Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
March 8, 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: Melissa Abbott, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – March 8, 2017

DATE: March 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 March meeting.
Material is arranged in order of the agenda.

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/FDA Safety Alerts – Appendix B

Action Item – Vote to Prior Authorize Nuplazid™ (Pimavanserin) – Appendix C

Action Item – Vote to Prior Authorize Veltassa® (Patiromer) – Appendix D

Action Item – Vote to Prior Authorize Kanuma® (Sebelipase Alfa) – Appendix E

Action Item – Vote to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel) – Appendix F

Action Item – Vote to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection) – Appendix G

Action Item – Vote to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection) – Appendix H

30-Day Notice to Prior Authorize Spinraza™ (Nusinersen) – Appendix I

Annual Review of Pulmonary Hypertension Medications – Appendix J

Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Zinbryta™ (Daclizumab) – Appendix K

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

Annual Review of Naloxone Medications – Appendix M

30-Day Notice to Prior Authorize Zinplava™ (Bezlotoxumab) – Appendix N

FDA and DEA Updates – Appendix O

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – March 8, 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. February 8, 2017 DUR Minutes – Vote

B. February 8, 2017 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/FDA Safety Alerts – See Appendix B

A. Medication Coverage Activity for February 2017

B. Pharmacy Help Desk Activity for February 2017

C. FDA Safety Alerts

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

5. Action Item – Vote to Prior Authorize Nuplazid™ (Pimavanserin) – See Appendix C

A. Introduction

B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Veltassa® (Patiromer) – See Appendix D

A. Introduction

B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Kanuma® (Sebelipase Alfa) – See Appendix E

A. Introduction

B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel) – See Appendix F

A. Introduction

B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection) – See Appendix G

A. Introduction

B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection) – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

11. 30-Day Notice to Prior Authorize Spinraza™ (Nusinersen) – See Appendix I

A. Spinal Muscular Atrophy
B. Market News and Updates
C. Spinraza™ (Nusinersen) Product Summary
D. College of Pharmacy Recommendations

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

12. Annual Review of Pulmonary Hypertension Medications – See Appendix J

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

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

13. Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Zinbryta™ (Daclizumab) – See Appendix K

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

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

14. Annual Review of Makena® and Vaginal Progesterone Products and 30-Day Notice to Prior Authorize Hydroxyprogesterone Caproate Injection – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Makena® and Vaginal Progesterone Products
C. Prior Authorization of Makena® and Vaginal Progesterone Products
D. Market News and Updates
E. Hydroxyprogesterone Caproate Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Makena® and Vaginal Progesterone Products

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

15. Annual Review of Naloxone Medications – See Appendix M

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

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

16. 30-Day Notice to Prior Authorize Zinplava™ (Bezlotoxumab) – See Appendix N

A. Introduction
B. Zinplava™ (Bezlotoxumab) Product Summary

C. College of Pharmacy Recommendations

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

17. FDA and DEA Updates – See Appendix O

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

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

A. Diabetic Medications
B. Antihypertensive Medications
C. Granulocyte-Colony Stimulating Factors (G-CSFs)
D. Osteoporosis Medications
E. Strensiq® (Asfotase Alfa)
F. Hemophilia Medications
G. Idiopathic Pulmonary Fibrosis Medications
H. Alpha$_1$-Proteinase Inhibitors

**Future business subject to change.*

19. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF FEBRUARY 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): Cac Nguyen, Michelle Lang	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	x	
Kelli Brodersen, Marketing Coordinator	x	
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:		
Pratik Parikh, Sarepta	Cheryl Donahue, Sarepta	Bill Mroczka, Alexion
Chris Stanfield, Supernus	Jonathon Raap, Alexion	Corinne Copeland, Eisai
John Loomis, Eisai	Chris Lawatsch, Eisai	Evan Rushing, Alkermes
Audrey Ratten, Alkermes	Toby Thompson, Pfizer	Doug Wood, Viiv
Dan Doyle, Trividia	Jim Chapman, Abbvie	Anne McNamara, Otonomy
Mark DeClerk, Lilly	J. Sika, OU student	Michele Puyear, Gilead
Jim Dunlap, PhRMA	Marc Parker, Sunovion	Erica Brumleve, GSK
Brent Hildebrand, Gilead	Chet Steckler, Purdue	Imani Baker, OUSWK
Mai Duong, Novartis	Kari Suttee, Novartis	Jeff Knappen, Allergan
Brian Maves, Pfizer	Jim Fowler, Astra Zeneca	Tyler Craddock, Medco
Sean Seago, Merck	Terry McCurren, Otsuka	Aaron Shaw, BI

PRESENT FOR PUBLIC COMMENT:	
John Loomis	Eisai

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. 12 SPEAKER: JOHN LOOMIS

ACTION: NONE REQUIRED

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

3A: DECEMBER 14, 2016 DUR MINUTES – VOTE

3B: DECEMBER 14, 2016 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ SOONERPSYCH PROGRAM UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR DECEMBER 2016

4B: PHARMACY HELP DESK ACTIVITY FOR DECEMBER 2016

4C: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2017

4D: PHARMACY HELP DESK ACTIVITY FOR JANUARY 2017

4E: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Abbott and Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE SYNDROS™ (DRONABINOL), SUSTOL® (GRANISETRON), AND BONJESTA® (DOXYLAMINE/PYRIDOXINE)**

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE VIEKIRA XR™ (DASABUVIR/ OMBITASVIR/PARITAPREVIR/RITONAVIR) AND EPCLUSA® (SOFOSBUVIR/VELPATASVIR)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE EXONDYS 51™ (ETEPLIRSEN)**

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Harrell moved to approve; seconded by Dr. Huddleston

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE OTOVEL® (CIPROFLOXACIN/ FLUOCINOLONE ACETONIDE)**

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE CINQAIR® (RESLIZUMAB) AND BEVESPI AEROSPHERE® (GLYCOPYRROLATE/FORMOTEROL FUMARATE)**

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **VOTE TO PRIOR AUTHORIZE FOSRENOL® (LANTHANUM CARBONATE), VELPHORO® (SUCROFERRIC OXYHYDROXIDE), AND AURYXIA™ (FERRIC CITRATE)**

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **VOTE TO PRIOR AUTHORIZE DEFITELIO® (DEFIBROTIDE SODIUM)**

11A: INTRODUCTION

11B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF SEIZURE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BRIVIACT® (BRIVARACETAM), FYCOMPA™ (PERAMPANEL ORAL SUSPENSION), AND CARNEXIV™ (CARBAMAZEPINE INJECTION)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF SEIZURE MEDICATIONS

12C: PRIOR AUTHORIZATION OF SEIZURE MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: BRIVIACT® (BRIVARACETAM) PRODUCT SUMMARY

12F: FYCOMPA™ (PERAMPANEL ORAL SUSPENSION) PRODUCT SUMMARY
12G: CARNEXIV™ (CARBAMAZEPINE INJECTION) PRODUCT SUMMARY
12H: COLLEGE OF PHARMACY RECOMMENDATIONS
12I: UTILIZATION DETAILS OF SEIZURE MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 14: ANNUAL REVIEW OF HYPERKALEMIA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VELTASSA® (PATIROMER)
14A: CHRONIC HYPERKALEMIA
14B: UTILIZATION OF POTASSIUM BINDERS
14C: MARKET NEWS AND UPDATES
14D: VELTASSA® (PATIROMER) PRODUCT SUMMARY
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF POTASSIUM BINDERS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: 30-DAY NOTICE TO PRIOR AUTHORIZE KANUMA® (SEBELIPASE ALFA)
15A: LYSOSOMAL ACID LIPASE DEFICIENCY (LAL-D) BACKGROUND INFORMATION
15B: KANUMA® (SEBELIPASE ALFA) PRODUCT SUMMARY
15C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF SOLARAZE® (DICLOFENAC SODIUM 3% GEL) AND 30-DAY NOTICE TO PRIOR AUTHORIZE PICATO® (INGENOL MEBUTATE 0.015% AND 0.05% GEL)
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF SOLARAZE® (DICLOFENAC 3% GEL)
16C: PRIOR AUTHORIZATION OF SOLARAZE® (DICLOFENAC 3% GEL)
16D: MARKET NEWS AND UPDATES
16E: PICATO® (INGENOL MEBUTATE GEL) PRODUCT SUMMARY
16F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF ANTI-MIGRAINE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ONZETRA® XSAIL® (SUMATRIPTAN NASAL POWDER) AND ZEMBRACE™ SYMTOUCH™ (SUMATRIPTAN INJECTION)
17A: CURRENT PRIOR AUTHORIZATION CRITERIA
17B: UTILIZATION OF ANTI-MIGRAINE MEDICATIONS
17C: PRIOR AUTHORIZATION OF ANTI-MIGRAINE MEDICATIONS

17D: MARKET NEWS AND UPDATES
17E: ONZETRA® XSAIL® (SUMATRIPTAN NASAL POWDER) PRODUCT SUMMARY
17F: ZEMBRACE™ SYMTOUCH™ (SUMATRIPTAN INJECTION) PRODUCT SUMMARY
17G: COLLEGE OF PHARMACY RECOMMENDATIONS
17H: UTILIZATION DETAILS OF ANTI-MIGRAINE MEDICATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF XURIDEN™ (URIDINE TRIACETATE)
18A: HEREDITARY OROTIC ACIDURIA OVERVIEW
18B: CURRENT PRIOR AUTHORIZATION CRITERIA
18C: UTILIZATION OF XURIDEN™ (URIDINE TRIACETATE)
18D: PRIOR AUTHORIZATION OF XURIDEN™ (URIDINE TRIACETATE)
18E: MARKET NEWS AND UPDATES
18F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; non-presentation; questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
20A: MULTIPLE SCLEROSIS MEDICATIONS
20B: ZINPLAVA™ (BEZLOTOXUMAB)
20C: PULMONARY HYPERTENSION MEDICATIONS
20D: ULCERATIVE COLITIS AND CROHN'S DISEASE MEDICATIONS
20E: NALOXONE MEDICATIONS
20F: GAUCHER DISEASE MEDICATIONS
20G: MAKENA® (HYDROXYPROGESTERONE CAPROATE) AND VAGINAL PROGESTERONE PRODUCTS
Future business subject to change.
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: ADJOURNMENT
The meeting was adjourned at 5:04 p.m.

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

Memorandum

Date: February 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 February 8, 2017

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Syndros™ (Dronabinol), Sustol® (Granisetron), and Bonjesta® (Doxylamine/Pyridoxine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Syndros™ (dronabinol oral solution), Sustol® (granisetron subcutaneous injection), and Bonjesta® (doxylamine/pyridoxine 20mg/20mg oral tablets) with the following criteria:

Marinol® and Syndros™ (Dronabinol) and Cesamet® (Nabilone) Approval Criteria:

1. Approval can be granted for six months for the diagnosis of HIV related loss of appetite.
2. The diagnosis of chemotherapy induced nausea and vomiting requires the following:
    a. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length will be based on duration of need.
4. For Marinol® (dronabinol) and Cesamet® (nabilone), a quantity limit of 60 capsules per 30 days will apply.

5. For Syndros™ (dronabinol) oral solution, the quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging.
6. For Syndros™ (dronabinol) oral solution, an age restriction of six years and younger will apply. Members older than six years of age will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used.

Sustol® (Granisetron Subcutaneous Injection) Approval Criteria:

1. An FDA approved indication for use in the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens; and
2. Chemotherapy regimen must be listed on the prior authorization request; and
3. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response is required for authorization in members receiving MEC; and
4. No ondansetron trial is required for authorization of granisetron in members receiving AC combination chemotherapy regimens; and
5. A patient-specific, clinically significant reason why the member cannot use Kytril® (granisetron hydrochloride injection); and
6. A quantity limit of one injection every seven days will apply.

Diclegis® and Bonjesta® (Doxylamine/Pyridoxine) Approval Criteria:

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy that is not responsive to conservative management; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin B_6 (pyridoxine).
4. If the daily net cost of Bonjesta® (doxylamine/pyridoxine 20mg/20mg) is greater than the daily net cost of Diclegis® (doxylamine/pyridoxine 10mg/10mg), authorization of Bonjesta® would also require a patient-specific, clinically significant reason why member cannot use Diclegis®.

Recommendation 3: Vote to Prior Authorize Viekira XR™ (Dasabuvir/ Ombitasvir/Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The prior authorization of Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Epclusa® (sofosbuvir/velpatasvir) with criteria similar to the other prior authorized hepatitis C medications.
2. The removal of the minimum METAVIR fibrosis score of F2. The removal of the fibrosis score requirement will be phased in as follows: Members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018.

3. Updating the criteria regarding alcohol and illicit IV drug use for all direct-acting antivirals (DAAs) to the following: Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy.

The following table highlights the preferred regimens for each genotype in treatment-naïve and PEG-IFN and RBV-experienced members (listed in alphabetical order). Additional regimens other than those listed may be considered based on patient-specific clinical situations.

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

Genotype	Patient Factors	Preferred Regimen(s)
Genotype-2		
2	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
Genotype-3		
3	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated or RAV Y93H) Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks (with RBV with RAV Y93H) Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, cirrhotic	Epclusa® + RBV for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
Genotype-4		
4	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
4	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks Harvoni® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
Genotype-5 or 6		

Genotype	Patient Factors	Preferred Regimen(s)
5 or 6	Treatment-naïve or experienced, non-cirrhotic or cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks

Not all regimens included are FDA approved.
All regimens are either FDA approved, recommended in AASLD/IDSA treatment guidance, or have study data indicating efficacy. If not specified, regimen applies to all genotypic subtypes.
RBV = Ribavirin; PEG IFN = peginterferon alfa; RAV= resistance-associated polymorphisms
Preferred regimens based on clinical efficacy data, guideline recommendations, supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Viekira Pak™ and Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), and Zepatier™ (elbasvir/grazoprevir) are the preferred direct-acting antivirals for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (daclatasvir) in combination for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira™, Epclusa®, Harvoni®, Sovaldi® with peginterferon and ribavirin, or Zepatier™ (elbasvir/grazoprevir) are not appropriate for the member. Detailed criteria for medications with no changes to the coverage criteria are not included in the criteria on the following pages. The criteria for each medication may include FDA approved regimens or AASLD guideline recommended regimens that are not included in the SoonerCare preferred regimens table. Preferred regimens for each genotype can be found in the preferred regimens table. Additional regimens other than those listed in the preferred regimens table may be considered based on patient-specific clinical situations.

Viekira Pak™ and Viekira XR™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)
Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and
4. Viekira Pak™ or Viekira XR™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, genotypic subtype, and cirrhosis will apply:
   a. **Genotype 1a, without cirrhosis:**
      i. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 12 weeks
   b. **Genotype 1a, with compensated cirrhosis:**

i. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 24 weeks
ii. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 12 weeks may be considered for some patients based on prior treatment history.

c. Genotype 1b, without cirrhosis or with compensated cirrhosis:

i. Viekira Pak™ or Viekira XR™ for 12 weeks

d. New regimens will apply as approved by the FDA

8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for those on ribavirin); and
16. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and
17. Member must not be taking the following medications: alfuzosin, ranolazine, dronedarone, carbamazepine, phenytoin, phenobarbital, colchicine, gemfibrozil, rifampin, lurasidone, pimozide, ergotamine, dihydroergotamine, methylergonovine, ethinyl estradiol, cisapride, St. John's wort, lovastatin, simvastatin, efavirenz, sildenafil, triazolam, oral midazolam, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine, and salmeterol; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Epclusa® (Sofosbuvir/Velpatasvir) Approval Criteria:

1. Member must be 18 years of age or older; and

2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1, genotype-2, genotype-3, genotype-4, genotype-5, or genotype-6; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and
4. Epclusa® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on cirrhosis status will apply:
    a. **Genotype-1, -2, -3, -4, -5, -6:**
        i. **Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A):**
            1. Epclusa® for 12 weeks
        ii. **Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C):**
            1. Epclusa® + weight-based ribavirin for 12 weeks
    b. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses greater than 40mg famotidine equivalent, amiodarone, omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses exceeding 10mg; and

16. If member is using antacids they must agree to separate antacid and Epclusa® administration by four hours; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 4: Vote to Prior Authorize Exondys 51™ (Eteplirsen)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Exondys 51™ (eteplirsen) with the following criteria:

Exondys 51™ (Eteplirsen) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping; and
2. 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 Otovel® (Ciprofloxacin/Fluocinolone Acetonide)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Otovel® (ciprofloxacin/fluocinolone 0.3%/0.025%) into Tier-2 of the Otic Anti-Infective Medications Product Based Prior Authorization (PBPA) category. Current Tier-2 criteria for this category will apply.

Otic Anti-Infective Medications		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	ciprofloxacin (Cetraxal®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	**ciprofloxacin/fluocinolone (Otovel®)**	
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Coly-Mycin® S)	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	
	ofloxacin (Floxin® Otic)	

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

Otic Anti-Infective Medications Tier-2 Approval Criteria:

1. Member must have an adequate 14-day trial of at least two Tier-1 medications; or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier-1 medications or infection by an organism not known to be covered by any of the Tier-1 medications.

Otic Anti-Infective Medications Special Prior Authorization (PA) Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent (within six months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

Recommendation 6: Vote to Prior Authorize Cinqair® (Reslizumab) and Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Cinqair® (reslizumab) and Bevespi Aerosphere® (glycopyrrolate/formoterol fumarate) with the following criteria:

Cinqair® (Reslizumab) Approval Criteria:

1. An FDA approved indication of add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype; and
2. Member must be 18 years of age or older; and
3. Member must have a blood eosinophil count of at least 400/mcL (within three to four weeks of dosing); and
4. Member must have had at least two asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least one additional controller medication; and
5. Member must have failed a high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination medications, the highest approved dose meets this criteria); and
6. Member must have failed at least one other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past three months; and
7. Cinqair® must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
8. Cinqair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last twelve months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of six months after which time compliance will be evaluated for continued approval.
10. Member's weight should be provided on prior authorization requests. Weights should have been taken within the last four weeks to provide accurate weight-based dosing.

Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components.

Recommendation 7: Vote to Prior Authorize Fosrenol® (Lanthanum Carbonate), Velphoro® (Sucroferric Oxyhydroxide), and Auryxia™ (Ferric Citrate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Velphoro® (sucroferric oxyhydroxide) and Auryxia™ (ferric citrate) with the following criteria:

Velphoro® (Sucroferric Oxyhydroxide) and Auryxia™ (Ferric Citrate) Approval Criteria:

1. A diagnosis of hyperphosphatemia in patients with chronic kidney disease (CKD) on dialysis; and
2. Documented trials of inadequate response to at least two of the phosphate binders available without a prior authorization or a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization.
3. For Auryxia™, a quantity limit of 12 tablets per day will apply based on maximum recommended dose.

Additionally, the College of Pharmacy recommends the prior authorization of Fosrenol® (lanthanum carbonate) 1,000mg chewable tablets, 750mg packets, and 1,000mg packets with the following criteria:

Fosrenol® (Lanthanum Carbonate) 1,000mg Chewable Tablets, 750mg Oral Powder, and 1,000mg Oral Powder Approval Criteria:

1. A diagnosis of hyperphosphatemia in patients with end stage renal disease (ESRD); and
2. Documented trials of inadequate response to at least two of the phosphate binders available without a prior authorization or a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization; and
3. For the approval of Fosrenol® oral powder, a patient-specific, clinically significant reason why a special formulation is needed over a phosphate binder available without a prior authorization, such as Fosrenol® 500mg or 750mg chewable tablets which can be crushed, must be provided; and
4. For the approval of Fosrenol® 1,000mg chewable tablets, a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization, such as Fosrenol® 500mg or 750mg chewable tablets, must be provided.

Based on the lower net cost of generic calcium acetate containing products, Phoslyra®, Renvela®, Renagel®, and Fosrenol® 500mg and 750mg chewable tablets, the College of Pharmacy does not recommend the prior authorization of these products at this time.

Recommendation 8: Vote to Prior Authorize Defitelio® (Defibrotide Sodium)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Defitelio® (defibrotide sodium) with the following criteria:

Defitelio® (Defibrotide Sodium) Approval Criteria:

1. An FDA approved diagnosis of hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation.
2. Initial approvals will be for one month of therapy. An additional month of therapy (maximum of 60 days) may be granted if the physician documents the continued need for therapy.

Recommendation 9: Annual Review of Seizure Medications and 30-Day Notice to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Nuplazid™ (Pimavanserin)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Hyperkalemia Medications and 30-Day Notice to Prior Authorize Veltassa® (Patiromer)

NO ACTION REQUIRED.

Recommendation 12: 30-Day Notice to Prior Authorize Kanuma® (Sebelipase Alfa)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Solaraze® (Diclofenac Sodium 3% Gel) and 30-Day Notice to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection)

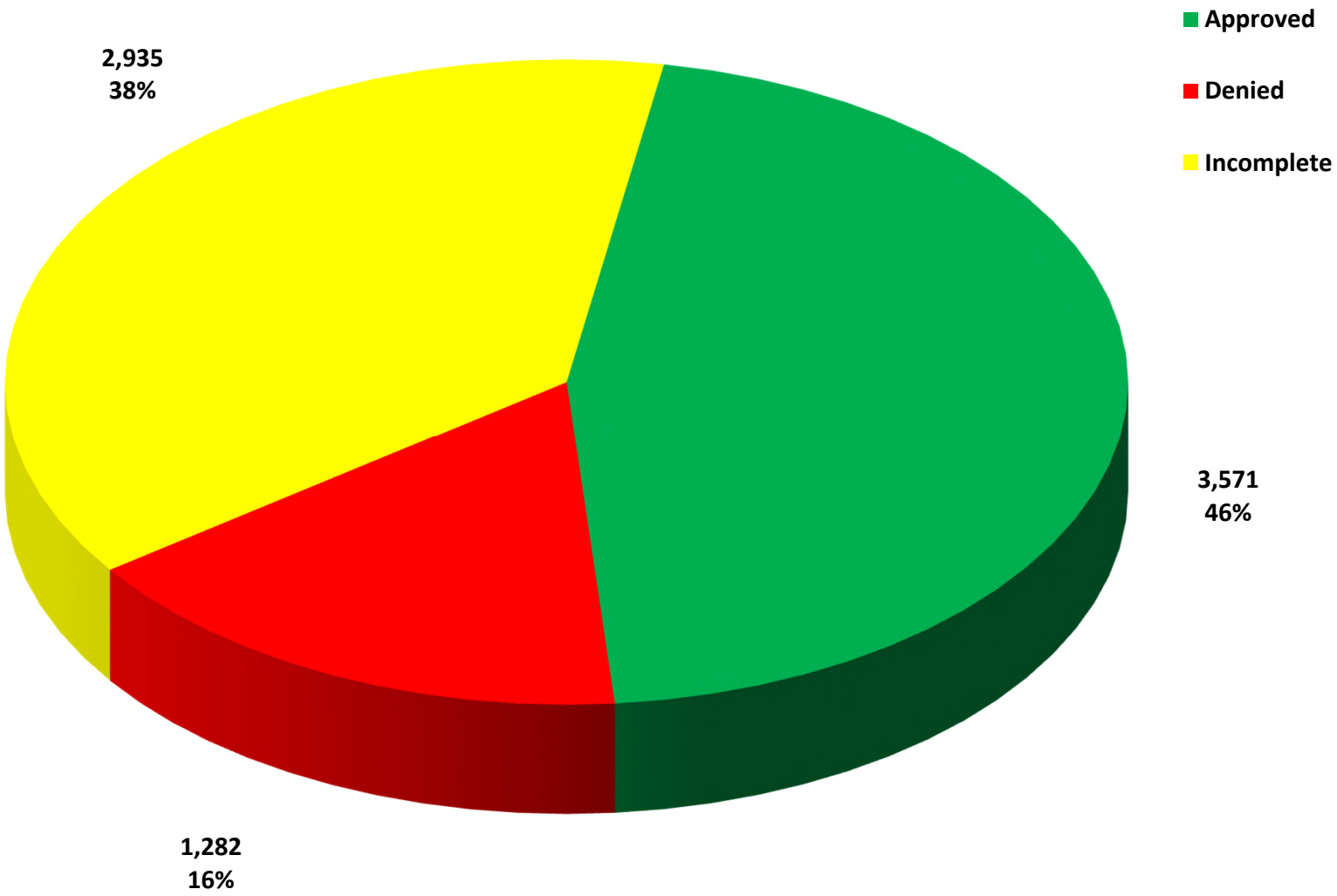
NO ACTION REQUIRED.

Recommendation 15: Annual Review of Xuriden™ (Uridine Triacetate)

NO ACTION REQUIRED.

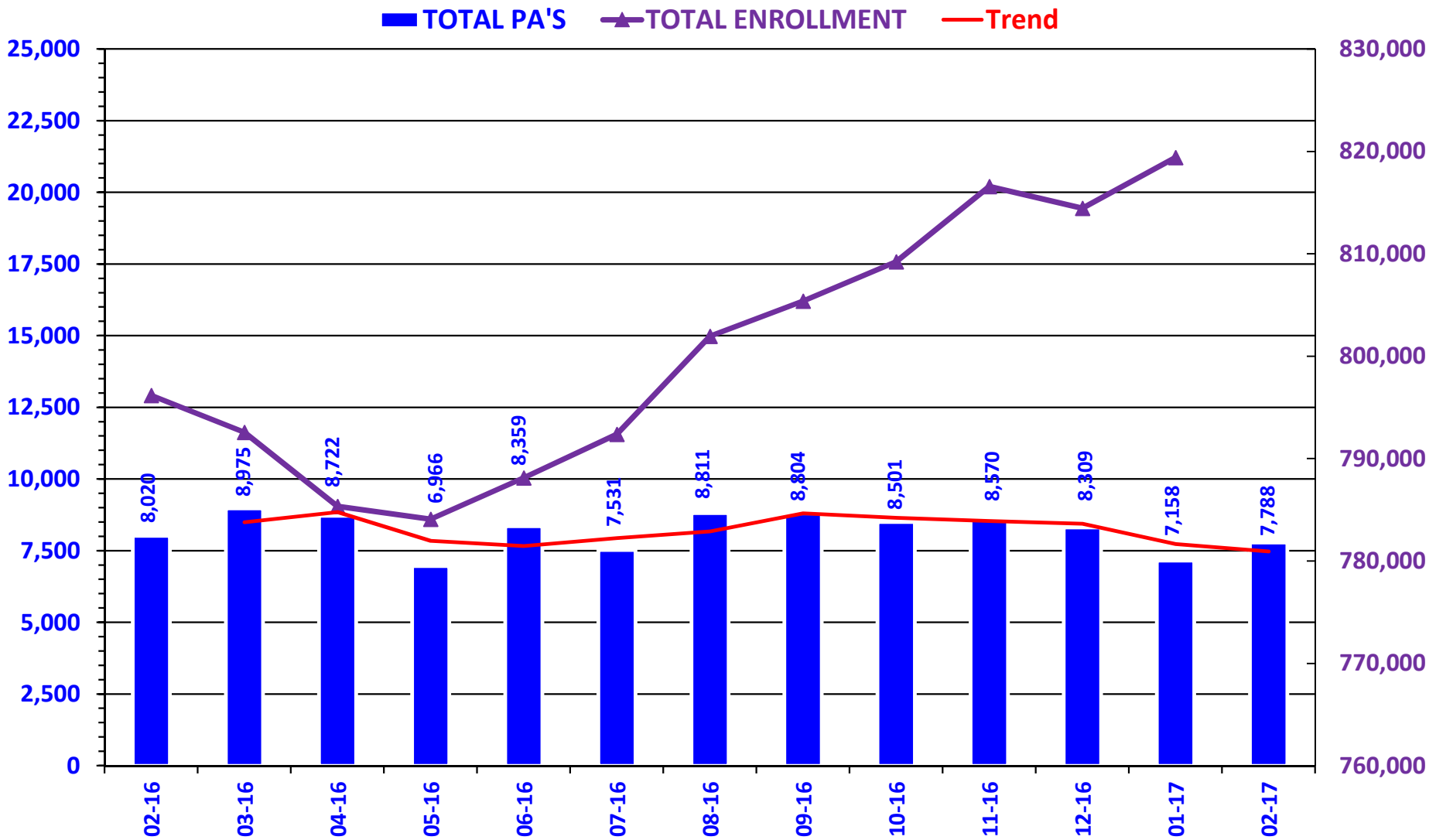
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY 2017



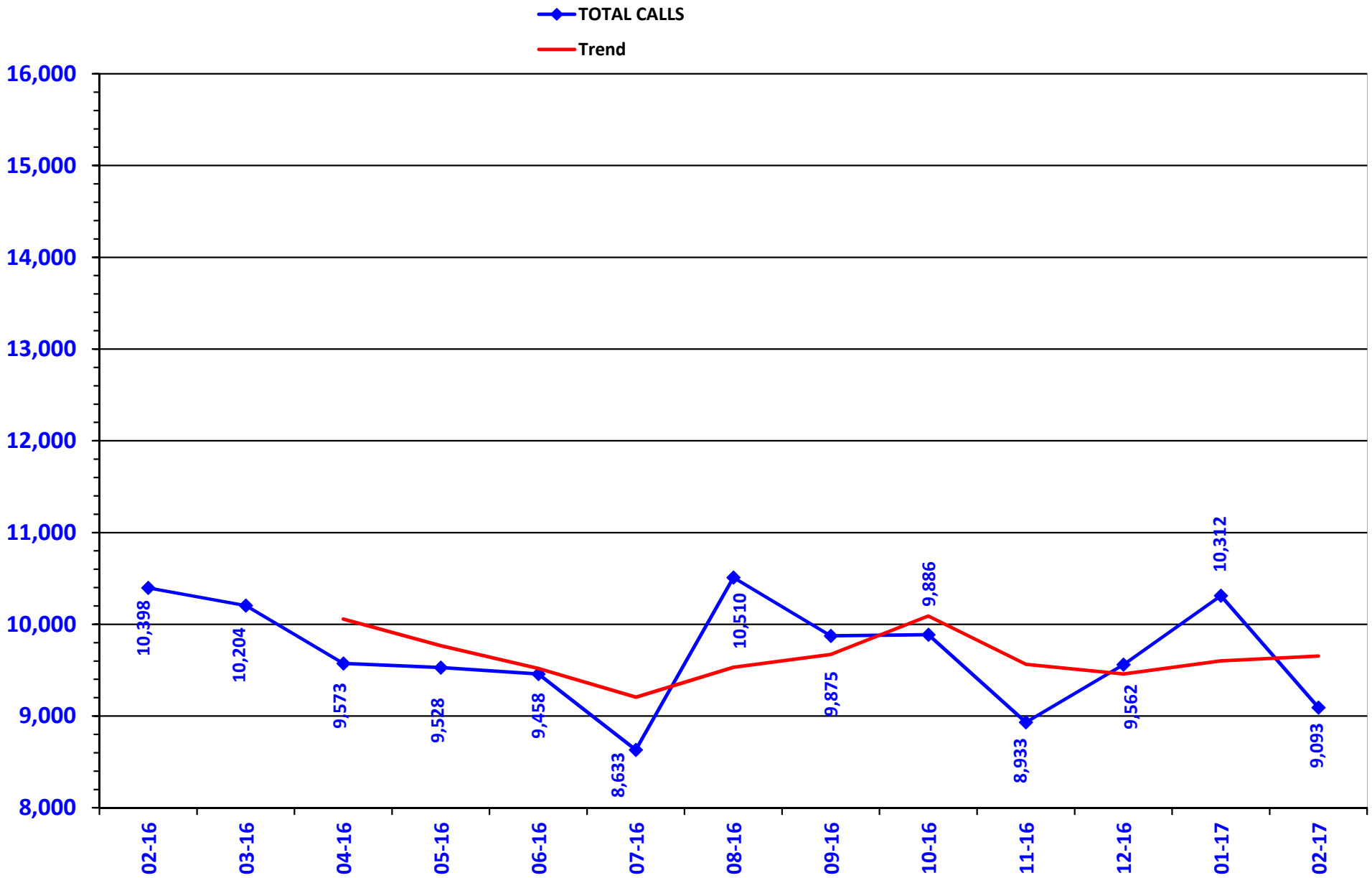
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: FEBRUARY 2016 – FEBRUARY 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
FEBRUARY 2016 – FEBRUARY 2017



Prior Authorization Activity
2/1/2017 Through 2/28/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	159	15	33	111	325
Analgesic - NonNarcotic	29	1	7	21	353
Analgesic, Narcotic	474	249	52	173	162
Angiotensin Receptor Antagonist	12	1	3	8	358
Antiasthma	34	9	11	14	335
Antibiotic	10	3	1	6	125
Anticonvulsant	111	50	16	45	321
Antidepressant	92	17	24	51	357
Antidiabetic	163	65	19	79	342
Antihistamine	247	202	8	37	352
Antimigraine	28	5	5	18	156
Antineoplastic	13	6	1	6	172
Antiparasitic	11	5	1	5	11
Antiulcers	141	24	49	68	159
Antiviral	71	44	12	15	8
Anxiolytic	62	39	6	17	275
Atypical Antipsychotics	181	99	26	56	345
Biologics	127	54	26	47	280
Bladder Control	43	9	9	25	300
Blood Thinners	190	103	19	68	320
Botox	51	31	14	6	334
Buprenorphine Medications	261	217	10	34	71
Cardiovascular	63	26	12	25	288
Cephalosporins	14	8	2	4	7
Chronic Obstructive Pulmonary Disease	177	21	58	98	358
Constipation/Diarrhea Medications	130	22	46	62	168
Contraceptive	22	13	2	7	306
Dermatological	96	10	52	34	60
Diabetic Supplies	455	248	29	178	188
Endocrine & Metabolic Drugs	80	60	6	14	134
Erythropoietin Stimulating Agents	20	10	2	8	101
Fibromyalgia	174	32	79	63	311
Fish Oils	15	0	7	8	0
Gastrointestinal Agents	81	16	19	46	119
Glaucoma	13	0	2	11	0
Growth Hormones	80	56	14	10	149
Hepatitis C	74	40	15	19	8
HFA Rescue Inhalers	55	18	15	22	282
Insomnia	41	8	13	20	134
Insulin	84	16	19	49	267
Miscellaneous Antibiotics	34	2	7	25	8
Multiple Sclerosis	51	25	6	20	184
Muscle Relaxant	49	12	14	23	77
Nasal Allergy	85	10	26	49	206
Neurological Agents	59	32	17	10	349
NSAIDs	209	30	70	109	223
Ocular Allergy	41	6	7	28	81

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Ophthalmic Anti-infectives	15	1	5	9	22
Osteoporosis	14	8	4	2	357
Other*	290	57	85	148	277
Otic Antibiotic	34	6	5	23	9
Respiratory Agents	36	26	3	7	136
Statins	64	7	19	38	314
Stimulant	789	368	78	343	338
Synagis	100	57	18	25	45
Testosterone	63	15	16	32	340
Topical Antifungal	42	4	10	28	16
Topical Corticosteroids	139	1	44	94	84
Vitamin	72	19	31	22	279
Pharmacotherapy	32	20	0	12	307
Emergency PAs	0	0	0	0	
Total	**6,402**	**2,558**	**1,209**	**2,635**	
Overrides					
Brand	42	24	5	13	256
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	5	1	1	3	361
Dosage Change	307	283	1	23	11
High Dose	4	0	0	4	0
Ingredient Duplication	26	23	0	3	11
Lost/Broken Rx	99	89	4	6	12
NDC vs Age	208	144	14	50	242
Nursing Home Issue	26	25	0	1	16
Opioid Quantity	19	15	4	0	142
Other*	34	30	0	4	12
Prescriber Temp Unlock	1	1	0	0	30
Quantity vs. Days Supply	576	347	43	186	239
STBS/STBSM	18	15	2	1	75
Stolen	19	16	1	2	11
Temporary Unlock	5	2	3	0	25
Third Brand Request	22	15	0	7	9
Overrides Total	**1,386**	**1,013**	**73**	**300**	
Total Regular PAs + Overrides	**7,788**	**3,571**	**1,282**	**2,935**	

Denial Reasons	
Unable to verify required trials.	2,332
Does not meet established criteria.	1,318
Lack required information to process request.	559

Other PA Activity	
Duplicate Requests	430
Letters	6,649
No Process	5
Changes to existing PAs	594
Helpdesk Initiated Prior Authorizations	705
PAs Missing Information	41

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

Overview of FDA Safety Alerts

Oklahoma Health Care Authority
March 2017

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

The following are recent U.S. Food and Drug Administration (FDA) safety alerts included for the Drug Utilization Review (DUR) Board's consideration. SoonerCare specific data may be presented where applicable. The College of Pharmacy will make recommendations as well as take recommendations from the DUR Board.

Date	Drug	Issue
08/31/2016	**Opioids and Benzodiazepines**	**Serious side effects and risk of death**
Issue Details: The FDA issued a Drug Safety Communication regarding the continued and increased use of opioids in combination with benzodiazepines. Depressed and difficult breathing and subsequent death can result from the combination of these two classes of drugs, both of which depress the central nervous system. **FDA Recommendations:** Boxed warnings have been added to the labels of all opioids and benzodiazepines in an effort to decrease the combined use of these two classes of drugs. In addition to opioids used for pain, those that are prescribed for cough were also included. Prescribers are advised to prescribe these drugs in combination only when alternatives are inadequate. If the combination is necessary, the doses should be prescribed at the lowest possible effective doses for the shortest duration. Alternatives to opioid cough medications should be prescribed for patients currently on benzodiazepines. **Pharmacy Claims Evaluation:** A thorough review of this issue was presented to the DUR Board in September 2016. As presented in the September 2016 review, in the 12 months prior to the report date, 7,859 SoonerCare members had concomitant use of at least one benzodiazepine and at least one opioid medication. Concomitant use was determined by paid claims for a benzodiazepine and an opioid medication concurrently for 90 consecutive days or greater. **SoonerCare Action:** Recommendations were made during the September 2016 review and included a targeted education to prescribers in specific counties with high rates of overdose deaths or concomitant benzodiazepine and opioid prescribing. Other potential interventions such as an edit to require prior authorization for reimbursement of concomitant benzodiazepine and opioid therapy for longer than 90 days if targeted education is ineffective at changing prescriber behaviors were also recommended.		

Date	Drug	Issue
10/04/2016	**Hepatitis C Direct-Acting Antivirals (DAAs)**	**Risk of reactivating Hepatitis B virus (HBV)**

Issue Details: The FDA issued a Drug Safety Communication regarding the incidence of HBV reactivation after treatment with DAA medications for Hepatitis C. Reactivation has led to serious liver problems and death. There were 24 cases reported to the FDA from November 2013 to July 2016 and, of the cases reported, two patients died and one required liver transplant. More cases were likely unreported.
FDA Recommendations: A boxed warning has been added to drug labels of DAA medications. Prescribers should evaluate patients for current or prior HBV infection before treatment for Hepatitis C and monitor for HBV flare-ups or reactivations during and after treatment.
Pharmacy Claims Evaluation: During the time indicated in the FDA Drug Safety Communication, SoonerCare provided DAA medications for Hepatitis C treatment to 709 members.
SoonerCare Action: Current SoonerCare Hepatitis C prior authorization criteria for DAA medications requires documentation of initiation of immunization with HBV vaccines or screening for HBV, as recommended in the American Association for the Study of Liver Disease (AASLD) guidelines, prior to approval. The College of Pharmacy does not recommend changes to the current prior authorization criteria for Hepatitis C DAA medications in light of the FDA recommendations.

Date	Drug	Issue
10/25/2016	**Testosterone and Other Anabolic Androgenic Steroids (AAS)**	**Risks of abuse and dependence**

Issue Details: Testosterone and other AAS are abused by adults and adolescents, including athletes and body builders. Abuse of testosterone, usually at doses higher than normally prescribed, can lead to serious adverse effects including heart attack, heart failure, stroke, depression, hostility, aggression, liver toxicity, and male infertility. Withdrawal symptoms such as depression, fatigue, irritability, loss of appetite, decreased libido, and insomnia have also been reported in individuals abusing high doses of testosterone.
FDA Recommendations: The FDA has approved class-wide labeling changes to the Warning and Precautions section and the Abuse and Dependence section for all prescription testosterone products.
Pharmacy Claims Evaluation: In fiscal year (FY) 2016, there were 165 SoonerCare members that had paid claims for testosterone products.
SoonerCare Action: Current SoonerCare criteria requires prior authorization for all testosterone products, and approval is based on diagnosis and lab values. The College of Pharmacy does not recommend changes to the current prior authorization criteria for testosterone products in light of the FDA recommendations.

Date	Drug	Issue
12/12/2016	**Pioglitazone**	**Increased risk of bladder cancer**

Issue Details: Based on the results of an updated review, the FDA has concluded that pioglitazone and pioglitazone-containing drugs may increase the risk of bladder cancer. The FDA previously issued safety alerts in September 2010 and June 2011 regarding the possible risk of bladder cancer based on interim results from a 10-year epidemiologic study. The FDA reviewed additional published studies and the results varied among the reviewed studies. Overall, the data suggest that pioglitazone use may be linked to an increased risk of bladder cancer.

FDA Recommendations: The labels of pioglitazone and pioglitazone-containing drugs were updated by the FDA in 2011 to include the warnings about this risk, but are now also required to include the results of the recent studies reviewed by the FDA. Pioglitazone and pioglitazone-containing drugs should not be used in patients with active bladder cancer and should be used cautiously in patients with a history of bladder cancer.

Pharmacy Claims Evaluation: In FY 2016, there were 521 SoonerCare members on pioglitazone or pioglitazone-containing medications, and there were 119 SoonerCare members with a bladder cancer diagnosis (all types). An association between these two SoonerCare patient groups cannot be inferred or determined.

Date	Drug	Issue
12/16/2016	**Varenicline (Chantix®) and Bupropion (Zyban®)**	**Risk of side effects on mood, behavior, or thinking**

Issue Details: A large clinical trial conducted at the request of the FDA has shown that the effects of varenicline and bupropion on mood, behavior, or thinking are not as serious as previously suspected. The risk of mental status changes while taking these drugs is still a possibility; however, the results of the trial confirm that the benefits of smoking cessation far outweigh the risks of the potential side effects of both of the drugs.

FDA Recommendations: The FDA is removing the boxed warning from the labels of varenicline and bupropion. The FDA will continue to evaluate the safety and effectiveness of these drugs. Patients taking these drugs should inform their health care professional if they experience serious changes in their mood or behavior and discontinue the drugs if indicated.

Pharmacy Claims Evaluation: During calendar year (CY) 2016, there were 2,249 SoonerCare members that had paid claims for one of these medications. Please note, other bupropion formulations not specifically indicated for smoking cessation may have been prescribed and/or dispensed, as bupropion formulations do not currently require prior authorization. Varenicline does not require prior authorization and may be used for up to 180 days per calendar year.

[1] FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Issued 08/31/2016. Last accessed 02/13/2017.

[2] FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm522932.htm. Issued 10/04/2016. Last accessed 02/13/2017.

[3] Testosterone and Other Anabolic Androgenic Steroids (AAS): FDA Statement - Risks Associated With Abuse and Dependence. Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm526151.htm. Issued 10/25/2016. Last accessed 02/13/2017.

[4] FDA Drug Safety Communication: Updated FDA review concludes that use of type 2 diabetes medicine pioglitazone may be linked to an increased risk of bladder cancer. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm519616.htm. Issued 12/12/2016. Last accessed 02/13/2017.

[5] FDA Drug Safety Communication: FDA revises description of mental health side effects of the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) to reflect clinical trial findings. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm532221.htm. Issued 12/16/2016. Last accessed 02/13/2017.

Appendix C

Vote to Prior Authorize Nuplazid™ (Pimavanserin)

Oklahoma Health Care Authority
March 2017

Introduction[1]

Nuplazid™ (pimavanserin) is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. Nuplazid™ is available as a 17mg oral tablet. The recommended dosing of pimavanserin is 34mg, taken orally as two 17mg tablets once daily, without titration. The wholesale acquisition cost (WAC) for Nuplazid™ is $32.50 per tablet, resulting in a cost per month of $1,950.00.

Recommendations

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.

[1] Nuplazid™ Prescribing Information. Acadia Pharmaceuticals Inc. Available online at: https://www.nuplazidhcp.com/pdf/NUPLAZID_Prescribing_Information.pdf. Last revised 04/2016. Last accessed 01/2017.

Appendix D

Vote to Prior Authorize Veltassa® (Patiromer)

Oklahoma Health Care Authority
March 2017

Introduction[1]

Veltassa® (patiromer) is a potassium binder indicated for the treatment of hyperkalemia. Patiromer should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action. Veltassa® is available as a powder for oral suspension. The recommended starting dose is 8.4grams orally once daily administered with food. The dose should be adjusted by 8.4grams daily as needed at one week intervals to obtain desired serum potassium target range. Other orally administered drugs should be taken at least three hours before or three hours after patiromer. The wholesale acquisition cost (WAC) for Veltassa® is $22.17 per packet.

Recommendations

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.

[1] Veltassa® Prescribing Information. Relypsa, Inc. Available online at: https://www.veltassa.com/pi.pdf. Last revised 11/2016. Last accessed 01/2017.

Appendix E

Vote to Prior Authorize Kanuma® (Sebelipase Alfa)

Oklahoma Health Care Authority
March 2017

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

Lysosomal acid lipase deficiency (LAL-D) is a rare autosomal recessive lysosomal storage disease. The age at onset and rate of progression vary greatly and this may relate to the nature of the underlying mutations. Infants with LAL-D typically have the most rapidly progressive disease and develop symptoms in the first weeks of life and rarely survive beyond six months of age. Children and adults typically present with some combination of hepatomegaly, elevated transaminases, dyslipidemia, and microvesicular steatosis of the liver on biopsy. In a large proportion of patients, liver damage with progression to fibrosis, cirrhosis, and liver failure occurs. Cardiovascular disease may present as early as childhood and elevated low-density lipoprotein cholesterol (LDL-c) levels and decreased high-density lipoprotein cholesterol (HDL-c) levels are common features.

In December 2015, the U.S. Food and Drug Administration (FDA) approved Kanuma® (sebelipase alfa) for the treatment of patients with a diagnosis of LAL-D. It is currently the only FDA-approved treatment for patients with LAL-D. Sebelipase alfa is a hydrolytic lysosomal cholesteryl ester and triacylglycerol-specific enzyme. It is available as 20mg/10mL solution in single-use vials. The recommended starting dose for patients with rapidly progressive LAL-D presenting within the first six months of life is 1mg/kg as an intravenous (IV) infusion once weekly. The dose may be increased to 3mg/kg once weekly for patients who do not achieve an optimal clinical response. For pediatric and adults patients with LAL-D, the recommended dosage is 1mg/kg as an IV infusion once every other week. The wholesale acquisition cost (WAC) of Kanuma® is $10,000 per 20mg/10mL vial. The average cost of treatment will vary depending on patient specific circumstances.

Recommendations

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.

[1] Reiner Z, Guardamagna O, Nair D, et al. Lysosomal acid lipase deficiency—An under recognized cause of dyslipidaemia and liver dysfunction. *Atherosclerosis*. 2014 Jul:235(1):21-30. Doi: 10.10106/j.atherosclerosis.2014.04.003.
[2] Hoffman EP, Barr ML, Giovanni MA, Murray MF. Lysosomal acid lipase deficiency. *GeneReviews®*. Available online at: http://www.ncbi.nlm.nih.gov/books/NBK305870/?report=printable. Last revised 09/01/2016. Last accessed 01/17/2017.
[3] LAL-D: A Life-Threatening Genetic Disease with Ongoing, Progressive, Multiorgan Damage Leading To Premature Death. Alexion Pharmaceuticals, Inc. Available online at: http://www.laldsource.com/. Last accessed 01/23/2017.
[4] FDA News Release: FDA Approves First Drug to Treat a Rare Enzyme Disorder in Pediatric and Adult Patients. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476013.htm. Issued 12/08/2015. Last accessed 01/17/2017.
[5] Kanuma® Prescribing Information. Alexion Pharmaceuticals, Inc. Available online at: http://www.kanuma.com/docs/full-prescribing-information.pdf. Last revised 12/2015. Last accessed 02/23/2017.

Appendix F

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

Oklahoma Health Care Authority
March 2017

Introduction[1]

Picato® (ingenol mebutate gel) is an inducer of cell death indicated for the topical treatment of actinic keratosis (AK). It is available in two dosage strengths: 0.015% and 0.05%. Picato® gel is supplied in unit dose laminate tubes and the tubes should be discarded after single use. The recommended dosage for the treatment of AK on the face or scalp is to apply the 0.015% gel to the affected area once daily for three consecutive days. The recommended dosage for the treatment of AK on the trunk or extremities is to apply the 0.05% gel to the affected area once daily for two consecutive days.

Recommendations

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.

[1] Picato® Prescribing Information. LEO Pharma, Inc. Available online at: https://www.picato.com/_pdf/PrescribingInformation.pdf. Last revised 10/2016. Last accessed 02/23/2017.

Appendix G

Vote to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) & Zembrace™ SymTouch™ (Sumatriptan Injection)

Oklahoma Health Care Authority
March 2017

Introduction[1,2]

- **Onzetra® Xsail® (sumatriptan nasal powder)** is a serotonin 5-HT1B/1D receptor agonist indicated for the acute treatment of migraine with or without aura in adults. It is supplied as a disposable nosepiece containing a capsule and a reusable breath-powered delivery device. Each capsule contains 11mg sumatriptan base (equivalent to 15.4mg of sumatriptan succinate nasal powder) in a clear, hypromellose capsule. A disposable nosepiece containing 11mg of sumatriptan powder is placed on the delivery device, the piercing button is used to pierce the inner capsule, and the nosepiece is inserted into the nostril while the mouthpiece is inserted between the lips. The patient blows forcefully through the mouthpiece to deliver the sumatriptan powder to the nasal cavity. This is repeated in the other nostril for the second 11mg dose (22mg total dose). The maximum recommended dose is two doses (44mg/4 nosepieces) in 24 hours.
- **Zembrace™ SymTouch™ (sumatriptan injection)** is a serotonin (5-HT1B/1D) receptor agonist indicated for the acute treatment of migraine with or without aura in adults. It is available as a prefilled, ready-to-use, single dose, disposable auto-injector containing 3mg sumatriptan. The recommended dose is 3mg of sumatriptan injected subcutaneously. One 3mg injection may be given up to four times a day with each injection at least one hour apart. The maximum cumulative dose that may be given in 24 hours is 12mg.

Recommendations

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®)*

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
			sumatriptan/naproxen (Treximet®)

*Requires a clinically significant reason why member cannot use all other available formulations of sumatriptan.

[1] Onzetra® Xsail® Prescribing Information. Avanir Pharmaceuticals, Inc. Available online at: https://www.onzetra.com/sites/default/files/onzetra_xsail_prescribing_information.pdf. Last revised 01/2016. Last accessed 02/2017.

[2] Zembrace™ Symtouch™ Prescribing Information. Dr. Reddy's Laboratories Ltd. Available online at: http://www.zembrace.com/Content/docs/zembrace-prescribing-information.pdf. Last revised 01/2016. Last accessed 02/2017.

Appendix H

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

Oklahoma Health Care Authority
March 2017

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

- **Briviact® (brivaracetam)** was approved by the U.S. Food and Drug Administration (FDA) in February 2016 and is indicated as adjunctive therapy in the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy. Brivaracetam is available as oral tablets, oral solution, and injection for intravenous (IV) use and can be initiated with either IV or oral administration.
- **Fycompa™ (perampanel) oral suspension** was approved by the FDA in April 2016 and is indicated as adjunctive therapy for the treatment of partial onset seizures with or without secondarily generalized seizures, and primary generalized tonic-clonic (PGTC) seizures in patients 12 years of age and older with epilepsy. Fycompa™ oral tablets were FDA approved in 2012 for the same indications.
- **SABRIL REMS,** a modified Risk Evaluations and Mitigation Strategy (REMS) program for **Sabril® (vigabatrin)**, was approved by the FDA in June 2016 and went into effect in July 2016. Streamlining of the REMS program is not due to any change in the risk of Sabril®-induced permanent vision loss. The SABRIL REMS program, formerly known as SHARE, has been changed after the FDA determined that some of the program's requirements are no longer necessary to ensure that the benefits of Sabril® outweigh the risks. The modified REMS program will alleviate some of the burden associated with prescribing Sabril®, as physicians will have fewer forms to submit (previously, five forms were required; now, only two forms are required).
- **Carnexiv™ (carbamazepine) injection for IV use** was approved by the FDA in October 2016 and is indicated as replacement therapy for oral carbamazepine formulations, when oral administration is temporarily not feasible, in adult patients with partial seizures with complex symptomatology, generalized tonic-clonic seizures, or mixed seizure patterns. Carbamazepine treatment should generally be initiated with an oral carbamazepine formulation. Carbamazepine is also available generically as various oral formulations, including suspension, chewable tablets, tablets, extended-release (ER) tablets, and ER capsules.

Recommendations

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.

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[1] Briviact® Prescribing Information. UCB, Inc. Available online at: https://www.briviact.com/briviact-PI.pdf?v=1479316368. Last revised 03/2016. Last accessed 02/09/2017.
[2] Briviact® Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/briviact-1/. Last revised 04/25/2016. Last accessed 02/09/2017.
[3] PR Newswire: Eisai Announces FDA Approval of Fycompa™ (perampanel) Oral Suspension for Adjunctive Therapy in the Treatment of Partial-Onset Seizures and Primary Generalized Tonic-Clonic Seizures. Available online at: http://www.prnewswire.com/news-releases/eisai-announces-fda-approval-of-fycompa-perampanel-oral-suspension-for-adjunctive-therapy-in-the-treatment-of-partial-onset-seizures-and-primary-generalized-tonic-clonic-seizures-300260456.html. Issued 05/02/2016. Last accessed 2/09/2017.
[4] Fycompa™ Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/fycompa/. Last revised 04/30/2016. Last accessed 02/09/2017.
[5] Lundbeck Press Release: U.S. FDA Approves Changes to the Sabril® (vigabatrin) REMS Program. Available online at: https://www.lundbeck.com/upload/us/files/pdf/2016_Releases/LundbeckUS.com_Sabril%20REMS%20Press%20Release_6.23.16.pdf. Issued 06/23/2016. Last accessed 02/09/2017.
[6] Carnexiv™ Prescribing Information. Lundbeck. Available online at: http://www.lundbeck.com/upload/us/files/pdf/Products/Carnexiv_PI_US_EN.pdf. Last revised 10/2016. Last accessed 02/09/2017.
[7] Carnexiv™ Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/carnexiv/. Last revised 10/20/2016. Last accessed 02/09/2017.
[8] Micromedex 2.0: Carbamazepine Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/. Last revised 02/07/2017. Last accessed 02/09/2017.

Appendix I

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

Oklahoma Health Care Authority
March 2017

Spinal Muscular Atrophy[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. Its inheritance pattern is autosomal recessive, resulting from deletions/mutations involving the survival motor neuron gene 1 (*SMN1*). 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. 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. 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. 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. Type IV SMA occurs in adulthood, usually after age 30. 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. In December 2016, the U.S. Food and Drug Administration (FDA) approved Spinraza™ (nusinersen) for the treatment of SMA. It is the first drug approved to treat SMA. The FDA granted the application fast track designation and priority review.

Market News and Updates[9,10,11,12,13,14,15]

Anticipated Patent Expiration(s):

- Spinraza™ (nusinersen): November 2030

Pipeline Update(s):

- **January 2016:** Cytokinetics, Inc. announced that its first Phase 2 clinical trial of CK-2127107, a novel fast skeletal muscle troponin activator, in patients with SMA has opened its enrollment. The trial is designed to assess the effect of CK-2127107 on multiple measures of muscle function in both ambulatory and non-ambulatory patients with SMA.
- **May 2016:** Roche announced feedback from the European Medicines Agency (EMA) and the FDA regarding the development of olesoxime, a neuroprotectant, for the treatment of SMA. The scientific advice received from both agencies concluded that current clinical evidence was not sufficient to conclusively determine the benefit/risk profile of olesoxime for treatment of SMA, and both health authorities have requested additional efficacy evidence for olesoxime by means of an additional study. In response, Roche announced it will be conducting a Phase 3 trial in patients with Type II and Type III SMA. Filing for olesoxime is now anticipated for 2020.
- **June 2016:** Novartis paused enrollment in the Phase 2 clinical study of their *SMN2* splice-modifying drug, LMI070, for treatment of Type I SMA due to animal safety studies showing unexpected injuries to the peripheral nerves, spinal cord, and blood vessels in the kidneys.
- **July 2016:** AveXis, Inc. announced that the FDA granted Breakthrough Therapy Designation for the company's gene therapy, AVXS-101, for the treatment of Type I SMA in pediatric patients. In October 2016, AveXis, Inc. presented interim data from the ongoing Phase 1 trial of AVXS-101. The interim data showed a favorable safety profile, extended event-free survival, increases in motor function, and achievement of developmental milestones in patients that received a one-time infusion.
- **January 2017:** The FDA granted orphan drug designation to PTC Therapeutics' RG7916 for the treatment of SMA. RG7916, a *SMN2* splice-modifying drug, is currently under investigation in two clinical studies: SUNFISH, a trial in Type II and III SMA patients, and FIREFISH, a trial in Type I SMA patients.

Spinraza™ (Nusinersen) Product Summary[16,17,18]

Indications: Spinraza™ (nusinersen) is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

Dosing:

- Spinraza™ is supplied as a 12mg/5mL preservative-free solution in a single-dose glass vial.
- Nusinersen is administered intrathecally.
- 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.
- A platelet count, coagulation laboratory testing, and quantitative spot urine protein testing should be obtained at baseline and prior to each dose.

Mechanism of Action: Nusinersen is an antisense oligonucleotide (ASO) designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using in vitro assays and studies in transgenic animal models of SMA, nusinersen was shown to increase exon 7 inclusion in *SMN2* messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein.

Contraindications: None.

Warnings and Precautions:

- Thrombocytopenia and Coagulation Abnormalities: Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some antisense oligonucleotides. Because of the risk of thrombocytopenia and coagulation abnormalities from nusinersen, patients may be at increased risk of bleeding complications. A platelet count and coagulation laboratory testing should be performed at baseline, prior to each administration of nusinersen, and as clinically needed.
- Renal Toxicity: Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Nusinersen is present and excreted by the kidney. Quantitative spot urine protein testing (preferably using a first morning urine specimen) should be conducted at baseline and prior to each dose of nusinersen. Repeat testing and further evaluation should be considered for urinary protein concentrations greater than 0.2g/L.

Adverse Reactions: The most common adverse reactions associated with nusinersen treatment that occurred in at least 20% of nusinersen-treated patients and occurred at least 5% more frequently than control patients were lower respiratory infection, upper respiratory infection, and constipation.

Use in Special Populations:

- Pregnancy: There are no adequate data on the developmental risk associated with the use of nusinersen in pregnant women. In animal studies in which nusinersen was administered by subcutaneous injection to mice and rabbits during pregnancy, no adverse effects on embryofetal development were observed.
- Lactation: There are no data on the presence of nusinersen in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for nusinersen and any potential adverse effects on the breastfed infant from nusinersen or from the underlying maternal condition.
- Pediatric Use: The safety and effectiveness of nusinersen in pediatric patients from newborn to 17 years of age have been established.
- Geriatric Use: SMA is largely a disease of children and young adults; therefore, there is no geriatric experience with nusinersen.

Efficacy: The efficacy of nusinersen was demonstrated in a double-blind, sham-procedure controlled clinical trial in symptomatic infantile-onset SMA patients and was supported by open-label clinical trials conducted in presymptomatic and symptomatic SMA patients.

- Infantile-Onset SMA: This study was a multicenter, randomized, double-blind, sham-procedure controlled study in 121 symptomatic infants ≤ 7 months of age at the time of first dose, who had been diagnosed with SMA (symptom onset before 6 months of age). Subjects were randomized 2:1 to receive either nusinersen or a sham injection. A planned interim efficacy analysis was conducted based on patients who died, withdrew, or completed at least 183 days of treatment. Age at first treatment ranged from 30 to 262 days (median age 181 days). Baseline demographics were balanced between the nusinersen and control groups with the exception of age at first treatment (median age 175 days vs. 206 days, respectively). The median disease duration was 14 weeks. The primary endpoint assessed at the time of interim analysis was the proportion of responders: subjects with an improvement in motor milestones according to Section 2 of the Hammersmith Infant Neurologic Exam (HINE). This endpoint evaluates seven different areas of motor milestone development, with a maximum score between two to four points for each, depending on the milestone, and a total maximum score of 26. A treatment responder was defined as any patient with at least a 2-point increase (or maximal score of four) in ability to kick (consistent with improvement by at least two milestones), or at least a 1-point increase in the motor milestones of head control, rolling, sitting, crawling, standing, or walking (consistent with improvement by at least one milestone). Patients needed to exhibit improvement in more categories of motor milestones than worsening to be classified as a responder. Of the 82 patients who were eligible for the interim analysis, 21 patients (40%) achieved a motor milestone response in the nusinersen group compared to zero patients (0%) in the sham-control group ($p<0.0001$). Additionally, treatment effects were assessed using the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), which is an evaluation of motor skills in patients with infantile-onset SMA. Of the nusinersen-treated patients, 33 (63%) had at least a 4-point improvement from baseline compared to one (3%) in the sham-control group; two patients (4%) had a worsening of at least 4-points in nusinersen group compared to 12 (40%) in the sham-group.
- Later-onset SMA consistent with Type II SMA: A phase III multicenter, double-blind, randomized, sham-procedure controlled study to assess the efficacy and safety of nusinersen in patients with later-onset SMA consistent with Type II SMA. Subjects were randomized 2:1 to receive either intrathecal nusinersen or a sham injection control, respectively. Inclusion criteria included a diagnosis of SMA; onset of clinical signs and symptoms consistent with SMA at greater than 6 months of age; able to sit independently, but never able to walk independently; and a Motor Function Score (Hammersmith Functional Motor Scale-Expanded [HFMSE]) greater than or equal to 10 and less than or equal to 54 at screening; an estimated life expectancy, in the opinion of the investigator, of greater than two years from screening; and meet age-appropriate institutional criteria for the use of anesthesia and sedation, if use is planned for study procedures. The primary endpoint is change from baseline in HFMSE score (at 15 months). The HFMSE is a validated instrument for measuring motor function in children

with Type II or III SMA and has demonstrated reliability, consistency, and correlation with the full Gross Motor Function Measure. In a pre-planned interim analysis, a significant difference (p=0.0000002) at 5.9 points in HFMSE was observed at 15 months between patients given nusinersen (n=84) compared to sham-procedure control (n=42). Patients receiving nusinersen experienced a mean improvement of 4.0 points in the HFMSE compared to a mean decrease of 1.9 points in the sham-procedure control group. A change of ≥ 3 points in the HFMSE has previously been determined to be clinically important. Results from other endpoints were consistent with a favorable response to nusinersen compared to sham-procedure control. Adverse events were mostly considered to be related to SMA disease, common events found in the general population, or events related to the lumbar puncture procedure. Nusinersen was well tolerated with a favorable safety profile.

- Open-Label Extension: The results of the controlled trial in infantile-onset SMA patients were supported by open-label uncontrolled trials conducted in symptomatic SMA patients who ranged in age from 30 days to 15 years at the time of first dose, and in presymptomatic patients, who ranged in age from 8 days to 42 days at the time of first dose. The patients in these studies had or were likely to develop Type I, II, or III SMA. Some patients achieved milestones such as ability to sit unassisted, stand, or walk when they would otherwise be unexpected to do so, maintained milestones at ages when they would be expected to be lost, and survived to ages unexpected considering the number of *SMN2* gene copies of patients enrolled in the studies.
- The overall findings of the controlled trial in infantile-onset SMA and the open-label uncontrolled trials support the effectiveness of nusinersen across the range of SMA patients, and appear to support early initiation of treatment with nusinersen.

Cost:

Medication	Cost per Dose*	Cost for First Year of Therapy	Cost per Year for Maintenance Dosing
Spinraza™ (nusinersen) 12mg/5mL	**$125,000**	**$750,000**	**$375,000**

*Cost based on Wholesale Acquisition Costs (WAC) and does not reflect rebated price or net cost.

Recommendations

The College of Pharmacy recommends the prior authorization of Spinraza™ (nusinersen) with the following criteria:

Spinraza™ (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
    a. Type I; or
    b. Type II; or
    c. Type III with symptoms; and
2. Molecular genetic testing to confirm biallelic pathogenic variants in the survival motor neuron gene 1 (*SMN1*); and

3. 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
4. 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
5. Spinraza™ must be administered in a healthcare facility by a specialist experienced in performing lumbar punctures; and
6. 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
7. 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
8. Approval quantity will be based on Spinraza™ prescribing information and FDA approved dosing regimen.

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Appendix J

Fiscal Year 2016 Annual Review of Pulmonary Hypertension Medications

Oklahoma Health Care Authority
March 2017

Current Prior Authorization Criteria

Revatio® (Sildenafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist.
3. A quantity limit of 90 tablets per 30 days will apply.

Revatio® (Sildenafil Suspension) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. An age restriction will apply. The oral suspension formulation may be approvable for ages six years and younger. Members seven years and older must have a patient-specific, clinically significant reason why the member is not able to use the oral tablet formulation.
4. A quantity limit of 224mL per 30 days (two bottles) will apply.

Adcirca® (Tadalafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. A patient-specific, clinically significant reason why the member cannot use generic sildenafil oral tablets; and
4. A quantity limit of 60 tablets per 30 days will apply.

Adempas® (Riociguat) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension; and
    a. Members with a diagnosis of pulmonary arterial hypertension 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 chronic thromboembolic pulmonary hypertension (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. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Adempas® REMS program.
5. A quantity limit of 90 tablets per 30 days will apply.

Orenitram® (Treprostinil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist or cardiologist; and
4. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist or cardiologist; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Opsumit® REMS program.
5. A quantity limit of 30 tablets per 30 days will apply.

Uptravi® (Selexipag) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Member must be 18 years of age or older; and
3. Previous failed trials of at least one of each of the following categories (alone or in combination):
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    c. Adempas® (riociguat); and
    d. Orenitram® (treprostinil); and
4. Medical supervision by a pulmonary specialist and/or cardiologist; and
5. A quantity limit of two tablets daily will apply for all strengths with an upper dose limit of 1,600mcg twice daily.

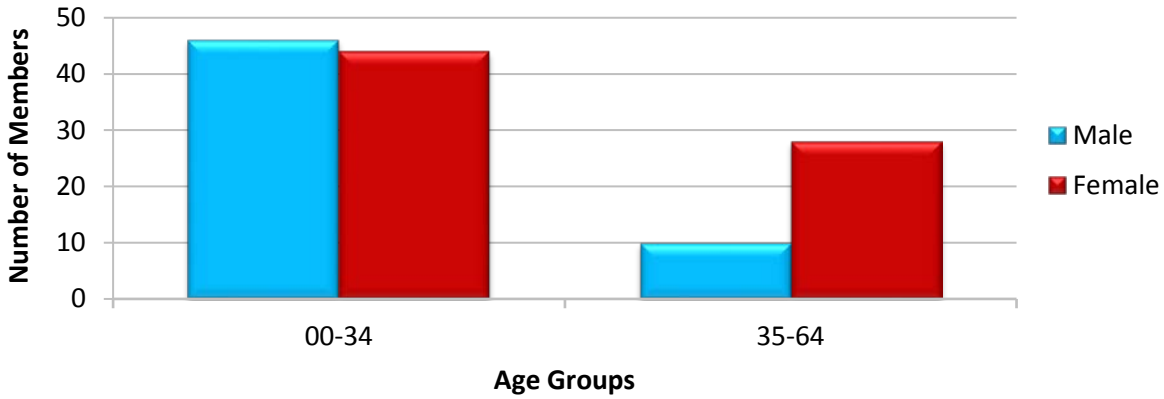
Utilization of Pulmonary Hypertension Medications: Fiscal Year 2016

Comparison of Fiscal Years

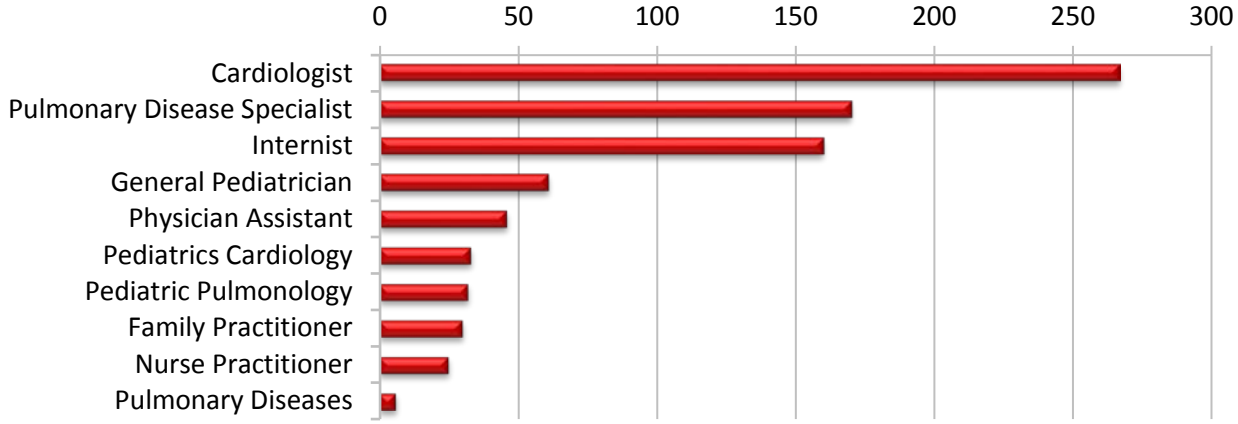
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	122	827	$2,441,564.38	$2,952.31	$97.61	113,627	25,014
2016	128	844	$3,387,475.58	$4,013.60	$132.73	82,269	25,522
% Change	**4.90%**	**2.10%**	**38.70%**	**35.90%**	**36.00%**	**-27.60%**	**2.00%**
Change	**6**	**17**	**$945,911.20**	**$1,061.29**	**$35.12**	**-31,358**	**508**

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

Demographics of Members Utilizing Pulmonary Hypertension Medications



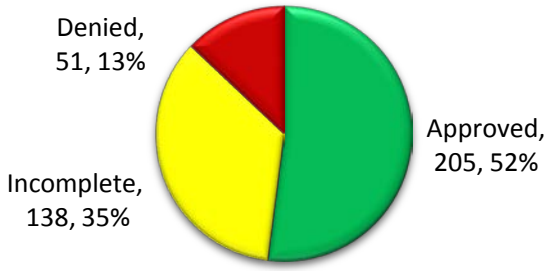
Top Prescriber Specialties of Pulmonary Hypertension Medications by Number of Claims



Prior Authorization of Pulmonary Hypertension Medications

There were 394 prior authorization requests submitted for pulmonary hypertension medications during fiscal year 2016. 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]

Anticipated Patent Expiration(s):

- Adcirca® (tadalafil): November 2020
- Adempas® (riociguat): April 2023
- Letairis® (ambrisentan): December 2027
- Opsumit® (macitentan): April 2029
- Uptravi® (selexipag): August 2030
- Orenitram® (treprostinil): January 2031

News:

- **January 2016:** The 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) were published in the *European Heart Journal*. A few changes compared with the 2009 ESC/ERS PH guideline include new developments on PH severity evaluation and on treatments, including combination therapy and two new recently approved drugs, Opsumit® (macitentan) and Adempas® (riociguat).
- **October 2016:** The U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) stating it could not approve United Therapeutics' New Drug Application (NDA) to allow the use of Remodulin® (treprostinil) with the Implantable System for Remodulin®, RemoSynch®, prior to the approval of the premarket approval application (PMA) for the implantable delivery device. The FDA rejected Medtronic's implantable device to deliver Remodulin® in March 2016. Medtronic has since submitted additional information to supplement its PMA to the FDA to address the issues raised in the FDA's rejection letter. United Therapeutics, the makers of Remodulin®, is working with Medtronic, Inc. to develop Medtronic's proprietary intravascular infusion catheter to be used with its SynchroMed® II implantable infusion pump and related infusion system components (together referred to as the Implantable System for Remodulin® or RemoSynch®) in order to deliver Remodulin® for the treatment of pulmonary arterial hypertension (PAH). United Therapeutics plans to resubmit the Remodulin® NDA for 60 day review in early 2017 or receive approval at the time the Medtronic PMA for RemoSynch® is approved.
- **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. Opsumit® (macitentan), an oral endothelin receptor antagonist FDA approved for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression, was among those medications listed for the potential serious risk of hepatic and hepatobiliary disorders. Tracleer® (bosentan), an oral endothelin receptor antagonist FDA approved for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to improve exercise ability and to decrease clinical worsening, was also on the list for serious potential risk of anaphylaxis and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Opsumit® and Tracleer® prescribing labels were updated to reflect the new warnings. 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.

- **November 2016:** The MERIT (Macitentan in thE tReatment of Inoperable chronic Thromboembolic pulmonary hypertension) study to assess the efficacy and safety of Opsumit® (macitentan) in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH; Pulmonary hypertension group 4) met its primary endpoint. In MERIT, 80 inoperable CTEPH patients were randomized 1:1 to receive either macitentan 10mg once daily or placebo over a 24 week treatment period. After 16 weeks the treatment effect was a significant 16% reduction in pulmonary vascular resistance (PVR) with macitentan compared with placebo [95% CI: -30%, -1%; p=0.04 intention-to-treat (ITT)]. The efficacy observed was consistent across all sub-groups, including patients receiving background PH specific therapy at baseline (61%), which included phosphodiesterase-5 enzyme (PDE-5) inhibitors (59%). Mean PVR did decrease from baseline in both macitentan and placebo groups. The study also showed a significant positive effect of macitentan compared to placebo on exercise capacity. After 24 weeks of treatment, the mean change in 6-minute walk distance (6-MWD) from baseline was an increase of 35 meters with macitentan and one meter with placebo.
- **January 2017:** Eiger BioPharmaceuticals, Inc. announced that the first patient has completed 24 weeks dosing in the double-blind Phase 2 LIBERTY study and has now received treatment with ubenimex in the open-label extension. After completing the blinded treatment period, each patient may be eligible to enroll in an open-label extension to receive ubenimex for at least 24 weeks. Ubenimex is a well-characterized, oral, small-molecule inhibitor of leukotriene A_4 hydrolase (LTA_4H), which blocks the production of leukotriene B_4 (LTB_4), an inflammatory mediator implicated in the pathogenesis of PAH. Ubenimex is approved in Japan (brand name Bestatin™) as an adjunct to chemotherapy agents to extend survival and to maintain remission after treatment for acute non-lymphocytic leukemia in adults. Ubenimex has been used for over 25 years in Japan. Ubenimex has been granted Orphan Drug Designation for treatment of PAH by the FDA and European Medicines Agency (EMA). Ubenimex is not currently approved for any indication in the U.S. or Europe.
- **January 2017:** The MAESTRO (MAcitentan in Eisenmenger Syndrome To RestOre exercise capacity) study to assess the efficacy and safety of Opsumit® (macitentan) in patients with PAH due to Eisenmenger Syndrome did not meet its primary objective of exercise capacity as measured in the 6-MWD. In MAESTRO, 226 patients were randomized in a 1:1 ratio to receive either 10mg macitentan or placebo once daily over a 16-week treatment period. After 16 weeks of treatment, the mean change in 6-MWD from baseline was an increase of 18.3 meters in the macitentan group and 19.7 meters in the placebo group. Eisenmenger Syndrome is a congenital heart defect that causes a shunt to develop between two chambers of the heart, so an increased blood flow returns to the lungs. The blood vessels in the lung arteries become stiff and narrow, resulting in PH. Eisenmenger Syndrome occurs when the pressure in the pulmonary circulation becomes so great that the direction of blood flow through the shunt

reverses. It is associated with the development of chronic cyanosis and limited exercise capacity.

- **January 2017:** The FDA approved new information to be added to the Adempas® (riociguat) drug label pertaining to PH associated with idiopathic interstitial pneumonias (PH-IIP) and updated information regarding use of PDE-5 inhibitors. Riociguat is contraindicated in patients with PH-IIP. Preliminary data from RISE-IIP showed a higher number of deaths (17 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. Further, there appeared to be no clinically significant benefit for those who took the drug. The *Contraindications*, *Drug Interactions*, and *Dose and Administration* sections were updated regarding the use of PDE-5 inhibitors stating riociguat should not be administered within 24 hours of sildenafil or 24 hours before or within 48 hours after tadalafil. Riociguat should be discontinued at least 24 hours prior to administering a PDE-5 inhibitor. In the PATENT PLUS LTE study, long-term therapy with riociguat in combination with sildenafil was associated with high rates of discontinuation due to hypotension, serious adverse effects, and deaths. Therefore, there were potentially unfavorable safety signals with sildenafil plus riociguat and no evidence of a positive benefit/risk ratio. Consequently, concomitant use of riociguat with PDE-5 inhibitors is contraindicated.
- **February 2017:** The EMA is reviewing the safety of Uptravi® (selexipag), an oral prostacyclin receptor agonist, following five patient deaths in France. Based on a preliminary review of available data, the EMA advises that selexipag may continue to be used, both in existing and new patients, but use must be in line with the current prescribing information. EMA's Pharmacovigilance Risk Assessment Committee (PRAC) will further explore all available data and once the review is completed, final conclusions will be published.

Recommendations

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

Adempas® (Riociguat) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension; and
    a. Members with a diagnosis of pulmonary arterial hypertension 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 chronic thromboembolic pulmonary hypertension (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.

Utilization Details of Pulmonary Hypertension Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
PHOSPHODIESTERASE-5 (PDE-5) INHIBITOR						
SILDENAFIL TAB 20MG	355	72	$17,660.56	$1.70	$49.75	0.52%
ADCIRCA TAB 20MG	123	22	$199,879.29	$52.05	$1,625.03	5.90%
REVATIO SUS 10MG/ML	118	34	$845,485.21	$208.09	$7,165.13	24.96%
SUBTOTAL	**596**	**128**	**$1,063,025.06**	**$58.08**	**$1,783.60**	**31.38%**
SOLUABLE GUANYLATE CYCLASE (sGC) STIMULATOR						
ADEMPAS TAB 0.5MG	3	2	$25,944.31	$288.27	$8,648.10	0.77%
ADEMPAS TAB 1MG	3	3	$19,887.25	$288.22	$6,629.08	0.59%
ADEMPAS TAB 2MG	3	1	$16,199.84	$305.66	$5,399.95	0.48%
ADEMPAS TAB 1.5MG	2	1	$8,654.26	$288.48	$4,327.13	0.26%
SUBTOTAL	**11**	**7**	**$70,685.66**	**$292.09**	**$6,425.97**	**2.10%**
ENDOTHELIN RECEPTOR ANTAGONISTS (ERA)						
TRACLEER TAB 62.5MG	43	8	$82,858.02	$65.24	$1,926.93	2.45%
LETAIRIS TAB 10MG	31	5	$253,880.17	$275.06	$8,189.68	7.49%
OPSUMIT TAB 10MG	29	6	$228,048.33	$262.12	$7,863.74	6.73%
LETAIRIS TAB 5MG	13	4	$97,745.00	$261.35	$7,518.85	2.89%
TRACLEER TAB 125MG	13	3	$119,359.45	$306.05	$9,181.50	3.52%
SUBTOTAL	**129**	**26**	**$781,890.97**	**$204.31**	**$6,061.17**	**23.08%**
PROSTACYCLIN VASODILATORS						
TYVASO REFIL SOL	30	4	$434,600.43	$517.38	$14,486.68	12.83%
REMODULIN INJ	20	3	$551,166.10	$918.61	$27,558.31	16.27%
REMODULIN INJ	13	3	$171,483.06	$439.70	$13,191.00	5.06%
FLOLAN INJ 1.5MG	12	1	$101,727.72	$280.24	$8,477.31	3.00%
ORENITRAM TAB	11	1	$18,065.74	$60.22	$1,642.34	0.53%
ORENITRAM TAB 1MG	11	2	$42,868.80	$129.91	$3,897.16	1.27%
REMODULIN INJ	4	1	$58,189.99	$484.92	$14,547.50	1.72%
VELETRI INJ 1.5MG	3	1	$4,170.54	$46.34	$1,390.18	0.12%
VENTAVIS SOL	1	1	$20,338.27	$677.94	$20,338.27	0.60%
ORENITRAM TAB	1	1	$1,702.44	$56.75	$1,702.44	0.05%
ORENITRAM TAB 2.5MG	1	1	$51,479.60	$1,715.99	$51,479.60	1.52%
TYVASO START SOL	1	1	$16,081.20	$574.33	$16,081.20	0.47%
SUBTOTAL	**108**	**20**	**$1,471,873.89**	**$467.11**	**$13,628.46**	**43.44%**
TOTAL	**844**	**128***	**$3,387,475.58**	**$132.73**	**$4,013.60**	**100.00%**

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

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Appendix K

Fiscal Year 2016 Annual Review of Multiple Sclerosis Medications and 30-day Notice to Prior Authorize Zinbryta™ (Daclizumab)

Oklahoma Health Care Authority
March 2017

Current Prior Authorization Criteria

Multiple Sclerosis Interferon Medications Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Authorization of Tier-2 medications requires previous failure of the preferred Tier-1 product defined as:
   a. Occurrence of an exacerbation after six months; or
   b. Significant increase in MRI lesions after six months; or
   c. Adverse reactions or intolerable side effects; and
3. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
4. Compliance will be checked for continued approval every six months.

Multiple Sclerosis Interferon Medications*	
Tier-1	**Tier-2**
Interferon β - 1a (Avonex®)	Interferon β - 1a (Rebif®)
Interferon β - 1b (Betaseron®)	Interferon β - 1a (Plegridy®)
	Interferon β - 1b (Extavia®)

*Tier structure based on supplemental rebate participation.

Ampyra® (Dalfampridine) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis; and
2. Kurtzke Expanded Disability Status Scale (EDSS) score between 3 and 7.5; and
3. Initial approvals will be for the duration of 90 days. If the member has responded well to treatment and the prescriber states that the member has shown improvement or the drug was effective, the member may receive authorization for one year; and
4. A quantity limit of 60 tablets for 30 days will apply.
5. Ampyra® may be used with other Multiple Sclerosis therapies.

Aubagio® (Teriflunomide) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. All of the following will be required for initiation of treatment:
   a. Verification that female members are not pregnant and currently using reliable contraception; and
   b. Verification that member has no active infection(s); and

c. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
d. Liver function tests and verification that levels are acceptable to the prescriber; and
e. Blood pressure measurement and verification that blood pressure is being monitored; and
f. Verification that member does not have tuberculosis, or completion of standard medical treatment for patients with tuberculosis; and

4. Initial approvals of Aubagio® will be for six months, after which time, all of the following will be required for further approval:
   a. Medication compliance; and
   b. Repeat CBC counts and verification that counts are acceptable to the prescriber; and
   c. Repeat liver function tests and verification that levels are acceptable to the prescriber; and
   d. Verification that female members are not pregnant and will continue using reliable contraception; and
   e. Verification that blood pressure and symptoms of renal failure are being monitored; and
5. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 30 tablets per 30 days will apply.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
4. Compliance will be checked for continued approval every six months.

Gilenya® (Fingolimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis with at least one relapse in the previous 12 months, or transitioning from existing Multiple Sclerosis 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. Compliance will be checked for continued approval every six months.

Lemtrada® (Alemtuzumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Member must have had an inadequate response to two or more medications indicated for the treatment of Multiple Sclerosis; and
3. Lemtrada® must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for two hours after each infusion; and

4. The prescriber must agree to monitor complete blood counts (CBC) with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose of Lemtrada®; and
5. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada® therapy; and
6. Member, prescriber, pharmacy, and healthcare facility must all enroll in the Lemtrada® REMS Program and maintain enrollment throughout therapy.

Tecfidera® (Dimethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; 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. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 60 tablets per 30 days will apply.

Tysabri® (Natalizumab) Approval Criteria:

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

Utilization of Multiple Sclerosis Medications: Fiscal Year 2016

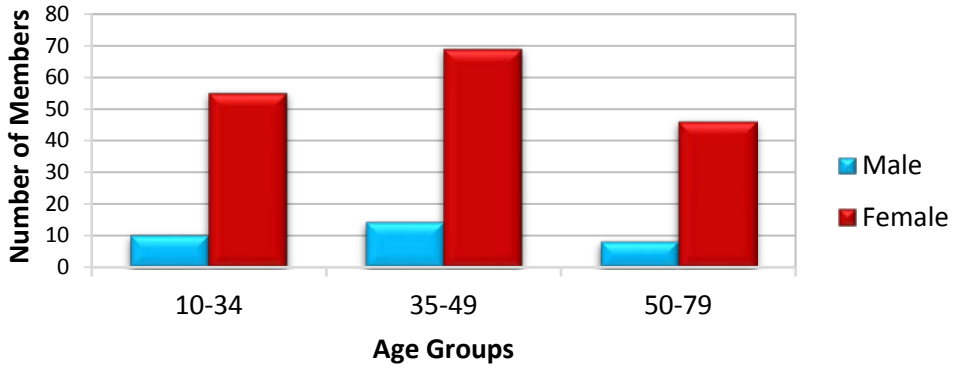
Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	216	1,599	$7,986,737.17	$4,994.83	$173.70	42,380	45,979
2016	202	1,533	$8,608,234.85	$5,615.29	$193.26	43,900	44,543
% Change	**-6.50%**	**-4.10%**	**7.80%**	**12.40%**	**11.30%**	**3.60%**	**-3.10%**
Change	**-14**	**-66**	**$621,497.68**	**$620.46**	**$19.56**	**1,520**	**-1,436**

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

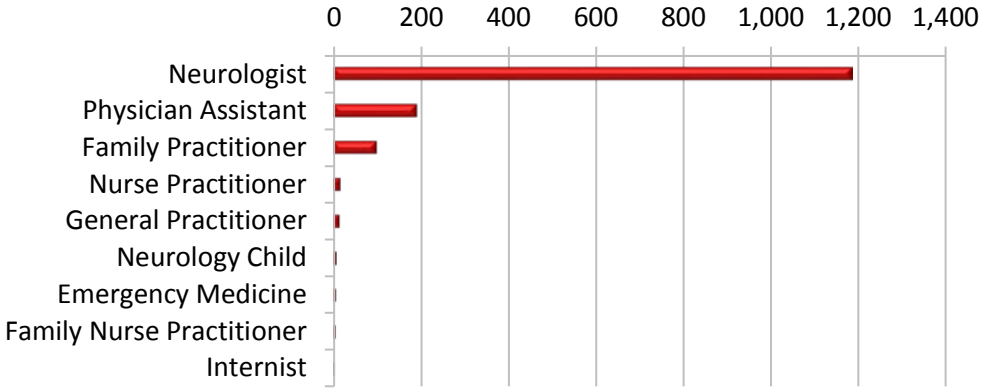
- Medical claim details for Multiple Sclerosis medications during fiscal year 2016 can be found at the end of this report.

Demographics of Members Utilizing Multiple Sclerosis Medications



All members under the age of 21 years were verified to have a diagnosis of Multiple Sclerosis (MS) in their diagnosis history, and their MS therapies were prescribed by a specialist in neurology.

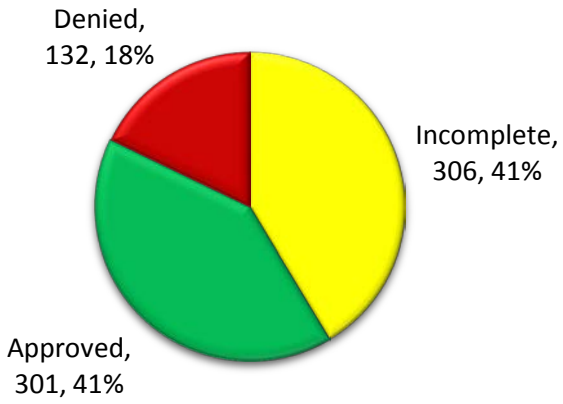
Top Prescriber Specialties of Multiple Sclerosis Medications by Number of Claims



Prior Authorization of Multiple Sclerosis Medications

There were 739 prior authorization requests submitted for 220 unique members for Multiple Sclerosis medications during fiscal year 2016. 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]

Anticipated and Recent Patent Expiration(s):

- Copaxone® (glatiramer acetate): There are no unexpired patents for the 20mg/mL strength; however, the 40mg/mL strength is patented until August 2030.
- Ampyra® (dalfampridine): May 2027
- Gilenya® (fingolimod): June 2027
- Tecfidera® (dimethyl fumarate): February 2028
- Aubagio® (teriflunomide): February 2034

Generic Formulation Update(s):

- **January 2017:** The U.S. Food and Drug Administration (FDA) approved Aurobindo Pharma's dalfampridine extended-release 10mg tablets for the treatment of MS. The FDA's Division of Bioequivalence determined the medication to be bioequivalent, and therefore therapeutically equivalent to the referenced listed drug, Ampyra®.

Safety Update(s):

- **February 2016:** The FDA approved an update to the Contraindications section and to the Warnings and Precautions section of the product labeling for Gilenya® (fingolimod). 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. Gilenya® 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. A complete blood count (CBC) should be obtained before initiating treatment with fingolimod and patients should be monitored for infection during treatment and for two months after discontinuation. Patients should not be started on fingolimod with an active infection. Cases of Kaposi's sarcoma have been reported in the postmarketing setting. Kaposi's sarcoma is an angioproliferative disorder that is associated with infection with human herpes virus 8. Patients with signs or symptoms consistent with Kaposi's sarcoma should be referred for prompt diagnostic evaluation and management. Cases of PML have occurred in patients who received fingolimod in the postmarketing setting. Fingolimod should be withheld at the first sign or symptom suggestive of PML. Cases of liver injury with hepatocellular and/or cholestatic hepatitis have also been reported with fingolimod in the postmarketing setting. Liver enzyme results should be obtained before initiation. Patients with severe hepatic impairment should be closely monitored and fingolimod should be discontinued if significant liver injury occurs. Basal cell carcinoma is associated with the use of fingolimod. Providers and patients are advised to monitor for suspicious skin lesions and if a suspicious skin lesion is observed, it should be promptly evaluated.
- **February 2016:** The FDA approved an update to the Warnings and Precautions section of the product labeling for Tecfidera® (dimethyl fumarate). PML has occurred in patients treated with dimethyl fumarate. A fatal case of PML occurred in a patient while

enrolled in a clinical trial. PML has also occurred in the postmarketing setting in the presence of lymphopenia persisting for more than six months. Dimethyl fumarate should be withheld at the first sign or symptom suggestive of PML and appropriate diagnostic evaluation should be performed.

- **May 2016:** According to a study published in the May 2016 online issue of *Neurology,* mitoxantrone may be associated with an increased risk of colorectal cancer. Mitoxantrone is used for aggressive types of relapsing-remitting or progressive MS that do not respond to other MS drugs, but its use is limited as previous studies have shown an increased risk of leukemia and heart damage. It was first developed as a chemotherapy drug for certain cancers. The study author noted that the study was relatively small and needs to be confirmed. He stated if the results are confirmed a colonoscopy should be given after treatment with mitoxantrone to screen for colorectal cancer, which can be treated more effectively if diagnosed early. Mitoxantrone is administered as an intravenous (IV) infusion.
- **October 2016:** The FDA is evaluating the need for regulatory action regarding the risk of drug-induced lupus with the use of β-interferons, based on reports of adverse events collected by the FDA Adverse Event Reporting System (FAERS) in the second quarter of 2016.
- **November 2016:** The prescribing information for Aubagio® (teriflunomide) was updated in June 2016 and again in November 2016. Additional information was added to the Warnings and Precautions section and to the Postmarketing Experience section regarding cases of thrombocytopenia that have been reported with teriflunomide in the postmarketing setting. A new Warnings and Precautions subsection was added and the Postmarketing Experience section was updated to include information regarding the risk of hypersensitivity and serious skin reactions (including toxic epidermal necrolysis and Stevens-Johnson syndrome). Additional information was also added to the Warnings and Precautions section (including a Boxed Warning) regarding the risk of teratogenicity and clarification in the Dosage and Administration section to exclude pregnancy prior to initiation. The Postmarketing Experience section was also updated to include reports of interstitial lung disease and pancreatitis. The Medication Guide has been updated to reflect these additions.
- **November 2016:** The FDA removed the Risk Evaluation and Mitigation Strategy (REMS) assessment for Gilenya® (fingolimod), which was initially approved in September 2010, after determining that the required communication plan was no longer necessary to ensure the benefits of the drug outweigh the risks.
- **January 2017:** The prescribing information for Tecfidera® (dimethyl fumarate) was updated to include a warning of potential liver injury that could require hospitalization. The new information notes that clinically significant cases of liver injury have been reported in patients treated with the drug in the postmarketing setting. The onset has ranged from a few days to several months after initiation of treatment. The signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal (ULN) and elevation of total bilirubin to greater than 2-fold the ULN, have been observed. These abnormalities resolved upon treatment

discontinuation. Some cases required hospitalization. The prescribing information states that the combination of new serum aminotransferase elevations with increased levels of bilirubin caused by drug-induced hepatocellular injury is an important predictor of serious liver injury that may lead to acute liver failure, liver transplant, or death in some patients. It recommends obtaining serum aminotransferase, alkaline phosphatase, and total bilirubin levels before treatment with dimethyl fumarate and during treatment, as clinically indicated, and that the drug be discontinued if clinically significant liver injury is suspected.

New FDA Approval(s):

- **May 2016:** The FDA approved Zinbryta™ (daclizumab) for the treatment of adults with relapsing forms of MS. It is a long-acting injection that is self-administered by the patient once a month.

Pipeline Update(s):

- **March 2016:** MediciNova, Inc. has announced that the experimental oral therapy MN-166 (ibudilast) has been designated by the FDA as a "Fast Track Product" for the possible treatment of progressive MS, including secondary progressive and primary progressive MS. Investigators are conducting a Phase 2 clinical trial of ibudilast in patients with progressive forms of MS and results are expected in 2017. Ibudilast did not reduce relapses or MRI-observed new lesions in a previous Phase 2 trial involving patients with relapsing MS. However, there is evidence that this agent could protect the nervous system from damage and is therefore undergoing further testing in patients with progressive forms of MS.
- **April 2016:** Clemastine fumarate, an antihistamine, partially reversed damage to the visual system in patients with MS in a preliminary study presented at the American Academy of Neurology (AAN) Annual Meeting. During the study, delays were reduced by an average of slightly less than two milliseconds in each eye per patient among those who received clemastine. The investigator cautioned that more research is needed with larger numbers of patients before physicians can recommend clemastine for patients with MS.
- **April 2016:** MedDay announced the results from the MS-SPI and MS-ON Phase 2b/3 trials of its therapeutic candidate, MD1003, in patients with MS. The trials included patients with "not active" progressive MS and those with either relapsing or progressive MS and visual loss, respectively. The data was presented at the AAN Annual Meeting and showed that MD1003 demonstrated better efficacy in reversing disease progression than a drug has previously achieved in "not active" progressive MS. MD1003 is a pharmaceutical formulation of high-dose biotin. It is already commercially available in certain European countries under early access programs. The studies also demonstrated good safety and tolerability data for MD1003.
- **June 2016:** Biogen reported the results from the Phase 2 SYNERGY study of opicinumab, an investigational, fully human monoclonal antibody being developed as a potential neuroreparative therapy in patients with relapsing forms of MS. Opicinumab missed the primary endpoint of the study, a multicomponent measure evaluating improvement of

physical function, cognitive decline, and disability. Opicinumab also did not meet the secondary efficacy endpoint in SYNERGY, which evaluated the slowing of disability progression. However, evidence of a clinical effect with a complex, unexpected dose-response was observed.

- **June 2016:** Genmab, working in collaboration with its partner Novartis, announced plans to begin a Phase 3 trial assessing the subcutaneous formulation of ofatumumab for relapsing MS. The trial will evaluate the efficacy and safety of ofatumumab compared to teriflunomide. A Phase 2 trial has been completed, and top-line results showed significant reduction in the cumulative number of new brain lesions.
- **August 2016:** Novartis announced the Phase 3 EXPAND study, evaluating the efficacy and safety of oral, once-daily, BAF312 (siponimod) in secondary progressive multiple sclerosis (SPMS), met its primary endpoint of a reduction in the risk of disability progression, compared with placebo. The EXPAND study represents the largest randomized, controlled study in SPMS to date.
- **September 2016:** Celgene International announced results from the 96-week blinded extension period of the RADIANCE Phase 2 trial of ozanimod, an investigational, oral, sphingosine-1-phosphate (S1P) receptor modulator, in patients with relapsing forms of MS. RADIANCE met its primary efficacy endpoint – reduction in the cumulative number of total gadolinium-enhancing (GdE) lesions, as determined by MRI, from week 12 to week 24. Ozanimod is in Phase 3 development for ulcerative colitis (UC) and MS. The company, Celgene, stated that the ongoing MS trials should have data to report in 2017, while data on UC trials could be released in 2018. The approval for treatment of MS could occur as early as 2018.
- **September 2016:** Laquinimod, an oral small molecule being developed by Teva Pharmaceuticals to treat MS and Huntington's Disease, is being evaluated for safety, efficacy, and tolerability in the CONCERTO study. In January 2016, the Data Monitoring Committee (DMC) supervising the trial recommended the use of higher doses be discontinued immediately after cardiovascular events were reported in eight patients. In September 2016, Active Biotech reported that the FDA had rescinded the special protocol assessment given to the study because the dose change was made without prior FDA approval. Teva plans to use the data from the CONCERTO trial to support the filing of a new marketing approval application in the U.S. and Europe.
- **September 2016:** Findings from a three-arm, Phase 3 trial of arbaclofen extended-release (ER) were presented at the Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). New research suggests that arbaclofen ER tablets can decrease spasticity related to MS with a better safety profile than baclofen. The Phase 3 trial included more than 300 patients with MS and those who received arbaclofen ER 20mg twice daily had significantly less spasticity after twelve weeks of treatment than those who received matching placebo, and had similar spasticity reductions as those who received baclofen 20mg four times a day. The arbaclofen ER group had significantly less drowsiness and dizziness than the baclofen group. The data have been presented to the FDA.
- **October 2016:** The latest data from the cladribine trials were presented at the Congress of the ECTRIMS 2016 meeting. The drug was rejected by the FDA and the European

Medicines Agency (EMA) in 2011. The agencies cited concerns about a signal of cancer risk in the initial results of the phase 3 CLARITY trial. Merck Serono has decided to try for a second time to gain approval with longer-term follow-up of clinical trials showing durable efficacy, without the safety signal that led to its initial rejection. The company has now filed a new approval application for cladribine with the EMA and is in discussions on how to proceed with the FDA. The drug is already approved for the treatment of hairy cell leukemia in the U.S.

- **December 2016:** The FDA has extended the Prescription Drug User Fee Act (PDUFA) date for its review of the biologics license application for Ocrevus™ (ocrelizumab) to March 2017. The extension is not related to the drug's efficacy or safety, but is the result of the submission of additional data by Roche regarding the commercial manufacturing process of ocrelizumab. Ocrelizumab is an investigational, humanized monoclonal antibody designed to selectively target CD20-positive B cells. Ocrelizumab showed superiority to interferon beta-1a in two Phase 3 studies in patients with relapsing forms of MS. Ocrelizumab also showed efficacy in patients with primary progressive MS. Roche states that ocrelizumab is the first investigational medicine to show such positive results in patients with both primary progressive and relapsing forms of MS.

Other News:

- **June 2016:** Data from the initial and extension phase of the CARE-MS II trial was reported at the Consortium of Multiple Sclerosis Centers (CMSC) Annual Meeting. In an analysis of the data, Lemtrada® (alemtuzumab) appeared to stabilize or improve disability in MS over five years. The mean change in the Kurtzke Expanded Disability Status Scale (EDSS) score over that time was +0.06. Most of the patients (60%) only received the standard two courses of alemtuzumab and did not require additional infusions. A third of patients achieved 12-month confirmed disability improvement (CDI), defined as at least a one-point decrease in EDSS scores, along with 43% who had a six-month CDI and 48% who had a three-month CDI. The rates of adverse events at five years looked similar to those seen at the end of the randomized controlled portion of the trial. Infections were common and remained so during the extension.
- **September 2016:** New guidelines for the treatment of MS are being reviewed in the U.S. and in Europe. A draft copy of the proposed new U.S. guidelines was made available on the AAN website for review and comment. The new European guidelines were the subject of a late-breaking news session at the Congress of the ECTRIMS 2016 meeting. Both sets of draft guidelines have been described by some MS experts as rather conservative. The U.S. document notes that the last AAN guidelines on the treatment of MS were issued in 2002 and only included β-interferon and glatiramer acetate. It points out that the treatment options for MS have changed considerably in the last 14 years, with more than 16 medications currently approved and widely prescribed for the treatment of MS in the U.S., with other agents nearing approval. The new AAN draft guidelines review evidence from published studies on all disease-modifying treatments

used in MS, and presents this in terms of effect on relapses, MRI lesions, disability, and adverse event related discontinuations for each individual drug.

- **October 2016:** Lemtrada® (alemtuzumab) is usually reserved for patients in the late stages of MS; however, in a study published online in *Neurology* alemtuzumab appears to offer long-term remission in newly diagnosed patients. In the study, 628 patients with relapsing-remitting MS who had not responded to at least one other MS drug were treated with either alemtuzumab 12mg or interferon β-1a. The researchers assessed disability levels at the start of the study and every three months for two years. Nearly 28% of patients treated with alemtuzumab had improved by at least one point on a 10-point disability test by the study's end, compared to about 15% of those receiving interferon β-1a. Alemtuzumab-treated patients had more favorable changes from baseline on Multiple Sclerosis Functional Composite (MSFC) and Sloan low-contrast letter acuity measures.

Zinbryta™ (Daclizumab) Product Summary[27]

Indications: Zinbryta™ (daclizumab) 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, Zinbryta™ (daclizumab) should generally be reserved for patients who have had an inadequate response to two or more medications indicated for the treatment of MS.

Dosing:

- 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. It is administered by subcutaneous injection. Patients can be trained to self-administer this medication.

Mechanism of Action: The precise mechanism by which daclizumab exerts its therapeutic effects in MS is unknown but is presumed to involve modulation of IL-2 mediated activation of lymphocytes through binding to CD25, a subunit of the high-affinity IL-2 receptor.

Boxed Warning: Hepatic Injury and Other Immune-Mediated Disorders

- Daclizumab can cause severe liver injury including life-threatening events, liver failure, and autoimmune hepatitis. Transaminase and bilirubin levels should be obtained prior to initiation of therapy with daclizumab and should be monitored monthly and for up to six months after the last dose. Daclizumab is contraindicated in patients with pre-existing hepatic disease or hepatic impairment.
- Immune-mediated disorders including skin reactions, lymphadenopathy, non-infectious colitis, and other immune-mediated disorders can occur with daclizumab.
- Zinbryta™ is available only through a restricted distribution program called the Zinbryta™ REMS Program.

Contraindications:

- Pre-existing hepatic disease or hepatic impairment, including alanine aminotransferase (ALT) or aspartate aminotransferase (AST) at least two times the upper limit of normal (ULN), because daclizumab can exacerbate existing liver disease.

- A history of autoimmune hepatitis or other autoimmune condition involving the liver.
- A history of hypersensitivity to daclizumab or any other components of the formulation. Anaphylaxis or life-threatening multi-organ hypersensitivity may occur in such patients.

Warnings and Precautions:

- Hypersensitivity Reactions: Daclizumab can cause anaphylaxis, angioedema, and urticaria after the first dose or at any time during treatment. If anaphylaxis or other allergic reactions occur, daclizumab should be discontinued and not re-started.
- Infections: Daclizumab increases the risk of infections. The most common types of infections observed were upper respiratory tract infections, urinary tract infections, and viral infections. If a serious infection develops, withholding daclizumab until the infection resolves should be considered.
- Depression and Suicide: Daclizumab should be administered with caution to patients with previous or current depressive disorders. Patients and/or caregivers should be advised to immediately report any symptoms of new or worsening depression and/or suicidal ideation to their healthcare provider. If a patient develops severe depression and/or suicidal ideation, discontinuation of daclizumab should be considered.

Adverse Reactions: The most common adverse reactions reported with daclizumab treatment (incidence ≥5% higher incidence than interferon β-1a) during clinical trials include the following:

- Nasopharyngitis
- Upper Respiratory Tract Infection
- Rash
- Influenza
- Dermatitis
- Oropharyngeal Pain
- Bronchitis
- Eczema
- Lymphadenopathy

The most common adverse reactions reported with daclizumab treatment (incidence ≥2% higher incidence than placebo) during clinical trials include the following:

- Depression
- Increased ALT
- Pharyngitis
- Upper Respiratory Tract Infection
- Rash

Drug Interactions:

- Hepatotoxic Drugs: Caution should be used when using hepatotoxic drugs, including non-prescription drugs, concomitantly with daclizumab. The need for the use of herbal products or dietary supplements that can cause hepatotoxicity should be carefully considered.

Use in Special Populations:

- Pregnancy: There are no adequate data on the developmental risk associated with the use of daclizumab in pregnant women. Administration of daclizumab to monkeys during gestation resulted in embryofetal death and reduced fetal growth at maternal exposures greater than 30 times that expected clinically.
- Lactation: There are no data on the presence of daclizumab in human milk, the effects on the breastfed child, or the effects of the drug on milk production. Daclizumab was

excreted in the milk of daclizumab-treated monkeys. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for daclizumab and any potential adverse effects on the breastfed child from daclizumab or from the underlying maternal condition.

- Pediatric Use: The safety and effectiveness of daclizumab in patients less than 17 years of age have not been established. Use of daclizumab is not recommended in pediatric patients due to the risks of hepatic injury and immune-mediated disorders.
- Geriatric Use: Clinical studies did not include a sufficient number of patients 65 years of age and older to determine whether they respond differently from younger patients.
- Hepatic Impairment: Clinical trials did not include patients with ALT or AST more than two times the ULN. Patients with signs or symptoms of hepatic impairment may be at increased risk for hepatotoxicity from daclizumab.

Efficacy: The efficacy of daclizumab was demonstrated in two randomized, double-blind, controlled studies (Study 1 and Study 2). Both studies evaluated subcutaneous daclizumab 150mg administered once every four weeks in patients with relapsing MS.

- Study 1: Active-Controlled Trial: Study 1 compared daclizumab to intramuscular Avonex® (interferon β-1a) 30mcg weekly in 1,841 patients. Treatment continued for up to 144 weeks until the last enrolled patient completed 96 weeks of treatment. The primary outcome measure of Study 1 was the annualized relapse rate (ARR). Daclizumab had a statistically significant effect on the ARR compared to interferon β-1a (0.216 vs. 0.393; 45% relative reduction in ARR; $p < 0.0001$).
- Study 2: Placebo-Controlled Trial: Study 2 compared daclizumab to placebo in 412 patients. Treatment duration was 52 weeks. The primary outcome measure of Study 2 was the ARR at Week 52. Daclizumab had a statistically significant effect on the ARR compared to placebo (0.211 vs. 0.458; 54% relative reduction in ARR; $p < 0.0001$).

Cost:

Medication	Cost per Month*	Cost per Year
Zinbryta™ (daclizumab)	**$6,833.33**	**$81,999.96**

*Cost based on Wholesale Acquisition Cost (WAC) and does not reflect rebated price or net cost.

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 with at least one relapse in the previous 12 months, or transitioning from existing Multiple Sclerosis 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; 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.

Utilization Details of Multiple Sclerosis Medications: Fiscal Year 2016

Pharmacy Claims: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 INTERFERON BETA-1A PRODUCTS					
AVONEX PEN KIT 30MCG	51	8	$291,721.26	$198.72	$5,720.02
AVONEX PREFL KIT 30MCG	51	7	$291,061.04	$196.40	$5,707.08
SUBTOTAL	**102**	**15**	**$582,782.30**	**$197.55**	**$5,713.55**
TIER-1 INTERFERON BETA-1B PRODUCTS					
BETASERON INJ 0.3MG	53	7	$325,297.30	$219.20	$6,137.68
SUBTOTAL	53	7	$325,297.30	**$219.20**	**$6,137.68**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 SUBTOTAL	**155**	**22**	**$908,079.60**	**$204.80**	**$5,858.58**
TIER-2 INTERFERON BETA-1A PRODUCTS					
REBIF INJ 44/0.5	67	10	$406,098.23	$214.87	$6,061.17
REBIF REBIDO INJ 44/0.5	66	11	$401,879.43	$216.53	$6,089.08
REBIF INJ 22/0.5	28	3	$168,550.13	$212.55	$6,019.65
REBIF REBIDO INJ TITRATN	2	2	$12,057.27	$200.95	$6,028.64
REBIF TITRTN INJ PACK	1	1	$5,741.70	$191.39	$5,741.70
SUBTOTAL	**164**	**27**	**$994,326.76**	**$214.80**	**$6,062.97**
TIER-2 PEGINTERFERON BETA-1A PRODUCTS					
PLEGRIDY INJ PEN	38	6	$218,005.23	$203.36	$5,736.98
PLEGRIDY PEN INJ STARTER	1	1	$5,315.61	$177.19	$5,315.61
SUBTOTAL	**39**	**7**	**$223,320.84**	**$202.65**	**$5,726.18**
TIER-2 SUBTOTAL	**203**	**34**	**$1,217,647.60**	**$212.47**	**$5,998.26**
DALFAMPRIDINE PRODUCTS					
AMPYRA TAB 10MG	155	22	$305,070.20	$65.61	$1,968.19
SUBTOTAL	**155**	**22**	**$305,070.20**	**$65.61**	**$1,968.19**
TERIFLUNOMIDE PRODUCTS					
AUBAGIO TAB 14MG	96	17	$561,962.64	$209.06	$5,853.78
AUBAGIO TAB 7MG	17	3	$97,072.48	$203.93	$5,710.15
SUBTOTAL	**113**	**20**	**$659,035.12**	**$208.29**	**$5,832.17**
GLATIRAMER ACETATE PRODUCTS					
COPAXONE INJ 40MG/ML	261	46	$1,428,942.00	$194.84	$5,474.87
COPAXONE INJ 20MG/ML	230	50	$1,484,438.21	$218.04	$6,454.08
GLATOPA INJ 20MG/ML	12	4	$65,831.50	$182.87	$5,485.96
SUBTOTAL	**503**	**100**	**$2,979,211.71**	**$205.43**	**$5,922.89**
FINGOLIMOD PRODUCTS					
GILENYA CAP 0.5MG	163	22	$1,051,140.40	$217.09	$6,448.71
SUBTOTAL	**163**	**22**	**$1,051,140.40**	**$217.09**	**$6,448.71**
DIMETHYL FUMARATE PRODUCTS					
TECFIDERA CAP 240MG	223	38	$1,386,955.51	$207.32	$6,219.53
TECFIDERA MIS STARTER	13	13	$81,476.94	$208.92	$6,267.46
SUBTOTAL	**236**	**51**	**$1,468,432.45**	**$207.41**	**$6,222.17**
NATALIZUMAB PRODUCTS					
TYSABRI INJ 300/15ML	5	2	$19,617.77	$140.13	$3,923.55
SUBTOTAL	**5**	**2**	**$19,617.77**	**$140.13**	**$3,923.55**
TOTAL	**1,533**	**202***	**$8,608,234.85**	**$193.26**	**$5,615.29**

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

Medical Claims: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ALEMTUZUMAB PRODUCTS					
LEMTRADA 10MG/1ML (J0202)	10	2	$191,221.40	5	$19,122.14
NATALIZUMAB PRODUCTS					
TYSABRI INJ 300MG/15ML (J2323)	123	18	$605,758.00	6.83	$4,924.86
TOTAL	**133**	**20***	**$796,979.40**	**6.65**	**$5,992.33**

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

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[27] 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 02/20/2017.

Appendix L

Fiscal Year 2016 Annual Review of Makena® (Hydroxyprogesterone Caproate) and Vaginal Progesterone Products and 30-Day Notice to Prior Authorize Hydroxyprogesterone Caproate Injection

Oklahoma Health Care Authority
March 2017

Current Prior Authorization Criteria

Makena® (Hydroxyprogesterone Caproate) Approval Criteria:

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and
3. Gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation.
4. Authorizations will be for once a week administration by a healthcare professional through 36 weeks, 6 days of gestation.

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

Crinone® (Progesterone Vaginal Gel) Approval Criteria:

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

Endometrin® (Progesterone Vaginal Insert) Approval Criteria:

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

Utilization of Makena® and Vaginal Progesterone Products: Fiscal Year 2016

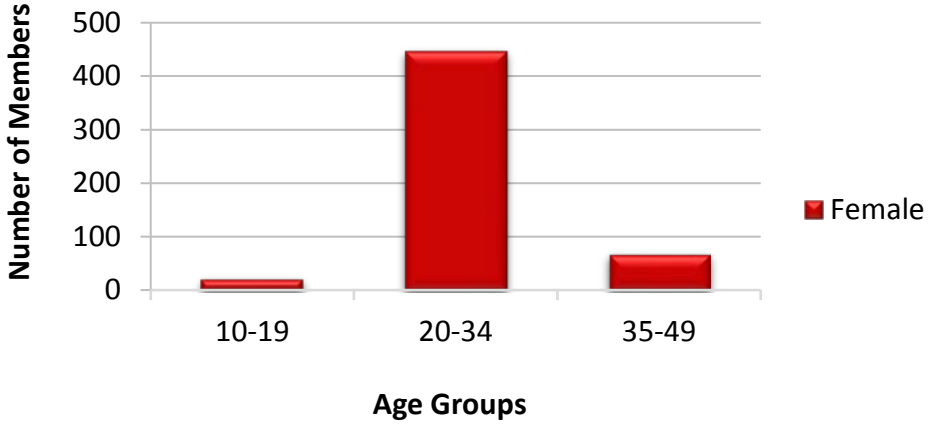
There was no SoonerCare utilization in fiscal year 2016 of the compounded hydroxyprogesterone caproate product (medical-only benefit); therefore, the following utilization details include pharmacy claims data only.

Comparison of Fiscal Years: Makena® and Vaginal Progesterone Products

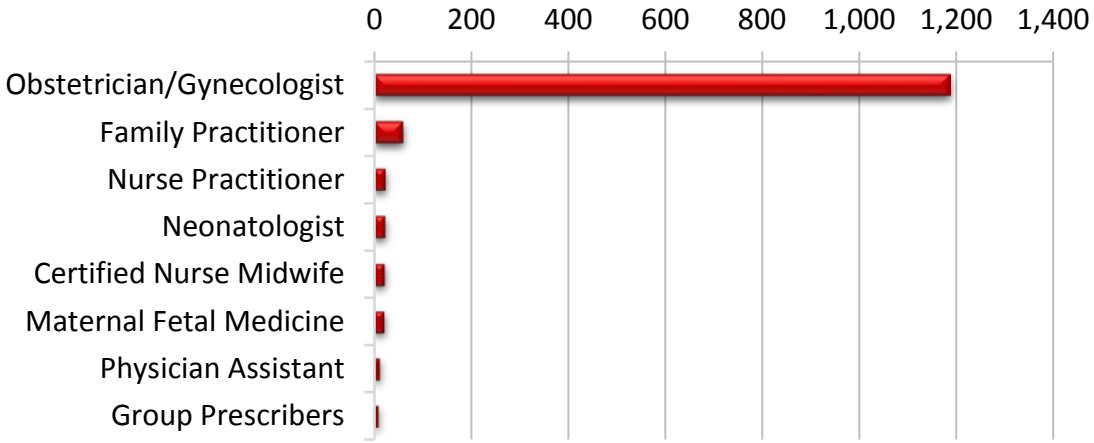
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	397	1,041	$3,708,533.00	$3,562.47	$109.47	5,393	33,876
2016	534	1,364	$4,897,513.07	$3,590.55	$112.59	7,063	43,500
% Change	**34.50%**	**31.00%**	**32.10%**	**0.80%**	**2.90%**	**31.00%**	**28.40%**
Change	**137**	**323**	**$1,188,980.07**	**$28.08**	**$3.12**	**1,670**	**9,624**

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

Demographics of Members Utilizing Makena® and Vaginal Progesterone Products

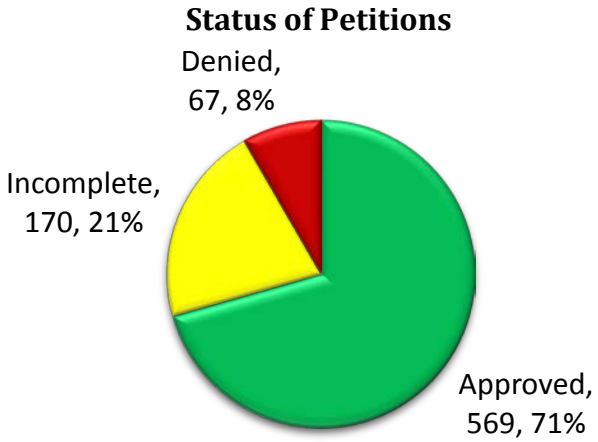


Top Prescriber Specialties of Makena® and Vaginal Progesterone Products by Number of Claims



Prior Authorization of Makena® and Vaginal Progesterone Products

There were 806 prior authorization requests submitted for Makena® and vaginal progesterone products during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3]

Anticipated Patent Expiration:

- Endometrin® (progesterone vaginal insert): November 2019

Anticipated Exclusivity Expiration:

- Makena® (hydroxyprogesterone caproate injection): February 2018

New FDA Approval:

- **August 2015:** The U.S. Food and Drug Administration (FDA) approved an Abbreviated New Drug Application (ANDA) for hydroxyprogesterone caproate 250mg/mL injection for use 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.

  Hydroxyprogesterone caproate 250mg/mL injection was approved as a generic for Delalutin®, which is no longer being marketed in the United States but was not withdrawn from sale for reasons of safety or effectiveness. Although the ANDA was FDA approved in August 2015, hydroxyprogesterone caproate injection did not become available on the market until June 2016.

Hydroxyprogesterone Caproate Product Summary[4,5,6]

Indications: Hydroxyprogesterone caproate 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.

Dosing:

- Hydroxyprogesterone caproate is available as a 250mg/mL injection for intramuscular (IM) use in 5mL multi-dose vials.
- Hydroxyprogesterone caproate injection should be administered IM into the upper outer quadrant of the gluteal muscle.
- Hydroxyprogesterone caproate vial should be stored upright in its box at a controlled room temperature (68° to 77°F) and protected from light. Any unused product should be discarded within 28 days after first use.
- For the treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV), the recommended dose is 1,000mg (or more) IM at once and then repeated with 1,000 to 7,000mg per week divided one or more times per week. Hydroxyprogesterone caproate should be discontinued when relapse occurs or after 12 weeks with no objective response.
- For the management of amenorrhea and abnormal bleeding due to hormonal imbalance in the absence of organic pathology, the recommended dose is a one-time dosage of hydroxyprogesterone caproate 375mg IM, which may be initiated at any time, or cyclic therapy (28-day cycle) to include estradiol valerate 20mg IM on day 1 followed by hydroxyprogesterone caproate 250mg IM with estradiol valerate 5mg IM 2 weeks later. For cyclic therapy, the cycle should be repeated every 4 weeks for 4 cycles, and the first cycle should be initiated after 4 days of desquamation or, if no bleeding, 21 days after hydroxyprogesterone caproate injection alone.
- As a test for endogenous estrogen production, the recommended dose is 250mg IM. For confirmation, may repeat 4 weeks after first injection.
- For the production of secretory endometrium and desquamation, the recommended dose for patients currently on estrogen therapy is a one-time dosage of hydroxyprogesterone caproate 375mg IM, which may be initiated at any time. For patients not on estrogen therapy, the recommended dose is cyclic therapy (28-day cycle) to include estradiol valerate 20mg IM on day 1 followed by hydroxyprogesterone caproate 250mg IM with estradiol valerate 5mg IM 2 weeks later.

Mechanism of Action: Hydroxyprogesterone caproate injection is a sterile, long-acting preparation of the caproate ester of the naturally-occurring progestational hormone, hydroxyprogesterone, in an oil solution for IM use. Hydroxyprogesterone is a potent, long-acting, progestational steroid ester which transforms proliferative endothelium into secretory endothelium, induces mammary gland duct development, and inhibits the production and/or

release of gonadotropic hormone. It also shows slight estrogenic, androgenic, or corticoid effects, but should not be relied upon for these effects.

Contraindications: Hydroxyprogesterone caproate is contraindicated as a diagnostic test for pregnancy and in patients with:

- Known or suspected carcinoma of the breast, other hormone-sensitive cancer, or history of these conditions
- Undiagnosed abnormal vaginal bleeding
- Liver dysfunction or disease
- Missed abortion
- Current or history of thrombotic or thromboembolic diseases
- History of hypersensitivity to the drug

Safety:

- Thrombotic and Thromboembolic Events: Hydroxyprogesterone caproate should be discontinued pending examination if there is a sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. Hydroxyprogesterone caproate should be stopped if examination reveals papilledema or retinal vascular lesions.
- Allergic Reactions: Hypersensitivity reactions to progestins have been reported. Hydroxyprogesterone caproate is contraindicated in women with a history of hypersensitivity to a progestin.
- Glucose Tolerance: Progestins may decrease glucose tolerance and the blood glucose concentration should be monitored in diabetic patients.
- Renal Impairment: The effect of renal impairment on the pharmacokinetics of hydroxyprogesterone caproate has not been evaluated.
- Hepatic Impairment: The effect of hepatic impairment on the pharmacokinetics of hydroxyprogesterone caproate has not been evaluated. Hydroxyprogesterone caproate is extensively metabolized and hepatic impairment may reduce the elimination of hydroxyprogesterone caproate.

Adverse Reactions: Common adverse reactions to hydroxyprogesterone caproate include injection site pain, swelling at injection site, urticaria, pruritus, injection site pruritus, nausea, injection site reaction, and diarrhea.

Cost: The wholesale acquisition cost (WAC) of hydroxyprogesterone caproate 250mg/mL injection is $340.91 per mL, resulting in a cost of $1,704.55 per 5mL multi-dose vial.

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).

Utilization Details of Makena® and Vaginal Progesterone Products: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
HYDROXYPROGESTERONE CAPROATE PRODUCTS						
MAKENA INJ 250MG/ML	1,335	520	$4,886,735.63	$113.55	$3,660.48	99.78%
SUBTOTAL	**1,335**	**520**	**$4,886,735.63**	**$113.55**	**$3,660.48**	**99.78%**
PROGESTERONE PRODUCTS						
CRINONE 8% VAG GEL	29	15	$10,777.44	$23.23	$371.64	0.22%
SUBTOTAL	**29**	**15**	**$10,777.44**	**$23.23**	**$371.64**	**0.22%**
TOTAL	**1,364**	**534***	**$4,897,513.07**	**$112.59**	**$3,590.55**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
The utilization details above include pharmacy claims data only, as there was no SoonerCare utilization in fiscal year 2016 of the compounded hydroxyprogesterone caproate product, which is available as a medical-only benefit. Please note, the current prior authorization criteria for vaginal progesterone products, in which use of Endometrin® is preferred over Crinone®, went into effect on 08/01/2016 and thus is not reflected in the above fiscal year 2016 utilization details.

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[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. Last revised 12/2016. Last accessed 02/10/2017.
[2] FDA ANDA Approval: Hydroxyprogesterone Caproate 250mg/mL Injection (Generic Delalutin®). Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/200271Orig1s000ltr.pdf. Issued 08/24/2015. Last accessed 02/15/2017.
[3] PR Newswire: ANI Pharmaceuticals Announces Launch of Hydroxyprogesterone Caproate Injection USP, 250mg/mL. Available online at: http://www.prnewswire.com/news-releases/ani-pharmaceuticals-announces-launch-of-hydroxyprogesterone-caproate-injection-usp-250mgml-300290857.html. Issued 06/28/2016. Last accessed 02/15/2017.
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Appendix M

Fiscal Year 2016 Annual Review of Naloxone Medications

Oklahoma Health Care Authority
March 2017

Current Prior Authorization Criteria

Naloxone injection and nasal spray are currently covered without prior authorization.

Evzio® (Naloxone Auto-Injector) Approval Criteria:

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

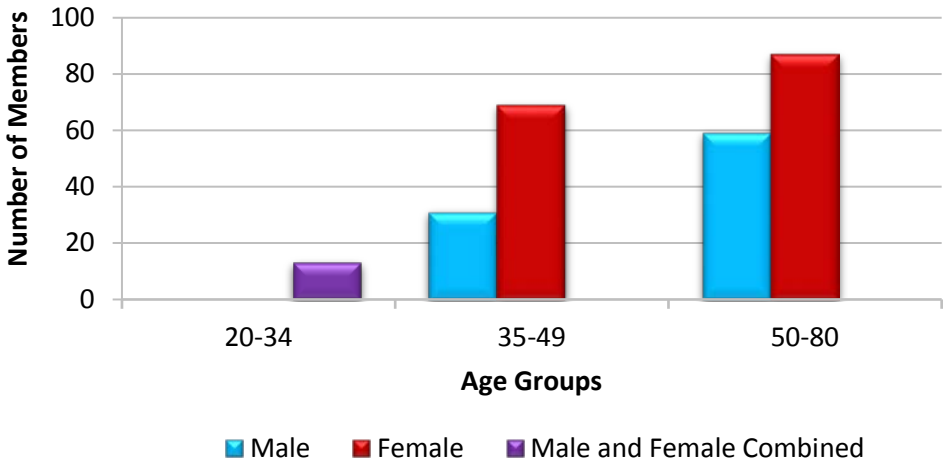
Utilization of Naloxone Medications: Fiscal Year 2016

Comparison of Fiscal Years

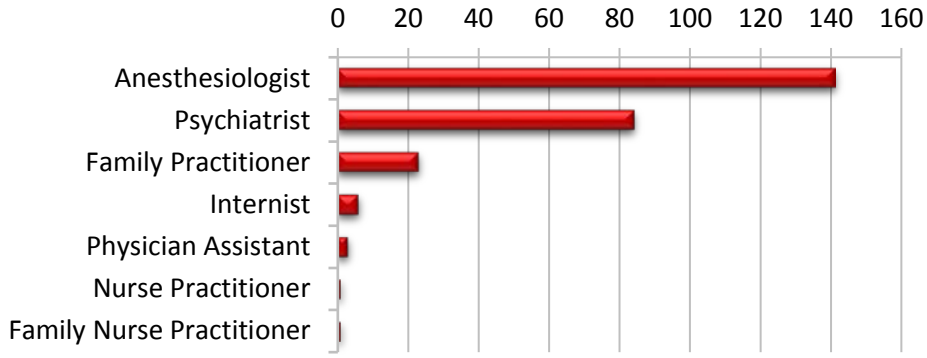
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	9	10	$1,602.99	$160.30	$11.70	3,022	137
2016	259	259	$22,988.12	$88.76	$3.57	591	6,445
% Change	**2,777.80%**	**2,490.00%**	**1,334.10%**	**-44.60%**	**-69.50%**	**-80.40%**	**4,604.40%**
Change	**250**	**249**	**$21,385.13**	**-$71.54**	**-$8.13**	**-2,431**	**6,308**

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

Demographics of Members Utilizing Naloxone Medications



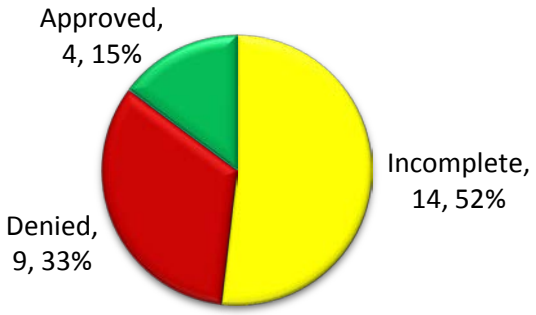
Top Prescriber Specialties of Naloxone Medications by Number of Claims



Prior Authorization of Naloxone Medications

There were 27 prior authorization requests submitted for naloxone medications during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Naloxone Statistics and Trends[1]

Fatal drug overdose has increased more than six-fold in the past three decades, and now claims the lives of over 47,000 Americans every year. Opioids, both prescription painkillers and heroin, are responsible for most of these deaths. The death rate from prescription opioid-associated overdose nearly quadrupled from 1999 to 2013, while deaths from heroin more than tripled from 2010 to 2014. Together, heroin and prescription pain medications take the lives of more than 28,000 Americans per year (over 75 people per day). They also cause hundreds of thousands of non-fatal overdoses. Opioid overdose is reversible through the timely administration of the medication naloxone and the provision of other emergency care. However, community access to naloxone was historically limited by laws and regulations that pre-date the overdose epidemic. In an attempt to reverse the unprecedented increase in preventable overdose deaths, the majority of states have recently amended those laws to increase access to emergency care and treatment for opiate overdose. By June 22, 2016, all but three states (KS, MT, WY) had passed legislation designed to improve layperson naloxone access. These states have made it easier for people who might be in a position to assist in an overdose to access the medication, encouraged those individuals to summon emergency responders, or both. In 2001, New Mexico became the first state to amend its laws to make it easier for medical professionals to prescribe and dispense naloxone, and for layperson

administrators to use it without fear of legal repercussions. As of 2016, 46 other states and the District of Columbia had made similar changes. Largely because of these legal changes, over 150,000 laypeople had received training and naloxone kits as of 2014, and naloxone program participants reported reversing more than 26,000 overdoses. In 2007, New Mexico became the first state to amend its laws to encourage Good Samaritans to summon aid in the event of an overdose. As of June 22, 2016, 35 other states and the District of Columbia had followed suit. Currently in Oklahoma, naloxone may be dispensed or sold by a pharmacy without a prescription under the supervision of a licensed pharmacist (if the pharmacy has an established protocol or collaborative practice agreement in place).

SoonerCare use of naloxone has recently been on the rise. In state fiscal year 2014 (SFY14), there was one claim for one member compared to SFY15 with ten claims for nine members. Then in SFY16, the utilization increased dramatically to 259 claims for 259 members. This upward trend in utilization began in September 2015, after a naloxone informational fax was sent to pharmacies from the Oklahoma Health Care Authority in August 2015. The fax informed pharmacies of the injectable formulations of naloxone available for SoonerCare members. Additionally, it highlighted the growing concern for opioid overdose deaths, the importance of naloxone to save lives in the event of an opioid overdose, and Oklahoma legislation aimed at increasing naloxone access. Based on the preceding information, continued efforts to increase awareness of naloxone access would further drive use of this life-saving medication.

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

Anticipated Patent Expiration(s):

- Evzio® (naloxone auto-injector): July 2034
- Narcan® (naloxone nasal spray): March 2035

New FDA Approval(s):

- **October 2016:** The U.S. Food and Drug Administration (FDA) approved a new drug application (NDA) for Evzio® 2mg (naloxone auto-injector). This provides a new strength of naloxone for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, and for immediate administration as emergency therapy in settings where opioids may be present. This NDA was originally submitted as a supplemental NDA (sNDA) but was administratively converted to an NDA. Evzio®, an opioid antagonist, will be available as two 2mg/0.4mL auto-injectors and a single Trainer. Evzio® was originally approved as a 0.4mg/0.4mL strength auto-injector in 2014 and was the first naloxone product approved for family member or caregiver use. The product incorporates audio and visual cues to help the user through the injection process. According to the manufacturer, Kaleo, Evzio® 0.4mg remains a safe and effective, FDA-approved option for treatment of an opioid emergency. However, Evzio® 0.4mg will no longer be manufactured. Kaleo also reports that Evzio® 2mg is the first and only take-home naloxone auto-injection system for use in opioid emergencies, including those with synthetic opioids like fentanyl, long-acting opioids, and partial agonists or mixed agonist/antagonists, which may require higher or repeat doses of naloxone.

- **January 2017:** The FDA approved Narcan® (naloxone) nasal spray 2mg for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. The 2mg dose is approved for use in opioid-dependent patients expected to be at risk for severe opioid withdrawal in situations where there is a low risk for accidental or intentional opioid exposure by household contacts. This approval comes just over one year after the FDA approved the first of its kind, ready-to-use, needle-free version of naloxone, Narcan® nasal spray 4mg, which has been commercially available since February 2016 following expedited FDA review and approval.

Other News:

- **November 2016:** The FDA published a consumer update entitled "What to Ask Your Doctor Before Taking Opioids." This publication lists questions for patients to ask prescribers regarding opioid prescriptions. This update also includes the reasoning behind each question and ideas on how to start the conversation. Of note, the question "Can I have an Rx for naloxone?" is included. Patients are encouraged to discuss naloxone with doctors and advised that naloxone is a drug that can reverse the effects of an opioid overdose and save lives. The update also states that in many cases it makes sense to be prepared for potential problems by keeping naloxone in the patient's home.
- **December 2016:** An article published in *The New England Journal of Medicine* addressed the rising cost of naloxone and naloxone access. While naloxone injection was FDA approved in 1971 and generic versions have been available since 1985, recent price hikes have limited access to naloxone in the face of a growing trend to increase access. Several states have passed laws and pursued initiatives designed to improve access to naloxone. As a result, between 2009 and 2015, the annual number of naloxone prescriptions increased only from 2.8 million to 3.2 million, but retail-prescriptions for naloxone were unchanged. Conversely, the proportion attributed to clinics and emergency medical services providers has grown from 14% to 29%. The relatively slow adoption of naloxone may be due in large part to stigmatization and lack of familiarity with the treatment among clinicians and opioid users. Another reason, however, may be its rising cost, which is probably enabled by the small number of manufacturers producing it. For example, naloxone 0.4mg/mL injection has increased in price by 129% since 2012, and the 1mg/mL injection increased by 95% in September 2014. Additionally, Narcan® (naloxone nasal spray) costs $150.00 for two doses, and Evzio® (naloxone auto-injector) costs $4,500.00 for two doses. Evzio® represents the biggest price hike at 500% in two years. Several strategies are suggested to promote price reductions such as purchasing bulk product, invoking federal law, and allowing importation of generics. The author recommends not only increasing access to naloxone, but also ensuring affordability as the government's responsibility in reducing the number of prescription-opioid and heroin overdoses in the United States.

Recommendations

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.

Utilization Details of Naloxone Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
NALOXONE INJ 1MG/ML	177	177	$7,725.35	$1.97	$43.65	33.60%
NARCAN SPRAY	79	79	$10,491.14	$4.26	$132.80	45.64%
EVZIO INJ	2	2	$4,755.31	$79.26	$2,377.6	20.69%
NALOXONE INJ 0.4MG/ML	1	1	$16.32	$16.32	$16.32	0.07%
TOTAL	**259**	**259***	**$22,988.12**	**$3.57**	**$88.76**	**100.00%**

*Total number of unduplicated members.

[1] Davis C, Chang S, Carr D. The Network for Public Health Law Legal. "Interventions to Reduce Overdose Mortality: Naloxone Access And Overdose Good Samaritan Laws." Available online at: https://www.networkforphl.org/_asset/qz5pvn/naloxone-_FINAL.pdf. Last revised 06/2016. Last accessed 02/09/2017.

[2] 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. Last revised 12/2016. Last accessed 02/07/2017.

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[7] Gupta R, Shah ND, Ross JS. The Rising Price of Naloxone - Risks to Efforts to Stem Overdose Deaths. *The New England Journal of Medicine* 2016; 375: 2213-2215.

Appendix N

30-Day Notice to Prior Zinplava™ (Bezlotoxumab)

Oklahoma Health Care Authority
March 2017

Introduction[1,2]

Clostridium 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. CDI can cause a spectrum of manifestations ranging from an asymptomatic carriage to fulminant disease with toxic megacolon. The basis for this range of clinical manifestations is not fully understood but may be related to various host and pathogen factors. Watery diarrhea is the cardinal symptom of *C. difficile*–associated diarrhea (CDAD) with colitis (greater than three loose stools in 24 hours). Other manifestations include lower abdominal pain and cramping, low-grade fever, nausea, anorexia, and leukocytosis. Fever is associated with CDAD in about 15% of cases. Leukocytosis, elevated creatinine, and elevated lactate in the setting of CDAD are common. CDAD is routinely associated with an average white blood cell count of 15,000/microL. Symptoms of CDI typically occur in the setting of antibiotic therapy and may begin during antibiotic therapy or five to ten days following antibiotic therapy. Rarely, symptoms present as late as ten weeks after cessation of antibiotic therapy. The antibiotics most frequently implicated in predisposition to CDI are fluoroquinolones, clindamycin, cephalosporins, and penicillins, though virtually any antibiotic can predispose to CDI. Additional risk factors for CDI include age greater than 65 years, recent hospitalization, and use of proton pump inhibitors. 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, although more data are needed.

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. Recurrent symptoms may be due to relapse of the initial infecting strain or reinfection with a new strain. Recurrent CDI often represents relapse rather than reinfection, regardless of the interval between episodes. Mild to moderate initial recurrence following therapy for CDI can be treated with metronidazole.

The decision to administer vancomycin as treatment for a first recurrence should be based upon the presence of markers of severe disease at the time of first recurrence rather than on previous drug exposure. There are no rigorous studies of management for multiple recurrences of CDI. Patients with multiple recurrences may benefit from vancomycin (administered in a pulse tapered fashion), fidaxomicin, or rifaximin, with or without the use of probiotics. Other useful treatments for patients with recurrent CDI may include: fecal microbiota transplant, intravenous immune globulin, anion-binding resins, and monoclonal antibodies. 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.

Zinplava™ (Bezlotoxumab) Product Summary[3,4,5]

Indications: Zinplava™ (bezlotoxumab) is a human monoclonal antibody that binds to *C. difficile* toxin B, 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.
Limitation of Use: Bezlotoxumab is not indicated for the treatment of CDI. Bezlotoxumab is not an antibacterial drug. Bezlotoxumab should only be used in conjunction with antibacterial drug treatment of CDI.

Dosing:

- Zinplava™ (bezlotoxumab) is supplied as a 1,000mg/40mL (25mg/mL) single-dose vial.
- The recommended dose is a single dose of 10mg/kg administered as an intravenous infusion over 60 minutes.
- Bezlotoxumab requires dilution prior to intravenous infusion, and administration via a low-protein binding 0.2 micron to 5 micron in-line or add-on filter.
- It is to be administered during antibacterial drug treatment for CDI.

Mechanism of Action: Bezlotoxumab is a human monoclonal antibody that binds to *C. difficile* toxin B and neutralizes its effects. It binds to an epitope on toxin B that is conserved across reported strains of *C. difficile*, although amino acid sequence variation within the epitope does occur. *In vitro* studies in cell-based assays using Vero cells or Caco-2 cells, suggest that bezlotoxumab neutralizes the toxic effects of *C. difficile* toxin B.

Contraindications: None.

Warnings and Precautions:

- Heart Failure: Heart failure was reported more commonly in the two Phase 3 clinical trials in bezlotoxumab-treated patients compared to placebo-treated patients. These adverse reactions occurred primarily in patients with underlying congestive heart failure (CHF). In patients with a history of CHF, 12.7% (15/118) of bezlotoxumab-treated patients and 4.8% (5/104) of placebo-treated patients had the serious adverse reaction of heart failure during the 12-week study period. Additionally, in patients with a history of CHF, there were more deaths in bezlotoxumab-treated patients, 19.5% (23/118), than in placebo-treated patients, 12.5% (13/104), during the 12-week study period. The causes of death varied and included cardiac failure, infections, and respiratory failure.

Adverse Reactions: The most common adverse reactions following treatment with bezlotoxumab (reported in ≥4% of patients) include the following:

- Nausea
- Pyrexia
- Headache

Infusion Related Reactions: Infusion specific adverse reactions reported in ≥0.5% of patients receiving bezlotoxumab and at a frequency greater than placebo include:

- Nausea
- Fatigue
- Pyrexia
- Dizziness
- Headache
- Dyspnea
- Hypertension

Use in Special Populations:

- Pregnancy: Adequate and well controlled studies with bezlotoxumab have not been conducted in pregnant women. No animal reproductive and developmental studies have been conducted with bezlotoxumab.
- Lactation: There is no information regarding the presence of bezlotoxumab in human milk, the effects on the breast-fed infant, or the effects on milk production.
- Pediatric Use: Safety and efficacy of bezlotoxumab in patients less than 18 years of age have not been established.
- Geriatric Use: Of the 786 patients treated with bezlotoxumab, 50% were 65 years of age and over, and 27% were 75 years of age and over. No overall differences in safety and efficacy were observed between these subjects and younger subjects. No dose adjustment is necessary for patients 65 years of age and over.

Efficacy: The safety and efficacy of bezlotoxumab were investigated in two randomized, double-blind, placebo-controlled, multicenter, Phase 3 trials (Trial 1 and Trial 2) in patients receiving standard of care (SoC) antibacterial drugs for treatment of CDI (metronidazole, vancomycin, or fidaxomicin). Inclusion criteria for the trials included patients 18 years of age or older with a confirmed diagnosis of CDI, which was defined as diarrhea (passage of three or more loose bowel movements in 24 or fewer hours), and a positive stool test for toxigenic *C. difficile* from a stool sample collected no more than seven days before study entry. Patients were excluded from the study if surgery for CDI was planned, or if they had uncontrolled chronic diarrheal illness. The following risk factors associated with a high risk of CDI recurrence or CDI-related adverse outcomes were present in the study population: 51% were ≥65 years of age, 39% received one or more systemic antibacterial drugs (during the 12-week follow-up period), 28% had one or more episodes of CDI within the six months prior to the episode under treatment (15% had two or more episodes prior to the episode under treatment), 21% were immunocompromised, and 16% presented at study entry with clinically severe CDI (as defined by a Zar score of ≥2). A hypervirulent strain (ribotypes 027, 078, or 244) was isolated in 22% of patients who had a positive baseline culture, of which 87% (189 of 217 strains) were ribotype 027. A Zar score is a prediction tool for the severity of CDI. One or two points are assigned to six variables and a total score ≥2 indicates severe disease. The variables include age >60 years, albumin <2.5mg/dL, white blood cell count >15x10^9/L, temperature >101˚F (38.3˚C), pseudomembranous colitis on colonoscopy, and intensive care unit (ICU) patient.

Patients received a 10- to 14-day course of oral SoC and a single infusion of bezlotoxumab or placebo was administered during the course of SoC. The day of the infusion of bezlotoxumab or placebo in relation to the start of SoC ranged from the day prior to the start of SoC to 14 days after the start of SoC with the median being day 3 of SoC. Patients were assessed for clinical cure of the presenting CDI episode, defined as no diarrhea for two consecutive days following the completion of a ≤14-day SoC regimen. Patients who achieved clinical cure were then assessed for recurrence of CDI through 12 weeks following administration of the infusion of bezlotoxumab or placebo. CDI recurrence was defined as the development of a new episode of diarrhea associated with a positive stool test for toxigenic *C. difficile* following clinical cure of the presenting CDI episode. Sustained clinical response was defined as clinical cure of the presenting CDI episode and no CDI recurrence through 12 weeks after infusion.

- Trial 1: In this trial, 403 patients were randomized to receive bezlotoxumab and 404 patients were randomized to receive placebo. Of the patients receiving bezlotoxumab, 60.1% met criteria for sustained clinical response. The recurrence rate was 17.4% and clinical failure rate was 22.5%. For placebo, there was a sustained clinical response of 55.2%, recurrence rate of 27.6%, and clinical failure of 17.2%. For sustained clinical response, there was 4.8% difference between bezlotoxumab and placebo. The clinical cure rate of the presenting CDI episode was lower in the bezlotoxumab arm as compared to the placebo arm in this trial.
- Trial 2: In this trial, 407 subjects were randomized to receive bezlotoxumab and 399 patients were randomized to receive placebo. Of the patients receiving bezlotoxumab, 66.8% met criteria for sustained clinical response. The recurrence rate was 15.7% and clinical failure rate was 17.5%. For placebo, there was a sustained clinical response of 52.1%, recurrence rate of 25.7%, and clinical failure of 22.2%. For sustained clinical response, there was 14.6% difference between bezlotoxumab and placebo. The clinical cure rate was lower in the placebo arm compared to the bezlotoxumab arm in this trial.

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-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 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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[1] Lamont JT. Clostridium difficile infection in adults: Clinical manifestations and diagnosis. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/clostridium-difficile-infection-in-adults-clinical-manifestations-and-diagnosis?source=search_result&search=clostridium+difficile&selectedTitle=2%7E150. Last revised 10/26/2016. Last accessed 02/08/2017.

[2] Kelly CP, Lamont JT. Clostridium difficile in adults: Treatment. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/clostridium-difficile-in-adults-treatment?source=search_result&search=clostridium+difficile&selectedTitle=1%7E150. Last revised 02/02/2017. Last accessed 02/08/2017.

[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 02/08/2017.

[4] 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 02/08/2017.

[5] Shah N, Shaaban H, Spira R, et al. Intravenous Immunoglobulin in the Treatment of Severe *Clostridium Difficile* Colitis. *Journal of Global Infectious Disease* 2014; 6(2): 82-85.

Appendix O

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

FDA NEWS RELEASE

For Immediate Release: February 9th, 2017
FDA approves drug to treat Duchenne muscular dystrophy

The U.S. Food and Drug Administration approved Emflaza (deflazacort) tablets and oral suspension to treat patients age 5 years and older with Duchenne muscular dystrophy (DMD), a rare genetic disorder that causes progressive muscle deterioration and weakness. Emflaza is a corticosteroid that works by decreasing inflammation and reducing the activity of the immune system.
Corticosteroids are commonly used to treat DMD across the world. This is the first FDA approval of any corticosteroid to treat DMD and the first approval of deflazacort for any use in the United States.
DMD is the most common type of muscular dystrophy. DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. The first symptoms are usually seen between 3 and 5 years of age and worsen over time. The disease often occurs in people without a known family history of the condition and primarily affects boys, but in rare cases it can affect girls. DMD occurs in about one of every 3,600 male infants worldwide.
People with DMD progressively lose the ability to perform activities independently and often require use of a wheelchair by their early teens. As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.
The effectiveness of deflazacort was shown in a clinical study of 196 male patients who were 5 to 15 years old at the beginning of the trial with documented mutation of the dystrophin gene and onset of weakness before age 5. At week 12, patients taking deflazacort had improvements in a clinical assessment of muscle strength across a number of muscles compared to those taking a placebo. An overall stability in average muscle strength was maintained through the end of study at week 52 in the deflazacort-treated patients. In another trial with 29 male patients that lasted 104 weeks, deflazacort demonstrated a numerical advantage over placebo on an assessment of average muscle strength. In addition, although not statistically controlled for multiple comparisons, patients on deflazacort appeared to lose the ability to walk later than those treated with placebo.
The side effects caused by Emflaza are similar to those experienced with other corticosteroids. The most common side effects include facial puffiness (Cushingoid appearance), weight gain, increased appetite, upper respiratory tract infection, cough, extraordinary daytime urinary frequency (pollakiuria), unwanted hair growth (hirsutism) and excessive fat around the stomach (central obesity).
Other side effects that are less common include problems with endocrine function, increased susceptibility to infection, elevation in blood pressure, risk of gastrointestinal perforation, serious skin rashes, behavioral and mood changes, decrease in the density of the bones and vision problems such as cataracts. Patients receiving immunosuppressive doses of corticosteroids should not be given live or live attenuated vaccines.
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.
The sponsor is receiving a rare pediatric disease priority review voucher under a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases. A voucher can be redeemed by a sponsor at a later date to receive priority review of a subsequent marketing application for a different product. This is the ninth rare pediatric disease priority review voucher issued by the FDA since the program began.
Emflaza is marketed by Marathon Pharmaceuticals of Northbrook, Illinois.

Safety Announcements

FDA Drug Safety Communication: FDA warns about rare but serious allergic reactions with the skin antiseptic chlorhexidine gluconate

[2/2/17] The U.S. Food and Drug Administration (FDA) is warning that rare but serious allergic reactions have been reported with the widely used skin antiseptic products containing chlorhexidine gluconate. Although rare, the number of reports of serious allergic reactions to these products has increased over the last several years. As a result, we are requesting the manufacturers of over-the-counter (OTC) antiseptic products containing chlorhexidine gluconate to add a warning about this risk to the Drug Facts labels. Prescription chlorhexidine gluconate mouthwashes and oral chips used for gum disease already contain a warning about the possibility of serious allergic reactions in their labels.

Patients and consumers should stop using the product that contains chlorhexidine gluconate and seek medical attention immediately or call 911 if they experience symptoms of a serious allergic reaction. These reactions can occur within minutes of exposure. Symptoms include wheezing or difficulty breathing; swelling of the face; hives that can quickly progress to more serious symptoms; severe rash; or shock, which is a life-threatening condition that occurs when the body is not getting enough blood flow.

Health care professionals should always ask patients if they have ever had an allergic reaction to any antiseptic before recommending or prescribing a chlorhexidine gluconate product. Advise patients to seek immediate medical attention if they experience any symptoms of an allergic reaction when using the products. Consider using alternative antiseptics such as povidone-iodine, alcohols, benzalkonium chloride, benzethonium chloride, or parachlorometaxylenol (PCMX) when any previous allergy to chlorhexidine gluconate is documented or suspected.

Chlorhexidine gluconate is mainly available in OTC products to clean and prepare the skin before surgery and before injections in order to help reduce bacteria that potentially can cause skin infections. These products are available as solutions, washes, sponges, and swabs and under many different brand names and as generics (see Facts about Chlorhexidine Gluconate). Chlorhexidine gluconate is also available as a prescription mouthwash to treat gingivitis and as a prescription oral chip to treat periodontal disease. In 1998, we issued a Public Health Notice to warn health care professionals about the risk of serious allergic reactions with medical devices such as dressings and intravenous lines between January that contain chlorhexidine gluconate.

We identified 52 cases of anaphylaxis with the use of chlorhexidine gluconate products applied to the skin. In the 46 years 1969 and early June 2015, FDA received reports of 43 cases worldwide. More than half of the 43 cases were reported after 2010, and after our 1998 Public Health Notice. This number includes only reports submitted to FDA, so there are likely additional cases about which we are unaware. The serious allergic reaction cases reported outcomes that required emergency department visits or hospitalizations to receive drug and other medical treatments. These allergic reactions resulted in two deaths. Eight additional cases of anaphylaxis were published in the medical literature between 1971 and 2015, and one case was identified in the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance (NEISS-CADES) database between 2004 and 2013.

We urge patients, consumers, and health care professionals to report side effects involving chlorhexidine gluconate or other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of February 21st, 2017):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Alitretinoin (Panretin) Gel	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
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***
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***
Methyldopate Hydrochloride 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***
Nimodipine (Nymalize) Oral Solution	***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***
Ranitidine Injection, USP	***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***
Sodium Acetate 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***
Sufentanil Citrate (Sufenta) Injection	***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***
Tobramycin Injection	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***