova, Teva	Jodi Jensen, Biogen

PRESENT FOR PUBLIC COMMENT:	
Brandon Ross	Merck
Pam Sardo	Avanir
Maria Agapova	Teva
Quynhchau Doan	AbbVie
Jodi Jensen	Biogen
Mai Duong	Novartis

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. 9 SPEAKER: PAM SARDO
2B: AGENDA NO. 11 SPEAKER: JODI JENSON
2C: AGENDA NO. 13 SPEAKER: MARIA AGAPOVA
2D: AGENDA NO. 13 SPEAKER: QUYNH CHAN DOAN
2E: AGENDA NO. 13 SPEAKER: MAI DUONG
2F: AGENDA NO. 16 SPEAKER: BRANDON ROSS

ACTION: NONE REQUIRED

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

3A: FEBURARY 8, 2017 DUR MINUTES – VOTE
3B: FEBURARY 8, 2017 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran
Dr. Preslar moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2017
4B: PHARMACY HELP DESK ACTIVITY FOR FEBRUARY 2017
4C: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE NUPLAZID™ (PIMAVANSERIN)**

5A: INTRODUCTION
5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Hardzog-Britt moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE VELTASSA® (PATIROMER)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Preslar moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE KANUMA® (SEBELIPASE ALFA)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott
Dr. Harrell moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE PICATO® (INGENOL MEBUTATE 0.015% AND 0.05% GEL)

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott
Dr. Hardzog-Britt moved to approve; seconded by Dr. Winegardner

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE ONZETRA® XSAIL® (SUMATRIPTAN NASAL POWDER) AND ZEMBRACE™ SYMTOUCH™ (SUMATRIPTAN INJECTION)

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Winegardner moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE BRIVIACT® (BRIVARACETAM), FYCOMPA™ (PERAMPANEL ORAL SUSPENSION), AND CARNEXIV™ (CARBAMAZEPINE INJECTION)

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Dr. Hardzog-Britt moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE SPINRAZA™ (NUSINERSEN)

11A: SPINAL MUSCULAR ATROPHY

11B: MARKET NEWS AND UPDATES

11C: SPINRAZA™ (NUSINERSEN) PRODUCT SUMMARY

11D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott
Dr. Winegardner recommended "add to exclude vent patients to criteria."
Dr. Preslar recommended "encourage physician to attend April meeting."

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF PULMONARY HYPERTENSION MEDICATIONS

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF PULMONARY HYPERTENSION MEDICATIONS

12C: PRIOR AUTHORIZATION OF PULMONARY HYPERTENSION MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 13: ANNUAL REVIEW OF MULTIPLE SCLEROSIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZINBRYTA™ (DACLIZUMAB)
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF MULTIPLE SCLEROSIS MEDICATIONS
13C: PRIOR AUTHORIZATION OF MULTIPLE SCLEROSIS MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: ZINBRYTA™ (DACLIZUMAB) PRODUCT SUMMARY
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF MULTIPLE SCLEROSIS MEDICATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF MAKENA® AND VAGINAL PROGESTERONE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE HYDROXYPROGESTERONE CAPROATE INJECTION
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF MAKENA® AND VAGINAL PROGESTERONE PRODUCTS
14C: PRIOR AUTHORIZATION OF MAKENA® AND VAGINAL PROGESTERONE PRODUCTS
14D: MARKET NEWS AND UPDATES
14E: HYDROXYPROGESTERONE CAPROATE PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF MAKENA® AND VAGINAL PROGESTERONE PRODUCTS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF NALOXONE MEDICATIONS
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF NALOXONE MEDICATIONS
15C: PRIOR AUTHORIZATION OF NALOXONE MEDICATIONS
15D: NALOXONE STATISTICS AND TRENDS
15E: MARKET NEWS AND UPDATES
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF NALOXONE MEDICATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: 30-DAY NOTICE TO PRIOR AUTHORIZE ZINPLAVA™ (BEZLOTOXUMAB)
16A: INTRODUCTION
16B: ZINPLAVA™ (BEZLOTOXUMAB) PRODUCT SUMMARY
16C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
18A: DIABETIC MEDICATIONS
18B: ANTIHYPERTENSIVE MEDICATIONS

18C: GRANULOCYTE-COLONY STIMULATING FACTORS (G-CSFS)
18D: OSTEOPOROSIS MEDICATIONS
18E: STRENSIQ® (ASFOTASE ALFA)
18F: HEMOPHILIA MEDICATIONS
18G: IDIOPATHIC PULMONARY FIBROSIS MEDICATIONS
18H: ALPHA1-PROTEINASE INHIBITORS
Future business subject to change.
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: ADJOURNMENT
The meeting was adjourned at 5:14 pm.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: March 9, 2017

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

From: Melissa Abbott, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of March 8, 2017

Recommendation 1: FDA Safety Alerts

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Nuplazid™ (Pimavanserin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Nuplazid™ (pimavanserin) with the following criteria:

Nuplazid™ (Pimavanserin) Approval Criteria:

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease psychosis; and
2. Member must have concomitant diagnosis of Parkinson's disease; and
3. Nuplazid™ will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis; and
4. Initial approvals will be for the duration of three months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication.
5. A quantity limit of two tablets daily will apply.

Recommendation 3: Vote to Prior Authorize Veltassa® (Patiromer)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Veltassa® (patiromer) with the following criteria:

Veltassa® (Patiromer) Approval Criteria:

1. An FDA approved diagnosis of hyperkalemia; and
2. A trial of a potassium-eliminating diuretic or documentation why a diuretic is not appropriate for the member; and
3. Documentation of a low potassium diet; and
4. A patient-specific, clinically significant reason why member cannot use sodium polystyrene sulfonate powder which is available without a prior authorization; and
5. A quantity limit of 30 packets per month will apply.

Recommendation 4: Vote to Prior Authorize Kanuma® (Sebelipase Alfa)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Kanuma® (sebelipase alfa) with the following criteria:

Kanuma® (Sebelipase Alfa) Approval Criteria:

1. An FDA approved diagnosis of Lysosomal Acid Lipase (LAL) deficiency; and
2. Kanuma® (sebelipase alfa) must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Recommendation 5: Vote to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Picato® (ingenol mebutate gel) with the following criteria:

Picato® (Ingenol Mebutate Gel) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK); and
2. Member must be 18 years of age or older; and
3. 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. Size of each lesion being treated; and
    c. Location of lesions being treated; and

4. Approval quantity and length will be based on patient-specific information provided, in accordance with Picato® prescribing information and FDA approved dosing regimen.

Recommendation 6: Vote to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Onzetra® Xsail® and Zembrace™ SymTouch™ into the Special Prior Authorization (PA) Tier of the Anti-Migraine Medications Product Based Prior Authorization (PBPA) category with the following criteria, shown in red. Additionally, for Onzetra® Xsail®, a quantity limit of eight doses (one kit containing 16 nosepieces) per 30 days will apply based on the prescribing information and recommended dosing. For Zembrace™ SymTouch™, a quantity limit of eight doses (two cartons) per 30 days will apply to be consistent with the other sumatriptan injectable products' quantity limits.

Anti-Migraine Medications Tier-2 Approval Criteria:

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

Anti-Migraine Medications Tier-3 Approval Criteria:

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

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zecuity®, Onzetra® Xsail®, and Zembrace™ SymTouch™ will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual ingredients separately or lower-tiered triptan medications.
4. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
5. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications and dihydroergotamine injection (D.H.E. 45®).

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan (Relpax®)	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)		zolmitriptan nasal spray (Zomig®)	sumatriptan injection (Imitrex®)
			sumatriptan injection (Sumavel® DosePro®)
			sumatriptan injection (Zembrace™ SymTouch™)*
			sumatriptan nasal powder (Onzetra® Xsail®)*
			sumatriptan nasal spray (Imitrex®)
			sumatriptan transdermal (Zecuity®)*
			sumatriptan/naproxen (Treximet®)

*Requires a clinically significant reason why member cannot use all other available formulations of sumatriptan.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendation 7: Vote to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the current criteria for Sabril® (vigabatrin) to include the new, modified REMS program, and recommends the prior authorization of Briviact® (brivaracetam), Fycompa™ (perampanel oral suspension), and Carnexiv™ (carbamazepine injection) with the following criteria:

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of refractory complex seizures in adults and pediatric patients 10 years or older, or infantile spasms in children ages 1 month to 2 years of age; and
2. Members with refractory complex seizures must have previous trials of at least three other antiepileptic medications; or
3. Members with infantile spasms must have had a previous trial with adrenocorticotropic hormone (ACTH) or have a diagnosis of infantile spasms with tuberous sclerosis; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the ~~SHARE~~ SABRIL REMS program and maintain enrollment throughout therapy.

Briviact® (Brivaracetam) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment 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 Briviact® and who have a seizure diagnosis will be grandfathered.
5. Approval length for Briviact® injection will be for a maximum of seven days of therapy. Further approval may be granted if prescriber documents an ongoing need for Briviact® intravenous (IV) therapy over oral Briviact® formulations.

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. (*Fycompa™ has currently provided a supplemental rebate to require a trial with one other medication; however, Fycompa™ will follow the original criteria and require trials with three other medications if the manufacturer chooses not to participate in supplemental rebates.)
4. For Fycompa™ oral suspension, a patient-specific, clinically significant reason why Fycompa™ oral tablets cannot be used.
5. Members currently stable on Fycompa™ and who have a seizure diagnosis will be grandfathered.

Carnexiv™ (Carbamazepine Injection) Approval Criteria:

1. An FDA approved indication; and
2. Initial prescription must be written by a neurologist; and
3. Member must currently be stable on oral carbamazepine; and
4. Member must have a current condition in which oral administration is temporarily not feasible and needing Carnexiv™ for replacement therapy; and
5. Approval length will be for a maximum of seven days of therapy. Further approval may be granted if prescriber documents an ongoing need for Carnexiv™ intravenous (IV) therapy over oral carbamazepine formulations.

Recommendation 8: 30-Day Notice to Prior Authorize Spinraza™ (Nusinersen)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Pulmonary Hypertension Medications

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Zinbryta™ (Daclizumab)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Makena® (Hydroxyprogesterone Caproate) and Vaginal Progesterone Products and 30-Day Notice to Prior Authorize Hydroxyprogesterone Caproate Injection

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Naloxone Medications

NO ACTION REQUIRED.

The College of Pharmacy recommends sending an educational mailing or fax to prescribers of members who receive opioids. The purpose of the mailing would be to encourage prescribers to educate members on the risks of opioids and the potential life-saving role of naloxone. Additionally, the mailing would include the naloxone medications available without prior authorization.

Recommendation 13: 30-Day Notice to Prior Authorize Zinplava™ (Bezlotoxumab)

NO ACTION REQUIRED.

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

March 31, 2017

FROM: Robert Katz, M.D.
Clinical Professor Pediatric/Pulmonary
OUHSC/Children's Hospital

RE: Approval for nusinersen (Spinraza) for patients with Spinal Muscle Atrophy (SMA)

SMA (spinal muscular atrophy) is a disease that robs people of physical strength by affecting the motor nerve cells in the spinal cord, taking away the ability to walk, eat, or breathe. Individuals with SMA have difficulty performing the basic functions of life, like breathing and swallowing. However, SMA does not affect a person's ability to think, learn, and build relationships with others. It is the number one genetic cause of death for infants. SMA affects approximately 1 in 10,000 babies, and about 1 in every 50 Americans is a genetic carrier. SMA can affect any race or gender. There are four primary types of SMA—I, II, III, and IV—based on age of onset and highest physical milestone achieved.

SMA is caused by a mutation in the survival motor neuron gene 1 (*SMN1*). In a healthy person, this gene produces a protein—called survival motor neuron protein or SMN protein—that is critical to the function of the nerves that control our muscles. Without it, those nerve cells cannot properly function and eventually die, leading to debilitating and often fatal muscle weakness.

All patients with SMA have at least one copy of survival motor neuron gene 2 (*SMN2*), often referred to as the SMA "backup gene." Due to a splicing error, most of the SMN protein made by *SMN2* is missing an important piece, called exon 7. Antisense drugs are small snippets of synthetic genetic material that bind to ribonucleic acid (RNA), so they can be used to fix splicing errors in genes such as *SMN2*. Nusinersen is antisense oligonucleotide that targets *SMN2*, causing it to make more complete SMN protein.

In December 2016 the FDA approved nusinersen for patients with all types of SMA. Spinraza is antisense oligonucleotide that targets *SMN2*, causing it to make more complete SMN protein. The clinical trial involving SMA-1 patients was stopped earlier than planned due to the positive effects of the drug. Open label studies have confirmed the effectiveness of the drug. Based on my review of the available literature there is little doubt in my mind that the drug can have a positive effect on many patients with SMA. The results of treatment can have a profound impact on the quality of life of these patients and their families.

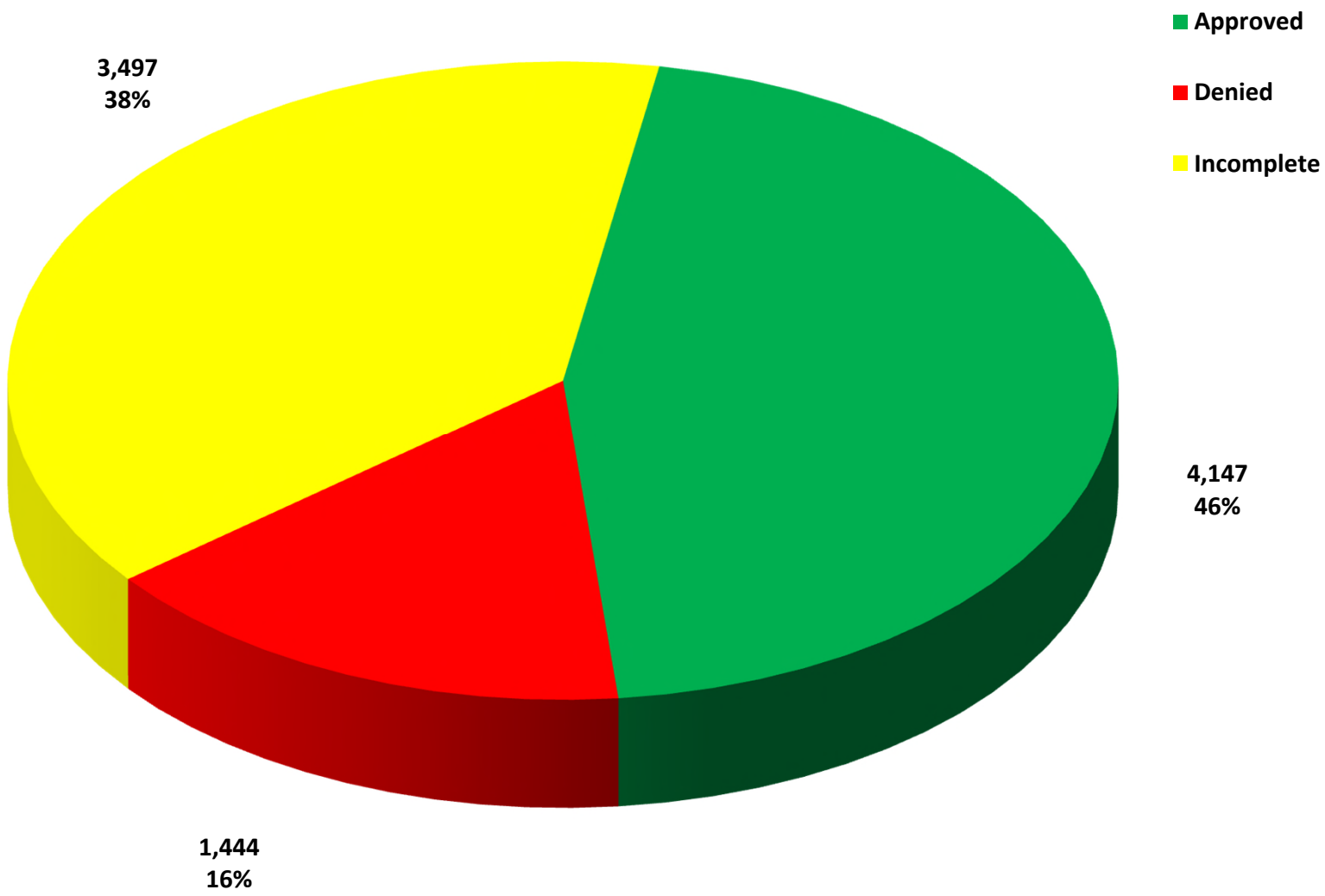
I would urge the Pharmacy Committee to approve the use of this medication for patients who are provided health benefits by the Oklahoma Health Care Authority. Based on the results available in the literature I think that all patients with SMA; including those on continuous ventilator support should be eligible to receive this medication. Due to the complexity, logistics

and the cost of the medication I certainly agree that the drug should be administered as part of a program where the outcomes are objectively monitored and that these results be used for continued coverage of the medication in individual patients. We are in the process of organizing such a program. I have also talked to and met with Jennifer Norman, M.D. who follows and manages many patients with SMA.

I apologize for being unable to attend this important meet but I am happy to answer any questions or concerns that the members of the committee may have for me. Thanks for your time and consideration of this important decision.

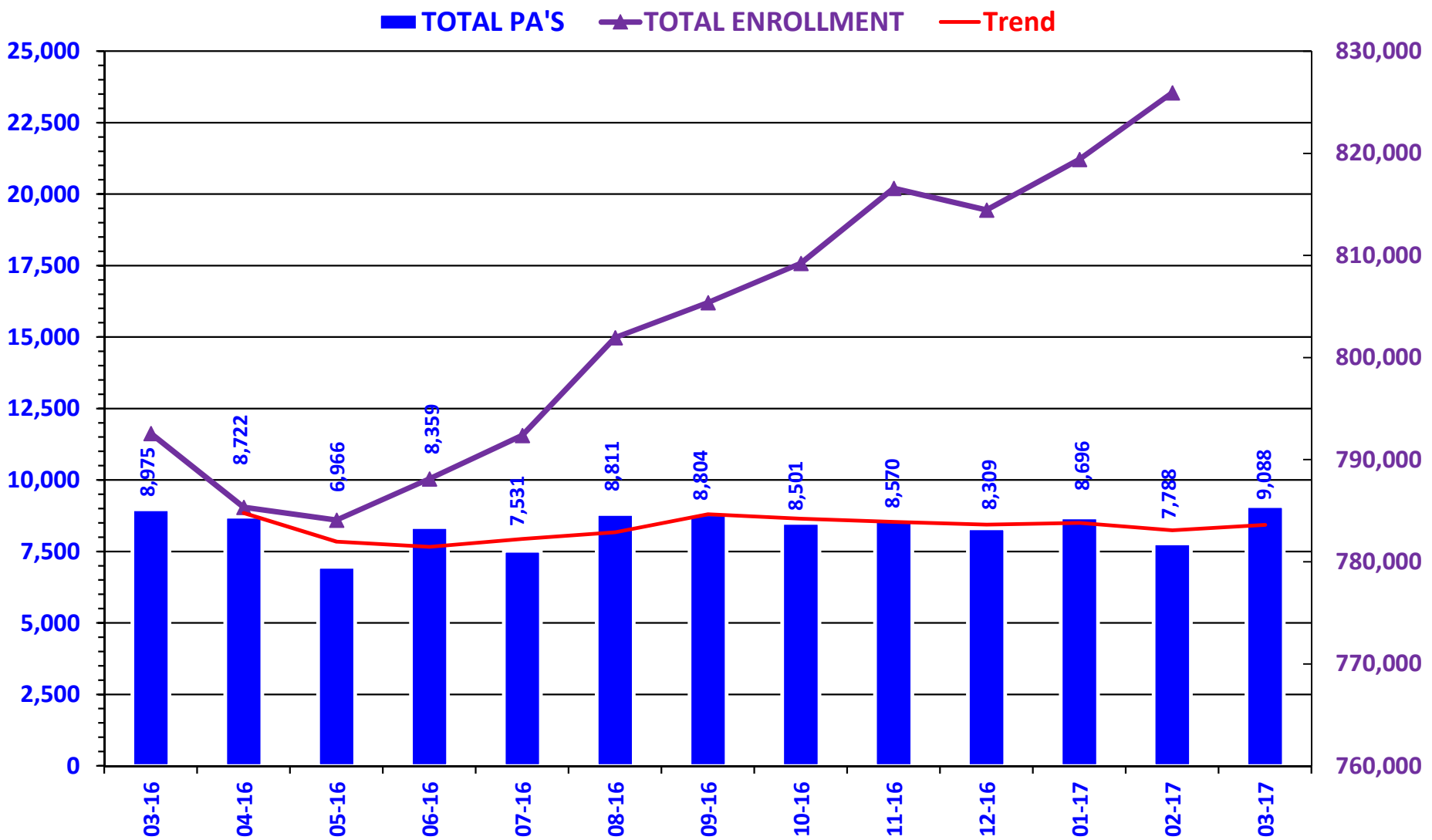
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH 2017



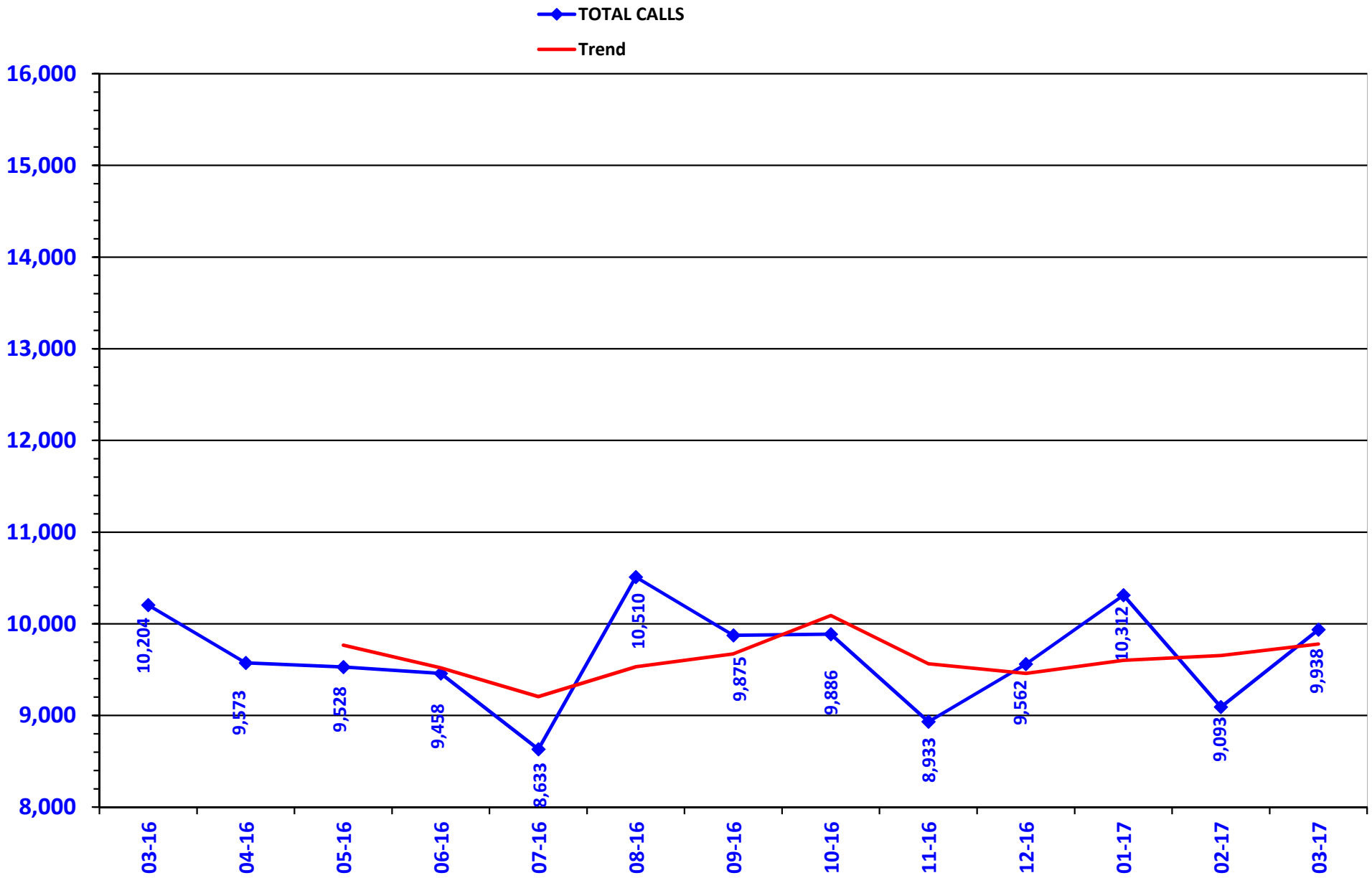
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MARCH 2016 – MARCH 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MARCH 2016 – MARCH 2017



Prior Authorization Activity
3/1/2017 Through 3/31/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	160	16	38	106	341
Analgesic - NonNarcotic	20	0	5	15	0
Analgesic, Narcotic	492	269	51	172	159
Angiotensin Receptor Antagonist	19	4	7	8	357
Antiasthma	48	8	14	26	323
Antibiotic	28	10	4	14	226
Anticonvulsant	150	52	21	77	329
Antidepressant	107	19	28	60	349
Antidiabetic	251	87	49	115	351
Antihistamine	262	221	9	32	356
Antimigraine	51	5	21	25	157
Antineoplastic	43	27	2	14	181
Antiulcers	167	31	49	87	202
Antiviral	92	47	17	28	11
Anxiolytic	51	27	2	22	272
Atypical Antipsychotics	239	123	23	93	324
Biologics	120	72	21	27	305
Bladder Control	49	15	10	24	347
Blood Thinners	213	128	17	68	323
Botox	24	15	7	2	316
Buprenorphine Medications	307	228	12	67	73
Cardiovascular	119	56	17	46	308
Cephalosporins	15	11	0	4	7
Chronic Obstructive Pulmonary Disease	222	22	56	144	288
Constipation/Diarrhea Medications	140	20	49	71	177
Contraceptive	10	9	1	0	283
Dermatological	126	21	64	41	143
Diabetic Supplies	603	310	31	262	195
Endocrine & Metabolic Drugs	88	56	3	29	129
Erythropoietin Stimulating Agents	19	13	3	3	111
Fibromyalgia	202	36	94	72	312
Fish Oils	27	0	13	14	0
Gastrointestinal Agents	118	25	25	68	124
Genitourinary Agents	17	7	4	6	198
Growth Hormones	99	78	5	16	148
Hematopoietic Agents	17	8	2	7	127
Hepatitis C	90	41	20	29	8
HFA Rescue Inhalers	69	13	11	45	321
Insomnia	37	4	13	20	180
Insulin	77	23	20	34	342
Miscellaneous Antibiotics	23	1	7	15	15
Multiple Sclerosis	80	25	18	37	127
Muscle Relaxant	61	16	18	27	84
Nasal Allergy	88	9	26	53	202
Neurological Agents	41	27	6	8	345
NSAIDs	213	17	77	119	226
Ocular Allergy	64	11	14	39	141
Ophthalmic Anti-infectives	11	3	4	4	37
Osteoporosis	22	8	5	9	328
Other*	348	69	84	195	254

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Otic Antibiotic	19	3	3	13	8
Passive Immunizing Agents	10	6	0	4	300
Respiratory Agents	21	8	2	11	175
Statins	86	15	19	52	359
Stimulant	899	429	106	364	340
Synagis	72	36	18	18	38
Testosterone	73	18	29	26	328
Topical Antifungal	56	2	10	44	68
Topical Corticosteroids	187	6	62	119	255
Vitamin	76	22	26	28	292
Pharmacotherapy	90	75	0	15	305
Emergency PAs	0	0	0	0	
Total	**7,528**	**2,963**	**1,372**	**3,193**	
Overrides					
Brand	45	27	6	12	284
Cumulative Early Refill	7	6	0	1	180
Diabetic Supplies	14	9	0	5	133
Dosage Change	362	342	0	20	12
High Dose	5	2	0	3	358
Ingredient Duplication	30	20	1	9	11
Lost/Broken Rx	85	79	0	6	13
NDC vs Age	242	156	16	70	260
Nursing Home Issue	78	69	3	6	12
Opioid Quantity	14	11	2	1	146
Other*	33	26	2	5	8
Quantity vs. Days Supply	611	413	39	159	254
STBS/STBSM	17	10	1	6	55
Stolen	15	12	1	2	20
Temporary Unlock	5	4	1	0	17
Third Brand Request	32	24	2	6	22
Overrides Total	**1,560**	**1,184**	**72**	**304**	
Total Regular PAs + Overrides	**9,088**	**4,147**	**1,444**	**3,497**	

Denial Reasons	
Unable to verify required trials.	2,672
Does not meet established criteria.	1,475
Lack required information to process request.	793

Other PA Activity	
Duplicate Requests	
Letters	7,730
No Process	
Changes to existing PAs	700
Helpdesk Initiated Prior Authorizations	760
PAs Missing Information	59

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

Nonsteroidal Anti-Inflammatory Drug (NSAID) Safety Mailing Update

Oklahoma Health Care Authority
April 2017

U.S. Food and Drug Administration (FDA) Safety Communication[1]

In July 2015, the U.S. Food and Drug Administration (FDA) strengthened existing label warnings for non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) regarding the increased risk of heart attack and stroke in patients using these medications. The warnings were strengthened after the FDA reviewed a variety of safety information including "observational studies and a combined analysis of clinical trials." Based on the FDA's review, prescription and over-the-counter (OTC) NSAID labels were updated to indicate the following:

- The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID and may increase with longer use and higher NSAID doses.
- It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient to determine that the risk of any particular NSAID is higher or lower than that of any other particular NSAID.
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease.
- In general, patients with heart disease or risk factors for heart disease have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.
- There is an increased risk of heart failure with NSAID use.

Prescriber Mailing Summary[1,2]

In May 2016, the College of Pharmacy and Oklahoma Health Care Authority sent an educational letter to 210 non-specialist prescribers of 272 patients who had at least a 90 day supply of NSAIDs and at least one cardiovascular risk factor. The time frame of analysis was October 1, 2015 to April 30, 2016 and the following cardiovascular risk factors were included in the analysis: smoking, diagnosis of hypertension, diagnosis of diabetes, elevated weight diagnosis, history of myocardial infarction, and diagnosis of cardiovascular disease. It is important to note that OTC medications were not included in this analysis as OTC NSAIDs are not covered by SoonerCare and are therefore not captured in a member's pharmacy claim history.

Prescribers were notified of the strengthened warnings regarding non-aspirin NSAIDs associated with heart attacks and strokes including the risk associated with early therapy, high NSAID doses, and for those with and without heart disease or risk factors for heart disease.

Prescribers were encouraged to educate patients to read all labels and accompanying literature for all medications and consider use of non-pharmacological treatment modalities (e.g., physical therapy, weight loss, massage) or acetaminophen, for otherwise healthy patients.

NSAID Safety Mailing Results

The mailing was sent to 210 prescribers of 272 chronic NSAID users with at least one cardiovascular risk factor. Of the 272 patients 54.41% had more than one cardiovascular risk factor. The majority of patients included had either hypertension (70.59%) or diabetes (43.75%); only 1.84% had a history of myocardial infarction. The most commonly used NSAID was meloxicam (88.97% of members).

The post-analysis of the mailing reviewed claims from June 1, 2016 to December 31, 2016. Results found 202 non-specialist prescribers of 273 chronic NSAID users with at least one cardiovascular risk factor. Of the 273 patients, 50.92% had more than one risk factor; this resulted in a 3.49% drop in chronic NSAID use in SoonerCare members with multiple cardiovascular risk factors. The majority of prescribers included in the mailing [n = 147 (70%)] no longer had patients included in the post-mailing analysis. The risk factor break down among chronic NSAID users in the post-mailing analysis was similar to the breakdown prior to the mailing and the most commonly used NSAID remained meloxicam (89.38% of members).

Conclusions[3]

Analysis of the NSAID safety mailing revealed a decrease in the number of members with multiple risk factors receiving chronic NSAID therapy. Additionally, the majority of prescribers who received an educational letter no longer had members with a cardiovascular risk factor receiving chronic NSAID therapy in the post-mailing analysis. While these results are promising, they may have been confounded by the March 2016 Centers for Disease Control and Prevention (CDC) guidelines for primary care clinicians who are prescribing opioids for chronic pain. The guidelines outlined twelve recommendations including the preference for nonopioid therapy such as NSAIDs for the treatment of chronic pain. This recommendation may result in more providers prescribing NSAIDs, after a risk-benefit analysis, in order to avoid prescribing opioid analgesics.

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[1] U.S. Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes. Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm451800.htm. Issued 07/09/2015. Last accessed 03/27/2017.

[2] Harvard Health Publications. Heart-safer NSAID alternatives. Harvard Men's Health Watch. Available online at: http://www.health.harvard.edu/heart-health/heart-safer-nsaid-alternatives. Issued 11/2015. Last accessed 03/27/2017.

[3] Centers for Disease Control and Prevention (CDC). CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. *Recommendations and Reports.* March 2016: 65(1); 1-49.

Appendix C

Vote to Prior Authorize Spinraza™ (Nusinersen)

Oklahoma Health Care Authority
April 2017

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

Spinal muscular atrophy (SMA) is a rare, neuromuscular disease characterized by degeneration of spinal cord motor neurons, which results in progressive muscular atrophy and weakness. The incidence of SMA ranges from 4 to 10 per 100,000 live births and a carrier frequency of approximately 1 in 50. SMA is the most common genetic cause of death in infants. Its inheritance pattern is autosomal recessive, resulting from deletions or mutations involving the survival motor neuron gene 1 (*SMN1*). SMA can either occur at birth or there can be an asymptomatic phase following birth. The asymptomatic phase for these patients can last for a variable length of time but is usually correlated with severity of disease, with earlier symptom onset correlating to more severe disease. Infants with the most severe form of SMA die within a few weeks after birth. SMA has been categorized into five subtypes based on age of symptom onset and motor function achieved: Type 0 (prenatal), Type I (severe, also known as infantile-onset or Werdnig-Hoffmann disease), Type II (intermediate), Type III (mild, also known as juvenile SMA or Kugelberg-Welander disease), and Type IV (adult onset).

- Type 0 SMA is the most severe form, and the first symptom is typically reduced fetal movement. The average life span is two to six months and, after birth, newborns may have little movement and have difficulty with swallowing and breathing.
- Type I SMA is a severe form that may be apparent at birth or within the first few months of life and features may include difficulty breathing or swallowing and inability to sit without support. Pulmonary disease secondary to neuromuscular weakness is the major cause of morbidity and mortality. With minimal or no respiratory support, the life span of patients with Type I SMA is usually less than two years.
- Type II SMA typically becomes apparent between 6 and 12 months of age. Children with Type II SMA may sit without support; however, they cannot stand or walk unaided. The primary cause of morbidity and mortality is pulmonary disease. Approximately 70% of patients with Type II SMA live to be at least 25 years of age.
- Type III SMA is a milder form of the disease and symptoms typically appear between early childhood and early adulthood. Individuals with Type III SMA are able to stand and walk without help; however, they usually lose this ability later in life. The life expectancy for Type III SMA is near normal.
- Type IV SMA occurs in adulthood, usually after age 30, and patients with Type IV SMA have a normal life expectancy. Symptoms of adult-onset SMA are usually mild-to-moderate and include muscle twitching, tremor, or weakness.

Treatment for SMA has been mainly supportive and directed at providing nutrition and respiratory assistance as needed, as well as treating or preventing complications of weakness. Spinraza™ (nusinersen) was approved by the U.S. Food and Drug Administration (FDA) for the

treatment of spinal muscular atrophy (SMA) in December 2016. It is the first drug approved for the treatment of SMA in pediatric and adult patients. Nusinersen is administered via an intrathecal injection and the recommended dosage is 12mg (5mL) per administration. Treatment is initiated with four loading doses; the first three loading doses should be administered at 14-day intervals; the fourth loading dose should be administered 30 days after the third dose; a maintenance dose should be administered once every four months thereafter. The cost per dose is $125,000. The cost for the first year of therapy is $750,000, followed by $375,000 per year for maintenance dosing.

Motor Function Tests Used in Nusinersen Clinical Trials[9,10,11,12,13,14,15]

Motor Function Test	Description
HINE	• HINE Section 2 is a motor function assessment tool designed to evaluate motor skills in infants from 2 months to 2 years of age • Exam includes 26 items that provide a comprehensive assessment of an infant's neuromuscular development • The overall score ranges from 0 to 78; with each item scored from 0 to 3 • The motor milestones portion includes 8 items: voluntary grasp, ability to kick, head control, rolling, sitting, crawling, standing, and walking • At 9 or 12 months, the scores ≥73 are regarded as optimal; healthy-term infants should have a median score ≥67 at 3 months and ≥70 at 6 months • Used to measure proportion of motor milestone responders in ENDEAR clinical study; a motor milestone responder was defined as a patient having more HINE categories with improvement than with worsening - Improvement: ≥2-point improvement in ability to kick (or maximal score), or ≥1-point improvement in any other milestone, excluding voluntary grasp - Worsening: ≥2-point worsening in ability to kick (or zero score), or ≥1-point worsening in any other milestone, excluding voluntary grasp
CHOP INTEND	• Used to evaluated the motor skills of infants with SMA • Assesses motor skills through 16 items: spontaneous movement of upper and lower extremity, hand grip, head in midline with visual stimulation, hip adductors, rolling elicited from legs and from arms, shoulder and elbow flexion and horizontal abduction, shoulder flexion and elbow flexion, knee extension, hip flexion and foot dorsiflexion, head control, elbow flexion, neck flexion, head/neck extension, and spinal incurvation • The total score ranges from 0 to 64; with each item scored from 0 to 4, where 0 is least function and 4 is the most function for each of the 16 items • Used as secondary endpoint in ENDEAR clinical study; a 4-point or greater improvement from baseline in total score was considered a responder
HFMSE	• Validated measure that has been used in several clinical trials to evaluate the motor function of children with SMA

Motor Function Test	Description
	• Expanded version of the original 20-items Hammersmith Functional Motor Scale that incorporates 13 items from the Gross Motor Function Measure assessment related to lying, rolling, crawling, kneeling, standing, walking, running, and jumping • Consists of 33 items investigating the child's ability to perform various activities; each activity is scored on a 3-point system, with a score of 2 for "performs without modification", 1 for "performs with modification/adaptation", and 0 for "unable to perform" • The total score can range from 0 to 66, with lower scores indicating poorer motor function • Used as primary endpoint in CHERISH clinical study to assess change from baseline; secondary endpoint of CHERISH was proportion of patients achieving a 3-point increase from baseline in HFMSE score at 15 months
ULM	• Specifically developed as an outcome measure to assess upper limb functional abilities in patients with SMA, including patients with severe contractures in the lower limbs and young children, in whom the possibility to detect functional changes, such as rolling or long sitting, is limited • Consists of 9 upper limb performance items that are reflective of activities of daily living such as removing the lid from a container and placing a coin in a box • The total score ranges from 0 to 18, with higher scores indicating greater functional abilities • An increase of 2 or more points in the ULM is considered to represent a clinically meaningful improvement • Quickly administered and has been evaluated in patients with SMA from age 30 months to 27 year • Used as secondary endpoint in CHERISH clinical study to assess change from baseline

HINE = Hammersmith Infant Neurological Exam; CHOP INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; HFMSE = Hammersmith Functional Motor Scale – Expanded; ULM = Upper Limb Module

Recommendations

The College of Pharmacy recommends the prior authorization of Spinraza™ (nusinersen) with the following criteria, with the addition of #3 based on the recommendation from the Drug Utilization Review (DUR) Board at the March DUR meeting:

Spinraza™ (Nusinersen) Approval Criteria:

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

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

[1] Markowitz JA, Singh P, Darras BT. Spinal Muscular Atrophy: A Clinical and Research Update. *Pediatric Neurology.* 46 (2012) 1-12.

[2] Wang CH, Finkel RS, Bertini ES, et al. Consensus Statement for Standard of Care in Spinal Muscular Atrophy. *Journal of Child Neurology*. 2007 Aug; 22(8):1027-49.

[3] Muralidharan K, Wilson RB, Ogino S, Nagan N, Curtis C, Schrijver I. Population Carrier Screening for Spinal Muscular Atrophy: A Position Statement of the Association for Molecular Pathology. *The Journal of Molecular Diagnostics: JMD.* 2011; 13(1):3-6. doi:10.1016/j.jmoldx.2010.11.012.

[4] Arnold WD, Kassar D, Kissel JT. Spinal Muscular Atrophy: Diagnosis and Management in a New Therapeutic Era. *Muscle & Nerve*. 2015; 51(2):157-167. doi:10.1002/mus.24497.

[5] Genetics Home Reference. U.S. National Library of Medicine. Spinal Muscular Atrophy. Available online at: https://ghr.nlm.nih.gov/condition/spinal-muscular-atrophy. Issued 02/14/2017. Last accessed 02/17/2017.

[6] National Institutes of Health. Spinal Muscular Atrophy. Available online at: https://rarediseases.info.nih.gov/diseases/7674/spinal-muscular-atrophy. Last revised 01/07/2016. Last accessed 02/23/2017.

[7] Bodamer OA. Spinal Muscular Atrophy. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/spinal-muscular-atrophy?source=search_result&search=spinal+muscular+atrophy&selectedTitle=1%7E53. Last revised 01/26/2017. Last accessed 02/17/2017.

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Appendix D

Vote to Prior Authorize Zinbryta™ (Daclizumab)

Oklahoma Health Care Authority
April 2017

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

- **Zinbryta™ (daclizumab)** was approved by the U.S. Food and Drug Administration (FDA) in May 2016. It is an interleukin (IL)-2 receptor blocking antibody indicated for the treatment of adult patients with relapsing forms of Multiple Sclerosis (MS). Due to its safety profile, daclizumab should generally be reserved for patients who have had an inadequate response to two or more medications indicated for the treatment of MS. Zinbryta™ is available in a carton containing a single-dose prefilled syringe providing 1mL of 150mg/mL of daclizumab. The recommended dosage is 150mg once monthly and is administered by subcutaneous injection. The wholesale acquisition cost (WAC) is $7,236.50 per syringe, resulting in a cost per year of $86,838.00.
- **Gilenya® (fingolimod)** product labeling was updated in February 2016. The FDA approved an update to the *Contraindications* section and to the *Warnings and Precautions* section. The update to the *Contraindications* section included information regarding hypersensitivity reactions, including rash, urticaria, and angioedema, that have been reported with fingolimod in postmarketing settings. Fingolimod is contraindicated in patients who have had a hypersensitivity reaction to fingolimod or any of the excipients in Gilenya®. The *Warnings and Precautions* section was updated to include information regarding the risk of infections with fingolimod, as well as reports of herpes viral infections, cases of progressive multifocal leukoencephalopathy (PML), liver injury, basal cell carcinoma, and hypersensitivity reactions.
- **Tecfidera® (dimethyl fumarate)** product labeling was updated in January 2017 to include a warning of potential liver injury that could require hospitalization.
- **Tysabri® (natalizumab)** product labeling was updated in May 2016 to include additional information regarding the risk of PML. MRI findings may be apparent before clinical signs or symptoms. Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML. Lower PML-related mortality and morbidity have been reported following discontinuation of treatment in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis. Because of the risk of PML, natalizumab is only available through a restricted distribution program called the TOUCH® Prescribing Program. It is recommended to test patients for JC Virus antibodies periodically. Additionally, information was added to the product label regarding the potential for antibody formation. Patients who received natalizumab for a short exposure (one to two infusions) followed by an extended period without treatment are at higher risk of developing anti-natalizumab antibodies and/or hypersensitivity reactions on re-exposure, compared to patients who regularly received scheduled treatment.

Recommendations

The College of Pharmacy recommends the prior authorization of Zinbryta™ (daclizumab) with the following criteria:

Zinbryta™ (Daclizumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis (MS); and
2. Member must have had an inadequate response to two or more medications indicated for the treatment of MS; and
3. The prescriber must agree to monitor serum transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] and total bilirubin levels prior to starting treatment, monthly, and for at least six months after treatment; and
4. Member must not have pre-existing hepatic disease (including hepatitis B or C) or hepatic impairment including ALT or AST at least two times the upper limit of normal; and
5. Member, prescriber, and pharmacy must all enroll in the Zinbryta™ REMS Program and maintain enrollment throughout therapy.

Additionally, the College of Pharmacy recommends updating the existing prior authorization criteria for Gilenya® (fingolimod) and Tecfidera® (dimethyl fumarate) with the changes noted in red:

Gilenya® (Fingolimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis (MS) with at least one relapse in the previous 12 months, or transitioning from existing MS therapy; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. The first dose should be observed in the doctor's office for signs and symptoms of bradycardia for six hours after first dose; and
4. Verification from the prescriber that member has no active infection(s); and
5. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
6. Liver function tests and verification that levels are acceptable to the prescriber; and
7. Compliance will be checked for continued approval every six months.

Tecfidera® (Dimethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis (MS); and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Compliance will be checked for continued approval every six months; and
7. A quantity limit of 60 tablets per 30 days will apply.

[1] Zinbryta™ Prescribing Information. Biogen. Available online at: https://www.zinbryta.com/content/dam/commercial/multiple-sclerosis/zinbryta/pat/en_us/pdfs/zinbryta-prescribing-information.pdf. Last revised 05/2016. Last accessed 03/16/2017.
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[4] Gilenya® Prescribing Information. Novartis. Available online at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gilenya.pdf. Last revised 02/2016. Last accessed 03/16/2017.
[5] Tecfidera® Prescribing Information. Biogen. Available online at: https://www.tecfidera.com/content/dam/commercial/multiple-sclerosis/tecfidera/pat/en_us/pdf/full-prescribing-info.pdf. Last revised 01/2017. Last accessed 03/16/2017.
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[8] Tysabri® Safety. Biogen. Available online at: https://www.tysabri.com/en_us/home/about/safety-side-effects.html. Last accessed 03/20/2017.

Appendix E

Vote to Prior Authorize Zinplava™ (Bezlotoxumab)

Oklahoma Health Care Authority
April 2017

Introduction[1,2,3]

Clostridium difficile (*C. difficile*) is a spore-forming, toxin-producing, gram-positive anaerobic bacterium that causes antibiotic-associated colitis. It colonizes the human intestinal tract after the normal gut flora has been altered by antibiotic therapy. *C. difficile* infection (CDI) is one of the most common healthcare-associated infections and a significant cause of morbidity and mortality among older adult hospitalized patients. Therapy for mild-to-moderate CDI consists of oral metronidazole or oral vancomycin. First-line treatment for severe CDI is oral vancomycin. Fidaxomicin may be considered in patients who cannot tolerate vancomycin.

Recurrent CDI is defined by complete abatement of CDI symptoms while on appropriate therapy, followed by subsequent reappearance of symptoms after treatment has been stopped. Up to 25% of patients experience recurrent CDI within 30 days of treatment. Less commonly, recurrent CDI can occur as late as two to three months after discontinuation of treatment. Once patients have experienced one recurrence, they are at significantly increased risk for further recurrences. Recurrent disease may be mild or severe. Risk factors for recurrence include age greater than 65 years, severe underlying medical disorders, need for ongoing therapy with concomitant antibiotics during treatment for CDI, and lack of an antibody-mediated immune response to *C. difficile* toxin B.

In October 2016, the U.S. Food and Drug Administration (FDA) approved the monoclonal antibody Zinplava™ (bezlotoxumab) for secondary prevention of CDI in patients at high risk for recurrence. Bezlotoxumab is a human monoclonal antibody that binds to *C. difficile* toxin B and neutralizes its effects. It is indicated to reduce recurrence of CDI in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence. Bezlotoxumab is not indicated for the treatment of CDI. It is not an antibacterial drug, and should only be used in conjunction with antibacterial drug treatment of CDI. Zinplava™ (bezlotoxumab) is supplied as a 1,000mg/40mL (25mg/mL) single-dose vial. The recommended dosing is a single dose of 10mg/kg administered as an intravenous infusion over 60 minutes.

Cost:

Medication	Cost Per mL	Cost Per Treatment*
Zinplava™ (bezlotoxumab)	**$95.00**	**$2,869.00 - $3,378.20**

Costs do not reflect rebated prices or net cost. Costs based on Wholesale Acquisition Costs (WAC); National Average Drug Acquisition Costs (NADAC) unavailable.
*Cost per treatment given as a range for average adult weight (75.5kg to 88.9kg) in the United States at recommended dose of 10mg/kg.

Recommendations

The College of Pharmacy recommends the prior authorization of Zinplava™ (bezlotoxumab) with the following criteria:

Zinplava™ (Bezlotoxumab) Approval Criteria:

1. An FDA approved diagnosis of *Clostridium difficile* infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence; and
    a. Prescriber must document the member has one or more of the following risk factors for high risk of CDI recurrence:
        i. Age of 65 years or older; or
        ii. One or more episodes of CDI within the six months prior to the episode under treatment; or
        iii. Need for ongoing therapy with concomitant antibiotics during treatment for CDI; or
        iv. Severe underlying medical disorders; or
        v. Immunocompromised; or
        vi. Clinically severe CDI (Zar score ≥ 2); and
2. Current or planned antibacterial drug for CDI must be provided on the prior authorization request to ensure medication is within standard of care; and
3. Prescriber must document that Zinplava™ (bezlotoxumab) will be administered while the member is receiving antibacterial drug treatment of CDI; and
4. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

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[2] Center for Disease Control and Prevention (CDC)/National Center for Health Statistics. Body Measurements: Measured average height, weight, and waist circumference for adults ages 20 years and over. Available online at: https://www.cdc.gov/nchs/fastats/body-measurements.htm. Last revised 07/15/2016. Last accessed 03/14/2017.

[3] Zinplava™ (bezlotoxumab) Prescribing Information. Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. Available online at: http://www.merck.com/product/usa/pi_circulars/z/zinplava/zinplava_pi.pdf. Last revised 10/2016. Last accessed 03/14/2017.

Appendix F

Vote to Prior Authorize Hydroxyprogesterone Caproate Injection (Generic Delalutin®)

Oklahoma Health Care Authority
April 2017

Introduction[1,2,3]

Hydroxyprogesterone caproate 250mg/mL injection was approved by the U.S. Food and Drug Administration (FDA) in August 2015 as a generic for Delalutin®. Delalutin® is no longer being marketed in the United States but was not withdrawn from sale for reasons of safety or effectiveness. Hydroxyprogesterone caproate is available as a 250mg/mL injection for intramuscular (IM) use in 5mL multi-dose vials and is indicated in non-pregnant women for:

- Treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV); and
- Management of amenorrhea (primary and secondary) and abnormal bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; and
- As a test for endogenous estrogen production and for the production of secretory endometrium and desquamation.

Recommendations

The College of Pharmacy recommends the prior authorization of hydroxyprogesterone caproate 250mg/mL injection with the following criteria:

Hydroxyprogesterone Caproate 250mg/mL Injection (Generic Delalutin®) Approval Criteria:

1. An FDA approved indication of one of the following in non-pregnant women:
    a. For the treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV); or
    b. For the management of amenorrhea (primary and secondary) or abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; or
    c. As a test for endogenous estrogen production or for the production of secretory endometrium and desquamation; and
2. The quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging.
3. Requests for the prevention of preterm birth in pregnant women with a history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation will not be approved for generic Delalutin® and should be resubmitted for authorization of Makena® (hydroxyprogesterone caproate).

[1] Hydroxyprogesterone Caproate Prescribing Information. ANI Pharmaceuticals, Inc. Available online at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=cdfa01cc-6315-44d4-ba79-3705fafe7ebe&type=display. Last revised 06/2016. Last accessed 03/09/2017.

[2] Hydroxyprogesterone Caproate Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/hydroxyprogesterone-caproate/. Last revised 06/03/2016. Last accessed 03/09/2017.

[3] Micromedex 2.0: Hydroxyprogesterone Caproate Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/. Last revised 11/18/2016. Last accessed 03/09/2017.

Appendix G

Vote to Update Adempas® (Riociguat) Approval Criteria

Oklahoma Health Care Authority
April 2017

Introduction[1,2]

Adempas® (riociguat) is a soluble guanylate cyclase (sGC) stimulator indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), World Health Organization (WHO) Group 4, after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class, and for the treatment of adults with pulmonary arterial hypertension (PAH), WHO Group 1, to improve exercise capacity, improve WHO functional class, and to delay clinical worsening.

In January 2017, the U.S. Food and Drug Administration (FDA) added a new contraindication to the drug label of Adempas® for use in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP). Riociguat is contraindicated in patients with PH-IIP due to preliminary data from RISE-IIP which showed a higher number of deaths (seventeen in the riociguat group and four in the placebo group) and serious events, including breathing problems and lung infections, in patients who took riociguat compared with those in the placebo group. Furthermore, there appeared to be no clinically significant benefit for those who took the drug.

Recommendations

The College of Pharmacy recommends the following changes noted in red to the Adempas® (riociguat) approval criteria:

Adempas® (Riociguat) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension (PAH) or chronic thromboembolic pulmonary hypertension (CTEPH); and
    a. Members with a diagnosis of PAH must have previous failed trials of at least one of each of the following categories:
        i. Revatio® (sildenafil) or Adcirca® (tadalafil); and
        ii. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    b. Members with a diagnosis of CTEPH must currently be on anticoagulation therapy; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. Member must not be on any concurrent phosphodiesterase (PDE) inhibitor therapy; and
4. Member must not have a diagnosis of pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP); and
5. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Adempas® REMS program.
6. A quantity limit of 90 tablets per 30 days will apply.

[1] Adempas® Prescribing Information. Bayer HealthCare Pharmaceuticals Inc. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Adempas_PI.pdf. Last revised 02/2017. Last accessed 02/23/2017.
[2] U.S. Food and Drug Administration (FDA) Supplement Approval. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/204819Orig1s006ltr.pdf. Issued 01/2017. Last accessed 03/2017.

Appendix H

Fiscal Year 2016 Annual Review of SoonerCare Pharmacy Benefit

Oklahoma Health Care Authority
April 2017

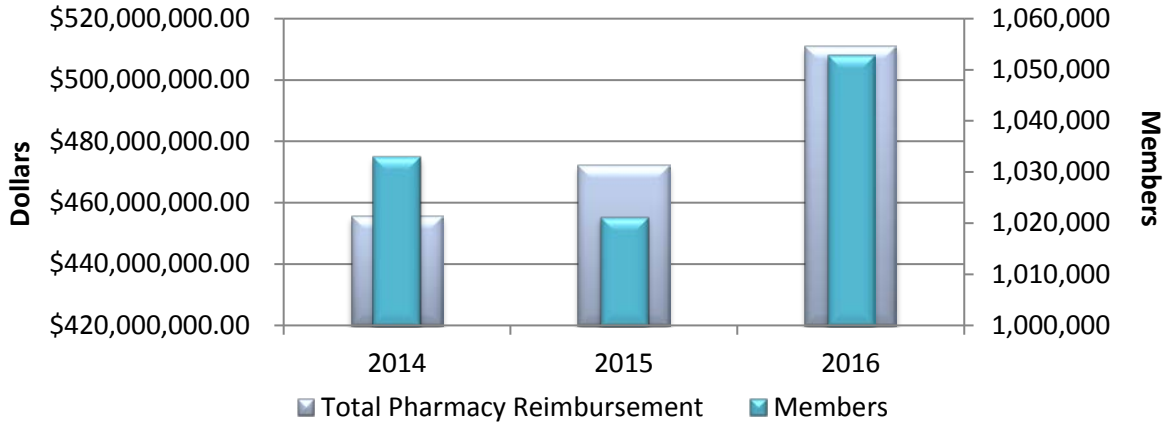
Summary[1]

During State Fiscal Year (SFY) 2016, prescription drugs accounted for $511 million of the approximate $5 billion in total SoonerCare funding. The cost per total members increased from $462.19 in SFY 2015 to $485.36 in SFY 2016, a 5.01% increase. Total reimbursement increases can largely be attributed to the 14.44% increase in cost per claim for specialty medications. Recently, the specialty pharmaceutical products total pharmacy reimbursement has been on the incline as a result of orphan drug approvals for rare diseases and the high costs associated with these therapies. Members utilizing the pharmacy benefit increased by 0.56% and number of medication claims increased by 1.54%; both of which also contributed to an increase in total medication reimbursement.

SFY	Members	Average Monthly Enrollment	Utilizers*	Claims	Reimbursement	Days	Cost/ Claim	Cost/ Day
2014	1,033,114	804,564	562,156	6,296,155	$455,453,990.13	155,648,597	$72.34	$2.93
2015	1,021,359	819,193	556,568	6,055,215	$472,062,067.55	149,723,249	$77.96	$3.15
2016	1,052,826	802,916	559,672	6,148,211	$511,004,775.43	155,407,873	$83.11	$3.29

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

Total Pharmacy Reimbursement and Member Enrollment Comparison



The Per Member Per Year (PMPY) value reflects the total pharmacy cost divided by the unduplicated number of members (total enrollees) for each time period. In order to reflect an accurate PMPY value, average monthly enrollment is used in place of annual enrollment and dual eligible members are excluded. The PMPY value is used across benefit plans with similar populations to accurately assess healthcare spending. The following table contains the adjusted PMPY values for the last three years. Calendar year (CY) 2016 saw a 7.25% increase from 2015 in

overall PMPY. This increase can be attributed to an increase in all pharmacy claims and a significant increase in reimbursement for specialty medications.

Calendar Year	CY 2014	CY 2015	CY 2016
Adjusted PMPY	$653	$690	$740

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

To measure the success of the SoonerCare pharmacy benefit management, Oklahoma's Medicaid statistics were compared to the Medicaid statistics of the largest PBM in the United States, Express Scripts (ESI). For CY 2015, ESI's Medicaid PMPY was $969 – 40% higher than OHCA's $690. If OHCA had experienced the same PMPY as ESI for CY 2015, it would have cost over $188 million more than the $472 million spent. Similarly, for CY 2016, ESI's Medicaid PMPY was $1,196 – 62% higher than OHCA's $740. At the ESI PMPY rate, it would have cost over $316 million more than the $511 million spent during calendar year 2016 for pharmacy reimbursement.

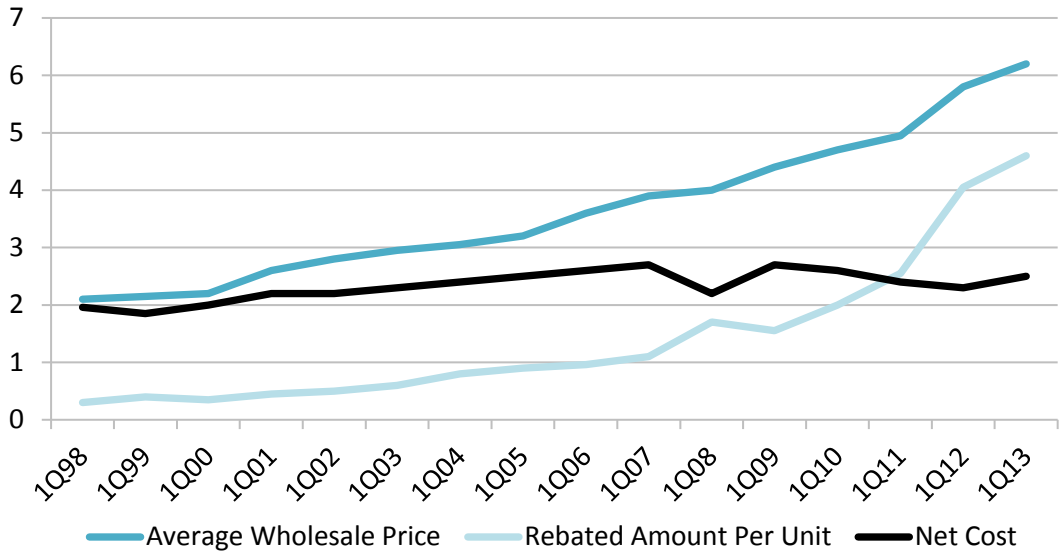
Calendar Year	ESI	OHCA	Percent Difference
2014	$883	$653	35%
2015	$969	$690	40%
2016	$1,196	$740	62%

Comparing the trend of the PMPY from 2015 to 2016, ESI experienced a 23.43% increase, while OHCA saw a 7.25% increase. SoonerCare prior authorization policies, coupled with quantity limits and monthly prescription limits, yield better than average results while still providing a comprehensive pharmacy benefit for 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 (ROI), using the overage generated by the ESI PMPY rate, for 2015 the ROI is $38 to $1 and for 2016 it is $63 to $1.

Medicaid Drug Rebate Program[2,3,4]

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



Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. In SFY 2016 OHCA collected $275 million in federal rebates and $14 million in state supplemental rebates, both of which increased from SFY 2015 ($237 million federal; $13 million state). These rebates are collected after reimbursement for the medication and are not reflected in this report.

Orphan Drugs[5,6,7,8,9]

The 1983 Orphan Drug Act was passed in order to encourage pharmaceutical companies to develop new medications and biologics for the treatment, diagnosis, and prevention of rare diseases that affect fewer than 200,000 patients in the United States.

- Orphan drug designation by the U.S. Food and Drug Administration (FDA) offers several lucrative incentives including FDA fee waivers, a 50% tax credit for clinical trials, and seven years of market exclusivity. Additionally, orphan drugs are given special consideration by the FDA for approval. Approximately two thirds of orphan drugs were approved with one controlled trial while non-orphan drugs typically require two or more controlled trials for approval.

- In 2016, 40% of all new medications approved received orphan drug designation. Since 1983, close to 450 orphan drugs have been approved, 70 of which were first approved by the FDA for mass market use, and approximately one third of which were either repurposed mass market drugs or drugs that received multiple orphan approvals.
- Ranked by annual sales, orphan drugs account for seven of the ten top-selling drugs of any kind. In 2014, the average annual cost for orphan drugs was $111,820.
- Critics of the Orphan Drug Act express concern that the seven year exclusivity allows pharmaceutical companies to charge whatever they want since there is no competition. Pharmaceutical companies cite research and development expenditures to justify high prices. An article in *Health Affairs* analyzed research and development costs for 15 drug companies that made the 20 best-selling drugs in 2015. The report found $116 billion in surplus revenue from drug sales while spending $76 billion on research and development. In December 2016, a HHS report found the cost of orphan drug development to be approximately $1 billion compared with $2.6 billion for non-orphan or mass market drugs.
- In March 2017, two groups of senators requested an investigation by the Government Accountability Office (GAO) into drugmakers of orphan drugs "after a growing chorus of complaints that some pharma companies are gaming the system to rake in profits. The GAO has agreed to officially investigate the issue."[10]

Examples of recent orphan drug approvals and their associated costs can be found in the following table:

Medication	Indication	Annual Cost Per Patient*
Emflaza™ (deflazacort)	Duchenne muscular dystrophy	$88,200[+]
Exondys 51™ (eteplirsen)	Duchenne muscular dystrophy	$582,400[+]
Ocaliva™ (obeticholic acid)	Primary biliary cholangitis	$68,400
Spinraza™ (nusinersen)	Spinal muscular atrophy	$750,000

*Cost based on Wholesale Acquisition Costs (WAC) and does not reflect rebated price or net cost.
[+]Dosing based on 40kg patient.

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). Traditional pharmaceuticals carry the bulk of the reimbursement costs accounting for 84% of the total pharmacy reimbursement in SFY 2016 and 99% of utilizers. Specialty products, in contrast, are typically injectable and require special handling such as refrigerated transport and special administration techniques. These products include treatments for hemophilia, rheumatoid arthritis, and genetic deficiencies, for example. During SFY 2016 the specialty pharmaceutical products comprised 16% and 0.6% of total pharmacy reimbursement costs and member utilization, respectively. The specialty pharmaceutical products total pharmacy reimbursement has continued to rise due to new emerging therapies and the high costs associated with these therapies.

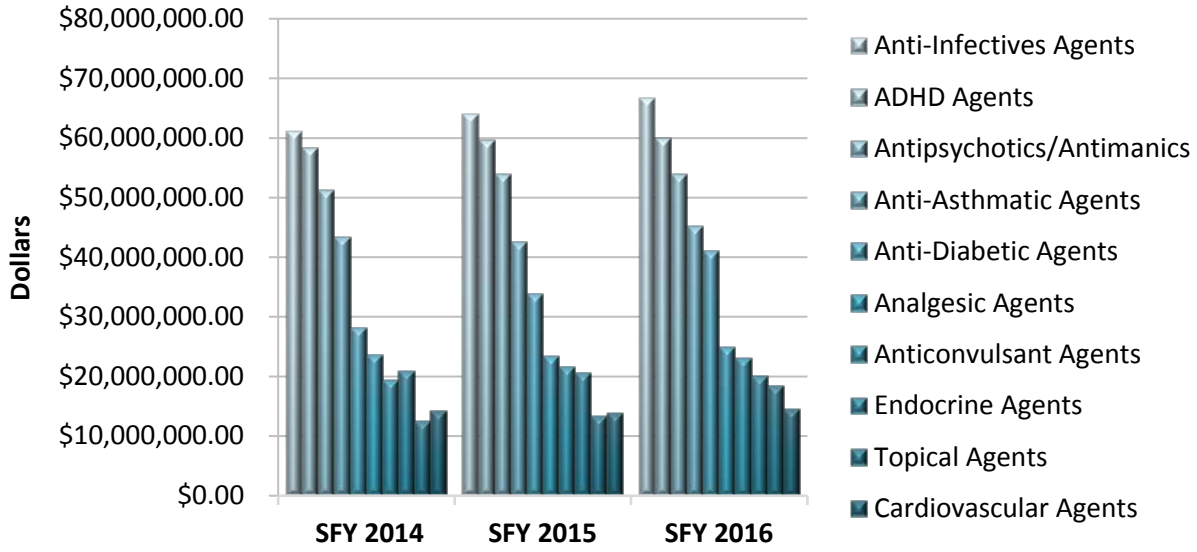
Top 10 Therapeutic Classes by Reimbursement: Fiscal Year 2016

Traditional 2016 therapeutic class reimbursement rankings changed slightly from the previous fiscal year with topical agents moving up from 10th in SFY 2015 to being the 9th largest traditional reimbursement class in SFY 2016. Traditional pharmaceutical classes that displayed the most significant change from SFY 2015 to SFY 2016 include anti-diabetic agents and topical agents.

- The topical agent class is comprised of dermatological, otic, ophthalmic, mouth/throat/dental agents, and anorectal products. Otic medications had the largest increase within this therapeutic class, increasing $3 million from the previous fiscal year. Generic ofloxacin otic products became three times more expensive and were moved to Tier-2 to alleviate the spending increase. Ciprodex® (ciprofloxacin/dexamethasone) otic solution utilization went up fivefold due to increased access following its move down in tier as a result of supplemental rebate participation; the increased utilization accounted for an increase in reimbursement and 87% of the total cost of the otic category. Costs in this report do not reflect federal or supplemental rebates that are provided by manufacturers.
- Long-acting insulin pens increased in price significantly resulting in a large spending increase in the anti-diabetic class. These products have significant federal rebates designed to keep the Medicaid net cost relatively flat; rebates are not accounted for in this analysis.
- Endocrine agents saw a decline in reimbursement in SFY 2016 as a result of prior authorizing the more costly corticosteroid oral solutions. The annual effect of this prior authorization won't be seen until SFY 2017 as the restrictions were not implemented until mid-SFY 2016.
- Anti-infective agent reimbursement can be accounted for by the costly therapies for the treatment of hepatitis C. The increase in hepatitis C medication spending is likely due to the increase in utilization as well as the increased cost of some of the new highly utilized regimens compared to the original regimens approved in 2013. The cost increase could also be accounted for by the use of two direct acting antiviral agents in combination as recommended by the guidelines for some less common hepatitis C viral genotypes. Combination regimen use should decrease as they are no longer preferred regimens as a result of increased availability of new regimens across multiple genotypes. Continual efforts are made to ensure optimal treatments with cost-effective outcomes.

Traditional Top 10 Classes by Reimbursement			
	SFY 2014	**SFY 2015**	**SFY 2016**
Anti-Infective Agents	$61,067,382.35	$63,894,993.65	$66,683,748.86
ADHD Agents	$58,357,734.65	$59,594,300.66	$59,942,177.34
Antipsychotics/Antimanics	$51,183,242.16	$53,904,373.75	$53,916,241.63
Anti-Asthmatic Agents	$43,367,208.57	$42,476,166.30	$45,212,373.87
Anti-Diabetic Agents	$28,058,844.39	$33,865,458.33	$40,929,564.55
Analgesic Agents	$23,569,728.18	$23,390,371.04	$24,973,663.88
Anticonvulsant Agents	$19,448,345.89	$21,634,647.57	$23,056,678.56
Endocrine Agents	$20,856,333.45	$20,558,655.33	$20,077,536.48
Topical Agents	$12,560,616.35	$13,343,152.46	$18,393,884.52
Cardiovascular Agents	$14,110,802.19	$13,764,645.61	$14,513,863.15

Top 10 Traditional Therapeutic Classes by Reimbursement



The high costs of specialty therapeutic products can largely be attributed to the orphan drug therapies indicated for rare diseases. Specialty 2016 therapeutic class reimbursement rankings differ from the previous fiscal year with biological agents and respiratory agents switching places in the 5th and 6th positions in SFY 2016. Specialty pharmaceutical classes that displayed the most significant change from SFY 2015 to SFY 2016 include pain agents and respiratory agents. Continuous review and management of hematological and neurological agents has promoted minimal reimbursement increases other than expected yearly price increases by product manufacturers and declines in reimbursement for anti-infective agents, nontherapeutic agents, and gastrointestinal agents.

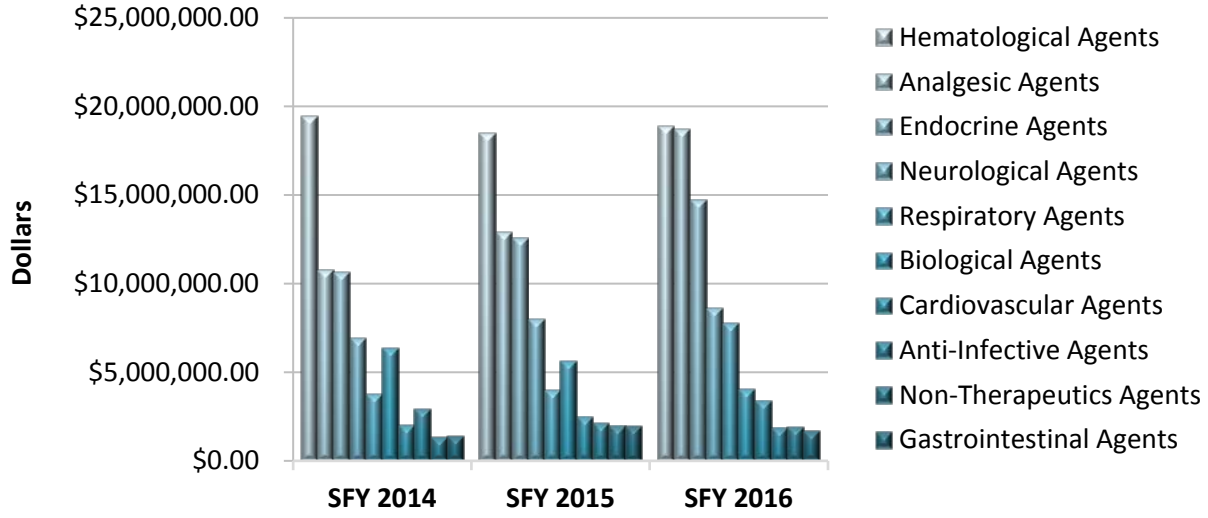
- Specialty pharmaceutical respiratory agents include medications for cystic fibrosis (CF), idiopathic pulmonary fibrosis (IPF), and emphysema. Orkambi® (lumacaftor/ivacaftor), a medication approved by the FDA in July 2015 for CF patients with two copies of the *F508del* mutation in their cystic fibrosis transmembrane regulator (CFTR) gene, contributed to $2,693,283 of total reimbursement for SFY 2016.[11]
- The cost of specialty pain products has increased by $5 million within the last fiscal year and the additional spend can be attributed to the cost inflation of targeted immunomodulator agents such as: Humira® (adalimumab), Enbrel® (etanercept), Ilaris® (canakinumab), Orencia® (abatacept), Simponi® (golimumab), Xeljanz® (tofacitinib), Otezla® (apremilast), and Kineret® (anakinra). This class will soon face biosimilar competition similar to generic competition for branded patent expirations. With the emergence of biosimilar FDA approvals, current branded product manufacturers raised their prices in anticipation of more market competition. All of the aforementioned products have increased in cost per claim by a minimum of $400 per claim with an average price increase of $617 per claim in SFY 2016. This cost increase was seen while utilization remained relatively flat. The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite price increases in medications that pay the brand penalty. The cost increases in this report do not reflect net cost increases. Additionally, the majority of utilization was seen in Tier-2

medications which are supplementally rebated medications. The supplemental rebated prices are also not reflected in this analysis.

- The decrease in reimbursement for biological agents can be attributed to the adoption of updated guidance for Synagis® (palivizumab).

Specialty Top 10 Classes by Reimbursement			
	SFY 2014	SFY 2015	SFY 2016
Hematological Agents	$19,464,704.37	$18,506,935.65	$18,859,832.35
Analgesic Agents	$10,745,209.58	$12,879,307.91	$18,734,339.24
Endocrine Agents	$10,643,828.94	$12,552,053.53	$14,732,068.87
Neurological Agents	$6,944,096.69	$7,986,737.17	$8,608,234.85
Respiratory Agents	$3,767,672.21	$3,976,385.33	$7,763,918.62
Biological Agents	$6,380,166.15	$5,638,501.56	$4,020,792.45
Cardiovascular Agents	$1,989,343.91	$2,441,564.38	$3,387,423.54
Anti-Infective Agents	$2,905,295.94	$2,101,669.49	$1,872,634.72
Non-Therapeutics Agents	$1,336,217.81	$1,930,027.69	$1,928,230.30
Gastrointestinal Agents	$1,390,862.30	$1,962,601.23	$1,642,701.27

Top 10 Specialty Therapeutic Classes by Reimbursement



Top 10 Medications by Reimbursement: Fiscal Year 2016

The top 10 medications by reimbursement typically contain highly utilized medications such as albuterol inhalers and maintenance asthma medications. Similar to the past two fiscal years, attention deficit therapies, atypical antipsychotics, and antivirals for the treatment of hepatitis C comprise the majority of the top 10 medications by reimbursement. The generic availability of aripiprazole resulted in a ranking of 3rd rather than a previous ranking of 1st seen in the last several fiscal years. The majority of top products are brand medications that participate in supplemental rebates including lisdexamfetamine, atomoxetine, paliperidone, and adalimumab. Reimbursement rankings do not account for federal or supplemental rebate participation. Top drug reimbursement rankings change from year to year only slightly for several reasons: high utilization, broad use between age demographics, and high costs of new therapies such as hepatitis C.

Top 10 Medications by Reimbursement*			
Rank	**2014**	**2015**	**2016**
1	aripiprazole oral	aripiprazole oral	lisdexamfetamine
2	sofosbuvir	lisdexamfetamine	ledipasavir/sofosbuvir
3	albuterol	albuterol	aripiprazole oral
4	lisdexamfetamine	sofosbuvir	albuterol
5	guanfacine ER	ledipasavir/sofosbuvir	atomoxetine
6	amphetamine/ dextroamphetamine ER	guanfacine ER	paliperidone palmitate inj
7	paliperidone palmitate inj	atomoxetine	sofosbuvir
8	methylphenidate ER	paliperidone palmitate inj	adalimumab
9	dexmethylphenidate ER	oseltamivir	fluticasone inh
10	fluticasone inh	fluticasone inh	somatropin inj

*Includes brand and generic where applicable.
inj = injection; inh = inhalation; ER = extended-release

Cost Per Claim

The SoonerCare cost per claim of brand medications rose by 21.07% in SFY 2016 in comparison to SFY 2015, 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.

Fiscal Year	Percent of Rx Spending on Generic Medications	Cost per Generic Claim	Cost per Brand Claim
2014	24%	$21.38	$310.61
2015	23%	$21.09	$340.13
2016	21%	$20.94	$411.78

The SoonerCare cost per claim of traditional medications rose by 5.17% in SFY 2016 in comparison to SFY 2015 and the cost per specialty claim increased by 14.44%. As mentioned previously, specialty costs are largely driven by the significant cost associated with medications for rare diseases as well as price increases of drugs that will soon face biosimilar competition.

Drug Class	SFY 2014	SFY 2015	SFY 2016
Traditional	$61.99	$66.43	$69.86
Specialty	$4,116.82	$4,341.50	$4,968.49

Conclusion

Even though costs have risen, they have not risen in direct proportion to the increase in membership, indicating cost-effective management measures were successful. New prior authorization categories during this fiscal year include breast cancer medications, granulocyte colony stimulating factors (G-CSFs), constipation/diarrhea medications, tetracycline and fluoroquinolone antibiotics, oral antifungal medications, Parkinson's disease medications,

ulcerative colitis and Crohn's disease medications, anthelmintic medications, bowel preparation medications, Gaucher disease medications, vasomotor symptom medications, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor medications, diabetic supplies, prostate cancer medications, and hemophilia medications. Modifications to the topical steroid tier structure and other generic categories reduced elevated spending on high-priced generic products which have been established on the market. When new drugs are approved and available on the market, a cost-effective analysis is performed to ensure spending is minimized while maintaining appropriate clinical care. The goal of the SoonerCare program is to provide members with the most appropriate healthcare in a fiscally responsible manner. For the pharmacy benefit this is accomplished by the use of a robust prior authorization program, limiting the number of total prescriptions and the number of brand name prescriptions allowed each month for non-institutionalized adults, continuous product pricing maintenance, and provider outreach and education. Constant market review and response to changes such as the introduction of new hepatitis C treatments and growth of the specialty market is necessary. SoonerCare will continue to strive to bring value-based pharmacy services to its members.

Top 100 Reimbursed Drugs by Fiscal Year

Top 100 Reimbursed Drugs By Fiscal Year		2016		2015	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Lisdexamfetamine	Vyvanse	1	$21,439,176.98	2	$15,888,742.06
Aripiprazole	Abilify*	2	$20,885,295.91	1	$25,409,147.99
Ledipasvir/Sofosbuvir	Harvoni	3	$19,459,629.97	7	$9,546,826.77
Albuterol	Multiple Products	4	$14,147,949.42	3	$13,201,344.55
Methylphenidate	Multiple Products	5	$14,009,206.64	4	$12,012,128.62
Atomoxetine	Strattera	6	$11,887,683.27	10	$8,772,650.66
Paliperidone Injection	Invega Trinz/Sust	7	$11,742,061.19	11	$8,462,946.85
Adalimumab	Humira	8	$10,641,255.60	12	$7,234,281.48
Insulin Glargine	Lantus/Toujeo	9	$9,652,704.25	8	$9,466,806.33
Sofosbuvir	Sovaldi	10	$9,461,859.18	6	$10,411,268.09
Fluticasone Inhalation	Flovent	11	$8,256,495.85	13	$7,179,215.02
Insulin Aspart	Novolog	12	$8,247,000.39	17	$6,168,551.39
Somatropin	Multiple Products	13	$7,893,708.41	15	$6,255,614.17
Lurasidone	Latuda	14	$7,227,761.27	21	$5,212,264.61
Oxycodone	Multiple Products	15	$7,006,876.59	18	$6,167,507.77
Insulin Detemir	Levemir	16	$6,998,616.65	20	$5,212,697.08
Amphetamine/Dextroamphetamine	Multiple Products	17	$5,797,633.31	14	$6,749,297.29
Epinephrine Injection	Multiple Products	18	$5,636,561.75	24	$4,381,410.19
Antihemophilic Factor (Recombinant)	Multiple Products	19	$5,614,917.62	16	$6,184,465.69
Dexmethylphenidate	Focalin*	20	$4,967,687.34	19	$5,861,044.32
Hydroxyprogesterone Caproate	Makena	21	$4,886,735.63	29	$3,703,814.63
Etanercept	Enbrel	22	$4,876,270.57	28	$3,796,652.26
Pregabalin	Lyrica	23	$4,842,721.00	25	$4,112,693.58
Fluticasone/Salmeterol	Advair	24	$4,764,493.17	23	$4,525,671.85
Insulin Lispro	Humalog	25	$4,258,682.60	31	$3,429,978.20

Top 100 Reimbursed Drugs By Fiscal Year		2016		2015	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Blood Glucose Test Strip	Multiple Products	26	$4,216,413.09	113	$837,241.66
Ciprofloxacin/Dexamethasone Otic	Ciprodex	27	$3,999,148.34	151	$597,637.06
Budesonide Inhalation	Pulmicort*	28	$3,994,726.46	22	$4,928,379.60
Hydrocodone/Acetaminophen	Multiple Products	29	$3,688,595.20	27	$3,838,960.81
Buprenorphine/Naloxone	Multiple Products	30	$3,616,867.59	38	$2,798,216.01
Lacosamide	Vimpat	31	$3,272,798.24	40	$2,646,905.87
Tiotropium	Spiriva	32	$3,264,798.90	33	$3,057,827.21
Quetiapine	Seroquel*	33	$3,088,194.63	30	$3,511,155.69
Glatiramer Acetate	Multiple Products	34	$2,979,211.71	37	$2,847,145.65
Antihemophilic Factor rAHF-PFM	Advate	35	$2,917,940.57	45	$2,057,889.15
Dornase Alfa	Pulmozyme	36	$2,869,372.27	42	$2,468,661.17
Lumacaftor/Ivacaftor	Orkambi	37	$2,693,283.71	NA	****
Palivizumab	Synagis	38	$2,628,429.93	26	$4,042,343.79
Corticotropin Injection	H.P. Acthar	39	$2,568,844.91	34	$2,949,049.31
Cefdinir	Omnicef*	40	$2,526,213.71	32	$3,070,388.59
Clobazam	Onfi	41	$2,498,298.34	54	$1,741,794.62
Paliperidone Tablet	Invega*	42	$2,481,250.84	35	$2,914,530.78
Azithromycin	Multiple Products	43	$2,384,994.11	43	$2,348,784.36
Daclatasvir	Daklinza	44	$2,372,858.81	NA	****
Sitagliptin	Januvia	45	$2,290,021.63	48	$1,867,047.03
Oxycodone/Acetaminophen	Multiple Products	46	$2,259,891.79	36	$2,847,462.41
Pancrelipase	Multiple Products	47	$2,172,192.30	47	$1,881,270.60
Oseltamivir	Tamiflu	48	$2,137,444.14	5	$10,569,992.12
Beclomethasone Inhalation	Qvar	49	$2,087,310.19	61	$1,573,178.18
Rifaximin	Xifaxan	50	$2,020,123.02	62	$1,523,295.88
Antiinhibitor Coagulant Complex	Feiba	51	$1,967,685.24	41	$2,566,216.73
Amoxicillin	Amoxil*	52	$1,947,608.83	46	$1,935,893.48
Montelukast	Singulair*	53	$1,900,345.72	55	$1,724,982.39
Ipratropium/Albuterol	Combivent*	54	$1,892,663.46	51	$1,835,792.19
Deferasirox	Jadenu/Exjade	55	$1,870,992.02	49	$1,864,538.26
Amoxicillin/Clavulanate	Augmentin*	56	$1,831,197.16	57	$1,690,029.10
Canakinumab	Ilaris	57	$1,820,996.15	104	$901,307.91
Eculizumab	Soliris	58	$1,729,571.78	56	$1,721,852.82
Cetirizine	Multiple Products	59	$1,692,303.49	63	$1,515,202.75
Budesonide/Formoterol Fumarate	Symbicort	60	$1,665,907.60	70	$1,387,905.63
Efavirenz/Emtricitabine/Tenofovir DF	Atripla	61	$1,636,427.63	50	$1,863,719.44
Ivacaftor	Kalydeco	62	$1,580,816.57	84	$1,103,321.47
Interferon Beta-1a	Rebif/Avonex	63	$1,577,109.06	60	$1,606,991.73
Divalproex	Depakote*	64	$1,559,083.15	44	$2,228,440.48
Liraglutide	Victoza	65	$1,528,648.45	77	$1,263,436.13
Emtricitabine/Tenofovir DF	Truvada	66	$1,493,182.93	66	$1,457,470.03
Clozapine	Multiple Products	67	$1,490,919.24	53	$1,773,514.79
Sulfamethoxazole/Trimethoprim	Bactrim*	68	$1,487,187.18	76	$1,276,808.71

Top 100 Reimbursed Drugs By Fiscal Year		2016		2015	
Generic Name	**Brand Name***	**Rank**	**Amount Paid**	**Rank**	**Amount Paid**
Dimethyl Fumarate	Tecfidera	69	$1,468,432.45	68	$1,439,449.09
Tobramycin Inhalation	Multiple Products	70	$1,414,853.31	58	$1,671,395.60
Tazarotene	Tazorac	71	$1,382,742.72	90	$994,846.20
Dasatinib	Sprycel	72	$1,371,022.90	120	$786,126.61
Oxcarbazepine	Multiple Products	73	$1,361,976.75	69	$1,407,320.71
Vigabatrin	Sabril	74	$1,316,496.46	73	$1,339,212.04
Imatinib	Gleevec*	75	$1,300,067.22	52	$1,791,821.98
Everolimus	Afinitor	76	$1,292,088.98	67	$1,441,086.94
Permethrin	Multiple Products	77	$1,269,834.46	71	$1,373,783.27
Rufinamide	Banzel	78	$1,251,142.14	87	$1,053,642.74
Gabapentin	Neurontin*	79	$1,247,676.00	64	$1,495,093.45
Prednisolone Sodium Phosphate	Multiple Products	80	$1,215,501.67	39	$2,712,636.07
Iloperidone	Fanapt	81	$1,205,612.97	72	$1,357,534.00
Sapropterin	Kuvan	82	$1,202,462.18	89	$1,043,775.80
Chlorpromazine	Thorazine*	83	$1,200,382.71	144	$639,115.40
Morphine Sulfate	Multiple Products	84	$1,194,342.29	65	$1,487,265.28
Metreleptin	Myalept	85	$1,174,044.90	146	$618,807.66
Levothyroxine	Multiple Products	86	$1,159,050.66	85	$1,091,544.18
Albendazole	Albenza	87	$1,120,242.48	114	$829,740.40
Sevelamer	Renvela	88	$1,110,542.88	102	$926,508.53
Spacer/Aerosol-Holding Chamber	Multiple Products	89	$1,110,249.12	74	$1,316,472.10
Varenicline	Chantix	90	$1,095,593.13	109	$852,371.04
Insulin Aspart	Novolog Mix	91	$1,092,667.85	98	$936,992.30
Guanfacine	Intuniv*	92	$1,089,295.46	9	$9,263,042.73
Elvitegrav/Cobic/Emtricitab/Tenofov DF	Stribild	93	$1,077,993.17	97	$940,510.57
Fluticasone Propionate Nasal	Flonase*	94	$1,059,605.90	88	$1,052,339.69
Infliximab	Remicade	95	$1,053,320.60	133	$703,564.45
Fingolimod	Gilenya	96	$1,051,140.40	79	$1,234,458.33
Etonogestrel Ethinyl Estradiol VA Ring	Nuvaring	97	$1,041,642.15	82	$1,151,982.08
Asenapine	Saphris	98	$1,031,226.87	112	$838,859.81
Risperidone Injection	Risperdal Consta	99	$1,021,897.87	83	$1,107,541.19
C1 Esterase Inhibitor (Human)	Multiple Products	100	$1,003,742.26	100	$935,796.59

*Includes brand and generic where applicable.
NA = not applicable, DF = disoproxil fumarate, VA = vaginal, Trinz = Trinza, Sust = Sustenna
Reimbursement does not reflect rebated costs or net costs.

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	251,334	108,487	$14,147,949.42	2.41	$56.29	2.32	$2.61	11.07%
2	Amoxicillin	Amoxil*	231,887	167,219	$1,947,608.83	11.95	$8.40	1.39	$0.87	1.52%
3	Cetirizine	Multiple	226,738	98,825	$1,692,303.49	3.02	$7.46	2.29	$0.25	1.32%
4	Hydrocodone/Acetaminophen	Multiple	209,476	75,306	$3,688,595.20	3.96	$17.61	2.78	$0.97	2.89%
5	Azithromycin	Zithromax*	135,934	102,792	$2,384,994.11	3.11	$17.55	1.32	$3.50	1.87%
6	Montelukast	Singulair*	129,224	37,862	$1,900,345.72	1.00	$14.71	3.41	$0.49	1.49%
7	Fluticasone Propionate Nasal	Flonase*	102,666	56,619	$1,059,605.90	0.45	$10.32	1.81	$0.29	0.83%
8	Lisdexamfetamine	Vyvanse	90,129	16,285	$21,439,176.98	1.00	$237.87	5.53	$8.01	16.78%
9	Omeprazole	Prilosec*	85,974	25,599	$671,296.76	1.25	$7.81	3.36	$0.22	0.53%
10	Clonidine	Catapres*	85,035	15,151	$522,423.36	1.45	$6.14	5.61	$0.20	0.41%
11	Gabapentin	Neurontin*	83,354	18,660	$1,247,676.00	3.14	$14.97	4.47	$0.48	0.98%
12	Methylphenidate	Multiple	81,770	12,777	$14,009,206.64	1.36	$171.32	6.4	$5.76	10.96%
13	Ibuprofen	Motrin*	79,206	56,677	$597,721.84	3.97	$7.55	1.4	$0.46	0.47%
14	Loratadine	Multiple	72,901	32,132	$608,507.15	2.58	$8.35	2.27	$0.27	0.48%
15	Sertraline	Zoloft*	71,720	18,101	$488,160.24	1.17	$6.81	3.96	$0.21	0.38%
16	Alprazolam	Xanax*	70,112	11,687	$360,905.00	2.33	$5.15	6	$0.18	0.28%
17	Amoxicillin/Clavulanate	Augmentin*	68,346	56,706	$1,831,197.16	8.76	$26.79	1.21	$2.69	1.43%
18	Cefdinir	Omnicef*	66,857	51,217	$2,526,213.71	6.76	$37.79	1.31	$3.77	1.98%
19	Trazodone	Desyrel*	61,962	15,345	$384,493.95	1.25	$6.21	4.04	$0.19	0.30%
20	Ondansetron	Zofran*	61,889	49,427	$567,232.43	1.91	$9.17	1.25	$1.35	0.44%
21	Fluoxetine	Prozac*	61,158	14,799	$575,896.57	1.26	$9.42	4.13	$0.29	0.45%
22	Lisinopril	Multiple	59,633	16,148	$233,711.23	1.09	$3.92	3.69	$0.09	0.18%
23	Prednisone	Multiple	59,362	43,836	$356,927.35	1.98	$6.01	1.35	$0.66	0.28%
24	Oxycodone/Acetaminophen	Multiple	59,207	26,451	$2,259,891.79	3.8	$38.17	2.24	$2.25	1.77%
25	Sulfamethoxazole/Trimethoprim	Bactrim*	58,718	47,357	$1,487,187.18	7.73	$25.33	1.24	$2.36	1.16%
26	Amphetamine/Dextroamphetamine	Multiple	57,209	9,049	$5,797,633.31	1.41	$101.34	6.32	$3.40	4.54%
27	Levothyroxine	Multiple	54,922	11,319	$1,159,050.66	1.00	$21.10	4.85	$0.52	0.91%
28	Cephalexin	Keflex*	53,398	46,326	$864,044.79	9.44	$16.18	1.15	$1.78	0.68%
29	Triamcinolone Topical	Multiple	52,856	37,481	$629,569.87	4.33	$11.91	1.41	$0.74	0.49%
30	Tramadol	Ultram*	51,294	20,459	$270,983.59	3.88	$5.28	2.51	$0.27	0.21%
31	Risperidone	Risperdal*	49,631	8,988	$633,807.35	1.51	$12.77	5.52	$0.41	0.50%

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	Prednisolone Sodium Phosphate	Multiple	49,166	37,601	$1,215,501.67	6.93	$24.72	1.31	$4.54	0.95%
33	Quetiapine	Seroquel*	46,997	9,029	$3,088,194.63	1.45	$65.71	5.21	$2.10	2.42%
34	Cyclobenzaprine	Multiple	44,063	21,265	$220,847.69	2.42	$5.01	2.07	$0.22	0.17%
35	Metformin	Multiple	44,051	11,037	$198,794.60	2.04	$4.51	3.99	$0.14	0.16%
36	Clonazepam	Klonopin*	42,902	8,874	$279,900.22	2.14	$6.52	4.83	$0.23	0.22%
37	Citalopram	Celexa*	41,521	11,838	$190,215.92	1.00	$4.58	3.51	$0.13	0.15%
38	Acetaminophen/Codeine	Multiple	41,497	27,938	$390,779.82	5.55	$9.42	1.49	$0.87	0.31%
39	Fluticasone Propionate Inhalation	Flovent	41,253	17,391	$8,256,495.85	0.35	$200.14	2.37	$6.02	6.46%
40	Guanfacine Extended-Release	Intuniv*	40,724	6,843	$1,089,295.46	1.00	$26.75	5.95	$0.90	0.85%
41	Mupirocin Topical	Bactroban*	40,337	34,372	$518,619.84	2.11	$12.86	1.17	$1.18	0.41%
42	Oxycodone	Multiple	40,178	6,373	$7,006,876.59	3.13	$174.40	6.3	$6.32	5.48%
43	Ranitidine	Zantac*	37,735	16,492	$302,568.79	3.37	$8.02	2.29	$0.27	0.24%
44	Prednisolone Syrup	Prelone*	37,423	29,621	$269,573.49	6.85	$7.20	1.26	$1.31	0.21%
45	Promethazine	Multiple	37,161	23,671	$322,512.34	5.56	$8.68	1.57	$1.01	0.25%
46	Dexmethylphenidate	Focalin*	36,044	4,815	$4,967,687.34	1.18	$137.82	7.49	$4.62	3.89%
47	Hydroxyzine Hydrochloride	Atarax*	32,703	16,744	$351,091.76	4.62	$10.74	1.95	$0.50	0.27%
48	Polyethylene Glycol	Multiple	32,406	17,385	$623,451.11	17.52	$19.24	1.86	$0.69	0.49%
49	Escitalopram	Lexapro*	32,177	8,535	$269,704.41	1.06	$8.38	3.77	$0.25	0.21%
50	Atomoxetine	Strattera	32,142	6,398	$11,887,683.27	1.08	$369.85	5.02	$12.48	9.30%

*Includes brand and generic where applicable.

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

Reimbursement does not reflect rebated costs or net costs.

Top Traditional Therapeutic Classes by Fiscal Year*

Anti-Infective Agents	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
Antiviral Agents	33,846	$44,910,210.63	83,466	$42,587,745.15
Anti-Infectives	103,263	$6,166,617.10	103,761	$6,065,355.06
Cephalosporins	131,989	$4,189,318.58	125,195	$4,645,941.74
Penicillins	313,303	$4,099,157.67	301,008	$3,957,717.56
Macrolide Antibiotics	139,986	$3,296,536.47	145,594	$3,022,834.25
Anthelmintic Agents	3,170	$1,159,334.44	2,627	$856,774.77
Antifungal Agents	27,720	$1,157,392.05	27,419	$1,011,220.18
Tetracyclines	23,754	$835,506.82	22,545	$1,132,962.64
Antimalarial Agents	4,257	$583,552.27	3,811	$309,542.60
Fluoroquinolones	24,999	$229,306.79	26,961	$249,993.14
Antimycobacterial Agents	370	$33,852.92	479	$32,558.52
Aminoglycosides	412	$21,841.15	412	$18,063.75
Sulfonamides	3	$1,121.97	9	$4,284.29
Amebicides	0	$0.00	0	$0.00
Total:	**807,072**	**$66,683,748.86**	**843,287**	**$63,894,993.65**

Attention Deficit Hyperactivity Disorder (ADHD) Agents	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
ADHD/Anti-Narcolepsy Agents	340,755	$59,942,177.34	316,760	$59,594,300.66
Total:	**340,755**	**$59,942,177.34**	**316,760**	**$59,594,300.66**

Antipsychotics	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
Antipsychotics	202,758	$53,916,241.63	199,429	$53,904,373.75
Total:	**202,758**	**$53,916,241.63**	**199,429**	**$53,904,373.75**

Anti-Asthmatic and Bronchodilator Agents	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
Anti-Asthmatic and Bronchodilator Agents	510,716	$45,212,373.87	484,615	$42,476,166.30
Total:	**510,716**	**$45,212,373.87**	**484,615**	**$42,476,166.30**

Anti-Diabetic Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Anti-Diabetic Agents		142,144	$40,929,564.55	137,069	$33,865,458.33
	Total:	**142,144**	**$40,929,564.55**	**137,069**	**$33,865,458.33**
Pain Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Analgesics - Narcotic		453,978	$22,213,624.32	484,585	$20,782,797.35
Analgesics - Anti-Inflammatory		159,791	$1,643,749.71	168,150	$1,663,307.67
Analgesics - Non-Narcotic		17,259	$484,158.62	20,953	$479,145.27
Migraine Agents		12,316	$438,075.07	11,607	$320,821.78
Gout Agents		6,400	$183,111.88	6,259	$133,165.39
Local Anesthetics - Parenteral		1,388	$7,268.27	1,352	$7,322.61
General Anesthetics		120	$3,676.01	178	$3,810.97
	Total:	**651,252**	**$24,973,663.88**	**693,084**	**$23,390,371.04**
Anticonvulsant Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticonvulsant Agents		328,694	$23,056,678.56	320,482	$21,634,647.57
	Total:	**328,694**	**$23,056,678.56**	**320,482**	**$21,634,647.57**
Endocrine Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Other Endocrine Agents		19,901	$7,866,567.89	20,173	$6,779,374.13
Contraceptives		107,054	$6,460,118.08	112,670	$7,130,461.71
Corticosteroids		183,502	$2,634,896.73	176,365	$4,073,708.85
Thyroid Agents		58,057	$1,252,359.21	56,683	$1,162,128.91
Estrogens		10,690	$971,083.18	11,677	$934,486.28
Progestins		5,397	$700,029.95	4,924	$277,693.74
Androgen - Anabolic Agents		567	$153,015.94	615	$153,064.33
Oxytocics		283	$39,465.50	328	$47,737.38
	Total:	**385,451**	**$20,077,536.48**	**383,435**	**$20,558,655.33**
Topical Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological Agents		216,426	$11,116,943.35	202,974	$9,431,485.84

Otic Agents		32,394	$4,586,498.31	47,384	$1,536,418.60
Ophthalmic Agents		71,319	$2,251,114.68	60,942	$1,978,911.20
Mouth/Throat/Dental Agents		24,385	$304,502.15	24,868	$321,086.99
Anorectal Agents		1,546	$134,826.03	1,426	$75,249.83
	Total:	**346,070**	**$18,393,884.52**	**337,594**	**$13,343,152.46**
Cardiovascular Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Vasopressors		10,829	$5,683,364.79	10,739	$4,416,986.79
Antihyperlipidemics		78,013	$2,510,435.58	78,280	$3,194,578.37
Antihypertensives		229,807	$2,173,709.28	226,394	$2,313,284.50
Beta Blockers		81,128	$1,892,836.66	81,083	$1,743,202.11
Antianginal Agents		8,942	$806,920.30	8,963	$706,409.08
Diuretics		56,996	$577,006.43	57,456	$544,449.95
Calcium Channel Blockers		39,985	$440,121.78	38,750	$447,152.65
Cardiotonics		3,668	$179,348.30	3,956	$213,741.02
Other Cardiovascular Agents		388	$127,352.69	286	$87,360.99
Antiarrhythmic Agents		2,333	$122,767.34	2,173	$97,480.15
	Total:	**512,089**	**$14,513,863.15**	**508,080**	**$13,764,645.61**
Antineoplastic Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antineoplastic Agents		12,625	$12,190,376.19	12,848	$10,868,100.95
	Total:	**12,625**	**$12,190,376.19**	**12,848**	**$10,868,100.95**
Gastrointestinal Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Ulcer Agents		195,580	$3,598,446.23	195,843	$3,434,728.68
Other Gastrointestinal Agents		13,656	$2,638,004.67	13,921	$2,503,230.57
Digestive Aids		1,721	$2,172,192.30	1,652	$1,881,270.60
Antiemetics		89,570	$1,205,365.75	93,113	$1,419,542.13
Laxatives		42,651	$907,310.61	39,698	$880,967.42
Antidiarrheals		3,006	$40,765.77	3,106	$38,815.14
Antacids		616	$3,378.32	529	$2,748.02
	Total:	**346,800**	**$10,565,463.65**	**347,862**	**$10,161,302.56**

Non-Therapeutic Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Diagnostic Agents		30,123	$4,230,096.11	6,141	$848,850.15
Assorted Classes		6,402	$2,050,134.46	6,055	$2,321,180.00
Medical Devices		62,022	$1,731,951.38	33,683	$1,471,639.61
Antidotes		2,413	$168,872.99	1,580	$96,635.92
Chemicals		11,318	$144,280.34	11,920	$217,511.00
Pharmaceutical Adjuvants		1,204	$57,935.30	1,171	$58,950.51
Antiseptics & Disinfectants		8	$189.51	7	$185.44
Alternative Medicines		6	$34.97	3	$20.57
	Total:	**113,496**	**$8,383,495.06**	**60,560**	**$5,014,973.20**
Antidepressants		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidepressants		417,903	$6,184,543.86	403,405	$6,347,776.63
	Total:	**417,903**	**$6,184,543.86**	**403,405**	**$6,347,776.63**
Psychotherapeutic/Neurologic Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Psychotherapeutic & Neurological Agents		18,787	$4,368,191.99	17,575	$4,580,157.46
	Total:	**18,787**	**$4,368,191.99**	**17,575**	**$4,580,157.46**
Allergy Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antihistamines		346,170	$2,879,174.85	318,325	$2,709,697.23
Systemic & Topical Nasal Agents		107,743	$1,350,737.53	100,942	$1,555,747.86
Cough/Cold/Allergy Agents		1,765	$50,986.12	1,495	$33,742.61
	Total:	**455,678**	**$4,280,898.50**	**420,762**	**$4,299,187.70**
Hematological Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Anticoagulants		14,717	$2,584,795.58	14,466	$2,395,702.05
Other Hematological Agents		14,465	$972,318.42	14,092	$685,107.06
Hematopoietic Agents		15,592	$268,261.61	15,653	$176,669.63
Hemostatics		205	$75,427.92	219	$54,599.09
	Total:	**44,979**	**$3,900,803.53**	**44,430**	**$3,312,077.83**

Genitourinary Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Urinary Anti-Infectives		18,839	$789,944.51	18,636	$840,810.49
Urinary Antispasmodics		13,554	$721,633.96	13,266	$787,709.26
Vaginal Agents		5,457	$662,766.52	5,652	$517,071.30
Other Genitourinary Agents		10,471	$596,573.67	11,634	$725,559.28
	Total:	**48,321**	**$2,770,918.66**	**49,188**	**$2,871,150.33**

Nutritional Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Multivitamins		37,478	$1,839,114.68	40,858	$1,308,025.08
Minerals & Electrolytes		24,089	$565,468.23	24,892	$537,489.60
Vitamins		704	$422,960.82	593	$231,314.74
Dietary Products		362	$152,873.52	405	$158,078.48
Nutrients		327	$54,312.58	307	$44,342.00
	Total:	**62,960**	**$3,034,729.83**	**67,055**	**$2,279,249.90**

Neuromuscular Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Musculoskeletal Therapy Agents		106,934	$1,416,935.42	110,285	$1,814,960.30
Antiparkinsonian Agents		25,633	$775,216.24	25,282	$738,046.03
Antimyasthenic Agents		207	$57,608.88	190	$59,705.83
Neuromuscular Agents		12	$2,065.95	2	$338.29
	Total:	**132,786**	**$2,251,826.49**	**135,759**	**$2,613,050.45**

Antianxiety Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Antianxiety Agents		197,914	$1,531,592.20	199,694	$1,602,456.53
	Total:	**197,914**	**$1,531,592.20**	**199,694**	**$1,602,456.53**

Hypnotics		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Hypnotics		44,945	$528,484.63	49,341	$497,327.56
	Total:	**44,945**	**$528,484.63**	**49,341**	**$497,327.56**

Biological Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Vaccines		6,284	$267,808.90	5,783	$176,520.44
Passive Immunizing Agents		52	$239,986.09	33	$98,089.76
Toxoids		882	$37,177.71	560	$23,055.98
Other Biological Agents		7	$1,855.05	*****	*********
	Total:	**7,225**	**$546,827.75**	**6,376**	**$297,666.18**

Specialized Respiratory Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Specialized Respiratory Agents		19	$139,087.33	*****	*********
	Total:	**19**	**$139,087.33**	*****	*********

Top Specialty Therapeutic Classes by Fiscal Year*

Hematological Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Other Hematological Agents		698	$16,463,906.42	669	$16,222,363.98
Hematopoietic Agents		635	$2,395,925.93	669	$2,284,571.67
	Total:	**1,333**	**$18,859,832.35**	**1,338**	**$18,506,935.65**

Pain Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Analgesics - Anti-Inflammatory		4,261	$18,733,433.45	3,736	$12,878,189.79
Local Anesthetics - Parenteral		35	$905.79	46	$1,118.12
	Total:	**4,296**	**$18,734,339.24**	**3,782**	**$12,879,307.91**

Endocrine Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Other Endocrine Agents		3,063	$10,291,717.16	2,770	$8,848,238.90
Progestins		1,188	$4,440,351.71	1,024	$3,703,814.63
	Total:	**4,251**	**$14,732,068.87**	**3,794**	**$12,552,053.53**

Psychotherapeutic/Neurologic Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Psychotherapeutic & Neurological Agents		1,533	$8,608,234.85	1,599	$7,986,737.17
	Total:	**1,533**	**$8,608,234.85**	**1,599**	**$7,986,737.17**

Specialized Respiratory Agents		2016		2015	
		Total Claims	Total Paid	Total Claims	Total Paid
Specialized Respiratory Agents		1,153	$7,763,918.62	945	$3,976,385.33
	Total:	**1,153**	**$7,763,918.62**	**945**	**$3,976,385.33**
Biological Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Passive Immunizing Agents		2,043	$3,650,627.90	2,763	$5,236,827.78
Other Biological Agents		11	$370,164.55	12	$401,673.78
	Total:	**2,054**	**$4,020,792.45**	**2,775**	**$5,638,501.56**
Cardiovascular Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Cardiovascular Agents		843	$3,387,423.54	827	$2,441,564.38
	Total:	**843**	**$3,387,423.54**	**827**	**$2,441,564.38**
Anti-Infective Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Aminoglycosides		309	$1,414,853.31	281	$1,671,395.60
Other Anti-Infective Agents		66	$423,791.39	69	$395,177.86
Antivirals		10	$33,990.02	11	$35,096.03
	Total:	**385**	**$1,872,634.72**	**361**	**$2,101,669.49**
Non-Therapeutic Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidotes		312	$1,928,230.30	302	$1,930,027.69
	Total:	**312**	**$1,928,230.30**	**302**	**$1,930,027.69**
Gastrointestinal Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Gastrointestinal Agents		332	$1,642,701.27	475	$1,962,601.23
	Total:	**332**	**$1,642,701.27**	**475**	**$1,962,601.23**
Topical Agents		**2016**		**2015**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological Agents		60	$793,104.30	48	$638,208.04
	Total:	**60**	**$793,104.30**	**48**	**$638,208.04**

Anti-Asthmatic and Bronchodilator Agents	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
Anti-Asthmatic and Bronchodilator Agents	78	$282,758.11	81	$269,672.99
Total:	**78**	**$282,758.11**	**81**	**$269,672.99**

Total	2016		2015	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Top Traditional and Specialty Therapeutic Classes	**6,148,069**	**$511,003,011.13**	**6,055,017**	**$472,054,906.95**

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

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Appendix I

Calendar Year 2016 Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Invokamet® XR (Canagliflozin/Metformin Extended-Release), Jentadueto® XR (Linagliptin/Metformin Extended-Release), Adlyxin® (Lixisenatide), Xultophy® 100/3.6 (Insulin Degludec/ Liraglutide), Soliqua™ 100/33 (Insulin Glargine/Lixisenatide), Synjardy® XR (Empagliflozin/Metformin Extended-Release), and Qtern® (Dapagliflozin/Saxagliptin)

Oklahoma Health Care Authority
April 2017

Current Prior Authorization Criteria

Diabetes Medications Tier-2 Approval Criteria:

1. A trial of a Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier-2 medications may be approved based on current American Association of Clinical Endocrinologists (AACE) or American Diabetes Association (ADA) guidelines.

Diabetes Medications Tier-3 Approval Criteria:

1. Member must have tried a Tier-2 medication in the same category and have a documented clinical reason why the Tier-2 medication is not appropriate. (For Tier-3 medications that do not have a similar category in Tier-2, a medication from any category in Tier-2 may be used.)

Diabetes Medications Special Prior Authorization (PA) Approval Criteria:

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

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

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

Toujeo® (Insulin Glargine) Approval Criteria:

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

Tresiba® (Insulin Degludec) Approval Criteria:

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

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

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

Basaglar® (Insulin Glargine) Approval Criteria:

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

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

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
SR = sustained-release, ER = extended-release, DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT-2 = sodium-glucose cotransporter-2

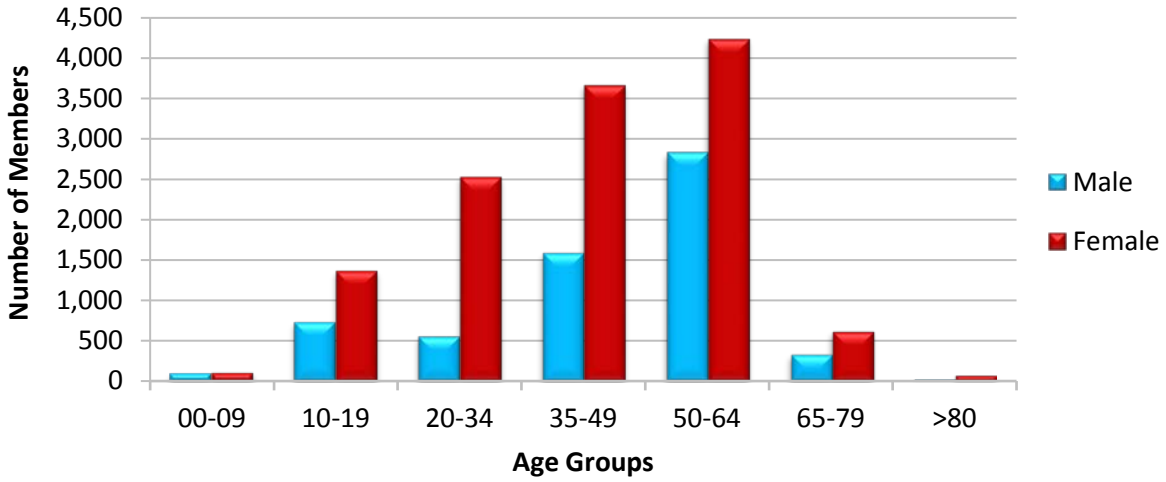
Utilization of Diabetes Medications: Calendar Year 2016

Comparison of Calendar Years

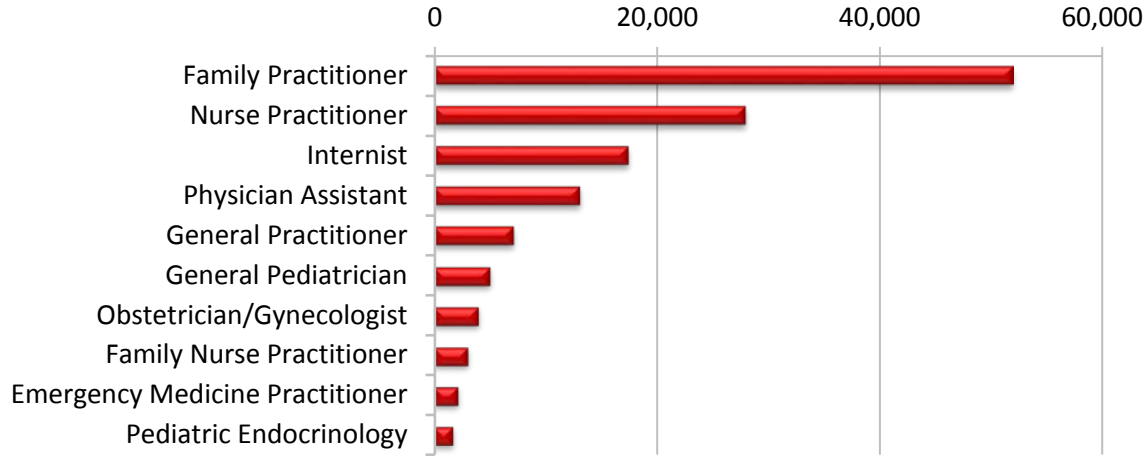
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	18,247	138,746	$37,429,356.42	$269.77	$7.93	5,815,320	4,720,437
2016	18,807	141,973	$42,509,004.45	$299.42	$8.68	5,901,152	4,899,032
% Change	**3.10%**	**2.30%**	**13.60%**	**11.00%**	**9.50%**	**1.50%**	**3.80%**
Change	**560**	**3,227**	**$5,079,648.03**	**$29.65**	**$0.75**	**85,832**	**178,595**

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

Demographics of Members Utilizing Diabetes Medications



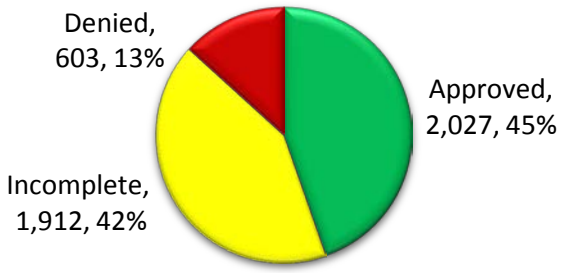
Top Prescriber Specialties of Diabetes Medications by Number of Claims



Prior Authorization of Diabetes Medications

There were 4,542 prior authorization requests submitted for diabetes medications during calendar year 2016. Of the 4,542 total prior authorizations submitted, 2,631 petitions were for oral diabetic medications and 1,911 were submitted for insulin requests. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Byetta® (exenatide): January 2020
- Januvia® (sitagliptin): November 2026
- Synjardy® (empagliflozin/metformin): April 2027
- Invokana® (canagliflozin): February 2029
- Invokamet® (canagliflozin/metformin): February 2029
- Jardiance® (empagliflozin): October 2029
- Farxiga® (dapagliflozin): May 2030
- Xigduo® XR (dapagliflozin/metformin extended-release[ER]): May 2030
- Glyxambi® (empagliflozin/linagliptin): June 2030
- Tradjenta® (linagliptin): March 2031

- Toujeo® (insulin glargine): May 2031
- Tresiba® (insulin degludec): February 2032
- Ryzodeg® 70/30 (insulin degludec/insulin aspart): February 2032
- Cycloset® (bromocriptine): April 2032
- Afrezza® (insulin human inhalation powder): July 2032
- Victoza® (liraglutide): September 2032

New Drug Approval(s):

- **May 2016:** Jentadueto® XR (linagliptin/metformin ER)
- **July 2016:** Adlyxin® (lixisenatide) injection
- **September 2016:** Invokamet® XR (canagliflozin/metformin ER)
- **November 2016:** Xultophy® 100/3.6 (insulin degludec 100 units/mL and liraglutide 3.6mg/mL injection)
- **November 2016:** Soliqua™ 100/33 (insulin glargine 100 units/mL and lixisenatide 33mcg/mL injection)
- **December 2016:** Synjardy® XR (empagliflozin/metformin ER)
- **February 2017:** Qtern® (dapagliflozin/saxagliptin)

New Indication Approval(s):

- **May 2016:** The U.S. Food and Drug Administration (FDA) approved Invokamet® (canagliflozin/metformin), a fixed-dose combination product containing a sodium glucose cotransporter (SGLT-2) inhibitor with a biguanide, for first-line treatment of adults with type 2 diabetes mellitus (DM). Invokamet® was originally FDA approved in August 2014 as an adjunct to diet and exercise to improve blood glucose control in adults with type 2 DM not adequately controlled by either canagliflozin or metformin or who were already being treated with both medications separately. The newly approved indication is in line with the most recent type 2 DM treatment guidelines which recommend initial dual therapy for patients with higher hemoglobin (Hb)A_{1c} levels. In September 2016, Invokamet® XR was also FDA approved as first-line treatment for type 2 DM in adults as an adjunct to diet and exercise.
- **December 2016:** The FDA approved a new indication for Jardiance® (empagliflozin) to reduce the risk of cardiovascular (CV) death in adult patients with type 2 DM and CV disease. The FDA's decision was based on a post-marketing study required by the FDA when Jardiance® was originally approved in 2014 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM. Jardiance® was studied in a post-market clinical trial of more than 7,000 patients with type 2 DM and CV disease. It was shown to reduce the risk of CV death compared to placebo when added to standard of care therapies for DM and atherosclerotic CV disease.
- **December 2016:** The FDA approved an expanded indication for Tresiba® (insulin degludec injection 100 units/mL, 200 units/mL), a once-daily, long-acting basal insulin, to be used in children one year of age and older with DM. Tresiba® was originally approved by the FDA in September 2015 for adult patients. It is now indicated to improve glycemic control in patients with type 1 and type 2 DM from the age of one through adulthood. Of note, Tresiba® is the only basal insulin approved for both type 1 and type 2 DM in patients as young as one year old.

Pipeline:

- **April 2016:** Merck announced that the company will not proceed with submitting marketing applications for omarigliptin, an investigational, once-weekly dipeptidyl peptidase-4 (DPP-4) inhibitor, in the United States or Europe. The company stated this decision was based on business reasons and did not result from concerns about the efficacy or safety of omarigliptin. Omarigliptin is approved in Japan and will continue to be marketed there as Marizev®.
- **May 2016:** Oramed Pharmaceuticals reported the investigational, oral insulin drug known as ORMD-0801 succeeded in significantly reducing night-time blood glucose in patients with type 2 DM according to initial data from a 28-day, 180-patient Phase 2 trial. Oramed is working with the FDA to proceed with a Phase 3 clinical trial in 2017.
- **August 2016:** Merck's New Drug Application (NDA) for its investigational insulin glargine biosimilar, MK-1293, was accepted for review by the FDA. The submission is following June 2016 results of two Phase 3 studies where MK-1293 achieved its primary endpoint by demonstrating non-inferiority in change from baseline HbA_{1c} and similar safety to Lantus® (insulin glargine) after 24 weeks in patients with type 1 and type 2 DM. Basaglar® (insulin glargine), approved by the FDA in December 2015, is the first Lantus® biosimilar available on the market.
- **December 2016:** Sotagliflozin, an investigational, first in class, oral dual inhibitor of SGLT type 1 and 2 for patients with type 1 DM, met its primary endpoint with mean HbA_{1c} reductions from baseline after 24 weeks of treatment of 0.39% with 200mg sotagliflozin and 0.37% with 400mg sotagliflozin (both $P<0.001$) vs 0.03% with placebo.
- **January 2017:** Results from the SUSTAIN-1 clinical trial for once-weekly semaglutide were published in *The Lancet* and demonstrated significant improvement in HbA_{1c} and bodyweight in patients with type 2 DM compared to placebo. The SUSTAIN-6 trial also showed a 26% lower risk of the primary composite outcome of first occurrence of CV death, nonfatal myocardial infarction (MI), or nonfatal stroke over two years compared to placebo as add-on to standard of care in patients with high CV risk. Novo Nordisk submitted a NDA to the FDA for once-weekly semaglutide for the treatment of adults with type 2 DM in December of 2016 based on the results from the SUSTAIN clinical trial program which included more than 8,000 adults with type 2 DM. Head-to-head studies between semaglutide and empagliflozin, sitagliptin, and liraglutide are currently underway.
- **March 2017:** The FDA has accepted NDAs for three treatments containing ertugliflozin, an investigational SGLT-2 inhibitor. The three treatments include a monotherapy formulation, a fixed-dose combination with sitagliptin, and a fixed-dose combination with metformin all for improving glycemic control in adults with type 2 DM. The clinical development program involved nine Phase 3 trials in over 12,000 adults with type 2 DM. The FDA has set a Prescription Drug User Fee Act (PDUFA) action date for December 2017.

News:

- **April 2016:** After a review of numerous studies published in medical literature, the FDA issued a Drug Safety Communication regarding label changes for all metformin-

containing medications, stating that metformin can be safely used in patients with mild, and some cases of moderate kidney impairment, for which it was previously contraindicated. The communication also stated that the measure of kidney function recommended is glomerular filtration rate estimating equation (eGFR) which provides a better estimate of kidney function in patients with kidney disease compared to blood creatinine concentration.

- **April 2016:** New *Warnings and Precautions* have been added to the labels of saxagliptin- and alogliptin-containing medications for the potential to increase the risk of heart failure. After an evaluation of two large clinical trials conducted in patients with heart disease, the FDA safety review has found that saxagliptin and alogliptin (both DPP-4 inhibitors) may increase the risk of heart failure, particularly in patients who have heart or kidney disease.
- **May 2016:** The FDA issued a Drug Safety Communication alerting the public about interim safety results from an ongoing clinical trial that found an increase in leg and foot amputations, mostly affecting the toes, in patients treated with canagliflozin-containing medications. The FDA has not determined whether there is a direct correlation between canagliflozin and an increased risk of leg and foot amputations, but is currently investigating the issue and will provide further updates when available.
- **June 2016:** The FDA issued a Drug Safety Communication strengthening the existing warning regarding the risk of acute kidney injury for canagliflozin and dapagliflozin containing medications. Based on recent reports, the warnings in the drug labels have been revised to include information about acute kidney injury and recommendations to minimize risks.
- **June 2016:** New data from the EMPA-REG OUTCOME trial published in *The New England Journal of Medicine* showed Jardiance® (empagliflozin) significantly reduced the risk for new-onset or worsening kidney disease by 39% versus placebo when added to standard of care in adults with type 2 DM with established CV disease. Previous data from the EMPA-REG OUTCOME trial published in 2015 showed empagliflozin significantly reduced the risk of the combined endpoint of CV death, non-fatal heart attack, or non-fatal stroke by 14% when added to standard of care in patients with type 2 DM at high risk of CV events. There was a 38% reduction in CV death with no significant difference in the risk of non-fatal heart attack or non-fatal stroke.
- **October 2016:** The FDA Adverse Events Reporting System (FAERS) quarterly publication put 27 drugs/drug classes on its watch list based on reports of adverse events. The SGLT-2 inhibitor class was among the medications listed for the potential serious risk of acute pancreatitis. The DPP-4 inhibitor class was also on the list for serious potential risk of pemphigoid, a group of rare autoimmune blistering diseases of the skin and mucosa. The FDA is investigating and evaluating the need for regulatory action. An adverse event on a quarterly FAERS watch list normally doesn't mean that the FDA has concluded there is a causal relationship, but that the FDA intends to investigate whether one exists. If the FDA's study does find a connection, the FDA could collect more data to better define the threat, revise the drug's label, order a Risk Evaluation and Mitigation Strategy (REMS), or in rare cases pull the drug from the market.

- **December 2016:** Based on the results of an updated review, the FDA has concluded that pioglitazone and pioglitazone-containing drugs may be linked to an increase risk of bladder cancer. The FDA previously issued safety alerts regarding the possible risk of bladder cancer in September 2010 and June 2011 based on interim results from a 10-year epidemiologic study. The FDA reviewed additional published studies and the results varied among the reviewed studies, however, the overall data suggest that pioglitazone use may be linked to an increased risk of bladder cancer. The FDA recommends pioglitazone and pioglitazone-containing drugs not be used in patients with active bladder cancer and be used cautiously in patients with a history of bladder cancer.

Guideline Update(s):

- **January 2017:** Oral Pharmacologic Treatment of Type 2 Diabetes Mellitus: A Clinical Practice Update from the American College of Physicians (ACP) was published in *Annals of Internal Medicine*. This guideline is an update from the ACP's previous 2012 guideline and includes newer oral medications that are now available since the last update. Metformin remains first-line for patients with type 2 DM when medication is needed to improve glycemic control. If a second medication is needed to improve high blood sugar, the ACP recommends physicians to consider adding either a sulfonylurea, thiazolidinedione, SGLT-2 inhibitor, or DPP-4 inhibitor to metformin. The ACP recommends that clinicians and patients discuss the benefits, adverse effects, and costs of additional medications. The increased cost, particularly of the more expensive medications, may not always support the added benefit.
- **January 2017:** The American Diabetes Association's (ADA) 2017 Standards of Medical Care in Diabetes (Standards) was published in *Diabetes Care* and emphasized psychological health, access to care, expanded and personalized treatment options, and tracking of hypoglycemia as key points. The guideline is produced annually by the ADA and focuses on screening, diagnosis, and treatment to provide better health outcomes for children and adults with type 1, type 2, or gestational DM, and to improve the prevention and delay of type 2 DM.

Invokamet® XR (Canagliflozin/Metformin Extended-Release) Product Summary[33]

Indications: Invokamet® XR (canagliflozin/metformin extended-release [ER]) is a SGLT-2 inhibitor and biguanide combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM when treatment with both canagliflozin and metformin is appropriate.

- Limitations of Use: Invokamet® XR is not for the treatment of type 1 DM or diabetic ketoacidosis.

Dosing:

- Invokamet® XR is available as a film-coated tablet in four strengths: 50mg canagliflozin/500mg metformin ER, 50mg canagliflozin/1,000mg metformin ER, 150mg canagliflozin/500mg metformin ER, and 150mg canagliflozin/1,000mg metformin ER.
- The recommended dosing for Invokamet® XR is two tablets once daily with the morning meal.

- In patients currently not treated with either canagliflozin or metformin, therapy should be initiated with two Invokamet® XR 50mg/500mg tablets.
- Patients already treated with canagliflozin and metformin should be switched to two Invokamet® XR tablets containing the same total daily dose of canagliflozin and the same, or nearest appropriate, total daily dose of metformin.
- In patients that require additional glycemic control that are taking a total daily dose of canagliflozin 100mg, the Invokamet® XR dose can be increased to canagliflozin 300mg once daily. A total daily canagliflozin dose of 300mg should not be exceeded.
- The metformin dose should be gradually escalated to reduce the gastrointestinal side effects while not exceeding a total daily dose of 2,000mg.
- Renal function should be assessed before initiating therapy and periodically thereafter.
- Invokamet® XR is contraindicated in patients with an eGFR below 45mL/min/1.73m^2.
- The dose of canagliflozin should be limited to two tablets, each tablet containing 50mg, daily in patients with an eGFR of 45 to less than 60mL/min/1.73m^2.
- Invokamet® XR should be swallowed whole and never crushed, cut, or chewed.

Efficacy: There have been no clinical efficacy studies conducted with Invokamet® XR. Bioequivalence studies were conducted comparing Invokamet® XR to canagliflozin and metformin co-administered as individual tablets and was demonstrated in healthy subjects.

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Invokamet® XR (canagliflozin/metformin ER) all strengths	**$7.11**	**$426.60**	**$5,119.20**
Synjardy® XR (empagliflozin/metformin ER) 12.5mg/1,000mg	$7.18	$430.80	$5,169.60
Invokana® (canagliflozin) 300mg	$13.71	$411.30	$4,935.60
metformin 1,000mg	$0.03	$1.80	$21.60

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

Jentadueto® XR (Linagliptin/Metformin Extended-Release) Product Summary[34]

Indications: Jentadueto® XR (linagliptin/metformin extended-release [ER]) is a DPP-4 inhibitor and biguanide combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM when treatment with both linagliptin and metformin is appropriate.

- Limitations of Use:
  - Jentadueto® XR is not for the treatment of type 1 DM or diabetic ketoacidosis.
  - Jentadueto® XR has not been studied in patients with a history of pancreatitis.

Dosing:

- Jentadueto® XR is available as oral tablets in two strengths: 2.5mg linagliptin/1,000mg metformin ER and 5mg linagliptin/1,000mg metformin ER.
- Jentadueto® XR should be individualized based on the patient's current regimen. The recommended dosing for Jentadueto® XR is once daily with a meal and the total daily dose should not exceed 5mg linagliptin and 2,000mg metformin per day.

- Jentadueto® XR should be swallowed whole and not split, crushed, dissolved, or chewed.
- Renal function should be assessed with eGFR before initiating Jentadueto® XR.
- Jentadueto® XR should not be used in patients with eGFR below 30mL/min/1.73m^2 and initiation is not recommended in patients with eGFR between 30 and 45mL/min/1.73m^2.
- The risk/benefit of continuing Jentadueto® XR should be assessed if eGFR falls below 45mL/min/1.73m^2 and Jentadueto® XR should be discontinued if eGFR falls below 30mL/min/1.73m^2.

Efficacy: The safety and efficacy of Jentadueto® XR were established based on adequate and well-controlled studies of linagliptin and metformin coadministered in patients with type 2 DM inadequately controlled on diet and exercise and in combination with a sulfonylurea.

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Jentadueto® XR (linagliptin/metformin ER) 5mg/1,000mg	**$12.70**	**$381.00**	**$4,572.00**
Jentadueto® XR (linagliptin/metformin ER) 2.5mg/1,000mg	**$6.35**	**$190.50**	**$2,286.00**
Tradjenta® (linagliptin) 5mg	$12.23	$366.90	$4,402.80
metformin 1,000mg	$0.03	$1.80	$21.60

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

Adlyxin® (Lixisenatide) Product Summary[35,36]

Indications: Adlyxin® (lixisenatide) is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM.

- Limitations of Use:
  - Adlyxin® has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Use of other antidiabetic therapies should be considered in patients with a history of pancreatitis.
  - Adlyxin® is not for treatment of type 1 DM or diabetic ketoacidosis.
  - Adlyxin® has not been studied in combination with short-acting insulin.
  - Adlyxin® has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

Dosing:

- Adlyxin® is available as an injection in two strengths: 50mcg/mL in a 3mL prefilled pen for 14 pre-set doses of 10mcg per dose and 100mcg/mL in a 3mL prefilled pen for 14 pre-set doses of 20mcg per dose.
- Adlyxin® should be initiated at 10mcg once daily for 14 days. On day 15, the dose should be increased to 20mcg once daily.
- Adlyxin® should be administered once daily within one hour before the first meal of the day.
- Adlyxin® should be injected subcutaneously in the abdomen, thigh, or upper arm.

Efficacy: The safety and efficacy of Adlyxin® were evaluated in ten clinical trials enrolling 5,400 patients with type 2 DM. Adlyxin® was evaluated both as monotherapy and in combination with other FDA-approved diabetic medications including metformin, sulfonylureas, pioglitazone, and basal insulin. Adlyxin® improved HbA_{1c} in these trials. A CV outcomes trial comparing Adlyxin® to placebo in more than 6,000 patients with type 2 DM at risk for atherosclerotic CV disease demonstrated use of Adlyxin® did not increase the risk of CV adverse events in these patients nor did it improve.

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Adlyxin® (lixisenatide) both strengths	**$92.87**	**$557.22**	**$6,686.64**
Victoza® (liraglutide) 18mg/3mL	$80.05	$720.45	$8,645.40
metformin 1,000mg	$0.03	$1.80	$21.60

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

Xultophy® 100/3.6 (Insulin Degludec/Liraglutide) Product Summary[37,38]

Indications: Xultophy® 100/3.6 (insulin degludec 100 units/mL and liraglutide 3.6mg/mL injection) is a combination of insulin degludec, a long-acting human insulin analog, and liraglutide, a GLP-1 receptor agonist, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM inadequately controlled on basal insulin (less than 50 units daily) or liraglutide (less than or equal to 1.8mg daily).

- Limitations of Use:
  - Xultophy® 100/3.6 is not recommended as first-line therapy for patients inadequately controlled on diet and exercise.
  - Xultophy® 100/3.6 has not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.
  - Xultophy® 100/3.6 is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.
  - Xultophy® 100/3.6 is not for treatment of type 1 DM or diabetic ketoacidosis.
  - Xultophy® 100/3.6 has not been studied in combination with prandial insulin.

Dosing:

- Xultophy® 100/3.6 is available as an injection containing 100 units of insulin degludec per mL and 3.6mg of liraglutide per mL in a single-patient-use pen. Xultophy® 100/3.6 pen delivers doses from 10 to 50 units with each injection; each Xultophy® 100/3.6 dosage unit contains 1 unit of insulin degludec and 0.036mg of liraglutide.
- Liraglutide and/or basal insulin therapy should be discontinued prior to initiation of Xultophy® 100/3.6.
- The recommended starting dosage of Xultophy® 100/3.6 is 16 units (16 units of insulin degludec and 0.58mg of liraglutide) given subcutaneously once daily.
- Xultophy® 100/3.6 should be administered once daily at same time each day with or without food.

- The maximum daily dosage is 50 units (50 units of insulin degludec and 1.8mg of liraglutide).
- Alternative antidiabetic products should be considered if patients require a Xultophy® 100/3.6 daily dosage persistently below 16 units or over 50 units.
- Xultophy® 100/3.6 should be injected subcutaneously in the thigh, upper arm, or abdomen.

Efficacy: The safety and efficacy of Xultophy® 100/3.6 was based on data from three randomized clinical trials involving 1,393 type 2 DM patients who were inadequately controlled on liraglutide or basal insulin therapy and switched to Xultophy® 100/3.6. Patients may have received oral antidiabetic (OAD) therapy during the study. The primary endpoint was a reduction in HbA_{1C} from baseline to week 26.

- In a study comparing Xultophy® 100/3.6 and OADs vs. liraglutide and OADs, there was a reduction in baseline HbA_{1C} of -1.31% for Xultophy® 100/3.6 and -0.36% for liraglutide ($p < 0.0001$ for superiority).
- In a study comparing Xultophy® 100/3.6 and metformin vs. insulin degludec and metformin, the reduction in baseline HbA_{1C} was -1.94% with Xultophy® 100/3.6 and -1.05% with insulin degludec ($p < 0.01$). This trial was designed to show the contribution of liraglutide to glycemic lowering and may not reflect real world clinical practice.
- In a study comparing Xultophy® 100/3.6 and metformin vs. insulin glargine and metformin, the reduction in baseline HbA_{1C} was -1.67% with Xultophy® 100/3.6 and -1.16% with insulin glargine ($p < 0.01$ for non-inferiority).

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Xultophy® 100/3.6 (insulin degludec/liraglutide)	**$63.55**	**$953.25**	**$11,439.00**
Victoza® (liraglutide) 18mg/3mL	$80.05	$720.45	$8,645.40
Lantus® (insulin glargine)	$24.07	$481.40¥	$5,776.80¥
metformin 1,000mg	$0.03	$1.80	$21.60

Costs do not reflect rebated prices or net costs.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
¥ Lantus® dose based on 50 units of insulin glargine per day and therefore requiring two vials per month.

Soliqua™ 100/33 (Insulin Glargine/Lixisenatide) Product Summary[39,40]

Indications: Soliqua™ 100/33 (insulin glargine 100 units/mL and lixisenatide 33mcg/mL injection) is a combination of a long-acting human insulin analog with a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM inadequately controlled on basal insulin (less than 60 units daily) or lixisenatide.

- Limitations of Use:
  - Soliqua™ 100/33 has not been studied in patients with a history of unexplained pancreatitis. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.
  - Soliqua™ 100/33 is not recommended for use in combination with any other product containing lixisenatide or another GLP-1 receptor agonist.
  - Soliqua™ 100/33 is not for treatment of type 1 DM or diabetic ketoacidosis.

- Soliqua™ 100/33 is not recommended for use in patients with gastroparesis.
- Soliqua™ 100/33 has not been studied in combination with prandial insulin.

Dosing:

- Soliqua™ 100/33 is available as an injection containing 100 units of insulin glargine per mL and 3.3mg of lixisenatide per mL in a 3mL single-patient-use pen. Soliqua™ 100/33 pen delivers doses from 15 to 60 units with each injection.
- Lixisenatide and/or basal insulin therapy should be discontinued prior to the initiation of Soliqua™ 100/33.
- In patients inadequately controlled on less than 30 units of basal insulin or on lixisenatide, the starting dosage is 15 units (15 units insulin glargine/5mcg lixisenatide) given subcutaneously once daily.
- In patients inadequately controlled on 30 to 60 units of basal insulin, the starting dosage is 30 units (30 units insulin glargine/10mcg lixisenatide) given subcutaneously once daily.
- Soliqua™ 100/33 should be injected subcutaneously in the thigh, upper arm, or abdomen once a day within the hour prior to the first meal of the day.
- The maximum daily dosage is 60 units (60 units of insulin glargine and 20mcg of lixisenatide).
- Alternative antidiabetic products should be used if patients require a Soliqua™ 100/33 daily dosage below 15 units or over 60 units.

Efficacy: The efficacy and safety of Soliqua™ 100/33 were demonstrated in a clinical study of 736 patients with type 2 DM randomized to Soliqua™ 100/33 or insulin glargine. The primary efficacy endpoint was the reduction in baseline HbA_{1C} at week 30.

- The Soliqua™ 100/33 group demonstrated a statistically significantly greater reduction in HbA_{1C} vs. the insulin glargine group (-1.1% vs. -0.6%, respectively; $p < 0.01$).
- The trial was designed to show the contribution of lixisenatide to glucose lowering and the results may not reflect real world clinical practice where alternative insulin glargine dosages can be used (60 units insulin dose cap used in study).

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Soliqua™ 100/33 (insulin glargine/lixisenatide)	**$42.33**	**$1,269.90⁺**	**$15,238.80⁺**
Adlyxin® (lixisenatide) both strengths	$92.87	$557.22	$6,686.64
Lantus® (insulin glargine)	$24.07	$481.40¥	$5,776.80¥
metformin 1,000mg	$0.03	$1.80	$21.60

Costs do not reflect rebated prices or net costs.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
⁺ Soliqua™ 100/33 cost based on two packages of five 3mL pens per month due to the maximum daily dosage of 60 units (60 units of insulin glargine and 20mcg of lixisenatide).
¥ Lantus® dose based on 60 units of insulin glargine per day and therefore requiring two vials per month.

Synjardy® XR (Empagliflozin/Metformin Extended-Release) Product Summary[41,42]

Indications: Synjardy® XR (empagliflozin/metformin extended-release [ER]) is a combination of empagliflozin, a SGLT-2 inhibitor and metformin ER, a biguanide, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM when treatment with both

empagliflozin and metformin is appropriate. Empagliflozin is indicated to reduce the risk of CV death in adults with type 2 DM and established CV disease. However, the effectiveness of Synjardy® XR on reducing the risk of CV death in adults with type 2 DM and CV disease has not been established.

- Limitations of Use: Synjardy® XR is not recommended for patients with type 1 DM or for the treatment of diabetic ketoacidosis.

Dosing:

- Synjardy® XR is available as an empagliflozin/metformin ER tablet in four strengths: 5mg/500mg, 5mg/1,000mg, 12.5mg/500mg, and 12.5mg/1,000mg.
- The maximum recommended dose of Synjardy® XR is 12.5mg empagliflozin/1,000mg metformin ER twice daily.
- Synjardy® XR should be taken twice daily with meals, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin.
- Synjardy® XR is contraindicated in patients with an eGFR below 45mL/min/1.73m^2.

Efficacy: There have been no clinical efficacy studies conducted with Synjardy® XR; however, bioequivalence of Synjardy® XR to empagliflozin and metformin ER coadministered as individual tablets was demonstrated in healthy subjects. Multiple clinical trials examining the co-administration of empagliflozin and metformin, alone or in combination with a sulfonylurea in adults with type 2 DM, produced clinically and statistically significant improvements in HbA_{1c} compared to placebo.

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Synjardy® XR (empagliflozin/metformin ER) 12.5mg/1,000mg	**$7.18**	**$430.80**	**$5,169.60**
Invokamet® XR (canagliflozin/metformin ER) all strengths	$7.11	$426.60	$5,119.20
Jardiance® (empagliflozin) 25mg	$13.78	$413.40	$4,960.80
metformin 1,000mg	$0.03	$1.80	$21.60

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

Qtern® (Dapagliflozin/Saxagliptin) Product Summary[43,44]

Indications: Qtern® (dapagliflozin/saxagliptin) is a SGLT-2 inhibitor and a DPP-4 inhibitor combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin.

- Limitations of Use:
  - Qtern® is not indicated for the treatment of type 1 DM or diabetic ketoacidosis.
  - Qtern® should only be used in patients who tolerate 10mg dapagliflozin.

Dosing:

- Qtern® is available as an oral 10mg dapagliflozin/5mg saxagliptin tablet.

- The recommended dose of Qtern® is one 10mg dapagliflozin/5mg saxagliptin tablet taken orally once daily in the morning with or without food.
- Qtern® should not be initiated if eGFR is below 60mL/min/1.73m^2 and should be discontinued it eGFR falls persistently below 60mL/min/1.73m^2.
- Qtern® should not be coadministered with strong cytochrome P450 3A4/5 inhibitors.
- Qtern® tablets should be swallowed whole and not be split or cut.

Efficacy: The efficacy of Qtern® was evaluated in a study of 315 type 2 DM patients. Patients were randomized to saxagliptin or placebo in combination with dapagliflozin and metformin.

- Patients treated with add-on saxagliptin therapy had significantly greater reductions in HbA_{1c} from baseline compared to placebo (-0.5% vs. -0.2%, respectively; difference between groups in HbA_{1c} -0.4%, $p < 0.0001$).
- The proportion of patients achieving HbA_{1c} less than7% at week 24 was 35.3% in the saxagliptin group vs. 23.1% in the placebo group.

Cost/Launch Date: Qtern® cost information and launch information are unknown at this time.

Recommendations

The College of Pharmacy recommends the following:

1. The placement of Invokamet® XR (canagliflozin/metformin extended-release), Jentadueto® XR (linagliptin/metformin extended-release), and Synjardy® XR (empagliflozin/metformin extended-release) into the special prior authorization (PA) tier of the Diabetes Medications Product Based Prior Authorization (PBPA) category.
2. The placement of Adlyxin® (lixisenatide), Xultophy® 100/3.6 (insulin degludec/liraglutide), Soliqua™ 100/33 (insulin glargine/lixisenatide), and Qtern® (dapagliflozin/saxagliptin) into Tier-3 of the Diabetes Medications PBPA category.
3. A clinical exception will apply for medications with the FDA approved diagnosis to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (DM) and CV disease for patients with the diagnosis of type 2 DM at high risk for CV events. Tier structure rules for this indication will apply.

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

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

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

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

Utilization Details of Non-Insulin Diabetes Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
METFORMIN PRODUCTS						
METFORMIN TAB 500MG	21,661	6,229	$96,897.38	$0.14	$4.47	1.21%
METFORMIN TAB 1000MG	16,798	4,203	$70,143.60	$0.13	$4.18	0.87%
METFORMIN TAB 500MG ER	4,829	1,535	$25,404.44	$0.15	$5.26	0.32%
METFORMIN TAB 850MG	1,330	361	$5,524.11	$0.13	$4.15	0.07%
METFORMIN TAB 750MG ER	509	159	$4,182.15	$0.22	$8.22	0.05%
SUBTOTAL	**45,127**	**12,487**	**$202,151.68**	**$0.14**	**$4.48**	**2.52%**
GLIMEPIRIDE PRODUCTS						
GLIMEPIRIDE TAB 4MG	1,555	386	$14,131.65	$0.24	$9.09	0.18%
GLIMEPIRIDE TAB 2MG	858	255	$5,906.84	$0.17	$6.88	0.07%
GLIMEPIRIDE TAB 1MG	412	114	$2,325.46	$0.14	$5.64	0.03%
SUBTOTAL	**2,825**	**755**	**$22,363.95**	**$0.20**	**$7.92**	**0.28%**
GLIPIZIDE PRODUCTS						
GLIPIZIDE TAB 5MG	2,751	774	$9,922.20	$0.10	$3.61	0.12%
GLIPIZIDE TAB 10MG	2,552	642	$10,232.30	$0.11	$4.01	0.13%
GLIPIZIDE ER TAB 10MG	1,114	334	$18,733.67	$0.44	$16.82	0.23%
GLIPIZIDE ER TAB 5MG	870	253	$9,154.70	$0.26	$10.52	0.11%
GLIPIZIDE XL TAB 10MG	573	185	$9,437.63	$0.50	$16.47	0.12%
GLIPIZIDE XL TAB 5MG	408	120	$4,444.75	$0.32	$10.89	0.06%
GLIPIZIDE ER TAB 2.5MG	226	99	$2,670.71	$0.27	$11.82	0.03%
GLIPIZIDE XL TAB 2.5MG	199	59	$2,290.66	$0.30	$11.51	0.03%
SUBTOTAL	**8,693**	**2,466**	**$66,886.62**	**$0.21**	**$7.69**	**0.83%**
GLYBURIDE PRODUCTS						
GLYBURIDE TAB 5MG	3,448	896	$42,482.27	$0.36	$12.32	0.53%
GLYBURIDE TAB 2.5MG	929	421	$7,299.02	$0.23	$7.86	0.09%
GLYBURIDE TAB 1.25MG	76	40	$621.90	$0.20	$8.18	0.01%
GLYBURID MCR TAB 3MG	64	15	$329.22	$0.13	$5.14	0.00%
GLYBURID MCR TAB 6MG	27	8	$231.24	$0.23	$8.56	0.00%
GLYBURID MCR TAB 1.5MG	13	6	$41.61	$0.11	$3.20	0.00%
SUBTOTAL	**4,557**	**1,386**	**$51,005.26**	**$0.33**	**$11.19**	**0.63%**
GLIPIZIDE/METFORMIN PRODUCTS						
GLIP/METFORM TAB 5-500MG	145	27	$5,977.40	$1.36	$41.22	0.07%
GLIP/METFORM TAB 2.5-500MG	99	25	$4,484.89	$1.44	$45.30	0.06%
GLIP/METFORM TAB 2.5-250MG	15	3	$356.48	$0.79	$23.77	0.00%
SUBTOTAL	**259**	**55**	**$10,818.77**	**$1.36**	**$41.77**	**0.13%**
GLYBURIDE/METFORMIN PRODUCTS						
GLYB/METFORM TAB 5-500MG	523	91	$5,007.18	$0.31	$9.57	0.06%
GLYB/METFORM TAB 2.5-500MG	175	32	$1,481.18	$0.27	$8.46	0.02%
GLYB/METFORM TAB 1.25-250MG	10	5	$60.15	$0.17	$6.02	0.00%
SUBTOTAL	**708**	**128**	**$6,548.51**	**$0.30**	**$9.25**	**0.08%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ACARBOSE PRODUCTS						
ACARBOSE TAB 25MG	85	18	$2,027.26	$0.82	$23.85	0.03%
ACARBOSE TAB 50MG	45	9	$1,293.63	$0.92	$28.75	0.02%
ACARBOSE TAB 100MG	12	3	$469.40	$1.30	$39.12	0.01%
PRECOSE TAB 50MG	2	2	$74.27	$1.24	$37.14	0.00%
SUBTOTAL	**144**	**32**	**$3,864.56**	**$0.90**	**$26.84**	**0.06%**
REPAGLINIDE PRODUCTS						
REPAGLINIDE TAB 1MG	42	7	$1,456.53	$1.14	$34.68	0.02%
REPAGLINIDE TAB 2MG	21	7	$1,211.48	$1.88	$57.69	0.02%
REPAGLINIDE TAB 0.5MG	8	5	$289.18	$1.20	$36.15	0.00%
SUBTOTAL	**71**	**19**	**$2,957.19**	**$1.37**	**$41.65**	**0.04%**
PIOGLITAZONE PRODUCTS						
PIOGLITAZONE TAB 30MG	853	228	$9,474.34	$0.26	$11.11	0.12%
PIOGLITAZONE TAB 15MG	697	199	$6,360.06	$0.22	$9.12	0.08%
PIOGLITAZONE TAB 45MG	463	133	$6,265.38	$0.29	$13.53	0.08%
SUBTOTAL	**2,013**	**560**	**$22,099.78**	**$0.26**	**$10.98**	**0.28%**
TIER-1 SUBTOTAL	**64,397**	**17,888**	**$388,696.32**	**$0.18**	**$6.04**	**4.85%**
TIER-2 PRODUCTS						
SAXAGLIPTIN PRODUCTS						
ONGLYZA TAB 5MG	1,674	342	$721,092.07	$12.82	$430.76	8.98%
ONGLYZA TAB 2.5MG	246	59	$108,304.57	$12.94	$440.26	1.35%
SUBTOTAL	**1,920**	**401**	**$829,396.64**	**$12.83**	**$431.98**	**10.33%**
SITAGLIPTIN PRODUCTS						
JANUVIA TAB 100MG	3,243	736	$1,795,502.15	$12.84	$553.65	22.35%
JANUVIA TAB 50MG	925	211	$534,466.19	$14.87	$577.80	6.65%
JANUVIA TAB 25MG	206	55	$98,898.43	$13.40	$480.09	1.23%
SUBTOTAL	**4,374**	**1,002**	**$2,428,866.77**	**$13.26**	**$555.30**	**30.23%**
SAXAGLIPTIN/METFORMIN PRODUCTS						
KOMBIGLYZE TAB 2.5-1000MG	140	33	$54,141.87	$12.70	$386.73	0.67%
KOMBIGLYZE TAB 5-1000MG	70	14	$34,689.66	$12.85	$495.57	0.43%
KOMBIGLYZE TAB 5-500MG	25	5	$9,580.01	$12.77	$383.20	0.12%
SUBTOTAL	**235**	**52**	**$98,411.54**	**$12.76**	**$418.77**	**1.22%**
SITAGLIPTIN/METFORMIN PRODUCTS						
JANUMET TAB 50-1000MG	1,209	215	$470,433.66	$12.14	$389.11	5.86%
JANUMET XR TAB 50-1000MG	353	65	$119,992.80	$11.27	$339.92	1.49%
JANUMET XR TAB 100-1000MG	287	59	$110,204.61	$12.72	$383.99	1.37%
JANUMET TAB 50-500MG	213	44	$84,860.59	$12.37	$398.41	1.06%
JANUMET XR TAB 50-500MG	12	4	$2,321.60	$6.45	$193.47	0.03%
SUBTOTAL	**2,074**	**387**	**$787,813.26**	**$12.07**	**$379.85**	**9.81%**
LINAGLIPTIN PRODUCTS						
TRADJENTA TAB 5MG	1,013	185	$380,667.08	$12.59	$375.78	4.74%
SUBTOTAL	**1,013**	**185**	**$380,667.08**	**$12.59**	**$375.78**	**4.74%**
LINAGLIPTIN/METFORMIN PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
JENTADUETO TAB 2.5-1000MG	93	22	$41,298.84	$12.63	$444.07	0.51%
JENTADUETO TAB 2.5-850MG	11	2	$2,455.77	$6.30	$223.25	0.03%
JENTADUETO TAB 2.5-500MG	8	4	$5,666.82	$12.59	$708.35	0.07%
SUBTOTAL	**112**	**28**	**$49,421.43**	**$12.02**	**$441.26**	**0.61%**
EXENATIDE PRODUCTS						
BYETTA INJ 10MCG	71	15	$55,073.31	$20.63	$775.68	0.69%
BYETTA INJ 5MCG	57	19	$34,470.52	$19.81	$604.75	0.43%
SUBTOTAL	**128**	**34**	**$89,543.83**	**$20.30**	**$699.56**	**1.12%**
LIRAGLUTIDE PRODUCTS						
VICTOZA INJ 18MG/3ML	2,594	591	$1,734,345.10	$21.32	$668.60	21.59%
SUBTOTAL	**2,594**	**591**	**$1,734,345.10**	**$21.32**	**$668.60**	**21.59%**
NATEGLINIDE PRODUCTS						
NATEGLINIDE TAB 120MG	47	7	$3,298.80	$2.35	$70.19	0.04%
NATEGLINIDE TAB 60MG	15	5	$904.03	$2.23	$60.27	0.01%
SUBTOTAL	**62**	**12**	**$4,202.83**	**$2.32**	**$67.79**	**0.05%**
CANAGLIFLOZIN PRODUCTS						
INVOKANA TAB 300MG	410	83	$165,677.64	$13.49	$404.09	2.06%
INVOKANA TAB 100MG	253	58	$101,008.56	$13.76	$399.24	1.26%
SUBTOTAL	**663**	**141**	**$266,686.20**	**$13.59**	**$402.24**	**3.32%**
CANAGLIFLOZIN/METFORMIN PRODUCTS						
INVOKAMET TAB 50-1000MG	26	6	$10,700.70	$13.72	$411.57	0.13%
INVOKAMET TAB 150-1000MG	11	5	$4,471.21	$13.55	$406.47	0.06%
INVOKAMET TAB 50-500MG	10	1	$4,001.93	$13.34	$400.19	0.05%
INVOKAMET TAB 150-500MG	7	3	$2,818.09	$13.42	$402.58	0.04%
SUBTOTAL	**54**	**15**	**$21,991.93**	**$13.58**	**$407.26**	**0.28%**
TIER-2 SUBTOTAL	**13,229**	**2,848**	**$6,691,346.61**	**$14.43**	**$505.81**	**83.30%**
TIER-3 PRODUCTS						
EXENATIDE PRODUCTS						
BYDUREON PEN INJ 2MG	560	118	$331,872.62	$20.58	$592.63	4.13%
BYDUREON INJ 2MG	172	49	$98,771.35	$19.90	$574.25	1.23%
BYDUREON INJ 2MG	3	2	$1,504.38	$17.10	$501.46	0.02%
SUBTOTAL	**735**	**169**	**$432,148.35**	**$20.41**	**$587.96**	**5.38%**
ALOGLIPTIN PRODUCTS						
NESINA TAB 25MG	26	5	$10,694.29	$12.73	$411.32	0.13%
ALOGLIPTIN TAB 25MG	16	5	$3,300.32	$6.88	$206.27	0.04%
SUBTOTAL	**42**	**10**	**$13,994.61**	**$10.60**	**$333.21**	**0.17%**
ALOGLIPTIN/PIOGLITAZONE PRODUCTS						
OSENI TAB 25-30MG	8	3	$6,827.71	$12.64	$853.46	0.08%
OSENI TAB 25-15MG	5	2	$1,900.28	$12.67	$380.06	0.02%
ALOG/PIOGLIT TAB 25-30MG	5	2	$2,263.12	$6.86	$452.62	0.03%
ALOG/PIOGLIP TAB 12.5-30MG	1	1	$205.52	$6.85	$205.52	0.00%
ALOG/PIOGLIT TAB 25-15MG	1	1	$205.52	$6.85	$205.52	0.00%
SUBTOTAL	**20**	**9**	**$11,402.15**	**$10.56**	**$570.11**	**0.13%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ALOGLIPTIN/METFORMIN PRODUCTS						
ALOG/MET TAB 12.5-1000MG	5	1	$1,027.60	$6.85	$205.52	0.01%
KAZANO TAB 12.5-1000MG	1	1	$361.66	$12.06	$361.66	0.00%
SUBTOTAL	**6**	**2**	**$1,389.26**	**$7.72**	**$231.54**	**0.01%**
EMPAGLIFLOZIN/LINAGLIPTIN PRODUCTS						
GLYXAMBI TAB 25-5MG	76	10	$35,701.58	$16.45	$469.76	0.44%
GLYXAMBI TAB 10-5MG	15	2	$8,045.70	$17.88	$536.38	0.10%
SUBTOTAL	**91**	**12**	**$43,747.28**	**$16.70**	**$480.74**	**0.54%**
EMPAGLIFLOZIN PRODUCTS						
JARDIANCE TAB 25MG	222	43	$89,873.75	$13.49	$404.84	1.12%
JARDIANCE TAB 10MG	110	38	$44,897.55	$13.61	$408.16	0.56%
SUBTOTAL	**332**	**81**	**$134,771.30**	**$13.53**	**$405.94**	**1.68%**
EMPAGLIFLOZIN/METFORMIN PRODUCTS						
SYNJARDY TAB 12.5-1000MG	8	2	$3,310.16	$13.79	$413.77	0.04%
SYNJARDY TAB 5-500MG	1	1	$413.27	$13.78	$413.27	0.01%
SUBTOTAL	**9**	**3**	**$3,723.43**	**$13.79**	**$413.71**	**0.05%**
ALBIGLUTIDE PRODUCTS						
TANZEUM INJ 30MG	76	18	$35,370.25	$15.90	$465.40	0.44%
TANZEUM INJ 50MG	34	11	$16,505.80	$16.88	$485.46	0.21%
SUBTOTAL	**110**	**29**	**$51,876.05**	**$16.20**	**$471.60**	**0.65%**
DULAGLUTIDE PRODUCTS						
TRULICITY INJ 1.5/0.5ML	126	29	$78,285.54	$21.45	$621.31	0.97%
TRULICITY INJ 0.75/0.5ML	73	25	$43,233.81	$22.02	$592.24	0.54%
SUBTOTAL	**199**	**54**	**$121,519.35**	**$21.65**	**$610.65**	**1.51%**
PIOGLITAZONE/METFORMIN PRODUCTS						
PIOGLITA/MET TAB 15-850MG	37	7	$5,144.64	$3.45	$139.04	0.06%
PIOGLITA/MET TAB 15-500MG	35	6	$4,393.66	$3.96	$125.53	0.05%
ACTOPLUS MET TAB XR	4	1	$2,561.19	$21.34	$640.30	0.03%
SUBTOTAL	**76**	**14**	**$12,099.49**	**$4.45**	**$159.20**	**0.14%**
DAPAGLIFLOZIN PRODUCTS						
FARXIGA TAB 10MG	156	22	$60,955.09	$13.54	$390.74	0.76%
FARXIGA TAB 5MG	86	17	$34,926.07	$13.54	$406.12	0.43%
SUBTOTAL	**242**	**39**	**$95,881.16**	**$13.54**	**$396.20**	**1.19%**
DAPAGLIFLOZIN/METFORMIN PRODUCTS						
XIGDUO XR TAB 10-1000MG	35	6	$14,146.56	$13.47	$404.19	0.18%
XIGDUO XR TAB 5-1000MG	17	2	$5,665.32	$11.11	$333.25	0.07%
SUBTOTAL	**52**	**8**	**$19,811.88**	**$12.70**	**$381.00**	**0.25%**
ROSIGLITAZONE PRODUCTS						
AVANDIA TAB 4MG	2	1	$476.22	$7.94	$238.11	0.01%
SUBTOTAL	**2**	**1**	**$476.22**	**$7.94**	**$238.11**	**0.01%**
MIGLITOL PRODUCTS						
MIGLITOL TAB 100MG	1	1	$175.39	$5.85	$175.39	0.00%
SUBTOTAL	**1**	**1**	**$175.39**	**$5.85**	**$175.39**	**0.00%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-3 SUBTOTAL	**1,917**	**432**	**$943,015.92**	**$16.58**	**$491.92**	**11.71%**
SPECIAL PRIOR AUTHORIZATION (PA) PRODUCTS						
PRAMLINTIDE PRODUCTS						
SYMLNPEN 120 INJ 1000MCG	1	1	$1,869.26	$62.31	$1,869.26	0.02%
SUBTOTAL	**1**	**1**	**$1,869.26**	**$62.31**	**$1,869.26**	**0.02%**
METFORMIN PRODUCTS						
METFORMIN ER TAB 1000MG	13	2	$7,598.65	$19.48	$584.51	0.09%
RIOMET SOL	3	3	$1,454.34	$19.39	$484.78	0.02%
SUBTOTAL	**16**	**5**	**$9,052.99**	**$19.47**	**$565.81**	**0.11%**
SPECIAL PA SUBTOTAL	**17**	**6**	**$10,922.25**	**$22.07**	**$642.49**	**0.13%**
TOTAL	**79,560**	**14,223***	**$8,033,981.10**	**$2.97**	**$100.98**	**100%**

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

Utilization Details of Insulin Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
NO PRIOR AUTHORIZATION REQUIRED PRODUCTS						
INSULIN LISPRO PRODUCTS						
HUMALOG KWIK INJ 100/ML	3,909	1,070	$2,591,991.88	$17.91	$663.08	7.52%
HUMALOG INJ 100/ML	3,294	750	$1,676,889.76	$17.22	$509.07	4.86%
HUMALOG INJ 100/ML	386	80	$193,235.98	$16.85	$500.61	0.56%
HUMALOG KWIK INJ 200/ML	20	4	$53,177.69	$99.21	$2,658.88	0.15%
SUBTOTAL	**7,609**	**1,904**	**$4,515,295.31**	**$17.77**	**$593.42**	**13.09%**
INSULIN ASPART PRODUCTS						
NOVOLOG INJ FLEXPEN	8,977	2,393	$6,100,716.21	$19.18	$679.59	17.70%
NOVOLOG INJ 100/ML	5,564	1,149	$2,673,065.41	$17.27	$480.42	7.75%
NOVOLOG INJ PENFILL	462	108	$224,873.81	$13.42	$486.74	0.65%
SUBTOTAL	**15,003**	**3,650**	**$8,998,655.43**	**$18.38**	**$599.79**	**26.10%**
INSULIN GLULISINE PRODUCTS						
APIDRA INJ SOLOSTAR	422	131	$293,884.26	$17.40	$696.41	0.85%
APIDRA INJ U-100	245	55	$103,170.73	$14.21	$421.11	0.30%
SUBTOTAL	**667**	**186**	**$397,054.99**	**$16.44**	**$595.28**	**1.15%**
REGULAR INSULIN (R) AND NPH (N) PRODUCTS						
HUMULIN R INJ U-100	1,228	309	$251,833.39	$7.72	$205.08	0.73%
NOVOLIN R INJ U-100	804	215	$156,785.73	$7.27	$195.01	0.45%
HUMULIN INJ 70/30	701	159	$241,777.88	$11.08	$344.90	0.70%
HUMULIN N INJ U-100	564	179	$150,314.68	$7.67	$266.52	0.44%
NOVOLIN N INJ U-100	534	152	$136,925.39	$8.13	$256.41	0.40%
NOVOLIN INJ 70/30	437	127	$145,744.20	$9.94	$333.51	0.42%
NOVOLIN N INJ RELION	286	86	$13,379.56	$1.47	$46.78	0.04%
HUMULIN N INJ U-100KWP	281	132	$157,669.15	$13.44	$561.10	0.46%
NOVOLIN R INJ RELION	272	114	$15,139.93	$1.65	$55.66	0.04%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
HUMULIN R INJ U-500	261	52	$414,288.90	$44.48	$1,587.31	1.20%
NOVOLIN70/30 INJ RELION	256	73	$14,895.12	$1.83	$58.18	0.04%
HUMULIN INJ 70/30 KWP	208	57	$131,871.25	$18.50	$634.00	0.38%
HUMULIN R INJ U-500	61	20	$96,830.51	$56.96	$1,587.39	0.28%
SUBTOTAL	**5,893**	**1,322**	**$1,927,455.69**	**$10.51**	**$327.08**	**5.58%**
INSULIN ASPART PROTAMINE COMBINATION PRODUCTS						
NOVOLOG MIX INJ FLEXPEN	1,093	261	$905,351.26	$24.49	$828.32	2.63%
NOVOLOG MIX INJ 70/30	311	97	$235,156.70	$22.57	$756.13	0.68%
SUBTOTAL	**1,404**	**358**	**$1,140,507.96**	**$24.07**	**$812.33**	**3.31%**
INSULIN LISPRO PROTAMINE COMBINATION PRODUCTS						
HUMALOG MIX INJ	282	64	$245,243.71	$25.57	$869.66	0.71%
HUMALOG MIX SUS 75/25	131	30	$82,095.99	$18.02	$626.69	0.24%
HUMALOG MIX INJ	77	17	$87,597.62	$37.97	$1,137.63	0.25%
HUMALOG MIX INJ 50/50	26	6	$21,842.70	$27.17	$840.10	0.06%
SUBTOTAL	**516**	**117**	**$436,780.02**	**$25.31**	**$846.47**	**1.26%**
LONG-ACTING PRODUCTS						
LANTUS INJ SOLOSTAR	10,937	2,844	$5,673,812.32	$12.14	$518.77	16.46%
LEVEMIR INJ FLEXTOUC	8,542	2,169	$5,239,442.93	$15.51	$613.37	15.20%
LANTUS INJ 100/ML	7,541	1,563	$3,644,494.95	$15.10	$483.29	10.57%
LEVEMIR INJ	3,718	903	$2,083,582.93	$18.00	$560.40	6.04%
LEVEMIR INJ FLEXPEN	7	6	$3,179.97	$12.23	$454.28	0.01%
LANTUS INJ SOLOSTAR	1	1	$405.02	$13.50	$405.02	0.00%
SUBTOTAL	**30,746**	**7,486**	**$16,644,918.12**	**$14.32**	**$541.37**	**48.28%**
SUBTOTAL	**61,838**	**15,376**	**$34,060,667.52**	**$15.63**	**$550.80**	**98.77%**
PRIOR AUTHORIZATION REQUIRED PRODUCTS						
INSULIN DEGLUDEC PRODUCTS						
TRESIBA FLEX INJ 200UNIT	87	29	$87,362.86	$28.22	$1,004.17	0.25%
TRESIBA FLEX INJ 100UNIT	35	12	$23,222.15	$16.31	$663.49	0.07%
SUBTOTAL	**122**	**41**	**$110,585.01**	**$24.47**	**$906.43**	**0.32%**
INSULIN GLARGINE PRODUCTS						
TOUJEO SOLO INJ 300U/ML	453	105	$303,770.82	$22.58	$670.58	0.88%
SUBTOTAL	**453**	**105**	**$303,770.82**	**$22.58**	**$670.58**	**0.88%**
SUBTOTAL	**575**	**146**	**$414,355.83**	**$23.06**	**$720.62**	**1.20%**
TOTAL	**62,413**	**8,380***	**$34,475,023.35**	**$15.69**	**$552.37**	**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.

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Appendix J

Calendar Year 2016 Annual Review of Ulcerative Colitis (UC) Medications and 30-Day Notice to Prior Authorize Giazo® (Balsalazide Disodium Tablets)

Oklahoma Health Care Authority
April 2017

Current Prior Authorization 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 corticosteroids; 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 that 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.

Dipentum® (Olsalazine Capsules) Quantity Limit Approval Criteria:

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

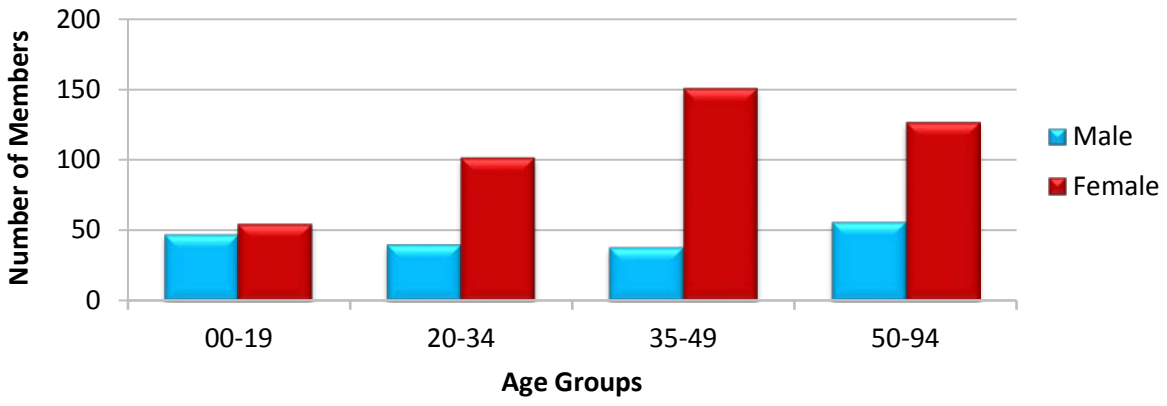
Utilization of Ulcerative Colitis (UC) Medications: Calendar Year 2016

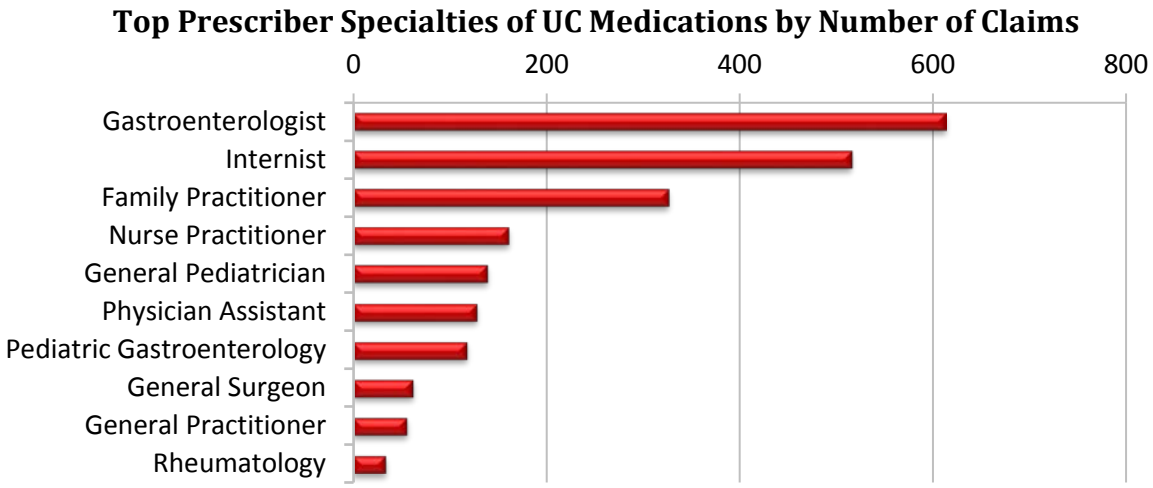
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	636	2,563	$1,024,989.33	$399.92	$13.58	386,815	75,460
2016	616	2,213	$782,433.94	$353.56	$11.91	321,437	65,679
% Change	**-3.10%**	**-13.70%**	**-23.70%**	**-11.60%**	**-12.30%**	**-16.90%**	**-13.00%**
Change	**-20**	**-350**	**-$242,555.39**	**-$46.36**	**-1.67**	**-65,378**	**-9,781**

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

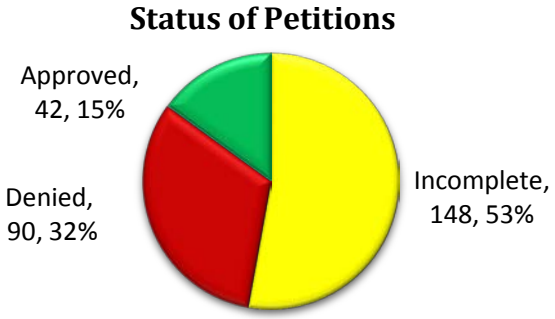
Demographics of Members Utilizing UC Medications





Prior Authorization of UC Medications

There were 280 prior authorization requests submitted for ulcerative colitis medications during calendar year 2016. The following chart shows the status of the submitted petitions.



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

Patent Expiration(s):

- Pentasa® (mesalamine controlled-release tablets), Dipentum® (olsalazine capsules), and Cortifoam® (10% hydrocortisone rectal aerosol foam): There are no unexpired patents; however, no generic formulations are available at this time.
- Delzicol® (mesalamine delayed-release tablets): April 2020
- Lialda® (mesalamine delayed-release tablets): June 2020
- Asacol® HD (mesalamine delayed-release tablets): November 2021
- Canasa® (mesalamine suppositories): June 2028
- Apriso® (mesalamine extended-release tablets): May 2030
- Giazo® (balsalazide tablets): June 2031

News:

- **May 2016:** The U.S. Food and Drug Administration (FDA) approved Entocort® EC (budesonide capsules) for the treatment of mild-to-moderate active Crohn's disease involving the ileum and/or ascending colon in patients 8 years of age and older. Entocort® EC was previously approved for the same indication in adult patients and for maintenance of clinical remission of mild-to-moderate Crohn's disease involving the

ileum and/or the ascending colon for up to three months in adult patients only. Entocort® EC is available generically.

- **September 2016:** An authorized generic for Asacol® HD (mesalamine delayed-release tablets) is now being marketed by Zydus Pharmaceuticals. In 2013, Warner Chilcott Co. granted Zydus a royalty license to market generic Asacol® HD to settle all outstanding patent litigation.

Giazo® (Balsalazide) Product Summary[6,7]

Indications: Giazo® (balsalazide tablets) is a locally acting aminosalicylate indicated for the treatment of mildly-to-moderately active UC in male patients 18 years of age and older.

- Limitations of Use:
  - Effectiveness in female patients was not demonstrated in clinical trials.
  - Safety and effectiveness of Giazo® beyond eight weeks have not been established.

Dosing:

- Giazo® is available as a 1.1 gram tablet.
- The recommended dosing of Giazo® is three 1.1 gram tablets two times a day (6.6 grams/day) with or without food for up to eight weeks.

Mechanism of Action: Balsalazide is a prodrug of mesalamine (5-aminosalicylic acid [5-ASA]). The mechanism of action of 5-ASA is unknown, but appears to be local to the colonic mucosa rather than systemic. Mucosal production of arachidonic acid metabolites, both through the cyclooxygenase pathways (i.e., prostanoids) and through the lipoxygenase pathways (i.e., leukotrienes and hydroxyeicosatetraenoic acids) is increased in patients with UC, and it is possible that 5-ASA diminishes inflammation by blocking production of arachidonic acid metabolites in the colon.

Contraindications: Giazo® is contraindicated in patients with hypersensitivity to salicylates, aminosalicylates or their metabolites, or to any of the components of Giazo® tablets.

Warnings and Precautions:

- Exacerbations of UC: In clinical trials, exacerbation of the symptoms of UC was reported. Patients should be observed closely for worsening of these symptoms while on treatment.
- Renal Impairment: Renal impairment has been reported in patients given products that release mesalamine in the gastrointestinal tract. Renal function should be evaluated at the beginning of treatment and periodically during treatment.
- Hepatic Impairment: There have been reports of hepatic failure in patients with pre-existing liver disease who have been administered mesalamine. Balsalazide is converted to mesalamine and should be used with caution in patients with pre-existing liver disease.

Adverse Reactions: The most common adverse reactions (incidence ≥2%) in male UC patients treated with Giazo® during clinical trials were anemia, diarrhea, pharyngolaryngeal pain, and urinary tract infection.

Efficacy: The safety and efficacy of Giazo® were based on an eight week clinical study of 250 patients with mildly-to-moderately active UC randomized to Giazo® 3.3g twice daily or placebo.

- The primary efficacy endpoint was the proportion of patients that achieved clinical improvement as well as improvement in rectal bleeding subscale of the Mayo Disease Activity Index (MMDAI) at the end of eight weeks of treatment.
- After eight weeks, the proportion of patients who met the definition of clinical improvement was greater for the Giazo® group compared to the placebo group in males only (57% Giazo® vs. 20% placebo). Effectiveness of Giazo® was not demonstrated in the female subpopulation in the clinical trial (54% Giazo® vs. 58% placebo).
- With adjustment for multiplicity, statistically significant differences were also seen in the male patients for clinical remission (35% Giazo® vs. 13% placebo) and for mucosal healing (52% Giazo® vs. 20% placebo).

Cost:

Medication	Cost Per Unit*	Cost Per Day	Cost Per 8 Weeks
Giazo® (balsalazide disodium) 1.1g tablet	**$5.28**	**$31.68**	**$1,774.08**
balsalazide disodium 750mg capsule	$0.47	$1.41	$78.96
sulfasalazine 500mg tablet	$0.17	$1.36	$76.16

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

Recommendations

The College of Pharmacy recommends the prior authorization of Giazo® (balsalazide) with the following criteria:

Giazo® (Balsalazide) Approval Criteria:

1. An FDA approved diagnosis of mildly-to-moderately active ulcerative colitis (UC); and
2. Member must be 18 years of age or older; and
3. Member must be male (effectiveness of Giazo® was not demonstrated in female patients in clinical trials); and
4. A patient-specific, clinically significant reason why the member cannot use generic balsalazide 750mg capsules or other products available without prior authorization*; and
5. Approvals will be for the duration of eight weeks. After eight weeks of treatment the prescriber must document a patient-specific, clinically significant reason the member needs a longer duration of treatment.

***The following medications do not require prior authorization:** sulfasalazine 500mg tablets, sulfasalazine delayed-release 500mg tablets, Rowasa® (mesalamine) rectal suspension enemas, Lialda® (mesalamine) delayed-release capsules, Colazal® (balsalazide) capsules, Dipentum® (olsalazine) capsules, Pentasa® (mesalamine) 250mg controlled-release capsules, Canasa® (mesalamine) suppositories, Apriso® (mesalamine) extended-release capsules, Delzicol® (mesalamine) delayed-release capsules, and hydrocortisone enemas.

Utilization Details of UC Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SULFASALAZINE PRODUCTS						
SULFASALAZIN TAB 500MG	615	192	$13,976.08	$0.78	$22.73	1.79%
SULFASALAZIN TAB 500MG	387	121	$12,061.09	$1.05	$31.17	1.54%
SULFASALAZIN POW	2	2	$121.42	$2.02	$60.71	0.02%
AZULFIDINE TAB 500MG	1	1	$32.03	$1.07	$32.03	0.00%
SUBTOTAL	**1,005**	**316**	**$26,190.62**	**$0.88**	**$26.06**	**3.35%**
MESALAMINE PRODUCTS						
LIALDA TAB 1.2GM	294	88	$195,592.13	$21.89	$665.28	25.00%
DELZICOL CAP 400MG	157	43	$74,829.87	$16.07	$476.62	9.56%
APRISO CAP 0.375GM	139	31	$60,385.19	$14.52	$434.43	7.72%
PENTASA CAP 500MG CR	133	47	$89,754.69	$25.00	$674.85	11.47%
ASACOL HD TAB 800MG	126	46	$99,289.94	$26.07	$788.02	12.69%
PENTASA CAP 250MG CR	75	40	$52,617.08	$23.35	$701.56	6.72%
CANASA SUP 1000MG	41	30	$33,379.47	$23.86	$814.13	4.27%
MESALAMINE ENE 4GM	22	12	$7,697.13	$14.89	$349.87	0.98%
MESALAMINE TAB 800MG	2	2	$1,765.54	$29.43	$882.77	0.23%
SUBTOTAL	**989**	**339**	**$615,311.04**	**$20.94**	**$622.15**	**78.64%**
BALSALAZIDE PRODUCTS						
BALSALAZIDE CAP 750MG	27	7	$3,349.26	$4.24	$124.05	0.43%
SUBTOTAL	**27**	**7**	**$3,349.26**	**$4.24**	**$124.05**	**0.43%**
OLSALAZINE MEDICATIONS						
DIPENTUM CAP 250MG	1	1	$1,578.28	$52.61	$1,578.28	0.20%
SUBTOTAL	**1**	**1**	**$1,578.28**	**$52.61**	**$1,578.28**	**0.20%**
BUDESONIDE PRODUCTS						
BUDESONIDE CAP 3MG DR	164	57	$112,909.82	$21.56	$688.47	14.43%
UCERIS TAB 9MG	12	5	$20,316.13	$56.43	$1,693.01	2.60%
SUBTOTAL	**176**	**62**	**$133,225.95**	**$23.80**	**$756.97**	**17.03%**
HYDROCORTISONE PRODUCTS						
HYDROCORT ENE 100MG	9	7	$875.45	$5.92	$97.27	0.11%
COLOCORT ENE 100MG	4	3	$441.01	$9.80	$110.25	0.06%
CORTIFOAM AER 90MG	2	1	$1,462.33	$24.37	$731.17	0.19%
SUBTOTAL	**15**	**11**	**$2,778.79**	**$10.98**	**$185.25**	**0.36%**
TOTAL	**2,213**	**616***	**$782,433.94**	**$11.91**	**$353.56**	**100.00%**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 10/2017. Last accessed 02/2017.

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[7] Giazo® Drug Approval Package. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/022205_giazo_toc.cfm. Issued 06/2013. Last accessed 02/2017.

Appendix K

Fiscal Year 2016 Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Byvalson™ (Nebivolol/Valsartan) and Qbrelis™ (Lisinopril Oral Solution)

Oklahoma Health Care Authority
April 2017

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 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 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. A U.S. Food and Drug Administration (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 (DUR) 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 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) Prior Authorization 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 blood urea nitrogen (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.

Nymalize® (Nimodipine Oral Solution) Approval Criteria:

1. A quantity limit of 2,838mL for 21 days will apply for Nymalize® oral solution.

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

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

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

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

ACE = angiotensin I converting enzyme, HCTZ = hydrochlorothiazide

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

CD = controlled delivery, ER = extended-release, SR = sustained-release, XR = extended-release, XL = extended-release, LA = long-acting

*All strengths other than the 360mg.

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

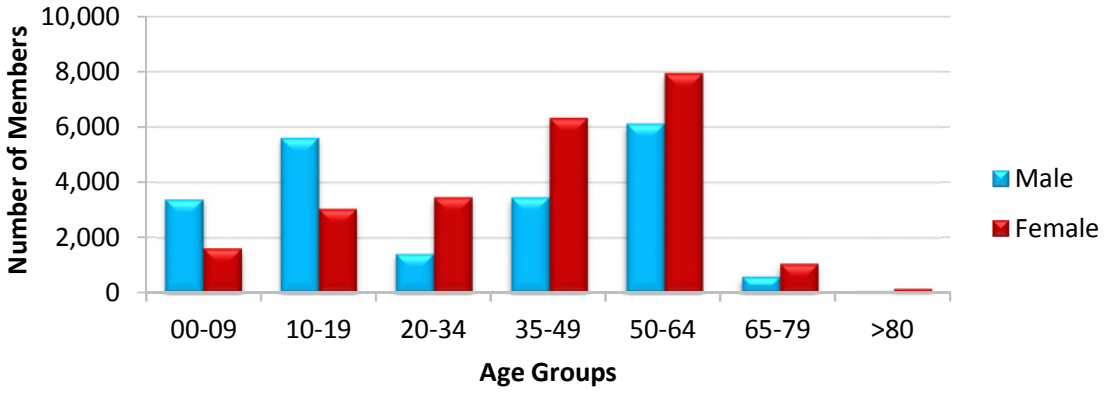
Utilization of Antihypertensive Medications: Fiscal Year 2016

Comparison of Fiscal Years

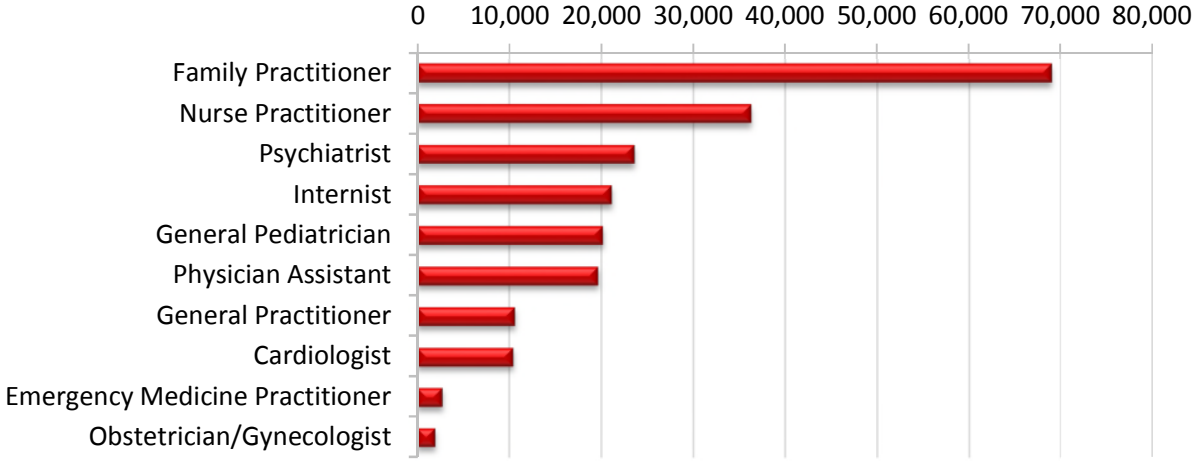
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	43,599	225,460	$2,346,983.91	$10.41	$0.27	10,596,963	8,576,545
2016	44,221	228,366	$2,145,771.60	$9.40	$0.25	10,821,506	8,745,581
% Change	**1.40%**	**1.30%**	**-8.60%**	**-9.70%**	**-7.40%**	**2.10%**	**2.00%**
Change	**622**	**2,906**	**-$201,212.31**	**-$1.01**	**-$0.02**	**224,543**	**169,036**

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

Demographics of Members Utilizing Antihypertensive Medications

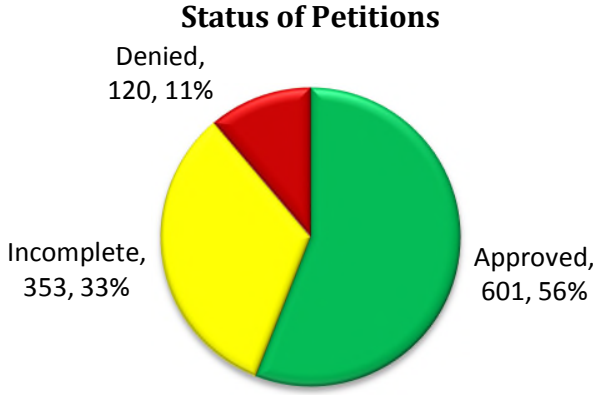


Top Prescriber Specialties of Antihypertensive Medications by Number of Claims



Prior Authorization of Antihypertensive Medications

There were 1,074 prior authorization requests submitted for antihypertensive medications during fiscal year 2016. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expiration(s):

- Tekturna® (aliskiren): February 2026
- Byvalson™ (nebivolol/valsartan): October 2027
- Edarbi® (azilsartan): March 2028
- Tekturna HCT® (aliskiren/hydrochlorothiazide): July 2028
- Hemangeol™ (propranolol hydrochloride oral solution): October 2028
- Prestalia® (perindopril arginine/amlodipine): October 2029
- Edarbyclor® (azilsartan/chlorthalidone): February 2030
- Epaned® (enalapril powder): November 2032
- Qbrelis™ (lisinopril oral solution): November 2035

New Generic Approval(s):

- **October 2016:** A generic version of Azor® (amlodipine/olmesartan) and Tribenzor® (olmesartan/amlodipine/hydrochlorothiazide) were launched.
- **October 2016:** A generic version of Benicar® (olmesartan) and Benicar HCT® (olmesartan/hydrochlorothiazide) was launched.

FDA Approval(s):

- **July 2016:** The FDA approved Byvalson™ (nebivolol/valsartan) 5mg/80mg tablets for the treatment of patients with hypertension to lower blood pressure. Byvalson™ is the first fixed-dose combination of a beta-blocker and an ARB available in the United States.
- **October 2016:** The FDA approved Qbrelis™ (lisinopril oral solution) for the treatment of hypertension in adult and pediatric patients 6 years of age and older, adjunct therapy for heart failure, and treatment of acute myocardial infarction in adults. Qbrelis™ is the first FDA-approved lisinopril oral solution.
- **January 2017:** The FDA approved a new formulation of Epaned® (enalapril oral solution) for the treatment of hypertension in adult and pediatric patients older than 1 month of

age, treatment of symptomatic heart failure, and treatment of asymptomatic left ventricular dysfunction. Epaned® was previously available as a powder for oral solution. The ready-to-use solution reduces the potential for errors as it does not require mixing.

FDA Safety Update(s):

- **November 2016:** The FDA approved safety information updates to the *Warnings and Precautions* section of the Prestalia® (perindopril/amlodipine) label. The information included the risk of hepatic failure and the risk of acute renal failure in patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) or ARBs. Additionally, the *Impaired Renal Function* section was updated to include the risk of developing acute renal failure with Prestalia® in patients who are taking NSAIDs or ARBs. The *Dosage Adjustment in Renal Impairment* subsection, *Clinical Pharmacology* section, and *Use in Specific Populations* section were also updated.

Guideline Update(s):

- **January 2017:** The American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) released the Pharmacologic Treatment of Hypertension in Adults Aged 60 Years or Older to Higher Versus Lower Blood Pressure Targets: A Clinical Practice Guideline. Some of the main recommendations to clinicians regarding adults aged 60 years or older included the following:
    - Initiating treatment in patients with systolic blood pressure (SBP) persistently at or above 150mmHg to achieve a target SBP less than 150mmHg to reduce the risk for mortality, stroke, and cardiac events.
    - Consider initiating or intensifying treatment in patients with a history of stroke or transient ischemic attack to achieve a target SBP less than 140mmHg to reduce the risk of recurrent stroke.
    - Consider initiating treatment or intensifying pharmacologic treatment in some adults aged 60 years or older at higher cardiovascular risk, based on individualized assessment, to achieve a target SBP less than 140mmHg to reduce the risk for stroke or cardiac events.
    - Treatment goals should be selected based on periodic discussions with the patient regarding the benefits and risks of specific blood pressure (BP) targets.

Other News:

- **August 2016:** At the European Society of Cardiology meeting, most audience members did not support a proposal for guideline committees to use the Systolic Blood Pressure Intervention Trial (SPRINT) to lower SBP targets. SPRINT compared the effects of antihypertensive treatment with a SBP of less than 120mmHg versus less than 140mmHg in hypertensive adults 50 years of age and older who had an average SBP of 130mmHg to 180mmHg and were at additional risk of cardiovascular disease (CVD). The main finding was that a primary composite outcome of myocardial infarction, non-myocardial acute coronary syndrome, stroke, acute decompensated heart failure, and CVD death was reduced by approximately 25% in the intensive treatment group compared with the standard treatment group. The thumbs down from the audience at the meeting was largely based on a strong argument from Dr. Sverre Kjeldsen who said the trial was difficult to interpret and he also stated the trial was unethical. One issue he pointed out was that the trial used an unprecedented and novel method to measure BP, making it impossible to

compare with previous trials. Other recent hypertension trials have measured BP using an automatic monitor in the presence of a healthcare professional. However, in SPRINT the healthcare professionals were trained to leave the room before the measurements started. This method has not been validated and Dr. Kjeldsen stated that multiple lines of evidence suggest this could lead to much lower BP readings. He said it was unethical not to report the unattended nature of the measurements, since many clinicians were not aware of this important change. He also noted the large number of patients that discontinued treatment during the trial or who were lost to follow-up.

Byvalson™ (Nebivolol/Valsartan) Product Summary[11]

Indications: Byvalson™ (nebivolol/valsartan) is a beta adrenergic blocker and an ARB indicated for the treatment of hypertension.

Dosing:

- Byvalson™ is available as an oral tablet containing 5mg of nebivolol and 80mg of valsartan per tablet.
- As initial therapy and in patients not adequately controlled on valsartan 80mg or nebivolol up to and including 10mg, the recommended dose is 5mg/80mg orally once daily. The maximum antihypertensive effects are attained within 2 to 4 weeks. Increasing the dose does not result in any meaningful further blood pressure reduction.
- Byvalson™ may be substituted for the individual components in patients already receiving 5mg nebivolol and 80mg valsartan.

Boxed Warning: Fetal Toxicity

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

Contraindications:

- Severe bradycardia
- Heart block greater than first degree
- Patients with cardiogenic shock
- Decompensated cardiac failure
- Sick sinus syndrome (unless a permanent pacemaker is in place)
- Patients with severe hepatic impairment (Child-Pugh >B)
- Hypersensitivity to any component of this product
- Co-administration of aliskiren with valsartan in patients with diabetes

Use in Specific Populations:

- Pregnancy: Nebivolol/valsartan can cause fetal harm when administered to a pregnant woman. Medications that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death.
- Lactation: There is no information regarding the presence of nebivolol/valsartan or its individual components in human milk, the effects on the breastfed infant, or the effects on milk production. Nebivolol and valsartan are present in rat milk. Because of the

potential for beta-blockers to produce serious adverse reactions in nursing infants, a nursing woman should be advised not to breastfeed with nebivolol/valsartan.

- Pediatric Use: The safety and effectiveness of nebivolol/valsartan in pediatric patients have not been established.
- Geriatric Use: No overall differences were observed in safety or effectiveness between elderly patients and younger patients who were treated with nebivolol/valsartan in clinical trials.
- Renal Impairment: Safety and effectiveness of nebivolol/valsartan in patients with moderate and severe renal impairment (creatinine clearance [CrCl] ≤60mL/min) have not been studied. No dosage adjustment is required for patients with mild or moderate renal impairment.
- Hepatic Impairment: There are no studies of nebivolol/valsartan in patients with hepatic insufficiency. No initial dosage adjustment is required for patients with mild hepatic impairment.

Clinical Studies: Byvalson™ was studied in a Phase 3, double-blind, placebo-controlled, dose-escalating, 8-week study in 4,161 patients with Stage 1 or 2 hypertension. Patients were randomized to one of eight treatment groups including: three fixed-dose combinations (FDC) of nebivolol and valsartan (5mg/80mg, 5mg/160mg, 10mg/160mg), nebivolol monotherapy (5mg, 20mg), valsartan monotherapy (80mg, 160mg), or placebo. After four weeks of treatment, all doses were doubled in the FDC groups, nebivolol monotherapy groups, and valsartan monotherapy groups. Treatment with Byvalson™ 5mg/80mg for four weeks resulted in placebo-adjusted reductions from baseline in SBP and diastolic blood pressure (DBP) of -8.3 and -7.2, respectively. Treatment with Byvalson™ 5mg/80mg resulted in greater reductions in SBP and DBP than did treatment with nebivolol 5mg alone ($P<0.0001$ for both SBP and DBP) or valsartan 80mg alone ($P=0.0007$ for SBP and $p<0.0001$ for DBP).

Qbrelis™ (Lisinopril Oral Solution) Product Summary[12]

Indications: Qbrelis™ (lisinopril oral solution) is an ACE inhibitor indicated for the following:

- Treatment of hypertension in adults and pediatric patients 6 years of age and older
- Adjunct therapy for heart failure
- Treatment of acute myocardial infarction

Dosing:

- Qbrelis™, 1mg/mL, is supplied as 150mL of oral solution.
- For treatment of hypertension, the recommended initial dose for adults is 10mg once daily. It is recommended to titrate the dose up to 40mg daily based on blood pressure response. It is recommended to initiate patients on diuretics at 5mg once daily.
- For pediatric patients with glomerular filtration rate greater than 30mL/min/1.73min^2 the recommended initial dose in patients 6 years of age and older is 0.07mg/kg (up to 5mg total) once daily.
- The recommended initial dose when used with diuretics and (usually) digitalis as adjunctive therapy for systolic heart failure is 5mg once daily. It is recommended to increase the dose as tolerated up to 40mg daily.

- In hemodynamically stable patients within 24 hours of the onset of symptoms of acute myocardial infarction (MI), the recommended dose is to give 5mg within 24 hours of MI followed by 5mg after 24 hours, then 10mg once daily.
- For patients with renal impairment (CrCl greater than or equal to 10mL/min and less than or equal to 30mL/min), it is recommended to halve the initial dose. For patients with CrCl less than 10mL/min or on hemodialysis, the recommended initial dose is 2.5mg.

Boxed Warning: Fetal Toxicity

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

Contraindications:

- Angioedema or a history of hereditary or idiopathic angioedema
- Hypersensitivity
- Co-administration of aliskiren with lisinopril in patients with diabetes

Use in Specific Populations:

- Pregnancy: Lisinopril oral solution can cause fetal harm when administered to a pregnant woman. Medications that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death.
- Lactation: There is no information regarding the presence of lisinopril in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions in nursing infants, women should be advised not to breastfeed during treatment with lisinopril.
- Pediatric Use: Antihypertensive effects and safety of lisinopril have been established in pediatric patients 6 to 16 years of age. No relevant differences between the adverse reaction profiles were identified for pediatric and adult patients. Safety and effectiveness of lisinopril have not been established in pediatric patients under the age of 6 or in pediatric patients with glomerular filtration rate <30mL/min/1.73 m^2.
- Geriatric Use: No dosage adjustment of lisinopril oral solution is necessary in elderly patients.
- Race: ACE inhibitors, including lisinopril, have an effect on blood pressure that is less in black patients than in non-black patients.
- Renal Impairment: Dose adjustment of lisinopril oral solution is required in patients undergoing hemodialysis or whose CrCl is ≤30mL/min.

Clinical Studies:

- Hypertension: In a clinical study involving 115 hypertensive patients 6 to 16 years of age, patients who weighed less than 50kg received either 0.625mg, 2.5mg, or 20mg of lisinopril once daily and patients who weighed greater than or equal to 50kg received either 1.25mg, 5mg, or 40mg of lisinopril once daily. Lisinopril was given as either tablets or in a suspension for those children who were unable to swallow tablets or who required a lower dose than is available in the tablet form. At the end of two weeks,

lisinopril lowered trough blood pressure in a dose-dependent manner with antihypertensive efficacy demonstrated at doses greater than 1.25mg (0.02mg/kg).

Cost Comparison:

Medication Name	Cost/ 5mg dose	Cost/ Month	Cost/ Year
Qbrelis™ (lisinopril oral solution)	**$16.45**	**$493.50**	**$5,922.00**
lisinopril tablet	$0.02	$0.60	$7.20

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

Recommendations

The College of Pharmacy recommends the prior authorization of Byvalson™ (nebivolol/valsartan) and Qbrelis™ (lisinopril oral solution) with the following criteria:

Byvalson™ (Nebivolol/Valsartan) Approval Criteria:

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

Qbrelis™ (Lisinopril Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use lisinopril oral tablets in place of the oral solution formulation.

Utilization Details of Antihypertensive Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CALCIUM CHANNEL BLOCKERS (CCBs)						
TIER-1 UTILIZATION						
AMLODIPINE TAB 10MG	15,404	4,163	$62,566.69	$0.09	$4.06	2.92%
AMLODIPINE TAB 5MG	11,798	3,570	$43,090.85	$0.09	$3.65	2.01%
AMLODIPINE TAB 2.5MG	1,604	478	$6,530.43	$0.10	$4.07	0.30%
NIFEDIPINE CAP 10MG	819	643	$38,340.44	$2.74	$46.81	1.79%
NIFEDICAL XL TAB 30MG	571	278	$9,514.88	$0.48	$16.66	0.44%
VERAPAMIL TAB 240MG ER	540	145	$6,760.06	$0.26	$12.52	0.32%
NIFEDIPINE TAB 30MG ER	493	173	$9,638.09	$0.50	$19.55	0.45%
NIFEDICAL XL TAB 60MG	479	143	$13,097.22	$0.74	$27.34	0.61%
NIFEDIPINE TAB 30MG ER	436	242	$7,803.02	$0.50	$17.90	0.36%
NIFEDIPINE TAB 60MG ER	430	149	$12,087.37	$0.73	$28.11	0.56%
NIFEDIPINE TAB 90MG ER	374	100	$15,917.76	$0.95	$42.56	0.74%
DILTIAZEM CAP 240MG CD	361	102	$8,133.62	$0.55	$22.53	0.38%
NIFEDIPINE TAB 60MG ER	332	109	$9,287.88	$0.80	$27.98	0.43%
DILTIAZEM CAP 180MG CD	320	107	$6,658.04	$0.52	$20.81	0.31%
DILTIAZEM TAB 120MG	314	68	$5,906.55	$0.55	$18.81	0.28%
VERAPAMIL TAB 120MG ER	313	92	$4,221.43	$0.35	$13.49	0.20%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
VERAPAMIL TAB 80MG	292	86	$1,777.50	$0.19	$6.09	0.08%
CARTIA XT CAP 240/24HR	290	84	$7,005.70	$0.51	$24.16	0.33%
VERAPAMIL TAB 180MG ER	287	80	$3,431.81	$0.27	$11.96	0.16%
CARTIA XT CAP 120/24HR	278	91	$5,067.05	$0.46	$18.23	0.24%
VERAPAMIL TAB 120MG	269	69	$1,868.35	$0.19	$6.95	0.09%
DILTIAZEM TAB 60MG	253	76	$3,498.25	$0.44	$13.83	0.16%
DILTIAZEM TAB 30MG	221	80	$2,193.90	$0.32	$9.93	0.10%
CARTIA XT CAP 180/24HR	219	70	$4,557.71	$0.48	$20.81	0.21%
DILTIAZEM CAP 120MG CD	200	67	$3,976.11	$0.46	$19.88	0.19%
DILTIAZEM TAB 90MG	196	48	$4,121.30	$0.68	$21.03	0.19%
NIFEDIPINE CAP 20MG	165	136	$18,904.04	$5.60	$114.57	0.88%
NIFEDIPINE TAB 90MG ER	161	45	$7,882.35	$1.04	$48.96	0.37%
DILTIAZEM CAP 180MG ER	161	51	$2,901.60	$0.50	$18.02	0.14%
DILT-XR CAP 240MG	139	31	$3,517.31	$0.65	$25.30	0.16%
VERAPAMIL TAB 40MG	130	53	$1,894.33	$0.46	$14.57	0.09%
DILTIAZEM CAP 120MG/24	129	26	$3,177.84	$0.81	$24.63	0.15%
DILTIAZEM CAP 240MG ER	127	38	$3,378.84	$0.61	$26.61	0.16%
DILTIAZEM CAP 180MG ER	117	25	$3,256.84	$0.76	$27.84	0.15%
VERAPAMIL CAP 240MG ER	116	38	$5,331.85	$1.07	$45.96	0.25%
VERAPAMIL CAP 120MG ER	107	41	$4,476.63	$1.07	$41.84	0.21%
DILTIAZEM CAP 120MG ER	102	50	$1,883.36	$0.44	$18.46	0.09%
DILTIAZEM CAP 240MG/24	92	19	$2,862.50	$0.92	$31.11	0.13%
TAZTIA XT CAP 360MG/24	91	24	$3,934.57	$0.85	$43.24	0.18%
DILTIAZEM CAP 180MG/24	87	24	$2,400.75	$0.67	$27.59	0.11%
DILTIAZEM CAP 120MG ER	86	26	$1,767.65	$0.55	$20.55	0.08%
VERAPAMIL CAP 360MG SR	77	18	$8,292.06	$2.54	$107.69	0.39%
VERAPAMIL CAP 240MG SR	66	22	$4,117.53	$1.24	$62.39	0.19%
DILTIAZEM CAP 240MG ER	61	31	$1,436.21	$0.52	$23.54	0.07%
VERAPAMIL CAP 180MG ER	56	20	$2,138.48	$0.89	$38.19	0.10%
DILTIAZEM CAP 300MG CD	55	13	$2,459.18	$0.85	$44.71	0.11%
DILT-XR CAP 180MG	54	18	$1,544.40	$0.60	$28.60	0.07%
DILTIAZEM CAP 90MG ER	52	14	$7,016.22	$3.68	$134.93	0.33%
DILTIAZEM CAP 60MG ER	52	17	$5,288.05	$3.15	$101.69	0.25%
TAZTIA XT CAP 180MG/24	45	9	$1,134.03	$0.58	$25.20	0.05%
DILTIAZEM CAP 120MG ER	44	15	$6,493.98	$4.14	$147.59	0.30%
FELODIPINE TAB 10MG ER	42	13	$1,356.86	$0.55	$32.31	0.06%
FELODIPINE TAB 5MG ER	38	7	$879.17	$0.42	$23.14	0.04%
DILTIAZEM CAP 360MG ER	37	14	$1,506.22	$0.98	$40.71	0.07%
DILT-XR CAP 120MG	33	9	$768.94	$0.63	$23.30	0.04%
TAZTIA XT CAP 120MG/24	31	12	$810.47	$0.55	$26.14	0.04%
TAZTIA XT CAP 240MG/24	29	8	$947.25	$0.80	$32.66	0.04%
AFEDITAB TAB 30MG CR	24	10	$504.28	$0.53	$21.01	0.02%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CARTIA XT CAP 300/24HR	21	6	$897.39	$0.91	$42.73	0.04%
TAZTIA XT CAP 300MG/24	18	3	$887.04	$1.14	$49.28	0.04%
VERAPAMIL CAP 120MG SR	16	12	$708.45	$0.94	$44.28	0.03%
DILTIAZEM CAP 360MG/24	16	3	$612.89	$0.93	$38.31	0.03%
VERAPAMIL CAP 180MG SR	16	5	$590.43	$0.89	$36.90	0.03%
DILTIAZEM ER TAB 360MG	15	4	$3,000.05	$3.45	$200.00	0.14%
NICARDIPINE CAP 20MG	12	1	$1,633.15	$4.54	$136.10	0.08%
DILTIAZEM CAP 300MG/24	11	2	$446.68	$1.35	$40.61	0.02%
DILTIAZEM ER TAB 420MG	11	2	$1,227.41	$3.72	$111.58	0.06%
DILTIAZEM ER TAB 180MG	9	6	$1,418.53	$2.49	$157.61	0.07%
DILTIAZEM CAP 300MG ER	6	3	$144.70	$0.80	$24.12	0.01%
NIFEDIPINE POW	6	3	$35.49	$0.24	$5.92	0.00%
DILTIAZEM CAP 420MG/24	5	3	$739.23	$1.54	$147.85	0.03%
VERAPAMIL POW	5	1	$55.07	$0.37	$11.01	0.00%
VERELAN CAP 240MG SR	4	1	$2,489.06	$6.95	$622.27	0.12%
AFEDITAB TAB 60MG CR	3	3	$102.95	$1.14	$34.32	0.00%
TIAZAC CAP 120MG/24	2	1	$72.58	$1.21	$36.29	0.00%
DILTIAZEM CAP 360MG ER	2	1	$1,021.92	$5.68	$510.96	0.05%
DILTIAZEM ER TAB 300MG	2	1	$201.28	$3.35	$100.64	0.01%
NIMODIPINE CAP 30MG	1	1	$1,458.94	$85.82	$1,458.94	0.07%
NICARDIPINE CAP 30MG	1	1	$154.74	$2.58	$154.74	0.01%
FELODIPINE TAB 2.5MG ER	1	1	$50.94	$0.57	$50.94	0.00%
VERAPAMIL INJ 2.5MG/ML	1	1	$21.00	$21.00	$21.00	0.00%
PROCARDIA CAP 10MG	1	1	$0.76	$0.76	$0.76	0.00%
TIER-1 SUBTOTAL	**39,884**	**12,256**	**$429,286.48**	**$0.26**	**$10.76**	**20.01%**
TIER-2 UTILIZATION						
AMLOD/ATORVA TAB 10-40MG	37	11	$11,394.85	$4.59	$307.97	0.53%
AMLOD/ATORVA TAB 10-20MG	29	10	$13,235.64	$5.26	$456.40	0.62%
AMLOD/ATORVA TAB 10-10MG	28	5	$4,630.27	$4.29	$165.37	0.22%
ISRADIPINE CAP 2.5MG	22	2	$1,471.44	$2.04	$66.88	0.07%
AMLOD/ATORVA TAB 5-10MG	20	3	$2,367.58	$3.59	$118.38	0.11%
MATZIM LA TAB 240MG/24	19	5	$2,081.08	$2.77	$109.53	0.10%
VERAPAMIL CAP 100MG ER	17	4	$1,618.80	$2.00	$95.22	0.08%
AMLOD/ATORVA TAB 10-80MG	16	4	$3,596.21	$4.61	$224.76	0.17%
AMLOD/ATORVA TAB 5-40MG	13	3	$2,628.93	$5.15	$202.23	0.12%
VERAPAMIL CAP 300MG ER	13	3	$870.59	$1.93	$66.97	0.04%
CARDIZEM LA TAB 120MG	11	3	$1,567.67	$4.02	$142.52	0.07%
AMLOD/ATORVA TAB 5-20MG	11	3	$2,177.08	$4.84	$197.92	0.10%
ISRADIPINE CAP 5MG	10	1	$1,792.35	$5.97	$179.24	0.08%
MATZIM LA TAB 180MG/24	3	3	$607.88	$2.29	$202.63	0.03%
MATZIM LA TAB 420MG/24	2	2	$238.94	$3.98	$119.47	0.01%
MATZIM LA TAB 300MG/24	2	1	$208.26	$3.47	$104.13	0.01%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MATZIM LA TAB 360MG/24	1	1	$339.59	$3.77	$339.59	0.02%
VERAPAMIL CAP 200MG ER	1	1	$38.70	$1.29	$38.70	0.00%
TIER-2 SUBTOTAL	**255**	**65**	**$50,865.86**	**$4.10**	**$199.47**	**2.37%**
TOTAL (CCBs)	**40,139**	**10,690***	**$480,152.34**	**$0.29**	**$11.96**	**22.38%**
ANGIOTENSIN RECEPTOR BLOCKERS (ARBs) AND COMBINATION PRODUCTS						
TIER-1 UTILIZATION						
LOSARTAN POT TAB 50MG	3,957	1,162	$20,981.76	$0.13	$5.30	0.98%
LOSARTAN POT TAB 100MG	2,975	852	$19,699.99	$0.14	$6.62	0.92%
LOSARTAN POT TAB 25MG	1,890	618	$8,626.87	$0.10	$4.56	0.40%
LOSARTAN/HCT TAB 100-25	1,422	391	$10,933.44	$0.16	$7.69	0.51%
LOSARTAN/HCT TAB 50-12.5	1,043	313	$6,818.70	$0.14	$6.54	0.32%
LOSARTAN/HCT TAB 100-12.5	596	167	$4,905.38	$0.18	$8.23	0.23%
VALSART/HCTZ TAB 160-12.5	354	82	$4,765.01	$0.32	$13.46	0.22%
IRBESARTAN TAB 150MG	304	72	$3,570.19	$0.25	$11.74	0.17%
VALSARTAN TAB 160MG	290	64	$6,090.09	$0.49	$21.00	0.28%
VALSART/HCTZ TAB 80-12.5	218	53	$2,957.31	$0.29	$13.57	0.14%
IRBESARTAN TAB 300MG	215	57	$3,313.05	$0.37	$15.41	0.15%
VALSART/HCTZ TAB 320-25MG	211	54	$4,542.34	$0.40	$21.53	0.21%
VALSARTAN TAB 320MG	205	45	$5,828.86	$0.55	$28.43	0.27%
VALSART/HCTZ TAB 160-25MG	187	58	$3,459.70	$0.34	$18.50	0.16%
VALSARTAN TAB 80MG	184	51	$3,549.26	$0.40	$19.29	0.17%
VALSART/HCTZ TAB 320-12.5	95	24	$1,579.09	$0.40	$16.62	0.07%
IRBESAR/HCTZ TAB 150-12.5	71	17	$1,120.44	$0.36	$15.78	0.05%
IRBESARTAN TAB 75MG	70	18	$642.65	$0.25	$9.18	0.03%
IRBESAR/HCTZ TAB 300-12.5	54	14	$1,152.80	$0.44	$21.35	0.05%
VALSARTAN TAB 40MG	45	15	$673.86	$0.36	$14.97	0.03%
COZAAR TAB 50MG	5	1	$783.42	$5.22	$156.68	0.04%
TIER-1 SUBTOTAL	**14,391**	**4,128**	**$115,994.21**	**$0.18**	**$8.06**	**5.41%**
TIER-2 UTILIZATION						
AMLOD/VALSAR TAB 10-320MG	137	15	$4,597.84	$1.12	$33.56	0.21%
TELMISARTAN TAB 80MG	133	18	$3,154.85	$0.76	$23.72	0.15%
BENICAR TAB 40MG	120	25	$43,397.48	$7.56	$361.65	2.02%
BENICAR HCT TAB 40-25MG	95	20	$35,606.94	$7.39	$374.81	1.66%
BENICAR TAB 20MG	85	22	$25,923.35	$5.47	$304.98	1.21%
BENICAR HCT TAB 40-12.5	74	17	$29,130.93	$7.65	$393.66	1.36%
BENICAR HCT TAB 20-12.5	73	18	$20,126.43	$5.78	$275.70	0.94%
TELMISARTAN TAB 40MG	69	15	$2,640.98	$0.65	$38.28	0.12%
AMLOD/VALSAR TAB /HCTZ	49	7	$5,944.53	$3.60	$121.32	0.28%
TRIBENZOR40- TAB 10-25MG	48	10	$16,667.54	$8.42	$347.24	0.78%
AMLOD/VALSAR TAB 5-160MG	43	8	$1,069.18	$0.83	$24.86	0.05%
AZOR TAB 5-40MG	38	8	$11,051.34	$8.37	$290.82	0.52%
AMLOD/VALSAR/HCTZ TAB	35	5	$3,053.81	$2.91	$87.25	0.14%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
AZOR TAB 10-40MG	34	5	$9,125.77	$8.45	$268.41	0.43%
BENICAR TAB 5MG	22	5	$4,215.30	$6.39	$191.60	0.20%
AMLOD/VALSAR/HCTZ TAB	21	4	$1,616.85	$2.57	$76.99	0.08%
AZOR TAB 5-20MG	21	4	$7,771.65	$6.64	$370.08	0.36%
MICARDIS TAB 80MG	18	3	$426.00	$0.79	$23.67	0.02%
TELMISARTAN TAB 20MG	17	2	$342.71	$0.67	$20.16	0.02%
AMLOD/VALSAR TAB 10-160MG	15	4	$291.56	$0.65	$19.44	0.01%
EXFORGE TAB 5-160-12.5MG	7	1	$1,317.92	$6.28	$188.27	0.06%
TRIBENZOR TAB 40-5-25MG	4	1	$3,054.00	$8.48	$763.50	0.14%
TRIBENZOR TAB 40-5-12.5MG	4	2	$2,487.72	$8.29	$621.93	0.12%
MICARDIS TAB 40MG	2	1	$1,083.16	$6.02	$541.58	0.05%
AMLOD/VALSAR TAB 5-320MG	1	1	$28.02	$0.93	$28.02	0.00%
TRIBENZOR TAB 20-5-12.5MG	1	1	$191.37	$6.38	$191.37	0.01%
TIER-2 SUBTOTAL	**1,166**	**222**	**$234,317.23**	**$4.85**	**$200.96**	**10.92%**
TIER-3 UTILIZATION						
TELMISA/HCTZ TAB 80-25MG	42	6	$4,273.39	$3.10	$101.75	0.20%
TELMISA/HCTZ TAB 80-12.5	37	8	$5,257.87	$3.58	$142.10	0.25%
TELMISA/HCTZ TAB 40-12.5	31	5	$3,178.26	$2.86	$102.52	0.15%
CANDESARTAN TAB 16MG	26	5	$2,395.29	$2.35	$92.13	0.11%
EDARBI TAB 80MG	22	4	$5,134.48	$5.70	$233.39	0.24%
CANDESARTAN TAB 8MG	20	4	$1,584.90	$1.76	$79.25	0.07%
CANDESARTAN TAB 32MG	20	4	$3,599.24	$3.53	$179.96	0.17%
EDARBYCLOR TAB 40-12.5	14	3	$3,633.20	$5.50	$259.51	0.17%
CANDESA/HCTZ TAB 32-12.5	7	2	$897.12	$1.55	$128.16	0.04%
EDARBYCLOR TAB 40-25MG	4	1	$1,992.48	$5.53	$498.12	0.09%
CANDESARTAN TAB 4MG	3	2	$299.86	$1.43	$99.95	0.01%
MICARDIS HCT TAB 80/12.5	3	1	$1,591.42	$5.89	$530.47	0.07%
CANDESA/HCTZ TAB 16-12.5	2	1	$154.85	$2.58	$77.43	0.01%
EPROSART MES TAB 600MG	2	1	$347.21	$2.89	$173.61	0.02%
EDARBI TAB 40MG	1	1	$165.51	$5.52	$165.51	0.01%
TIER-3 SUBTOTAL	**234**	**48**	**$34,505.08**	**$3.42**	**$147.46**	**1.61%**
TOTAL (ARBs)	**15,791**	**3,868***	**$384,816.52**	**$0.55**	**$24.37**	**17.93%**
ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIs) AND COMBINATION PRODUCTS						
TIER-1 UTILIZATION						
LISINOPRIL TAB 20MG	19,402	5,915	$76,141.29	$0.09	$3.92	3.55%
LISINOPRIL TAB 10MG	18,370	5,790	$64,252.66	$0.08	$3.50	2.99%
LISINOPRIL TAB 40MG	9,573	2,644	$50,886.37	$0.11	$5.32	2.37%
LISINOPRIL TAB 5MG	7,818	2,537	$25,580.63	$0.08	$3.27	1.19%
LISINOP/HCTZ TAB 20-12.5	5,684	1,773	$22,506.40	$0.09	$3.96	1.05%
LISINOP/HCTZ TAB 20-25MG	5,550	1,830	$24,754.70	$0.09	$4.46	1.15%
LISINOPRIL TAB 2.5MG	3,331	1,053	$10,466.73	$0.08	$3.14	0.49%
LISINOP/HCTZ TAB 10-12.5	3,101	1,109	$10,886.72	$0.08	$3.51	0.51%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ENALAPRIL TAB 10MG	1,662	389	$31,219.02	$0.48	$18.78	1.45%
ENALAPRIL TAB 20MG	1,658	355	$44,748.23	$0.69	$26.99	2.09%
ENALAPRIL TAB 5MG	1,527	338	$29,880.58	$0.55	$19.57	1.39%
LISINOPRIL TAB 30MG	1,139	342	$6,383.55	$0.14	$5.60	0.30%
ENALAPRIL TAB 2.5MG	933	186	$16,464.15	$0.52	$17.65	0.77%
BENAZEPRIL TAB 20MG	610	146	$2,973.55	$0.11	$4.87	0.14%
BENAZEPRIL TAB 40MG	466	109	$2,653.20	$0.12	$5.69	0.12%
FOSINOPRIL TAB 40MG	311	57	$3,394.61	$0.30	$10.92	0.16%
BENAZEPRIL TAB 10MG	278	85	$1,583.02	$0.12	$5.69	0.07%
RAMIPRIL CAP 10MG	245	53	$1,899.79	$0.17	$7.75	0.09%
ENALAPR/HCTZ TAB 10-25MG	237	49	$2,577.88	$0.26	$10.88	0.12%
CAPTOPRIL TAB 25MG	211	44	$13,133.46	$1.90	$62.24	0.61%
QUINAPRIL TAB 40MG	174	33	$1,767.20	$0.21	$10.16	0.08%
QUINAPRIL TAB 20MG	153	33	$1,453.10	$0.22	$9.50	0.07%
FOSINOPRIL TAB 20MG	150	33	$1,264.33	$0.24	$8.43	0.06%
CAPTOPRIL TAB 50MG	147	26	$13,774.28	$3.06	$93.70	0.64%
RAMIPRIL CAP 2.5MG	131	35	$827.97	$0.13	$6.32	0.04%
RAMIPRIL CAP 5MG	129	37	$1,027.67	$0.17	$7.97	0.05%
FOSINOPRIL TAB 10MG	128	26	$1,230.26	$0.24	$9.61	0.06%
CAPTOPRIL TAB 12.5MG	100	20	$4,807.98	$1.21	$48.08	0.22%
BENAZEP/HCTZ TAB 20-25MG	98	23	$5,204.12	$1.17	$53.10	0.24%
BENAZEP/HCTZ TAB 20-12.5	90	19	$4,336.66	$1.35	$48.19	0.20%
BENAZEPRIL TAB 5MG	78	22	$403.16	$0.12	$5.17	0.02%
ENALAPR/HCTZ TAB 5-12.5MG	74	15	$592.39	$0.23	$8.01	0.03%
BENAZEP/HCTZ TAB 10-12.5	70	16	$4,594.54	$1.32	$65.64	0.21%
RAMIPRIL CAP 1.25MG	48	17	$491.32	$0.22	$10.24	0.02%
QUINAPRIL TAB 5MG	29	7	$220.75	$0.22	$7.61	0.01%
QUINAPRIL TAB 10MG	25	9	$331.45	$0.21	$13.26	0.02%
CAPTOPR/HCTZ TAB 25-15MG	24	5	$1,491.59	$1.36	$62.15	0.07%
CAPTOPR/HCTZ TAB 50-25MG	24	4	$2,419.27	$2.69	$100.80	0.11%
QNAPRIL/HCTZ TAB 20-25MG	21	5	$548.79	$0.55	$26.13	0.03%
CAPTOPRIL TAB 100MG	19	3	$1,912.66	$2.77	$100.67	0.09%
QNAPRIL/HCTZ TAB 20-12.5	16	4	$634.04	$0.79	$39.63	0.03%
TRANDOLAPRIL TAB 1MG	14	2	$268.55	$0.33	$19.18	0.01%
VASOTEC TAB 20MG	8	4	$156.40	$0.65	$19.55	0.01%
TRANDOLAPRIL TAB 2MG	8	1	$68.38	$0.28	$8.55	0.00%
QNAPRIL/HCTZ TAB 10-12.5	6	3	$290.53	$0.69	$48.42	0.01%
CAPTOPR/HCTZ TAB 25-25MG	5	2	$230.88	$0.59	$46.18	0.01%
TRANDOLAPRIL TAB 4MG	5	2	$83.84	$0.31	$16.77	0.00%
MOEXIPRIL TAB 15MG	4	1	$99.04	$0.83	$24.76	0.00%
PERINDOPRIL TAB 4MG	3	1	$138.27	$0.51	$46.09	0.01%
MOEXIPR/HCTZ TAB 15-25MG	3	1	$198.74	$0.74	$66.25	0.01%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
PERINDOPRIL TAB 8MG	1	1	$50.26	$0.56	$50.26	0.00%
TIER-1 SUBTOTAL	**83,891**	**25,214**	**$493,304.96**	**$0.14**	**$5.88**	**22.99%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
EPANED SOL 1MG/ML	557	145	$157,852.31	$6.67	$283.40	7.36%
SPECIAL PA SUBTOTAL	**557**	**145**	**$157,852.31**	**$6.67**	**$283.40**	**7.36%**
TOTAL (ACEIs)	**84,448**	**21,766***	**$651,157.27**	**$0.18**	**$7.71**	**30.35%**
ACE INHIBITOR/CALCIUM CHANNEL BLOCKER COMBINATIONS (ACEI/CCB)						
TIER-1 UTILIZATION						
AMLOD/BENAZP CAP 10-20MG	184	40	$4,473.88	$0.50	$24.31	0.21%
AMLOD/BENAZP CAP 10-40MG	134	33	$3,839.68	$0.50	$28.65	0.18%
AMLOD/BENAZP CAP 5-20MG	134	21	$2,711.55	$0.50	$20.24	0.13%
AMLOD/BENAZP CAP 5-10MG	44	10	$1,331.95	$0.58	$30.27	0.06%
AMLOD/BENAZP CAP 5-40MG	28	5	$630.20	$0.47	$22.51	0.03%
AMLOD/BENAZP CAP 2.5-10MG	14	3	$448.71	$0.75	$32.05	0.02%
TIER-1 SUBTOTAL	**538**	**112**	**$13,435.97**	**$0.51**	**$24.97**	**0.63%**
TIER-2 UTILIZATION						
TRANDO/VERAP TAB 1-240 CR	11	1	$1,200.27	$3.64	$109.12	0.06%
TRANDO/VERAP TAB 4-240 ER	6	2	$1,926.61	$5.84	$321.10	0.09%
TARKA TAB 4-240 CR	2	1	$1,105.34	$11.05	$552.67	0.05%
TARKA TAB 2-240 CR	1	1	$165.60	$5.52	$165.60	0.01%
TIER-2 SUBTOTAL	**20**	**5**	**$4,397.82**	**$5.57**	**$219.89**	**0.20%**
TOTAL (ACEI/CCB)	**558**	**109***	**$17,833.79**	**$0.66**	**$31.96**	**0.83%**
DIRECT RENIN INHIBITORS (DRIs)						
TEKTURNA TAB 300MG	11	2	$2,806.26	$6.24	$255.11	0.13%
TEKTURNA HCT TAB 300-12.5	1	1	$545.90	$6.07	$545.90	0.03%
TEKTURNA HCT TAB 150-25MG	1	1	$142.34	$4.74	$142.34	0.01%
TOTAL (DRIs)	**13**	**4***	**$3,494.50**	**$6.13**	**$268.81**	**0.16%**
CLONIDINE PRODUCTS						
NO PRIOR AUTHORIZATION REQUIRED						
CLONIDINE TAB 0.1MG	57,866	12,137	$326,542.20	$0.18	$5.64	15.22%
CLONIDINE TAB 0.2MG	22,059	3,880	$129,156.33	$0.19	$5.86	6.02%
CLONIDINE TAB 0.3MG	4,788	787	$30,383.83	$0.20	$6.35	1.42%
CLONIDINE POW	27	6	$157.51	$0.19	$5.83	0.01%
SUBTOTAL	**84,740**	**16,810**	**$486,239.87**	**$0.19**	**$5.74**	**22.66%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
CLONIDINE DIS 0.1/24HR	112	25	$8,326.45	$2.63	$74.34	0.39%
CLONIDINE DIS 0.3/24HR	100	26	$16,811.69	$6.09	$168.12	0.78%
CLONIDINE DIS 0.2/24HR	75	27	$8,501.06	$3.90	$113.35	0.40%
CATAPRES TAB 0.2MG	8	1	$2,544.29	$10.60	$318.04	0.12%
SPECIAL PA SUBTOTAL	**295**	**79**	**$36,183.49**	**$4.34**	**$122.66**	**1.69%**
TOTAL (CLONIDINE)	**85,035**	**15,151***	**$522,423.36**	**$0.20**	**$6.14**	**24.35%**
SOTALOL PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
NO PRIOR AUTHORIZATION REQUIRED						
SOTALOL HCL TAB 80MG	218	52	$2,142.52	$0.30	$9.83	0.10%
SOTALOL HCL TAB 120MG	110	21	$1,224.15	$0.38	$11.13	0.06%
SOTALOL AF TAB 80MG	54	9	$583.32	$0.36	$10.80	0.03%
SOTALOL HCL TAB 160MG	49	11	$683.23	$0.46	$13.94	0.03%
SOTALOL AF TAB 160MG	3	1	$51.39	$0.57	$17.13	0.00%
SOTALOL HCL TAB 240MG	1	1	$26.50	$0.88	$26.50	0.00%
SOTALOL AF TAB 120MG	1	1	$9.96	$0.33	$9.96	0.00%
SUBTOTAL	**436**	**96**	**$4,721.07**	**$0.35**	**$10.83**	**0.22%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
SOTYLIZE SOL 5MG/ML	22	4	$12,017.76	$20.13	$546.26	0.56%
SPECIAL PA SUBTOTAL	**22**	**4**	**$12,017.76**	**$20.13**	**$546.26**	**0.56%**
TOTAL (SOTALOL)	**458**	**88***	**$16,738.83**	**$1.19**	**$36.55**	**0.78%**
MISCELLANEOUS COMBINATION PRODUCTS (MISC.)						
NO PRIOR AUTHORIZATION REQUIRED						
ATENOL/CHLOR TAB 50-25MG	288	91	$6,000.29	$0.43	$20.83	0.28%
BISOPRL/HCTZ TAB 5-6.25MG	279	67	$1,578.88	$0.13	$5.66	0.07%
ATENOL/CHLOR TAB 100-25MG	190	46	$4,884.54	$0.54	$25.71	0.23%
BISOPRL/HCTZ TAB 10/6.25	149	46	$1,029.75	$0.15	$6.91	0.05%
BISOPRL/HCTZ TAB 2.5/6.25	122	33	$740.27	$0.13	$6.07	0.03%
METOPRL/HCTZ TAB 50-25MG	121	36	$6,478.20	$1.22	$53.54	0.30%
METOPRL/HCTZ TAB 100-25MG	64	20	$4,711.47	$1.47	$73.62	0.22%
BIDIL TAB	59	16	$18,528.31	$10.78	$314.04	0.86%
PROPRAN/HCTZ TAB 40/25	23	6	$1,145.22	$1.49	$49.79	0.05%
PROPRAN/HCTZ TAB 80/25	17	4	$809.64	$1.42	$47.63	0.04%
METOPRL/HCTZ TAB 100-50MG	16	2	$1,131.29	$1.57	$70.71	0.05%
DUTOPROL TAB 25-12.5	11	4	$2,224.85	$6.18	$202.26	0.10%
DUTOPROL TAB 100-12.5	8	2	$2,382.90	$5.67	$297.86	0.11%
METHYLD/HCTZ TAB 250/25	4	1	$221.41	$1.85	$55.35	0.01%
METHYLD/HCTZ TAB 250/15	4	1	$145.55	$1.21	$36.39	0.01%
DUTOPROL TAB 50-12.5	1	1	$168.56	$5.62	$168.56	0.01%
TOTAL (MISC.)	**1,356**	**361***	**$52,181.13**	**$0.85**	**$38.48**	**2.43%**
PROPRANOLOL SOLUTION PRODUCTS						
NO PRIOR AUTHORIZATION REQUIRED						
PROPRANOLOL SOL 20MG/5ML	541	145	$10,728.01	$0.68	$19.83	0.50%
PROPRANOLOL SOL 40MG/5ML	15	9	$237.88	$0.55	$15.86	0.01%
SUBTOTAL	**556**	**154**	**10,966**	**$0.68**	**$19.72**	**0.51%**
SPECIAL PRIOR AUTHORIZATION UTILIZATION						
HEMANGEOL SOL 4.28/ML	12	1	$6,007.97	$27.69	$500.66	0.28%
SUBTOTAL	**12**	**1**	**$6,007.97**	**$27.69**	**$500.66**	**0.28%**
TOTAL (PROPRANOLOL)	**568**	**153***	**$16,973.86**	**$1.03**	**$29.88**	**0.79%**
TOTAL	**228,366**	**44,221***	**$2,145,771.60**	**$0.25**	**$9.40**	**100.00%**

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

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Appendix L

Fiscal Year 2016 Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Fosamax® (Alendronate 40mg Tablets)

Oklahoma Health Care Authority
April 2017

Current Prior Authorization Criteria

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate (Fosamax®)	alendronate + D (Fosamax® +D)	alendronate effervescent tablets (Binosto®)
calcium + vitamin D*	ibandronate (Boniva®)	alendronate solution (Fosamax®)
	risedronate (Actonel®)	denosumab (Prolia®)
		ibandronate (Boniva® IV)
		risedronate 30mg tablet (Actonel®)
		risedronate delayed-release tablets (Atelvia®)
		teriparatide (Forteo®)
		zoledronic acid (Reclast®)

*Must be used in combination with a bisphosphate to count as a Tier-1 trial.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Osteoporosis Medications Tier-2 Approval Criteria:

1. A trial of at least one Tier-1 medication, compliantly used for at least six months concomitantly with calcium + vitamin D, that failed to prevent fracture, or improve bone mineral density (BMD) scores; or
2. Hypersensitivity to or intolerable adverse effects with all Tier-1 medications.
3. Quantity limits apply based on FDA approved maximum doses.

Osteoporosis Medications Special Prior Authorization (PA) Approval Criteria:

1. **Forteo® (Teriparatide):**
   a. A Bone Mineral Density test (T-score) at or below -2.5 within the last month; and
   b. One of the following:
      i. A minimum of a 12 month trial with a bisphosphonate plus adequate calcium and vitamin D; or
      ii. A 12 month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or
   c. The diagnosis of non-healing fracture may be approved for six months.
   d. Approval will be for a maximum of 2 years of therapy.
2. **Prolia® (Denosumab), Reclast® (Zoledronic Acid), and Boniva® (Ibandronate IV):**
   a. A minimum of a 12 month trial with a Tier-1 or Tier-2 bisphosphonate plus adequate calcium and vitamin D; or

b. Contraindication to or intolerable adverse effects with Tier-1 and Tier-2 medications.
c. Clinical exceptions may apply for members with:
    i. Severe esophageal disease (e.g., ulcerations, strictures)
    ii. Inability to take anything by mouth
    iii. Inability to sit or stand for prolonged periods
    iv. Inability to take bisphosphonates orally or other special medical circumstances that justify this method of administration
    v. Intravenous zoledronic acid may be approved for a diagnosis of Paget disease of the bone

3. **Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets), and Actonel® (Risedronate 30mg Tablets):**
    a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 medications.
    b. Members with diagnosis in history of Paget's disease will not require prior authorization.
4. **Fosamax® (Alendronate Oral Solution):**
    a. An FDA approved diagnosis of osteoporosis or Paget's disease; and
    b. A patient-specific, clinically significant reason the member cannot use the oral tablet formulation.
5. **Quantity Limits apply based on U.S. Food and Drug Administration (FDA) approved maximum doses.**

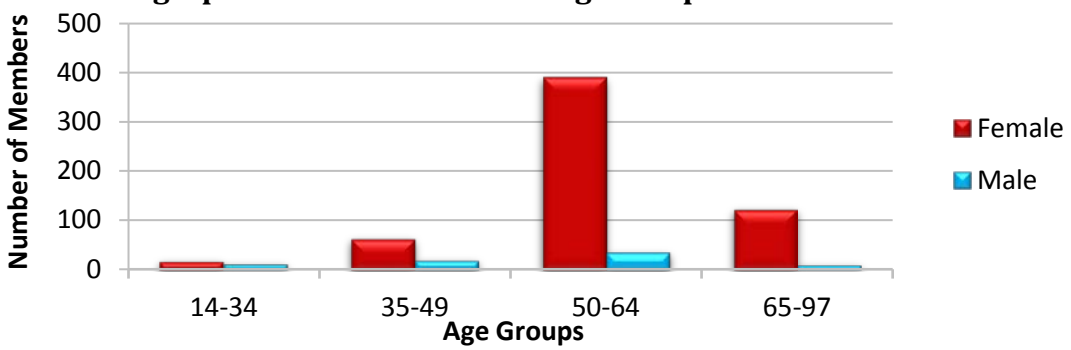
Utilization of Osteoporosis Medications: Fiscal Year 2016

Comparison of Fiscal Years

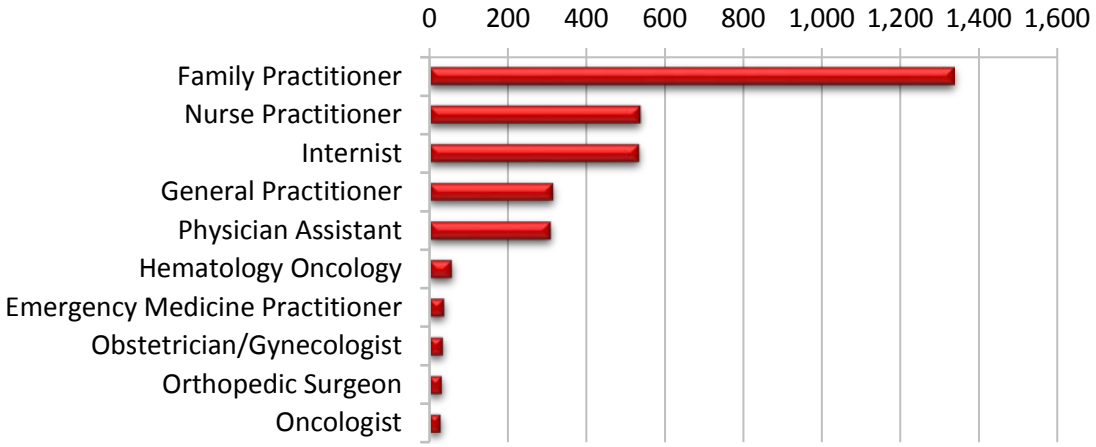
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	753	3,749	$395,283.76	$105.44	$3.37	22,866	117,342
2016	662	3,381	$423,563.48	$125.28	$4.11	21,866	102,998
% Change	**-12.10%**	**-9.80%**	**7.20%**	**18.80%**	**22.00%**	**-4.40%**	**-12.20%**
Change	**-91**	**-368**	**$28,279.72**	**$19.84**	**$0.74**	**-1,000**	**-14,344**

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

Demographics of Members Utilizing Osteoporosis Medications



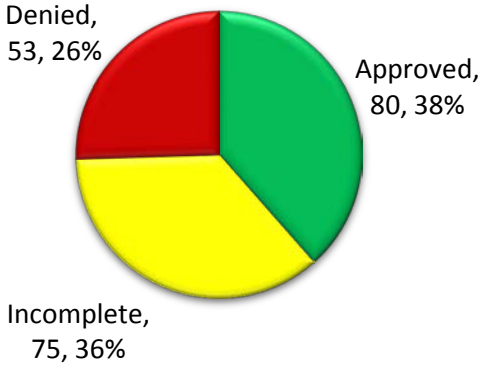
Top Prescriber Specialties of Osteoporosis Medications by Number of Claims



Prior Authorization of Osteoporosis Medications

There were 208 prior authorization requests submitted for osteoporosis medications during fiscal year 2016. Computer edits are in place to detect lower tiered medications in the member's 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]

Anticipated Patent Expiration(s):

- Fosamax® Plus D (alendronate/cholecalciferol): January 2019
- Binosto® (alendronate effervescent tablets): August 2023
- Forteo® (teriparatide): March 2025
- Reclast® (zoledronic acid): August 2028

Guideline Update(s):

- **September 2016:** The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) published clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis. According to the AACE, the guidelines use the best evidence, taking into consideration the economic impact of the disease and the need for efficient and effective evaluation and treatment of

postmenopausal women with osteoporosis. Guidance for diagnosis, treatment selection, duration of treatment, and specialty referral is provided in the guidelines.

- It is recommended that all postmenopausal women age 50 years or older be evaluated for osteoporosis risk. Osteoporosis should be diagnosed based on presence of fragility fractures in the absence of other metabolic bone disorders or a T-score of −2.5 or lower in the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius even in the absence of a prevalent fracture.
- Additionally, serum 25-hydroxyvitamin D (25[OH]D) should be measured with a goal of maintaining levels at greater than or equal to 30ng/mL in patients with osteoporosis (preferable range, 30 to 50ng/mL). Supplementing with vitamin D_3 is recommended, if needed. Dosing of 1,000 to 2,000 international units (IU) of daily maintenance therapy is typically needed to maintain an optimal serum 25(OH)D level.
- Patients should be counseled to maintain adequate dietary intake of calcium to a total intake (including diet plus supplement, if needed) of 1,200mg/day for women 50 years of age or older.
- Pharmacological therapy is strongly recommended for the following patients: those with osteopenia or low bone mass and a history of fragility fracture of the hip or spine; those with a T-score of −2.5 or lower in the spine, femoral neck, total hip, or 33% radius; those with a T-score in the spine, femoral neck, total hip, or 33% radius, between −1.0 and −2.5 if the FRAX® 10-year probability for major osteoporotic fracture is greater than or equal to 20% or the 10-year probability of hip fracture is greater than or equal to 3%.
- The guidelines suggest use of alendronate, risedronate, zoledronic acid, and denosumab as initial therapy for most patients at high risk of fracture. Teriparatide, denosumab, or zoledronic acid should be considered for patients unable to use oral therapy and as initial therapy for patients at especially high fracture risk. Raloxifene or ibandronate may be appropriate for initial therapy in some cases where patients require drugs with spine-specific efficacy.
- Successful treatment of osteoporosis is defined as stable or increasing bone mineral density (BMD) with no evidence of new fractures or fracture progression. Duration of treatment varies and is specific to the treatment used. Referral to an endocrinologist or osteoporosis specialist is recommended when a patient with normal BMD sustains a fracture without major trauma, when recurrent fractures or continued bone loss occurs in a patient receiving therapy without obvious treatable causes of bone loss, or other when secondary conditions complicate treatment.

News:

- **April 2016:** The International Osteoporosis Foundation (IOF) Fracture Working Group convened to review existing literature and vote on appropriateness of care for fracture healing. The panel concluded that there was no negative effect of osteoporosis medications, such as bisphosphonates, on fracture healing, and that it is safe to start osteoporosis medications as soon as possible after both vertebral and non-vertebral fracture. However, the panel agreed that after the occurrence of an atypical femur

fracture, bisphosphonate therapy should be stopped. Treatment with an anabolic agent, such as teriparatide, should be considered to improve healing. Further, the panel suggested guidelines for future trial design to understand the role of osteoporosis medications on fracture healing.

- **September 2016:** Amgen published positive results from a Phase 3 trial comparing Prolia® (denosumab) with risedronate in patients receiving oral glucocorticoid therapy. The study met all primary and secondary endpoints at 12 months. The data showed that Prolia® treatment led to significantly greater gains in BMD at the lumbar spine and total hip, both in patients receiving continuing glucocorticoid therapy and in patients newly initiating glucocorticoid therapy. A total of 795 patients enrolled in the 24-month study, receiving 60mg of denosumab subcutaneously every six months, compared with oral risedronate at 5mg daily. Further analysis is ongoing, and the study will remain double-blinded for an additional 12 months.
- **September 2016:** At the American Society of Bone and Mineral Research (ASBMR) 2016 Meeting, experts confronted the reality that federal funding for dual-energy x-ray absorptiometry (DEXA) no longer makes screening for osteoporosis viable. ASBMR president Douglas Kiel, MD, MPH, professor of medicine, Harvard Medical School, reported that one of the major focuses of the meeting is the osteoporosis crisis. Dr. Kiel explained that this crisis, at least in part, is the result of declining reimbursement for DEXA, the gold-standard screening test to identify patients with osteoporosis. The reimbursement has reached a level where clinics cannot afford to run the DEXA machines and pay the technicians to keep the units functioning. This results in declining rates of detection, as well as declining levels of treatment for patients with osteoporosis. In addition to lack of funding, oral bisphosphonate use declined by more than 50% between 2008 and 2012. The decline in oral bisphosphonate use coincided with largely media-driven hysteria surrounding safety concerns with these bone-building agents, even though neither the U.S. Food and Drug Administration (FDA) nor the ASBMR had concerns enough themselves to put restrictions on their use. Many patients refuse to accept treatment for osteoporosis, at least with a bisphosphonate, including those who have already experienced a hip fracture, and many of those who are already taking a bisphosphonate want to stop treatment. Some of that concern appears to have filtered down to prescribing physicians, as fewer than 20% of patients discharged from the hospital after a hip fracture are receiving treatment.

Pipeline:

- **Abaloparatide:** The results of a randomized clinical trial for abaloparatide were published in *The Journal of the American Medical Association* (*JAMA*) in August 2016. Abaloparatide is a selective activator of the parathyroid hormone type 1 receptor. The study was intended to determine the efficacy and safety of abaloparatide 80mcg versus placebo for prevention of new vertebral fracture in postmenopausal women at risk of osteoporotic fracture. The Abaloparatide Comparator Trial In Vertebral Endpoints (ACTIVE) was a Phase 3, double-blind, randomized control trial at 28 sites in ten countries. Postmenopausal women with a BMD T-score less than or equal to −2.5 and greater than −5.0 at the lumbar spine or femoral neck or thoracic vertebral fracture or history of a low-trauma non-vertebral fracture within the past five years were eligible.

Blinded, daily subcutaneous injections of placebo (n = 821), abaloparatide 80mcg (n = 824), or open-label teriparatide 20mcg (n = 818) were given for 18 months. The primary end point was percentage of participants with new vertebral fracture in the abaloparatide versus placebo groups. The study showed the use of subcutaneous abaloparatide, compared with placebo, reduced the risk of new vertebral and non-vertebral fractures over 18 months. Further research is needed to evaluate the risks and benefits of abaloparatide treatment, and the efficacy of abaloparatide versus other osteoporosis treatments.

- **Romosozumab:** In April 2016, Amgen and UCB Pharma reported that the results of a new open-label Phase 3 study (STRUCTURE trial) showed that their investigational agent romosozumab significantly promoted BMD at the hip and spine compared with teriparatide (Forteo®) in postmenopausal women with osteoporosis who were transitioning from bisphosphonate therapy. Romosozumab, which is administered subcutaneously once a month, is a humanized monoclonal antibody that inhibits sclerosin, an osteocyte-derived inhibitor of osteoblast activity. The drug has the dual effect of promoting bone formation and inhibiting resorption**.** By September 2016, Amgen and UCB Pharma announced that the FDA accepted for review the Biologics License Application (BLA) for romosozumab. The BLA is based on data from the pivotal Phase 3 placebo-controlled FRActure study in postmenopausal woMen with ostEoporosis (FRAME) in approximately 7,200 patients. FRAME is a multicenter, international, randomized, double-blind, placebo-controlled, parallel-group study in postmenopausal women with osteoporosis, defined as low BMD at the total hip or femoral neck. Patients were randomized 1:1 to receive either 210mg romosozumab subcutaneous (SC) monthly (QM) or placebo SC QM for the 12-month double-blind study period. After the placebo-controlled study period, patients entered the open-label phase where all patients received 60mg denosumab SC every six months (Q6M) for 12 months, while remaining blinded to initial treatment. An additional 12 month extension period of open-label 60mg denosumab SC Q6M is currently ongoing.
- **TBRIA™ (calcitonin-salmon [rDNA origin] delayed-release tablets):** TARSA Therapeutics, Inc. announced that their New Drug Application (NDA) for TBRIA™ (calcitonin-salmon [rDNA origin] delayed-release tablets) submitted to the FDA in July 2015, has been accepted for review. TBRIA™ is a once-daily oral recombinant salmon calcitonin tablet for the treatment of postmenopausal osteoporosis in women greater than five years post menopause when alternative treatments are not suitable (e.g., patients for whom other therapies are contraindicated or for patients who are intolerant or unwilling to use other therapies). TBRIA™ demonstrated positive safety and efficacy as a treatment for postmenopausal osteoporosis in the global, randomized, double-blind ORACAL trial. It met its primary endpoint and demonstrated statistical superiority to both placebo and nasal calcitonin spray in increasing BMD at the lumbar spine after 48 weeks of use. The safety profile of TBRIA™ did not substantially differ from nasal calcitonin or placebo. If approved, TBRIA™ would be the first FDA approved oral calcitonin.

Cost Comparison[10]

There are several strengths of alendronate available for the treatment and prevention of osteoporosis. Alendronate 40mg differs from other strengths in that it is only FDA approved for the treatment of Paget's disease. Additionally, the cost of alendronate 40mg differs greatly from the cost of other strengths of alendronate. The wholesale acquisition cost (WAC) of alendronate 40mg is $5.78 per tablet. This results in a 30-day supply costing $173.40. As shown below, a 30-day supply of the other available strengths of alendronate is less than $5.00.

Cost Comparison:

Medication	Cost Per Tablet	Cost for 30 Days of Therapy*
Fosamax® 40mg (alendronate tablet)	**$5.78[+]**	**$173.40[+]**
Fosamax® 70mg (alendronate tablet)	$0.36[Δ]	$1.44[Δ]
Fosamax® 35mg (alendronate tablet)	$0.53[Δ]	$2.12[Δ]
Fosamax® 10mg (alendronate tablet)	$0.16[Δ]	$4.80[Δ]
Fosamax® 5mg (alendronate tablet)	$0.15[Δ]	$4.50[Δ]

*30 days of therapy based on usual dose of medication
[+]WAC = Wholesale Acquisition Cost
[Δ]NADAC = National Average Drug Acquisition Cost

Recommendations

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

1. The placement of Fosamax® (alendronate) 40mg tablets into the Special Prior Authorization (PA) Tier of the Osteoporosis Medications Product Based Prior Authorization (PBPA) category due to the wholesale acquisition cost (WAC) in comparison to other alendronate strengths. The following criteria shown in red would apply:
    a. **Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets), Actonel® (Risedronate 30mg Tablets), and Fosamax® (Alendronate 40mg Tablets):**
        i. A patient specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 products.
        ii. Members with diagnosis in history of Paget's disease will not require prior authorization.
2. Placement of Reclast® (zoledronic acid) into the Tier-2 of the Osteoporosis Medications PBPA category due to WAC.

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate (Fosamax®)	alendronate + D (Fosamax® +D)	alendronate effervescent tablets (Binosto®)
calcium + vitamin D*	ibandronate (Boniva®)	alendronate solution (Fosamax®)
	risedronate (Actonel®)	**alendronate 40mg tablet (Fosamax®)**
	zoledronic acid (Reclast®)	denosumab (Prolia®)
		ibandronate (Boniva® IV)
		risedronate 30mg tablet (Actonel®)
		risedronate delayed-release tablets (Atelvia®)
		teriparatide (Forteo®)

*Must be used in combination with a bisphosphate to count as a Tier-1 trial.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization Details of Osteoporosis Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
ALENDRONATE PRODUCTS						
ALENDRONATE TAB 70MG	2,524	491	$11,109.15	$0.15	$4.40	2.62%
ALENDRONATE TAB 35MG	324	75	$1,435.71	$0.16	$4.43	0.34%
ALENDRONATE TAB 10MG	93	26	$715.52	$0.26	$7.69	0.17%
ALENDRONATE TAB 5MG	24	6	$145.37	$0.20	$6.06	0.03%
ALENDRONATE TAB 40MG	5	3	$487.71	$2.62	$97.54	0.12%
SUBTOTAL	**2,970**	**601**	**$13,893.46**	**$0.16**	**$4.68**	**3.28%**
TIER-1 SUBTOTAL	**2,970**	**601**	**$13,893.46**	**$0.16**	**$4.68**	**3.28%**
TIER-2 PRODUCTS						
ALENDRONATE PRODUCTS						
FOSAMAX + D TAB 70-5600	11	1	$1,747.02	$5.67	$158.82	0.41%
SUBTOTAL	**11**	**1**	**$1,747.02**	**$5.67**	**$158.82**	**0.41%**
IBANDRONATE PRODUCTS						
IBANDRONATE TAB 150MG	93	23	$5,782.04	$1.16	$62.17	1.37%
SUBTOTAL	**93**	**23**	**$5,782.04**	**$1.16**	**$62.17**	**1.37%**
RISEDRONATE PRODUCTS						
RISEDRONATE TAB 35MG	48	7	$9,062.18	$6.71	$188.80	2.15%
ACTONEL TAB 35MG	39	5	$9,581.81	$8.77	$245.69	2.26%
RISEDRONATE TAB 5MG	12	1	$1,808.66	$5.38	$150.72	0.43%
RISEDRONATE TAB 150MG	7	2	$1,107.31	$5.27	$158.19	0.26%
SUBTOTAL	**106**	**15**	**$21,559.96**	**$7.22**	**$203.40**	**5.10%**
TIER-2 SUBTOTAL	**210**	**39**	**$29,089.02**	**$3.51**	**$138.52**	**6.88%**
SPECIAL PA PRODUCTS						
ALENDRONATE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ALENDRONATE SOL 70/75ML	20	2	$1,236.08	$2.15	$61.80	0.29%
SUBTOTAL	**20**	**2**	**$1,236.08**	**$2.15**	**$61.80**	**0.29%**
DENOSUMAB PRODUCTS						
PROLIA SOL 60MG/ML	27	21	$24,924.79	$5.21	$923.14	5.88%
SUBTOTAL	**27**	**21**	**$24,924.79**	**$5.21**	**$923.14**	**5.88%**
TERIPARATIDE PRODUCTS						
FORTEO SOL 600/2.4	153	25	$354,282.89	$81.93	$2,315.57	83.64%
SUBTOTAL	**153**	**25**	**$354,282.89**	**$81.93**	**$2,315.57**	**83.64%**
ZOLEDRONIC PRODUCTS						
ZOLEDRONIC INJ 5/100ML	1	1	$137.24	$0.38	$137.24	0.03%
SUBTOTAL	**1**	**1**	**$137.24**	**$0.38**	**$137.24**	**0.03%**
SPECIAL PA SUBTOTAL	**201**	**49**	**$380,581.00**	**$37.87**	**$1,893.44**	**89.84%**
TOTAL	**3,381**	**662***	**$423,563.48**	**$4.11**	**$125.28**	**100.00%**

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

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Appendix M

Fiscal Year 2016 Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs)

Oklahoma Health Care Authority
April 2017

Current Prior Authorization Criteria

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

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

Currently, Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are available without prior authorization. Neulasta® was included in the implementation of the original prior authorization of G-CSFs in April 2016 (which also included Granix® and Zarxio®); however, after an analysis of cost effectiveness, the prior authorization requirement for Neulasta® was removed in October 2016.

Utilization of G-CSFs: Fiscal Year 2016

Comparison of Fiscal Years for G-CSFs: Pharmacy Claims

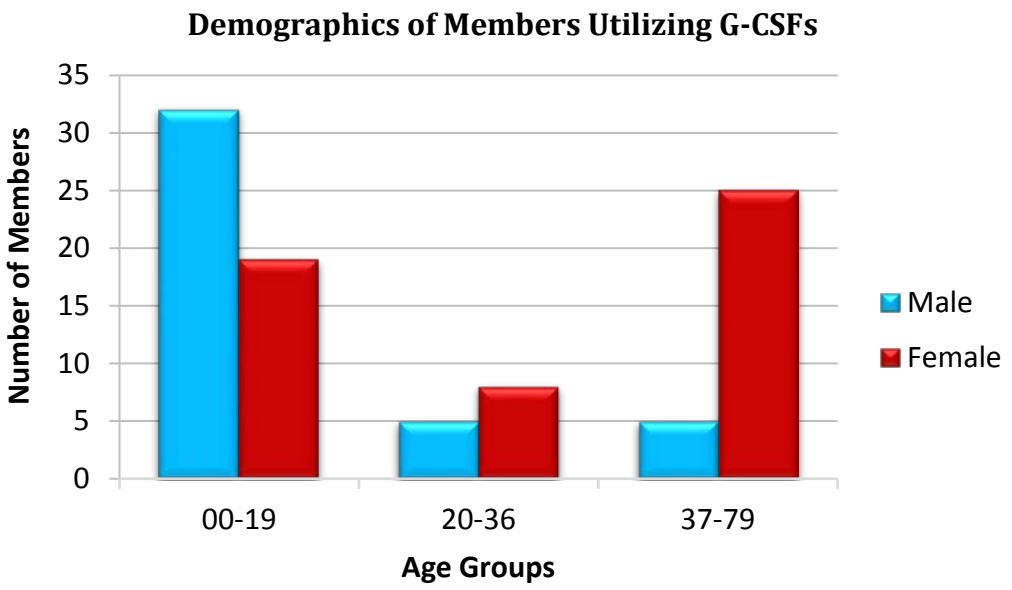
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2015	63	242	$926,403.83	$3,828.12	3.84
2016	94	306	$1,138,099.21	$3,719.28	3.26
% Change	**49.20%**	**26.40%**	**22.90%**	**-2.80%**	**-15.25%**
Change	**31**	**64**	**$211,695.38**	**-$108.84**	**-0.59**

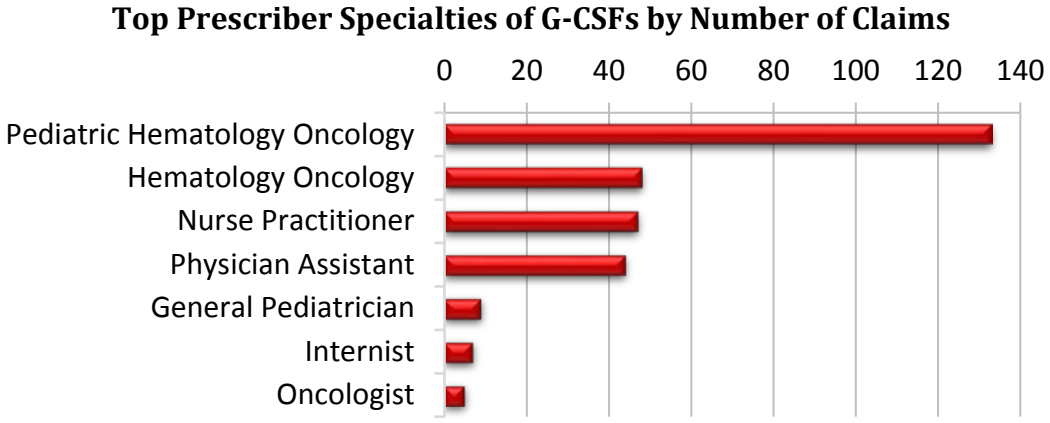
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Fiscal Years for G-CSFs: Medical Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2015	343	1,385	$3,910,285.79	$2,823.31	4.04
2016	258	1,187	$3,127,319.46	$2,634.64	4.60
% Change	**-24.78%**	**-14.30%**	**-20.02%**	**-6.68%**	**13.94%**
Change	**-85**	**-198**	**-$782,966.33**	**-$188.67**	**0.56**

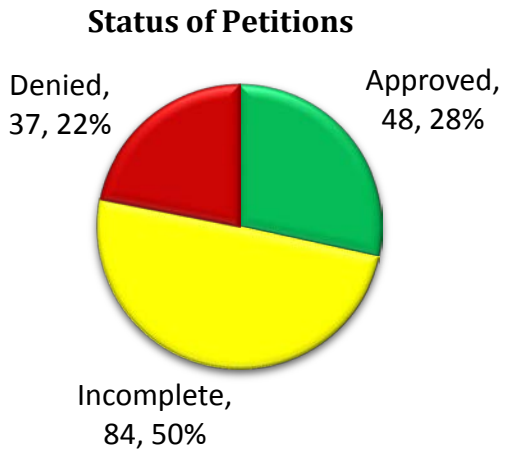
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of G-CSFs

There were 169 prior authorization requests submitted for G-CSFs during fiscal year 2016. The following chart shows the status of the submitted petitions.



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

Safety Update:

- **October 2016:** The U.S. Food and Drug Administration (FDA) is evaluating the need for regulatory action regarding the risk of glomerulonephritis with the use of Granix® (tbo-filgrastim), based on reports of adverse events collected by the FDA Adverse Event Reporting System (FAERS) in the second quarter of 2016.

Pipeline Updates:

- **December 2014:** Apotex submitted a Biologics License Application (BLA) to the FDA for a proposed biosimilar for Neulasta® (pegfilgrastim), followed by submission of a BLA for a proposed biosimilar for Neupogen® (filgrastim) in February 2015. However, after ongoing litigation with Amgen regarding possible patent infringement of Amgen's products, Neulasta® and Neupogen®, the FDA goal date set under the Biosimilar User Fee Act (BsUFA) is unknown for both proposed biosimilar products.
- **June 2016:** The FDA declined to approve Sandoz's proposed biosimilar for Neulasta® (pegfilgrastim) and issued a complete response letter for the product. Novartis, Sandoz's parent pharmaceutical company, indicated that Sandoz is working with the agency to address remaining questions. Sandoz has agreed with the FDA to move forward with an additional study to address their data request and are expected to submit the results of that study to the FDA in 2018. Novartis also withdrew their application for a proposed pegfilgrastim biosimilar product from the European Medicines Agency (EMA) in January 2017. At the time of the withdrawal from the EMA, the company had not demonstrated that their proposed biosimilar product is highly similar to Neulasta® and an inspection to confirm that it was being manufactured according to Good Manufacturing Practice (GMP) standards had not yet taken place.
- **October 2016:** Coherus Biosciences submitted a BLA to the FDA for a proposed biosimilar for Neulasta® (pegfilgrastim). The BsUFA action date is set for June 9, 2017.
- **February 2017:** Mylan and Biocon submitted a BLA to the FDA for a proposed biosimilar for Neulasta® (pegfilgrastim). The FDA goal date set under the BsUFA is October 9, 2017.

Recommendations

The College of Pharmacy does not recommend any changes to the Granulocyte Colony-Stimulating Factors (G-CSFs) category at this time.

Utilization Details of G-CSFs: Fiscal Year 2016

G-CSFs: Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FILGRASTIM PRODUCTS						
NEUPOGEN INJ 300MCG	180	50	$624,676.05	$3,470.42	3.60	54.89%
NEUPOGEN INJ 480/0.8	36	18	$142,755.93	$3,965.44	2.00	12.54%
NEUPOGEN INJ 300/0.5	29	15	$78,179.05	$2,695.83	1.93	6.87%
NEUPOGEN INJ 480MCG	4	4	$17,068.14	$4,267.04	1.00	1.50%
SUBTOTAL	**249**	**87**	**$862,679.17**	**$3,464.57**	**2.86**	**75.80%**
PEGFILGRASTIM PRODUCTS						
NEULASTA INJ 6MG/0.6M	54	21	$271,240.59	$5,022.97	2.57	23.83%
SUBTOTAL	**54**	**21**	**$271,240.59**	**$5,022.97**	**2.57**	**23.83%**
FILGRASTIM-SNDZ PRODUCTS						
ZARXIO INJ 300/0.5	2	1	$3,492.58	$1,746.29	2.00	0.31%
SUBTOTAL	**2**	**1**	**$3,492.58**	**$1,746.29**	**2.00**	**0.31%**
TBO-FILGRASTIM PRODUCTS						
GRANIX INJ 480/0.8	1	1	$686.87	$686.87	1.00	0.06%
SUBTOTAL	**1**	**1**	**$686.87**	**$686.87**	**1.00**	**0.06%**
TOTAL	**306**	**94***	**$1,138,099.21**	**$3,719.28**	**3.26**	**100.00%**

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

G-CSFs: Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PEGFILGRASTIM PRODUCTS						
NEULASTA INJ J2505	773	219	$2,894,796.88	$3,744.89	3.53	92.56%
SUBTOTAL	**773**	**219***	**$2,894,796.88**	**$3,744.89**	**3.53**	**92.56%**
FILGRASTIM PRODUCTS						
NEUPOGEN J1442	289	39	$155,022.90	$536.41	7.41	4.96%
SUBTOTAL	**289**	**39***	**$155,022.90**	**$536.41**	**7.41**	**4.96%**
TBO-FILGRASTIM PRODUCTS						
GRANIX J1446	70	14	$20,813.04	$297.33	5.00	0.67%
GRANIX J1447	55	8	$56,686.64	$1,030.67	6.88	1.81%
SUBTOTAL	**125**	**20***	**$77,499.68**	**$620.00**	**6.25**	**2.48%**
TOTAL	**1,187**	**258***	**$3,127,319.46**	**$2,634.64**	**4.60**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Zarxio® (filgrastim-sndz) had no medical utilization in fiscal year 2016.

[1] U.S. Food and Drug Administration (FDA): Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System (FAERS) April through June 2016. Available online at: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm523358.htm. Last revised 10/05/2016. Last accessed 03/16/2017.

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Appendix N

Fiscal Year 2016 Annual Review of Idiopathic Pulmonary Fibrosis (IPF) Medications

Oklahoma Health Care Authority
April 2017

Introduction[1,2,3]

Idiopathic pulmonary fibrosis (IPF) is a chronic, incurable lung condition that is characterized by varying degrees of fibrosis, collagen deposits, and distortion of the pulmonary architecture. Clinical manifestations of IPF include progressive symptoms of dyspnea, cough, and worsening pulmonary function. Over time, fibrosis of the lungs increases until the lungs can no longer provide enough oxygen to the body's organs and tissues. The prognosis of IPF is poor, with a median survival of approximately three years after diagnosis.

It is estimated that IPF affects approximately 100,000 individuals in the United States, with 30,000 to 40,000 new cases being diagnosed each year.[4] IPF is usually diagnosed in adults over the age of 50 years and is more common in men than in women.

Pharmacologic treatments for IPF are limited. The U.S. Food and Drug Administration (FDA) granted approval through a process of fast track, orphan product, breakthrough designation, and priority review to two new products for the treatment of IPF, Ofev® (nintedanib) and Esbriet® (pirfenidone), in October 2014. Ofev® and Esbriet® slow the rate of progressive lung function decline, but do not cure IPF or lead to improvement of lung function.

Prior to the FDA approval of Ofev® and Esbriet®, no medications were approved for the treatment of IPF. Traditional approaches to treat IPF have included prednisone, azathioprine, and N-acetylcysteine, either alone or in combination; however, this approach does not seem to be effective and there is not adequate evidence to support the use of these medications. Treatment has predominantly been limited to supportive care (e.g., oxygen therapy, pulmonary rehabilitation), with lung transplantation as an option for selected patients.

Current Prior Authorization Criteria

Ofev® (Nintedanib) Approval Criteria:

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

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by a pulmonologist or pulmonary specialist; and

4. A quantity limit of 270 capsules or tablets per 30 days will apply for the 267mg strength capsules and tablets, and a quantity limit of 90 tablets per 30 days will apply for the 801mg strength tablets.

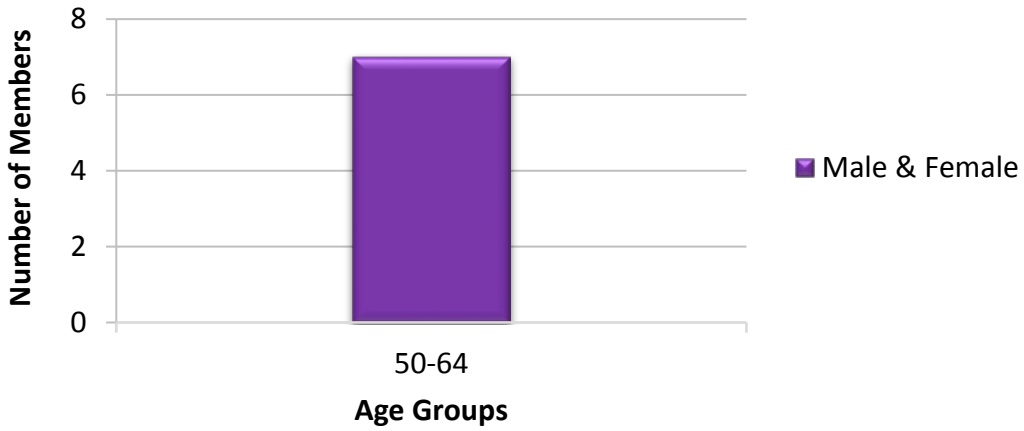
Utilization of IPF Medications: Fiscal Year 2016

Comparison of Fiscal Years: IPF Medications

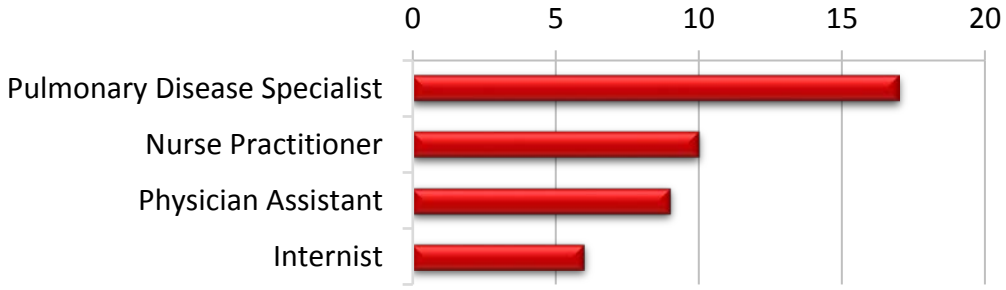
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	3	13	$109,400.33	$8,415.41	$280.51	1,200	390
2016	7	42	$350,664.96	$8,349.17	$278.31	7,350	1,260
% Change	**133.30%**	**223.10%**	**220.50%**	**-0.80%**	**-0.80%**	**512.50%**	**223.10%**
Change	**4**	**29**	**$241,264.63**	**-$66.24**	**-$2.20**	**6,150**	**870**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Please note, both Ofev® and Esbriet® were FDA approved in October 2014, therefore were not available for the entire 2015 fiscal year.

Demographics of Members Utilizing IPF Medications

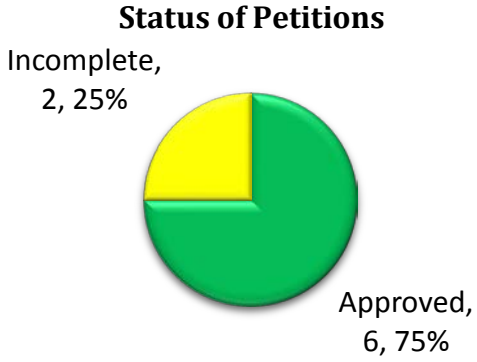


Top Prescriber Specialties of IPF Medications by Number of Claims



Prior Authorization of IPF Medications

There were 8 prior authorization requests submitted for IPF medications during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates[5,6,7,8,9,10]

Anticipated Patent Expiration(s):

- Ofev® (nintedanib): April 2024
- Esbriet® (pirfenidone capsules): August 2033

Anticipated Exclusivity Expiration(s):

- Esbriet® (pirfenidone tablets): October 2021

New FDA Approval:

- **January 2017:** The FDA approved Esbriet® (pirfenidone) 267mg and 801mg tablets for the treatment of IPF. The recommended dosing regimen for Esbriet® is 267mg three times daily for one week, then 534mg three times daily for one week, followed by the recommended dosage of 801mg three times daily. Esbriet® 267mg capsules were FDA approved in 2014. Esbriet® tablets are not currently available on the market; therefore, cost information is not yet available. A cost comparison between Esbriet® capsules and tablets will be completed once the tablets are available on the market to determine if preference should be given to one dosage form over the other. The quantity limits for Esbriet® have been updated to include the tablet formulation and strengths available, and the changes are noted in red in the *Current Prior Authorization Criteria* section of this report.

News:

- **March 2017:** Two studies published in the *Journal of Managed Care and Specialty Pharmacy* concluded that Esbriet® (pirfenidone) can improve life expectancy compared with best supportive care and lower the risk of lung function decline for patients with IPF. The first study showed that pirfenidone can increase life expectancy in patients by 2.47 years compared to best supportive care. The second study concluded that pirfenidone may reduce the odds of experiencing a decline in percent predicted forced vital capacity (FVC) of greater than or equal to 10% compared with placebo in the first

year of treatment. The results of the analysis also suggest that pirfenidone improves survival.

- **March 2017:** There is currently a Phase 4, twelve week, open-label, randomized, parallel-group study ongoing to evaluate the safety, tolerability, and pharmacokinetics of nintedanib in combination with pirfenidone, compared to treatment with nintedanib alone, in patients with IPF. The estimated study completion date was February 2017; however, the study still appears to be ongoing and study results are not yet available.

Recommendations

The College of Pharmacy does not recommend any changes to the Idiopathic Pulmonary Fibrosis (IPF) Medications category at this time.

Utilization Details of IPF Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
PIRFENIDONE PRODUCTS						
ESBRIET CAP 267MG	23	4	$189,476.90	$274.60	$8,238.13	54.03%
SUBTOTAL	**23**	**4**	**$189,476.90**	**$274.60**	**$8,238.13**	**54.03%**
NINTEDANIB PRODUCTS						
OFEV CAP 150MG	19	3	$161,188.06	$282.79	$8,483.58	45.97%
SUBTOTAL	**19**	**3**	**$161,188.06**	**$282.79**	**$8,483.58**	**45.97%**
TOTAL	**42**	**7***	**$350,664.96**	**$278.31**	**$8,349.17**	**100.00%**

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

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Appendix O

Fiscal Year 2016 Annual Review of Strensiq® (Asfotase Alfa)

Oklahoma Health Care Authority
April 2017

Introduction[1,2,3]

Hypophosphatasia (HPP) is a rare autosomal disease characterized by abnormal mineralization of bone and dental tissues. It is caused by deficiency of tissue-nonspecific alkaline phosphatase due to mutations in the tissue-non-specific alkaline phosphatase (*TNSALP*) gene. The earlier the presentation, the more severe the disease. Early loss of primary incisors may be the first and only sign in mild disease. The severe forms of the disease are present in the perinatal period and in infancy. Patients with the infantile form present within the first six months of life with generalized skeletal demineralization, hypercalcemia, hypercalciuria, fractures, early fusion of the bones of the skull, short extremities, failure to thrive, and respiratory infections. Approximately 50% of affected patients die during infancy. The childhood and adult forms are less severe than the infantile form. They typically present with premature loss of deciduous teeth. The manifestations of childhood HPP include early fusion of the bones of the skull, short stature, bone pain, spontaneous fractures, and scoliosis. Muscle pain, stiffness, and proximal lower-limb weakness also may occur. In the adult form, dental disease often precedes the onset of symptomatic osteomalacia. Severe forms of HPP affect an estimated 1 in 100,000 newborns. Milder cases, such as those that appear in childhood or adulthood, may occur more frequently.

HPP is diagnosed through blood sampling that demonstrates low serum alkaline phosphatase (ALP) concentration or elevated concentrations of phosphoethanolamine and pyrophosphate. Affected patients also may have increased urinary excretion of phosphoethanolamine.

In October 2015, the U.S. Food and Drug Administration (FDA) approved Strensiq® (asfotase alfa) a tissue nonspecific alkaline phosphatase indicated for the treatment of patients with perinatal, infantile, and juvenile-onset HPP. By replacing the deficient ALP, Strensiq® improves bone mineralization. The recommended dosage regimen of Strensiq® for the treatment of perinatal, infantile, and juvenile-onset HPP is 6mg/kg per week administered subcutaneously in divided doses. Other treatments include individualized supportive care, vitamin B_6 for associated seizures, routine dental care, and nonsteroidal anti-inflammatory drugs (NSAIDs) for osteoarthritis, bone pain, and osteomalacia.

Current Prior Authorization Criteria

Strensiq® (Asfotase Alfa) Approval Criteria:

1. An FDA approved indication for the treatment of patients with perinatal/infantile-onset and juvenile-onset hypophosphatasia (HPP); and
2. Confirmed diagnosis by laboratory testing of:
    a. Low age-adjusted alkaline phosphatase (ALP) activity; and
    b. Elevated pyridoxal 5'-phophate (PLP) levels; and

3. Member's weight (kg) must be provided and have been taken within the last four weeks to ensure accurate weight-based dosing; and
4. The 80mg/0.8mL vial should not be used in pediatric patients weighing less than 40kg.

Utilization of Strensiq® (Asfotase Alfa): Fiscal Year 2016

Fiscal Year 2016 Utilization: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2	16	$326,488.76	$20,405.55	$728.77	110	448

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

- Strensiq® (asfotase alfa) was FDA approved in October 2015, within fiscal year 2016; therefore, there was no utilization during fiscal year 2015.

Demographics of Members Utilizing Strensiq® (Asfotase Alfa)

- Due to the small number of members utilizing Strensiq® (asfotase alfa) during fiscal year 2016, detailed demographic information could not be provided.

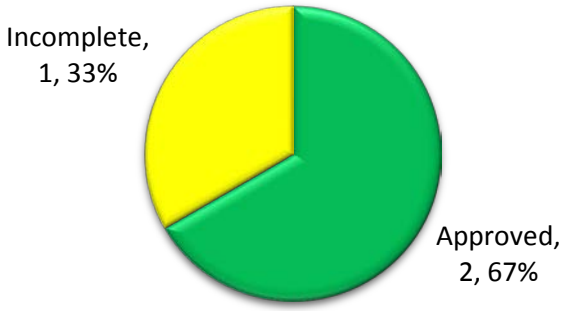
Top Prescriber Specialties of Strensiq® (Asfotase Alfa) by Number of Claims

- The only prescriber specialty listed on paid claims for Strensiq® (asfotase alfa) during fiscal year 2016 was an internist specializing in clinical genetics.

Prior Authorization of Strensiq® (Asfotase Alfa)

There were 3 prior authorization requests submitted for Strensiq® (asfotase alfa) during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[4]

- **October 2016:** Alexion Pharmaceuticals received supplemental approval from the FDA to add severe hypersensitivity reactions to the *Warnings and Precautions* section of the Strensiq® (asfotase alfa) prescribing information, as well as patient labeling. The *Warnings and Precautions* section now includes a warning for anaphylaxis. Signs and symptoms consistent with anaphylaxis are listed and include: difficulty breathing, choking sensation, nausea, periorbital edema, and dizziness. The manufacturer reports reactions have occurred within minutes after subcutaneous administration of Strensiq® and can occur in patients on treatment for more than one year. Other hypersensitivity reactions that have also been reported in Strensiq®-treated patients include: vomiting, fever, headache, flushing, irritability, chills, skin erythema, rash, pruritus, and oral hypoesthesia.

Recommendations

The College of Pharmacy does not recommend any changes to the Strensiq® (asfotase alfa) prior authorization criteria at this time.

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Appendix P

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

FDA NEWS RELEASE

For Immediate Release: February 28th, 2017

FDA approves Xermelo for carcinoid syndrome diarrhea

The U.S. Food and Drug Administration approved Xermelo (telotristat ethyl) tablets in combination with somatostatin analog (SSA) therapy for the treatment of adults with carcinoid syndrome diarrhea that SSA therapy alone has inadequately controlled.

Carcinoid syndrome is a cluster of symptoms sometimes seen in people with carcinoid tumors. These tumors are rare, and often slow-growing. Most carcinoid tumors are found in the gastrointestinal tract. Carcinoid syndrome occurs in less than 10 percent of patients with carcinoid tumors, usually after the tumor has spread to the liver. The tumors in these patients release excess amounts of the hormone serotonin, resulting in diarrhea. Complications of uncontrolled diarrhea include weight loss, malnutrition, dehydration, and electrolyte imbalance.

Xermelo, in a regimen with SSA therapy, is approved in tablet form to be taken orally three times daily with food. Xermelo inhibits the production of serotonin by carcinoid tumors and reduces the frequency of carcinoid syndrome diarrhea.

The safety and efficacy of Xermelo were established in a 12-week, double-blind, placebo-controlled trial in 90 adult participants with well-differentiated metastatic neuroendocrine tumors and carcinoid syndrome diarrhea. These patients were having between four to 12 daily bowel movements despite the use of SSA at a stable dose for at least three months. Participants remained on their SSA treatment, and were randomized to add placebo or treatment with Xermelo three times daily. Those receiving Xermelo added on to their SSA treatment experienced a greater reduction in average bowel movement frequency than those on SSA and placebo. Specifically, 33 percent of participants randomized to add Xermelo on to SSA experienced an average reduction of two bowel movements per day compared to 4 percent of patients randomized to add placebo on to SSA.

The most common side effects of Xermelo include nausea, headache, increased levels of the liver enzyme gamma-glutamyl transferase, depression, accumulation of fluid causing swelling (peripheral edema), flatulence, decreased appetite and fever. Xermelo may cause constipation, and the risk of developing constipation may be increased in patients whose bowel movement frequency is less than four bowel movements per day. Patients treated with a higher than recommended dosage of Xermelo developed severe constipation in clinical trials. One patient required hospitalization and two other patients developed complications of either intestinal perforation or intestinal obstruction. Patients should be monitored for severe constipation. If a patient experiences severe constipation or severe, persistent or worsening abdominal pain, they should discontinue Xermelo and contact their healthcare provider.

The FDA granted this application fast track designation and priority review. The drug also received orphan drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases. Xermelo is manufactured by Woodlands, Texas-based Lexicon Pharmaceuticals, Inc.

FDA NEWS RELEASE

For Immediate Release: March 3rd, 2017

FDA approves first treatment for frequent urination at night due to overproduction of urine

The U.S. Food and Drug Administration approved Noctiva (desmopressin acetate) nasal spray for adults who awaken at least two times per night to urinate due to a condition known as nocturnal polyuria (overproduction of urine during the night). Noctiva is the first FDA-approved treatment for this condition.

Nocturia (wakening at night to urinate) is a symptom that can be caused by a wide variety of conditions, such as congestive heart failure, poorly controlled diabetes mellitus, medications, or diseases of the bladder or prostate. Before considering Noctiva, health care providers should evaluate each patient for possible causes for the nocturia, and optimize the treatment of underlying conditions that may be contributing to the night-time urination. Because Noctiva is approved only for adults with nocturia caused by nocturnal polyuria, health care providers should confirm overproduction of urine at night with a 24-hour urine collection, if one has not been obtained previously. Health care providers should also be mindful of underlying conditions that can cause

nocturia, but that make treatment with Noctiva unsafe, such as excessive drinking of fluids or symptomatic congestive heart failure.
Noctiva is taken daily, approximately 30 minutes before going to bed. It works by increasing the absorption of water through the kidneys, which leads to less urine production.
Noctiva's efficacy was established in two 12-week, randomized, placebo-controlled trials in 1,045 patients 50 years of age and older with nocturia due to nocturnal polyuria. Although these trials showed a small reduction in the average number of night-time urinations with Noctiva compared to placebo, more patients treated with Noctiva were able to at least halve their number of night-time urinations, and patients treated with Noctiva had more nights with one or fewer night-time urinations.
Noctiva is being approved with a boxed warning and a Medication Guide because it can cause low sodium levels in the blood (hyponatremia). Severe hyponatremia can be life-threatening if it is not promptly diagnosed and treated, leading to seizures, coma, respiratory arrest or death. Health care providers should make sure the patient's sodium level is normal before starting Noctiva, and should check sodium levels within one week and approximately one month after starting treatment and periodically thereafter. The lower Noctiva dose is recommended as the starting dose for those who may be at risk for hyponatremia, such as the elderly. Noctiva should not be used in patients at increased risk of severe hyponatremia, such as those with excessive fluid intake, those who have illnesses that can cause fluid or electrolyte imbalances, certain patients with kidney damage, and in those using certain medicines, known as loop diuretics or glucocorticoids.
Noctiva should also not be used in patients with symptomatic congestive heart failure or uncontrolled hypertension because fluid retention can worsen these underlying conditions. Use of Noctiva should be discontinued temporarily in patients with certain nasal conditions such as colds or allergies until those conditions have resolved.
Noctiva is also not recommended for the treatment of nocturia in pregnant women. Nocturia is usually related to normal changes in pregnancy that do not require treatment with Noctiva. Noctiva should not be used in children.
The most common side effects of Noctiva in clinical trials included nasal discomfort, cold symptoms (nasopharyngitis), nasal congestion, sneezing, high or increased blood pressure, back pain, nose bleeds, bronchitis and dizziness.
Although there are other FDA-approved medications that also contain desmopressin, none of those medications are approved to treat nocturia.
Noctiva is manufactured by Renaissance Lakewood, LLC for Milford, Pennsylvania-based Serenity Pharmaceuticals, LLC.

FDA NEWS RELEASE

For Immediate Release: March 21st, 2017

FDA approves drug to treat Parkinson's disease

The U.S. Food and Drug Administration approved Xadago (safinamide) tablets as an add-on treatment for patients with Parkinson's disease who are currently taking levodopa/carbidopa and experiencing "off" episodes. An "off" episode is a time when a patient's medications are not working well, causing an increase in Parkinson's symptoms, such as tremor and difficulty walking.
An estimated 50,000 Americans are diagnosed with Parkinson's disease each year, according to the National Institutes of Health, and about one million Americans have the condition. The neurological disorder typically occurs in people over age 60, though it can occur earlier, when cells in the brain that produce a chemical called dopamine become impaired or die. Dopamine helps transmit signals between the areas of the brain that produce smooth, purposeful movement – such as eating, writing, and shaving. Early symptoms of the disease are subtle and occur gradually. In some people, Parkinson's disease progresses more quickly than in others.
The efficacy of Xadago in treating Parkinson's disease was shown in a clinical trial of 645 participants who were also taking levodopa and were experiencing "off" time. Those receiving Xadago experienced more beneficial "on" time, a time when Parkinson's symptoms are reduced, without troublesome uncontrolled involuntary movement (dyskinesia), compared to those receiving a placebo. The increase in "on" time was accompanied by a reduction in "off" time and better scores on a measure of motor function assessed during "on" time than before treatment.
In another clinical trial of 549 participants, the participants adding Xadago to their levodopa treatment had more "on" time without troublesome uncontrolled involuntary movement compared to those taking a placebo, and also had better scores on a measure of motor function assessed during "on" time than before treatment.

Certain patients should not take Xadago. These include patients who have severe liver problems, or who take a medicine used to treat a cough or cold called dextromethorphan. It also should not be taken by patients who take another medicine called a monoamine oxidase inhibitor (MAOI) because it may cause a sudden severe increase in blood pressure, or by those who take an opioid drug, St. John's wort, certain antidepressants (such as serotonin-norepinephrine reuptake inhibitors, tricyclics, tetracyclics, and triazolopyridines), or cyclobenzaprine, because it may cause a life-threatening reaction called serotonin syndrome.
The most common adverse reactions observed in patients taking Xadago were uncontrolled involuntary movement, falls, nausea, and trouble sleeping or falling asleep (insomnia).
Serious, but less common, risks include the following: exacerbated high blood pressure (hypertension); serotonin syndrome when used with MAOIs, antidepressants, or opioid drugs; falling asleep during activities of daily living; hallucinations and psychotic behavior; problems with impulse control/compulsive behaviors; withdrawal-emergent hyperpyrexia (fever) and confusion; and retinal pathology.
The FDA granted approval of Xadago to Newron Pharmaceuticals.

FDA NEWS RELEASE

For Immediate Release: March 23rd, 2017

FDA approves first treatment for rare form of skin cancer

The U.S. Food and Drug Administration granted accelerated approval to Bavencio (avelumab) for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC), including those who have not received prior chemotherapy. This is the first FDA-approved treatment for metastatic MCC, a rare, aggressive form of skin cancer.
According to the National Cancer Institute, approximately 1,600 people in the United States are diagnosed with MCC every year. While the majority of patients present with localized tumors that can be treated with surgical resection, approximately half of all patients will experience recurrence, and more than 30 percent will eventually develop metastatic disease. In patients with metastatic MCC, the cancer has spread beyond the skin into other parts of the body.
Bavencio targets the PD-1/PD-L1 pathway (proteins found on the body's immune cells and some cancer cells). By blocking these interactions, Bavencio may help the body's immune system attack cancer cells.
Bavencio received an Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need using clinical trial data that is thought to predict a clinical benefit to patients. Further clinical trials are required to confirm Bavencio's clinical benefit and the sponsor is currently conducting these studies.
Approval of Bavencio was based on data from a single-arm trial of 88 patients with metastatic MCC who had been previously treated with at least one prior chemotherapy regimen. The trial measured the percentage of patients who experienced complete or partial shrinkage of their tumors (overall response rate) and, for patients with a response, the length of time the tumor was controlled (duration of response). Of the 88 patients who received Bavencio in the trial, 33 percent experienced complete or partial shrinkage of their tumors. The response lasted for more than six months in 86 percent of responding patients and more than 12 months in 45 percent of responding patients.
Common side effects of Bavencio include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reactions, rash, decreased appetite and swelling of the limbs (peripheral edema). The most common serious risks of Bavencio are immune-mediated, where the body's immune system attacks healthy cells or organs, such as the lungs (pneumonitis), liver (hepatitis), colon (colitis), hormone-producing glands (endocrinopathies) and kidneys (nephritis). In addition, there is a risk of serious infusion-related reactions. Patients who experience severe or life-threatening infusion-related reactions should stop using Bavencio. Women who are pregnant or breastfeeding should not take Bavencio because it may cause harm to a developing fetus or a newborn baby.
The FDA granted this application Priority Review and Breakthrough Therapy designation. Bavencio also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted accelerated approval of Bavencio to EMD Serono Inc.

FDA NEWS RELEASE

For Immediate Release: March 27th, 2017

FDA approves maintenance treatment for recurrent epithelial ovarian, fallopian tube or primary peritoneal cancers

The U.S. Food and Drug Administration approved Zejula (niraparib) for the maintenance treatment (intended to delay cancer growth) of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, whose tumors have completely or partially shrunk (complete or partial response, respectively) in response to platinum-based chemotherapy.
Epithelial ovarian, fallopian tube or primary peritoneal cancer is a cancer of the tissue covering the ovary or lining the fallopian tube or abdominal wall (peritoneum). The National Cancer Institute estimates that more than 22,000 women will be diagnosed with these cancers in 2017 and more than 14,000 will die of these diseases.
Zejula is a poly ADP-ribose polymerase (PARP) inhibitor that blocks an enzyme involved in repairing damaged DNA. By blocking this enzyme, DNA inside the cancerous cells may be less likely to be repaired, leading to cell death and possibly a slow-down or stoppage of tumor growth.
The safety and efficacy of Zejula were studied in a randomized trial of 553 patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who had received at least two prior treatments of platinum-based chemotherapy and who had experienced a complete or partial response to their most recent chemotherapy treatment. Patients were tested with an FDA-approved test to determine whether they had a specific gene mutation, called a deleterious or germline BRCA mutation. The trial measured the length of time the patients' tumors did not grow after treatment (progression-free survival) in patients with and without the mutation. The median progression-free survival for patients taking Zejula who had a germline BRCA mutation was 21 months compared to 5.5 months for the same patient population taking a placebo. The median progression-free survival for patients taking Zejula who did not have a germline BRCA mutation was 9.3 months compared to 3.9 months for the same patient population taking a placebo.
Common side effects of Zejula include low levels of red blood cells (anemia), low levels of blood platelets (thrombocytopenia), low levels of white blood cells (neutropenia or leukopenia), heart palpitations, nausea, constipation, vomiting, abdominal pain/swelling (distention), inflammation of the mucous membranes (mucositis), diarrhea, indigestion (dyspepsia), dry mouth, fatigue, decreased appetite, urinary tract infection, liver problems (AST/ALT elevation), muscle pain (myalgia), back pain, joint pain (arthralgia), headache, dizziness, unusual taste sensation (dysgeusia), insomnia, anxiety, cold-like symptoms (nasopharyngitis), trouble breathing (dyspnea), cough, rash and high blood pressure (hypertension). Zejula is associated with serious risks, such as hypertension, severe increase in blood pressure (hypertensive crisis), bone marrow problems (myelodysplastic syndrome), a type of cancer of the blood called acute myeloid leukemia and low levels of blood cells in the bone marrow (bone marrow suppression).Women who are pregnant or breastfeeding should not take Zejula because it may cause harm to a developing fetus or a newborn baby.
The FDA granted this application Fast Track, Priority Review and Breakthrough Therapy designations.
Zejula also received Orphan Drug designation specifically for its use in treating recurrent epithelial ovarian cancer. This designation provides incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted the approval of Zejula to Tesaro, Inc.

FDA NEWS RELEASE

For Immediate Release: March 28th, 2017

FDA approves new eczema drug Dupixent

The U.S. Food and Drug Administration approved Dupixent (dupilumab) injection to treat adults with moderate-to-severe eczema (atopic dermatitis). Dupixent is intended for patients whose eczema is not controlled adequately by topical therapies, or those for whom topical therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
Atopic dermatitis, a chronic inflammatory skin disease, is often referred to as "eczema," which is a general term for several types of inflammation of the skin. Atopic dermatitis is the most common of the many types of eczema; onset typically begins in childhood and can last through adulthood. The cause of atopic dermatitis is a combination of genetic, immune and environmental factors. In atopic dermatitis, the skin develops red, scaly and crusted bumps, which are extremely itchy. Scratching leads to swelling, cracking, "weeping" clear fluid, and finally, coarsening and thickening of the skin.
Dupixent is administered as an injection under the skin. Dupixent's active ingredient is an antibody (dupilumab) that binds to a protein [interleukin-4 (IL-4) receptor alpha subunit (IL-4Ra)], that causes inflammation. By binding to this protein, Dupixent is able to inhibit the inflammatory response that plays a role in the development of atopic dermatitis.
The safety and efficacy of Dupixent were established in three placebo-controlled clinical trials with a total of 2,119 adult participants with moderate-to-severe atopic dermatitis not adequately controlled by topical

medication(s). Overall, participants who received Dupixent achieved greater response, defined as clear or almost clear skin, and experienced a reduction in itch after 16 weeks of treatment.
Dupixent can cause side effects such as serious allergic reactions and eye problems, such as pink eye (conjunctivitis) and inflammation of the cornea (keratitis). If patients experience new or worsening eye symptoms such as redness, itching, pain or visual changes, they should consult a health care provider. The most common side effects include injection site reactions; cold sores in the mouth or on the lips; and eye and eyelid inflammation, including redness, swelling and itching.
The safety and efficacy of Dupixent have not been established in the treatment of asthma. Patients who also have asthma should not adjust or stop their asthma treatment without talking to their physicians.
The FDA granted the application for Dupixent Priority Review and Breakthrough Therapy designation.
The FDA granted the approval of Dupixent to Regeneron Pharmaceuticals, Inc.

Safety Announcements

FDA Drug Safety Communication: FDA warns about increased risk of serious pancreatitis with irritable bowel drug Viberzi (eluxadoline) in patients without a gallbladder

[3/15/17] The U.S. Food and Drug Administration (FDA) is warning that Viberzi (eluxadoline), a medicine used to treat irritable bowel syndrome with diarrhea (IBS-D), should not be used in patients who do not have a gallbladder. An FDA review found these patients have an increased risk of developing serious pancreatitis that could result in hospitalization or death. Pancreatitis may be caused by spasm of a certain digestive system muscle in the small intestine. As a result, the FDA is working with the Viberzi manufacturer, Allergan, to address these safety concerns.
Patients should talk to their health care professional about how to control their symptoms of irritable bowel syndrome with diarrhea (IBS-D), particularly if they do not have a gallbladder. The gallbladder is an organ that stores bile, one of the body's digestive juices that helps in the digestion of fat. Patients should stop taking Viberzi right away and get emergency medical care if they develop new or worsening stomach-area or abdomen pain, or pain in the upper right side of the stomach-area or abdomen that may move to the back or shoulder. This pain may occur with nausea and vomiting. These may be symptoms of pancreatitis, an inflammation of the pancreas an organ important in digestion; or spasm of the sphincter of Oddi, a muscular valve in the small intestine that controls the flow of digestive juices to the gut.
Health care professionals should not prescribe Viberzi in patients who do not have a gallbladder and should consider alternative treatment options in these patients. Hospitalizations and deaths due to pancreatitis have been reported with Viberzi use in patients who do not have a gallbladder. Symptoms of pancreatitis have occurred with just one or two doses of Viberzi at the recommended dosage for patients who do not have a gallbladder (75 mg), and who do not consume alcohol.
Physicians can consider both over-the-counter (OTC) or FDA-approved prescription medicines to treat symptoms associated with IBS-D such as OTC bismuth subsalicylate (Kaopectate and Pepto-Bismol), OTC loperamide (Imodium), and prescription medicine diphenoxylate/ atropine (Lomotil) for diarrhea. Also consider OTC medicines for gas relief such as simethicone (Gas-X, Mylicon). Other FDA-approved prescription medicines for IBS-D include alosetron hydrochloride (Lotronex) and the antibiotic rifaximin (Xifaxan).
Viberzi is a prescription medicine used to treat irritable bowel syndrome in adults when the main symptom is diarrhea (IBS-D). IBS-D affects the large intestine and causes cramping, stomach-area or abdomen pain, bloating, gas, and diarrhea. The cause of IBS-D is not known. Viberzi works by decreasing bowel contractions, which leads to less diarrhea. In patients with IBS-D, Viberzi can help ease stomach-area or abdomen pain and improve stool consistency.
From May 2015, when Viberzi was first approved, through February 2017, FDA received 120 reports of serious cases of pancreatitis or death. Among the 68 patients who reported their gallbladder status, 56 of them did not have a gallbladder and received the currently recommended dosage of Viberzi. Seventy-six patients were hospitalized, of which two patients died. These two patients did not have a gallbladder. Some cases of serious pancreatitis or death also reported sphincter of Oddi spasm (n=6) or abdomen pain (n=16).
The FDA urges patients and health care professionals to report side effects involving Viberzi (eluxadoline) or other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of April 3rd, 2017):

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

Albuterol Sulfate Inhalation Solution (0.5%, 0.021%, and 0.042%)	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***

Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Estradiol Valerate Injection, USP	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Hydroxyamphetamine Hydrobromide/Tropicamide (Paremyd)	***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***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nitrous Oxide, Gas	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine (Transderm Scop) Transdermal System Patch	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sterile Talc Powder	***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***