

Drug Utilization Review Board

Oklahoma
Health Care
Authority

Wednesday,
October 12, 2016
4 p.m.

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





The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members
FROM: Bethany Holderread, Pharm.D.
SUBJECT: Packet Contents for Board Meeting – October 12, 2016
DATE: October 1, 2016
NOTE: The DUR Board will meet at 4:00 p.m. The meeting will be held at 4345 N Lincoln Blvd.

*Enclosed are the following items related to the October 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

Action Item – Vote on 2017 Meeting Dates – Appendix B

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

Action Item – Vote to Prior Authorize Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL) – Appendix D

Action Item – Vote to Prior Authorize Xiidra™ (Lifitegrast 5% Ophthalmic Solution) – Appendix E

Action Item – Vote to Prior Authorize Allzital® (Butalbital/Acetaminophen 25mg/325mg) & Esgic® Capsules (Butalbital/Acetaminophen/Caffeine 50mg/325mg/40mg) – Appendix F

Action Item – Annual Review of Breast Cancer Medications – Appendix G

Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), & Imlygic® (Talimogene Laherparepvec) – Appendix H

Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Relistor® (Methylnaltrexone) Tablets – Appendix I

Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szzs), & Amjevita™ (Adalimumab-atto) – Appendix J

Action Item – Annual Review of Bladder Control Medications – Appendix K

Annual Review of Lidoderm® (Lidocaine 5% Patch) and 30-Day Notice to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch) – Appendix L

Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Ultravate® Lotion (Halobetasol Propionate 0.05%), Sernivo™ (Betamethasone Dipropionate Spray 0.05%), & Flurandrenolide 0.05% Cream and Lotion – Appendix M

Annual Review of Corlanor® (Ivabradine) and Entresto™ (Sacubitril/Valsartan) – Appendix N

Annual Review of Growth Hormone – Appendix O

FDA and DEA Updates – Appendix P

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board (DUR Board)

Meeting – October 12, 2016 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

- A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

- A. 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. September 14, 2016 DUR Minutes – Vote
- B. September 14, 2016 DUR Recommendations Memorandum
- C. Correspondence

Items to be presented by Dr. Muchmore, Chairman:

4. Action Item – Vote on 2017 Meeting Dates – See Appendix B

- A. 2017 Drug Utilization Review Board Meeting Dates – Vote

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

5. Update on Medication Coverage Authorization Unit/Long-Acting Beta Agonist Utilization: Pediatric Members – See Appendix C

- A. Medication Coverage Activity for September 2016
- B. Pharmacy Help Desk Activity for September 2016
- C. Long-Acting Beta Agonist Utilization: Pediatric Members

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

6. Action Item – Vote to Prior Authorize Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL) – See Appendix D

- A. Introduction
- B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Xiidra™ (Lifitegrast 5% Ophthalmic Solution) – See Appendix E

- A. Introduction
- B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Allzital® (Butalbital/Acetaminophen 25mg/325mg) & Esgic® Capsules (Butalbital/Acetaminophen/Caffeine 50mg/325mg/40mg) – See Appendix F

- A. Introduction
- B. College of Pharmacy Recommendations

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

9. Action Item – Annual Review of Breast Cancer Medications – See Appendix G

- A. Introduction
- B. Utilization of Breast Cancer Medications

- C. Prior Authorization of Breast Cancer Medications
- D. Market News and Updates
- E. Recommendations
- F. Utilization Details of Breast Cancer Medications

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

10. Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), & Imlygic® (Talimogene Laherparepvec) – See Appendix H

- A. Introduction
- B. Utilization of Skin Cancer Medications
- C. Market News and Updates
- D. Product Summaries
- E. Recommendations
- F. Utilization Details of Skin Cancer Medications

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

11. Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Relistor® (Methylnaltrexone) Tablets – See Appendix I

- A. Current Prior Authorization Criteria
- B. Utilization of Constipation and Diarrhea Medications
- C. Prior Authorization of Constipation and Diarrhea Medications
- D. Market News and Updates
- E. Relistor® (Methylnaltrexone) Tablets Product Summary
- F. Cost Comparison: Medications for Opioid Induced Constipation (Chronic Non-Cancer Pain)
- G. College of Pharmacy Recommendations
- H. Utilization Details of Constipation and Diarrhea Medications
- I. Utilization Details of Xifaxan® (Rifaximin)

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

12. Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szsz), & Amjevita™ (Adalimumab-atto) – See Appendix J

- A. Current Prior Authorization Criteria
- B. Utilization of Targeted Immunomodulator Agents
- C. Prior Authorization of Targeted Immunomodulator Agents
- D. Market News and Updates
- E. Xeljanz® XR (Tofacitinib Extended-Release) Product Summary
- F. Taltz® (Ixekizumab) Product Summary
- G. Inflectra™ (Infliximab-dyyb) Product Summary
- H. Erelzi™ (Etanercept-szsz) Product Summary
- I. Amjevita™ (Adalimumab-atto) Product Summary
- J. Noninfectious Intermediate Uveitis, Posterior Uveitis, & Panuveitis Summary
- K. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and Familial Mediterranean Fever (FMF) Summary
- L. College of Pharmacy Recommendations
- M. Utilization Details of Targeted Immunomodulator Agents

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

13. Action Item – Annual Review of Bladder Control Medications – See Appendix K

- A. Current Prior Authorization Criteria
- B. Utilization of Bladder Control Medications
- C. Prior Authorization of Bladder Control Medications
- D. Market News and Updates
- E. Pricing Trend(s)
- F. College of Pharmacy Recommendations

G. Utilization Details of Bladder Control Medications

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

14. Annual Review of Lidoderm® (Lidocaine 5% Patch) and 30-Day Notice to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch) – See Appendix L

- A. Current Prior Authorization Criteria
- B. Utilization of Lidoderm® (Lidocaine 5% Patch)
- C. Prior Authorization of Lidoderm® (Lidocaine 5% Patch)
- D. Synera® (Lidocaine/Tetracaine Topical Patch) Product Summary
- E. College of Pharmacy Recommendations

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

15. Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Ultravate® Lotion (Halobetasol Propionate 0.05%), Sernivo™ (Betamethasone Dipropionate Spray 0.05%), & Flurandrenolide 0.05% Cream and Lotion – See Appendix M

- A. Current Prior Authorization Criteria
- B. Utilization of Topical Corticosteroids
- C. Prior Authorization of Topical Corticosteroids
- D. Market News and Updates
- E. Ultravate® (Halobetasol Lotion 0.05%) Product Summary
- F. Sernivo™ (Betamethasone Dipropionate Topical Spray 0.05%) Product Summary
- G. Flurandrenolide 0.05% Cream and Lotion Product Summary
- H. College of Pharmacy Recommendations
- I. Utilization Details of Topical Corticosteroids

Non-presentation; Questions only:

16. Annual Review of Corlanor® (Ivabradine) and Entresto™ (Sacubitril/Valsartan) – See Appendix N

- A. Current Prior Authorization Criteria
- B. Utilization of Corlanor® and Entresto™
- C. Prior Authorization of Corlanor® and Entresto™
- D. Market News and Updates
- E. College of Pharmacy Recommendations
- F. Utilization Details of Corlanor® and Entresto™

Non-presentation; Questions only:

17. Annual Review of Growth Hormone – See Appendix O

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

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

18. FDA and DEA Updates – See Appendix P

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

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

- A. Cystic Fibrosis Medications
- B. Keveyis™ (Dichlorphenamide)
- C. Various Systemic Antibiotics
- D. Ophthalmic Anti-Inflammatories
- E. Hepatitis C Medications
- F. Iron Overload Medications
- G. Pancreatic Enzymes

**Future business subject to change.*

20. Adjournment



Appendix A



**OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF SEPTEMBER 14, 2016**

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director		X
Melissa Abbott, Pharm.D.; Clinical Pharmacist		X
Michyla Adams, Pharm.D.; Clinical Pharmacist	X	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Erin Ford, Pharm.D.; Clinical Pharmacist		X
Bethany Holderread, Pharm.D.; Clinical Coordinator	X	
Shellie Keast, Ph.D.; Assistant Professor	X	
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): Yen Le, Jiayu Lin	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	
Ed Long, Chief Communications 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:		
Matt Phillips, Zylera	Tyler Craddock, The Medicines Co.	Chris Stanfield, Supernus
Kimberly Lyles, Shire	Suzanne Hensley, MannKind	Melvin Nwamadi, Abbott
Mai Duong, Novartis	Richard Ponder, J & J	Mary Stewart Crane, J & J
Marc Parker, Sunovion	David Williams, Allergan	Jimmy Boland, Sun Pharma
Marc Welborn, Intercept	Jim Chapman, AbbVie	Sean Seago, Merck
Jim Fowler, AstraZeneca	Kirsten Mar, AstraZeneca	Doug Wood, ViiV HC
Jason Schwier, Amgen	Brian Maves, Pfizer	Terry McCurren, Otsuka
Scott Sabrsula, ZS Pharma	Ron Schnare, Shire	Gay Thomas, BMS

PRESENT FOR PUBLIC COMMENT:	
Matt Phillips	Zylera
Kirsten Mar	AstraZeneca
Kimberly Lyles	Shire

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA NO. 12 SPEAKER: MATT PHILLIPS

2B: AGENDA NO. 13 SPEAKER: KIRSTEN MAR

2C: AGENDA NO. 16 SPEAKER: KIMBERLY LYLES

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: JULY 13, 2016 DUR MINUTES – VOTE

3B: JULY 13, 2016 DUR RECOMMENDATIONS MEMORANDUM

3C: AUGUST 10, 2016 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

**AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION
UNIT/CONCOMITANT BENZODIAZEPINE AND OPIOID UTILIZATION**

4A: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2016

4B: PHARMACY HELP DESK ACTIVITY FOR AUGUST 2016

4C: CONCOMITANT BENZODIAZEPINE AND OPIOID UTILIZATION

Materials included in agenda packet; presented by Dr. Holderread

Dr. Winegardner recommends *“I think targeted education would be more effective than casting the wide net.”*

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

ACTION: MOTION CARRIED

**AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE DEXILANT™ SOLUTAB
(DEXLANSOPRAZOLE DELAYED-RELEASE ORALLY DISINTEGRATING TABLETS)**

5A: INDICATION(S) AND DOSING

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE AK-TRACIN® (BACITRACIN) AND BLEPH-10® (SULFACETAMIDE SODIUM) OPHTHALMIC OINTMENT

6A: INDICATION(S)

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE BETOPTIC® (BETAXOLOL OPHTHALMIC SOLUTION), TIMOPTIC-XE® (TIMOLOL MALEATE OPHTHALMIC GEL-FORMING SOLUTION), & BETIMOL® (TIMOLOL OPHTHALMIC SOLUTION)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE NASAREL® (FLUNISOLIDE NASAL SPRAY)

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Winegardner moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE OCALIVA™ (OBETICHOIC ACID)

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Garton moved to approve; seconded by Dr. Huddleston
Dr. Garton and Dr. Muchmore recommend wording changed to *“must confirm the lack of improvement in liver function test not caused by superimposed liver disease and confirm superimposed liver disease is being adequately managed.”*

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE BELBUCA™ (BUPRENORPHINE BUCCAL FILM), DOLOPHINE® (METHADONE), MORPHABOND™ (MORPHINE EXTENDED-RELEASE), XTAMPZA™ ER (OXYCODONE EXTENDED-RELEASE), & PROBUPHINE® (BUPRENORPHINE IMPLANT)

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread
Dr. Harrell moved to approve; seconded by Dr. Rhymer

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE VIVLODEX™ (MELOXICAM CAPSULES)

11A: INTRODUCTION

11B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF PREDNISOLONE SPECIAL FORMULATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MILLIPRED™ (PREDNISOLONE SODIUM PHOSPHATE ORAL SOLUTION 10MG/5ML)

12A: INTRODUCTION

12B: CURRENT PRIOR AUTHORIZATION CRITERIA

12C: UTILIZATION OF PREDNISOLONE SPECIAL FORMULATIONS

12D: PRIOR AUTHORIZATION OF PREDNISOLONE SPECIAL FORMULATIONS

- 12E: PREDNISOLONE SPECIAL FORMULATIONS CLAIMS ANALYSIS**
12F: MILLIPRED™ (PREDNISOLONE SODIUM PHOSPHATE ORAL SOLUTION 10MG/5ML) PRODUCT SUMMARY
12G: COLLEGE OF PHARMACY RECOMMENDATIONS
12H: UTILIZATION DETAILS OF PREDNISOLONE SPECIAL FORMULATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)

- 13A: CURRENT PRIOR AUTHORIZATION CRITERIA**
13B: UTILIZATION OF PALIVIZUMAB
13C: PRIOR AUTHORIZATION OF PALIVIZUMAB
13D: SEASON COMPARISON
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ANTIHYPERLIPIDEMICS

- 14A: CURRENT PRIOR AUTHORIZATION CRITERIA**
14B: UTILIZATION OF ANTIHYPERLIPIDEMICS
14C: PRIOR AUTHORIZATION OF ANTIHYPERLIPIDEMICS
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF STATIN MEDICATIONS AND ZETIA® (EZETIMIBE)
14G: UTILIZATION DETAILS OF OMEGA-3 FATTY ACIDS
14H: UTILIZATION DETAILS OF JUXTAPID® (LOMITAPIDE) AND KYNAMRO® (MIPOMERSEN)
14I: UTILIZATION DETAILS OF PCSK9 INHIBITORS
Materials included in agenda packet; presented by Dr. Adams
Dr. Winegardner moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS

- 15A: CURRENT PRIOR AUTHORIZATION CRITERIA**
15B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
15C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF ANTICOAGULANTS
15G: UTILIZATION DETAILS OF PLATELET AGGREGATION INHIBITORS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Preslar moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF DRY EYE DISEASE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE XIIDRA™ (LIFITEGRAST 5% OPHTHALMIC SOLUTION)

- 16A: UTILIZATION OF DRY EYE DISEASE PRODUCTS**
16B: DRY EYE DISEASE
16C: XIIDRA™ (LIFITEGRAST OPHTHALMIC SOLUTION) PRODUCT SUMMARY
16D: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF BUTALBITAL PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ALLZITAL® (BUTALBITAL/ACETAMINOPHEN 25MG/325MG) & ESGIC® CAPSULES BUTALBITAL/ACETAMINOPHEN/CAFFEINE 50MG/325MG/40MG)

- 17A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 17B: UTILIZATION OF BUTALBITAL PRODUCTS**
- 17C: PRIOR AUTHORIZATION OF BUTALBITAL PRODUCTS**
- 17D: PRICING TREND(S)**
- 17E: ALLZITAL® (BUTALBITAL/ACETAMINOPHEN 25MG/325MG) PRODUCT SUMMARY**
- 17F: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 17G: UTILIZATION DETAILS OF BUTALBITAL PRODUCTS**

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: FDA AND DEA UPDATES

Materials included in agenda packet; presented by Dr. Keast

ACTION: NONE REQUIRED

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

- 19A: HEART FAILURE MEDICATIONS**
- 19B: TARGETED IMMUNOMODULATOR AGENTS**
- 19C: BREAST CANCER MEDICATIONS**
- 19D: SKIN CANCER MEDICATIONS**
- 19E: CONSTIPATION AND DIARRHEA MEDICATIONS**
- 19F: TOPICAL CORTICOSTEROIDS**
- 19G: BLADDER CONTROL MEDICATIONS**
- 19H: TOPICAL LIDOCAINE MEDICATIONS**
- 19I: GROWTH HORMONE**

**FUTURE BUSINESS SUBJECT TO CHANGE.*

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: ADJOURNMENT

The meeting was adjourned at 5:20 p.m.



The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: September 15, 2016

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

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

Subject: DUR Board Recommendations From Meeting of September 14, 2016

Recommendation 1: Concomitant Benzodiazepine and Opioid Utilization

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

- Working with the Oklahoma Health Care Authority and the Prescription Drug Fatality Task Force on targeting education to prescribers in specific counties with high rates of overdose death rates or concomitant benzodiazepine and opioid prescribing. Educational interventions may include practice facilitator education to prescribers, targeted educational letters to prescribers (particularly those who have members who are using the same prescriber for both prescriptions), and newsletter articles.
- If targeted educational interventions are ineffective at changing prescriber behaviors, consider implementation of an edit that would require prior authorization for reimbursement of concomitant benzodiazepine and opioid therapy for longer than 90 days. The edit would need to be phased in over a period of time to allow for adequate tapering. The edit would not go into effect until all patient and prescriber groups had been notified. Additionally, medication groups would be selected and implemented over time to ensure a smoother transition.

Recommendation 2: Vote to Prior Authorize Dexilant™ SoluTab (Dexlansoprazole Delayed-Release Orally Disintegrating Tablets)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Dexilant™ SoluTab into Tier-3 of the Anti-Ulcer Product Based Prior Authorization (PBPA) category. Current Tier-3 criteria for this category would apply.

Anti-Ulcer Medications*		
Tier-1	Tier-2	Tier-3
omeprazole (Prilosec®)	dexlansoprazole (Dexilant®)	dexlansoprazole (Dexilant™ SoluTab)
pantoprazole (Protonix®)	lansoprazole (Prevacid® and ODT)	esomeprazole magnesium (Nexium®)
	rabeprazole (Aciphex®)	esomeprazole strontium
		omeprazole suspension (Prilosec®)
		pantoprazole (Protonix® suspension)
		rabeprazole (Aciphex® sprinkles)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).

ODT = orally disintegrating tablet

Anti-Ulcer Medications Tier-2 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 medications titrated up to the recommended dose that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 medications; or
3. An indication not covered by lower tiered medications.

Anti-Ulcer Medications Tier-3 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 and Tier-2 medications that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 and Tier-2 medications; or
3. An indication not covered by lower tiered medications.
4. Special formulations including orally disintegrating tablets (ODTs), sprinkle capsules, granules, suspensions, and solutions for intravenous (IV) use require patient-specific, clinically significant reasoning why the member cannot use standard dosage formulations.

Recommendation 3: Vote to Prior Authorize AK-Tracin® (Bacitracin) and Bleph-10® (Sulfacetamide Sodium) Ophthalmic Ointment

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the ophthalmic antibiotics category:

1. Move AK-Tracin® (bacitracin) ophthalmic ointment and Bleph-10® (sulfacetamide sodium) ophthalmic ointment from Tier-1 to Tier-2 of the Ophthalmic Antibiotic Ointments Tier Chart based on increases in state maximum allowable costs (SMAC). Current Tier-2 criteria for this category will apply.

2. Move Maxitrol® suspension and ointment (neomycin/polymyxin B/dexamethasone) from Tier-2 to Tier-1 of the Ophthalmic Antibiotics/Steroid Combination Products Tier Chart based on low net costs.

Ophthalmic Antibiotics: Liquids		
Tier-1	Tier-2	Tier-3
ciprofloxacin (Ciloxan®)	levofloxacin (Quixin®)	azithromycin (Azasite®)
gentamicin (Gentak®)		besifloxacin (Besivance®)
neomycin/polymyxin B/gramicidin (Neosporin®)		gatifloxacin (Zymaxid®)
ofloxacin (Ocuflox®)		moxifloxacin (Vigamox®, Moxeza®)
polymyxin B/trimethoprim (Polytrim®)		
sulfacetamide sodium (Bleph-10®)		
tobramycin (Tobrex®)		
Ophthalmic Antibiotics: Ointments		
Tier-1	Tier-2	
bacitracin/polymyxin B (AK-Poly-Bac®)	bacitracin (AK-Tracin®)	
erythromycin (Ilotycin™, Roymcin®)	ciprofloxacin (Ciloxan®)	
gentamicin (Gentak®)	sulfacetamide sodium (Bleph-10®, Sodium Sulamyd®)	
neomycin/polymyxin B/bacitracin (Neosporin®)		
tobramycin (Tobrex®)		
Ophthalmic Antibiotics/Steroid Combination Products		
Tier-1	Tier-2	
neomycin/polymyxin B/dexamethasone (Maxitrol®) susp & oint	bacitracin/polymyxin B/neomycin/HC oint	
sulfacetamide/prednisolone 10%-0.23% solution	gentamicin/prednisolone (Pred-G®) susp & oint	
	neomycin/polymyxin B/HC (Cortisporin®) susp	
	sulfacetamide/prednisolone 10%-0.2% (Blephamide®) susp & oint	
	tobramycin/dexamethasone (Tobradex®) susp & oint	
	tobramycin/loteprednol (Zylet®) susp	

oint = ointment; susp = suspension; HC = hydrocortisone

Tier structures based on rebated prices and/or state maximum allowable cost (SMAC).

Ophthalmic Antibiotic Tier-2 Approval Criteria:

1. An approved indication/suspected infection by an organism not known to be covered by Tier-1 products, or failure of a Tier-1 product; or
2. Known contraindication to all indicated Tier-1 medications; or
3. Prescription written by optometrists/ophthalmologists; or
4. When requested medication is being used for pre/post-operative prophylaxis.

Ophthalmic Antibiotic Tier-3 Approval Criteria:

1. An approved indication/suspected infection by an organism not known to be covered by Tier-2 products, or failure of a Tier-2 product; or
2. Known contraindication to all indicated Tier-2 medications; or
3. Prescription written by optometrists/ophthalmologists; or
4. When requested medication is being used for pre/post-operative prophylaxis.

Ophthalmic Antibiotic/Steroid Combination Tier-2 Approval Criteria:

1. Prescription written by optometrists/ophthalmologists; or
2. When requested medication is being used for pre/post-operative prophylaxis.

Recommendation 4: Vote to Prior Authorize Betoptic® (Betaxolol Ophthalmic Solution), Timoptic-XE® (Timolol Maleate Ophthalmic Gel-Forming Solution), & Betimol® (Timolol Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

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

1. Move betaxolol ophthalmic solution (Betoptic®) and timolol maleate ophthalmic gel-forming solution (Timoptic-XE®) to Tier-2 based on an increased state maximum allowable cost (SMAC). The existing Tier-2 criteria for this category will apply.
2. Move Betimol® (timolol ophthalmic solution) to Tier-2 based on increased net cost. The existing Tier-2 criteria for this category will apply.
3. Update the Glaucoma Medications tier chart to remove the discontinued medications: Propine® (dipivefrin), Rescula® (unoprostone), and Izba® (travoprost 0.003%).

Glaucoma Medications*	
Tier-1	Tier-2
Beta-Blockers	
carteolol (Ocupress® 1%)	betaxolol (Betoptic® , Betoptic-S®)
dorzolamide/timolol (Cosopt®)	brimonidine/timolol (Combigan®)
levobunolol (Betagan®)	dorzolamide/timolol (Cosopt® PF)
metipranolol (OptiPranolol®)	timolol (Betimol®)
timolol maleate (Istalol®, Timoptic®)	timolol maleate (Timoptic-XE® , Timoptic Ocadose®)
Prostaglandin Analogs	
latanoprost (Xalatan®)	bimatoprost (Lumigan®)
travoprost 0.004% (Travatan-Z®)	tafluprost (Zioptan™)
	travoprost 0.004% (Travatan®)
	unoprostone (Rescula®)
	travoprost 0.003% (Izba®)
Adrenergic Agonists	
dipivefrin (Propine®)	
Alpha-2 Adrenergic Agonists	
brimonidine 0.2%	apraclonidine (Iopidine®)
brinzolamide/brimonidine (Simbrinza™)	brimonidine (Alphagan-P® 0.1%, 0.15%)
	brimonidine/timolol (Combigan®)
Carbonic Anhydrase Inhibitors	

Glaucoma Medications*	
Tier-1	Tier-2
acetazolamide (Diamox®)+	dorzolamide/timolol (Cosopt® PF)
brinzolamide (Azopt®)	
brinzolamide/brimonidine (Simbrinza™)	
dorzolamide/timolol (Cosopt®)	
dorzolamide (Trusopt®)	
methazolamide (Neptazane®)+	
(*Indicates Available Oral Products)	
Cholinergic Agonists/Cholinesterase Inhibitors	
pilocarpine (Isopto® Carpine, Pilopine HS®)	carbachol (Miostat® 0.01%)
	echothiophate iodide (Phospholine Iodide®)

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation. Please note, combination products are included in both applicable pharmaceutical classes; therefore, are each listed twice in the tier chart.

Recommendation 5: Vote to Prior Authorize Nasarel® (Flunisolide Nasal Spray)

MOTION CARRIED by unanimous approval.

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

1. Move Astelin® (azelastine) and Qnasl® 80mcg (beclomethasone) from Tier-3 to Tier-2 based on state maximum allowable costs (SMAC) and net costs after rebates. The existing criteria for this category will apply.
2. Move flunisolide (Nasalide®, Nasarel®) from Tier-1 to Tier-3 based on increases in SMAC. The existing criteria for this category will apply.
3. Move beclomethasone (Beconase® AQ) from Tier-2 to Tier-1 based on net costs after rebates.
4. Initiate a prescriber/pharmacy mailing or fax to inform providers of Nasal Allergy PBPA category changes.

Nasal Allergy Medications*		
Tier-1	Tier-2	Tier-3
beclomethasone (Beconase® AQ)	azelastine (Astelin®)	azelastine (Astepro®)
fluticasone (Flonase®)	beclomethasone (Qnasl® 80mcg)	azelastine/fluticasone (Dymista®)
		beclomethasone (Qnasl® 40mcg)
		budesonide (Rhinocort AQ®)
		ciclesonide (Omnaris®, Zetonna®)
		flunisolide (Nasalide®, Nasarel®)
		fluticasone (Veramyst®)
		mometasone (Nasonex®)
		olopatadine (Patanase®)

*Tier structure based on rebate participation and/or state maximum allowable cost (SMAC).

Nasal Allergy Medications Tier-2 Approval Criteria:

1. Failure with all Tier-1 medications defined as no beneficial response after at least three weeks use at the maximum recommended dose; or
2. Documented adverse effect or contraindication to all Tier-1 medications.

3. No grandfathering of Tier-2 or Tier-3 medications will be allowed for this category.
4. For 2 to 4 year old members, the age-appropriate, lower-tiered generic medications must be tried prior to the approval of higher tiered medications.
5. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or chronic obstructive pulmonary disease (COPD), in which case authorizations will be for the duration of one year.

Nasal Allergy Medications Tier-3 Approval Criteria:

1. All Tier-2 criteria must be met; and
2. Failure with all available Tier-2 medications defined as no beneficial response after at least three weeks use at the maximum recommended dose; or
3. Documented adverse effect or contraindication to all Tier-2 medications.
4. No grandfathering of Tier-2 or Tier-3 medications will be allowed for this category.
5. For 2 to 4 year old members, the age-appropriate, lower-tiered generic medications must be tried prior to the approval of higher tiered medications.
6. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.

Recommendation 6: Vote to Prior Authorize Ocaliva™ (Obeticholic Acid)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ocaliva™ (obeticholic acid) with the following criteria:

Ocaliva™ (Obeticholic Acid) Approval Criteria:

1. An FDA approved diagnosis of primary biliary cholangitis (PBC); and
2. Member must have taken ursodeoxycholic acid (UDCA) at an appropriate dose for at least one year and prescriber must confirm a lack of improvement in liver function tests **is not caused by a superimposed liver disease, confirm that if the member has a superimposed liver disease it is being adequately treated**, proper timing of bile acid sequestrants if co-administered with UDCA (four hours before or four hours after), and patient compliance with UDCA; and
3. Ocaliva™ must be taken in combination with UDCA. For Ocaliva™ monotherapy consideration, the prescriber must document a patient-specific, clinically significant reason why the member is unable to take UDCA; and
4. A quantity limit of one tablet daily will apply.

Recommendation 7: Vote to Prior Authorize Belbuca™ (Buprenorphine Buccal Film), Dolophine® (Methadone), MorphaBond™ (Morphine Extended-Release), Xtampza™ ER (Oxycodone Extended-Release), & Probuphine® (Buprenorphine Implant)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The placement of Belbuca™ (buprenorphine buccal film), MorphaBond™ (morphine extended-release), and Xtampza™ ER (oxycodone extended-release) into Tier-3 of the Opioid Analgesics Product Based Prior Authorization (PBPA) category. Current Tier-3 criteria for this category will apply.
2. Moving methadone from Tier-1 to Tier-3 of the Opioid Analgesics PBPA category based on CMS recommendations and the disproportionate share of opioid-related overdose deaths associated with methadone when used for pain. Current Tier-3 criteria for this category will apply.
3. The prior authorization of Probuphine® (buprenorphine implant) with the criteria listed in red.

Probuphine® (Buprenorphine Implant) Approval Criteria:

1. An FDA approved diagnosis of maintenance treatment of opioid dependence; and
2. Members must be currently on a maintenance dose of 8mg per day or less of a Subutex® or Suboxone® sublingual tablet or its transmucosal buprenorphine product equivalent; and
3. Member must have been stable on current transmucosal buprenorphine dose (of 8mg per day or less) for three months or longer without any need for supplemental dosing or adjustments; and
4. Members must have had no positive urine toxicology results or paid claims for opioids for the last three months. Concomitant treatment with opioids (including tramadol) will be denied; and
5. Probuphine® must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a DEA (X) number; and
6. Prescribers must verify they have considered the following factors in determining clinical stability and suitability for Probuphine®:
 - a. Period free from illicit opioid drug use
 - b. Stability of living environment
 - c. Participation in a structured activity/job
 - d. Consistency in participation in recommended behavioral therapy/peer support program
 - e. Consistency in compliance with clinic visit requirements
 - f. Minimal to no desire or need to use illicit opioids
 - g. Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis interventions
 - h. Social support system
7. The prescriber must verify enrollment in the Probuphine® Risk Evaluation and Mitigation Strategy (REMS) program; and
8. Approvals will be for one kit (four implants) per six months. Reauthorizations for an additional six months may be granted if the member does not have ongoing use of supplemental dosing with transmucosal buprenorphine or opioid analgesics while utilizing Probuphine®.

Opioid Analgesics*

Tier-1	Tier-2	Tier-3	Special PA
<p>Long-Acting: oxycodone ER 10mg, 15mg, 20mg only (Oxycontin[®])[◇]</p> <p>Short-Acting: ASA/butalbital/caffeine/codeine (Fiorinal with Codeine[®]) codeine codeine/APAP hydrocodone/APAP (Norco[®]) hydrocodone/IBU (Vicoprofen[®], Ibudone[®], Reprexain[™]) hydromorphone (Dilaudid[®]) morphine IR (MSIR[®]) oxycodone IR (Oxy IR[®]) oxycodone/APAP (Percocet[®]) oxycodone/ASA (Percodan[®]) oxycodone/ibuprofen (Combunox[™]) tramadol/APAP (Ultracet[®]) tramadol (Ultram[®])</p>	<p>Long-Acting: buprenorphine (Butrans[®]) fentanyl patches (Duragesic[®]) hydrocodone bitartrate ER (Hysingla[™] ER) morphine ER tablets (MS Contin[®]) oxycodone ER (Oxycontin[®])[◇]</p> <p>Short-Acting: oxymorphone IR (Opana[®]) tapentadol IR (Nucynta[®])</p>	<p>Long-Acting: buprenorphine ER buccal film (Belbuca[™]) hydrocodone bitartrate ER (Zohydro[™] ER) hydromorphone ER (Exalgo[®]) methadone (Dolophine[®]) morphine sulfate ER (Avinza[®]) morphine sulfate ER (Kadian[®]) morphine sulfate ER (MorphaBond[™]) morphine/naltrexone (Embeda[®]) oxycodone ER (Xtampza[™] ER) oxymorphone (Opana[®] ER)⁺ tapentadol ER (Nucynta[®] ER) tramadol ER (Ultram ER[®], Ryzolt[®])</p> <p>Short-Acting: hydrocodone/APAP (Xodol[®], Zamiset[®], Liquicet[®]) hydrocodone/APAP/caffeine (Trezix[™]) oxycodone/APAP (Primlev[™], Xolox[®]) oxycodone (Oxecta[®])</p>	<p>Long-Acting: oxycodone/APAP ER (Xartemis[™] XR)</p> <p>Oncology Only: fentanyl sublingual tablet (Abstral[®]) fentanyl transmucosal lozenge (Actiq[®]) fentanyl buccal tablet (Fentora[®]) fentanyl nasal spray (Lazanda[®]) fentanyl buccal film (Onsolis[®]) fentanyl sublingual spray (Subsys[™])</p>

APAP = Acetaminophen, ASA = Aspirin, IBU = Ibuprofen, IR = Immediate-Release, ER = Extended-Release

*Tier Structure based on supplemental rebate participation and/or state maximum allowable cost. Tier-2 medications subject to move to Tier-3.

[◇]Brand name preferred.

⁺Brand name Opana[®] ER preferred. Generic oxymorphone extended-release tablets require special authorization. The generic formulation is not abuse-deterrent.

- Tier-1 products are covered with no prior authorization necessary.
- Members with an oncology-related diagnosis are exempt from the prior authorization process, and do not require pain contracts.
- Only one long-acting and one-short acting agent can be used concurrently.
- Short-acting, solid dosage formulation products are limited to a quantity of four units per day or a quantity of 120 units per 30 days.
- An age restriction applies on oral liquid narcotic analgesic products for all members older than 12 years of age and oral solid dosage forms for all members younger than 10 years of age.

Opioid Analgesics Tier-2 Approval Criteria:

1. A documented 30-day trial/titration period with at least one Tier-1 medication(s) within the last 90 days is required for a Tier-2 long-acting medication; or
2. A documented 30-day trial with at least two Tier-1 short-acting medications within the last 90 days is required for a Tier-2 short-acting medication; or
3. A chronic pain diagnosis requiring time-released medication (for long-acting medication requests).

Opioid Analgesics Tier-3 Approval Criteria:

1. A documented 30-day trial with at least two Tier-2 long-acting medications within the last 90 days is required for approval of a long-acting Tier-3 medication; or
2. A documented 30-day trial with at least two Tier-2 short-acting medications within the last 90 days is required for approval of a Tier-3 short-acting medication; or
3. A documented allergy or contraindication to all available Tier-2 medications.

Recommendation 8: Vote to Prior Authorize Vivlodex™ (Meloxicam Capsules)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The placement of Vivlodex™ (meloxicam capsules) into the Special Prior Authorization (PA) Tier of the NSAID Product Based Prior Authorization (PBPA) category. Current Special PA criteria for this category will apply.
2. The addition of an age restriction on meloxicam suspension. Members older than 7 years of age would require a reason why they need the liquid formulation and cannot use the oral tablet formulation.
3. Move indomethacin 25mg and 50mg immediate-release capsules from the Special PA Tier to Tier-1. A quantity limit of eight capsules per day would apply. The suspension and extended-release formulation would remain in the Special PA Tier.
 - a. Indomethacin capsules were previously included in the Special PA Tier due to a poor adverse effect profile compared to other NSAIDs. Due to the low net cost of indomethacin and similar adverse effect profile to other non-selective NSAIDs the College of Pharmacy recommends moving indomethacin to Tier-1.
4. Move piroxicam capsules from the Special PA Tier to Tier-2 based on decreases in state maximum allowable cost (SMAC). The current Tier-2 criteria for this category will apply.

NSAIDs Tier-2 Approval Criteria:

1. Previous use of at least two Tier-1 NSAID products (from different product lines) plus a proton pump inhibitor (PPI) within the last 120 days; or
2. For those with a prior gastrointestinal (GI) bleed who must have an NSAID, a Tier-2 product may be approved (celecoxib should be taken with a PPI).

NSAIDs Special Prior Authorization (PA) Approval Criteria:

1. A unique indication for which a Tier-1 or Tier-2 medication is not appropriate; or
2. Previous use of at least two Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 product.
4. Additionally, use of Tivorbex™ will require a patient-specific, clinically significant reason why the member cannot use all other available generic indomethacin products.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier-1	Tier-2	Special PA
diclofenac ER (Voltaren® XR)	celecoxib (Celebrex®)	diclofenac (Zorvolex®)
diclofenac potassium (Cataflam®)	diclofenac sodium/ misoprostol (Arthrotec®)	diclofenac epolamine (Flector® patch)
diclofenac sodium (Voltaren®) 50mg and 75mg tablets	diclofenac sodium (Voltaren®) 25mg tablets	diclofenac potassium (Cambia® powder pack)
etodolac (Lodine®) 400mg and 500mg tablets	etodolac (Lodine®) 200mg and 300mg capsules	diclofenac potassium (Zipsor® capsule)
flurbiprofen (Ansaid®)	etodolac ER (Lodine® XL)	diclofenac sodium (Dyloject™)
ibuprofen (Motrin®)	fenoprofen (Nalfon®)	diclofenac sodium (Pennsaid® topical drops)
indomethacin immediate-release capsules (Indocin®)	meclofenamate (Meclomen®)	diclofenac sodium (Voltaren Gel®)
ketoprofen (Orudis®)	naproxen sodium (Anaprox®) 275mg and 550mg tablets	ibuprofen/famotidine (Duexis®)
meloxicam (Mobic®)	oxaprozin (Daypro®)	indomethacin suspension and extended-release capsules (Indocin®)
nabumetone (Relafen®)	piroxicam (Feldene®)	indomethacin (Tivorbex™)
naproxen (Naprosyn®)	tolmetin (Tolectin®)	ketoprofen ER (Oruvail®)
naproxen EC (Naprosyn®)		mefenamic acid (Ponstel®)
sulindac (Clinoril®)		meloxicam capsules (Vivlodex™)
		naproxen sodium ER (Naprelan®)
		naproxen/esomeprazole (Vimovo®)

ER = Extended-Release, EC = Enteric Coated

Tier structure based on supplemental rebate participation and/or state maximum allowable cost.

Recommendation 9: Annual Review of Prednisolone Special Formulations and 30-Day Notice to Prior Authorize Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Synagis® (Palivizumab)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Antihyperlipidemics

MOTION CARRIED by unanimous approval.

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

1. Update the Statin Medications and Zetia® (ezetimibe) tier chart and criteria to remove the discontinued medications, Simcor® (simvastatin/niacin CR) and Advicor® (lovastatin/niacin CR).

2. Add a clinical exception for Crestor® (rosuvastatin) for pediatric members with homozygous familial hypercholesterolemia (HoFH) based on the newly expanded indication. None of the current Tier-1 statin medications are indicated for the treatment of pediatric HoFH.
3. Update the PCSK9 Inhibitors criteria to reflect the new dosage form available for Repatha® (evolocumab).
4. Monitor the state maximum allowable cost (SMAC) of generic rosuvastatin and move it to Tier-1 once the SMAC has stabilized and is comparable to other Tier-1 statin medications.

Statin Medications and Zetia® (Ezetimibe)*		
Tier-1	Tier-2	Special PA
atorvastatin (Lipitor®)	ezetimibe (Zetia®)	fluvastatin (Lescol® & Lescol® XL)
lovastatin (Mevacor®)	rosuvastatin (Crestor®) [†]	lovastatin (Altoprev®)
pravastatin (Pravachol®)		lovastatin/niacin CR (Advicor®)
simvastatin (Zocor®)		pitavastatin (Livalo®)
		simvastatin/ezetimibe (Vytorin®)
		simvastatin/niacin CR (Simcor®)

*Tier structure based on state maximum allowable cost (SMAC) and/or supplemental rebate participation.

[†]Crestor® 5mg and Crestor® 10mg require special reason for use.

CR = controlled-release

Statin Medications and Zetia® (Ezetimibe) Tier-2 Approval Criteria:

1. Member must have a documented trial with atorvastatin, consisting of at least 8 weeks of continuous therapy titrated to 40mg, which did not yield adequate LDL reduction. The minimum starting dose of the Tier-2 medication may only be at the moderate-to-high LDL lowering doses (20mg rosuvastatin or higher); or
2. A documented adverse effect or contraindication to all available lower tiered products; or
3. A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high-risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome, **or for pediatric members with homozygous familial hypercholesterolemia (HoFH)**; and
4. Clinical exceptions for Zetia® (ezetimibe) include the following:
 - a. Documented active liver disease; or
 - b. Documented unexplained, persistent elevations of serum transaminases; or
 - c. Documented statin-related myopathy.

Statin Medications and Zetia® (Ezetimibe) Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used; **and**
 - ~~a. Simcor® (simvastatin/niacin) and Advicor® (lovastatin/niacin) will also require a patient-specific, clinically significant reason why the member cannot use the individual products separately.~~

PCSK9 Inhibitors Approval Criteria:

1. An FDA approved diagnosis of heterozygous familial hypercholesterolemia (HeFH) defined by the presence of one of the following criteria:
 - a. A documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or

- b. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or
- 2. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
 - a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
 - b. An untreated total cholesterol greater than 500mg/dL and at least one of the following:
 - i. Documented evidence of definite HeFH in both parents; or
 - ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
- 3. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
 - a. High cardiovascular risk confirmed by Framingham risk score; and
 - i. Supporting diagnoses/conditions signifying this risk level; or
 - b. Documented history of Coronary Heart Disease (CHD); and
 - i. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and
- 4. Member must be 18 years of age or older for the diagnosis of HeFH or clinical atherosclerotic cardiovascular disease, or must be 13 years of age or older for the diagnosis of HoFH; and
- 5. Member must be on high-dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
 - a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
 - b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
 - c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
 - d. Tier structure rules still apply; and
- 6. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
- 7. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
- 8. ~~Repatha® requests for the dosing regimen of 420mg once monthly require a diagnosis of HoFH or require a patient-specific, clinically significant reason why the member cannot use Repatha® at the dosing regimen of 140mg every 2 weeks; and~~
- 9. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent®. A quantity limit of 2 syringes or autoinjectors per 28 days will apply for Repatha® 140mg and a quantity limit of one autoinjector per 28 days for Repatha® 420mg. ~~Patients with the diagnosis of HoFH needing 3 Repatha® syringes or autoinjectors per 30 days (for the dosing regimen of 420mg once monthly) will be approved for a quantity limit override upon meeting PCSK9 inhibitors approval criteria. Patients requesting Repatha® 420mg strength will not be approved for multiple 140mg syringes but instead should use one 420mg autoinjector.~~
- 10. Initial approvals will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the

effectiveness of this medication, and compliance will be checked at that time and every six months thereafter for continued approval.

Recommendation 12: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the Pradaxa® (dabigatran), Brilinta® (ticagrelor), Xarelto® (rivaroxaban), and Effient® (prasugrel) approval criteria as seen in red:

Pradaxa® (Dabigatran) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
 - a. Non-valvular atrial fibrillation; or
 - b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with a parenteral anticoagulant for 5 to 10 days; or
 - c. To reduce the risk of recurrent DVT or PE in patients who have been previously treated; or
 - d. **For the prophylaxis of DVT and PE in patients who have undergone hip replacement surgery.**

Brilinta® (Ticagrelor) Approval Criteria:

1. The first 90 days of therapy do not require prior authorization.
2. Approved diagnostic criteria include:
 - a. Acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction) with or without percutaneous coronary intervention (PCI); or
 - b. **History of myocardial infarction (MI); and**
3. Approvals will be for the duration of one year.

Xarelto® (Rivaroxaban) Approval Criteria:

1. Approved diagnostic criteria: non-valvular atrial fibrillation, **treatment** of deep vein thrombosis (DVT), pulmonary embolism (PE), to reduce the risk of recurrent DVT and PE, **or for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery.**
2. Xarelto® (rivaroxaban) 15mg and 20mg:
 - a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required.
3. Xarelto® (rivaroxaban) 10mg:
 - a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use in patients following hip or knee replacement surgery.

Effient® (Prasugrel) Approval Criteria:

1. The first 90 days of therapy do not require prior authorization; and
2. Approved diagnostic criteria: unstable angina/non-ST-segment elevated myocardial infarction (UA/non-STEMI) and ST-segment elevated myocardial infarction (STEMI)

- patients who are to be managed with percutaneous coronary intervention (PCI), primary or delayed (stent placement); and
3. Effient® (prasugrel) will not be approved for members with the following situations:
 - a. Coronary Artery Bypass Graft surgery (CABG); or
 - b. Members with a history of transient ischemic attack (TIA) or stroke; and
 4. Members greater than 75 years of age will generally not be approved without supporting information; and
 5. Approvals will be for the duration of one year.
 6. ~~After the end of 15 months, prescribers should provide supporting information for the continuation of this product.~~

Recommendation 13: Annual Review of Dry Eye Disease Products and 30-Day Notice to Prior Authorize Xiidra™ (Lifitegrast 5% Ophthalmic Solution)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Butalbital Products and 30-Day Notice to Prior Authorize Allzital® (Butalbital/Acetaminophen 25mg/325mg) & Esgic® Capsules (Butalbital/Acetaminophen/Caffeine 50mg/325mg/40mg)

NO ACTION REQUIRED.



Mercy Clinic
Pediatrics

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Nancy Nesser, Pharm.D.

It has been brought to my attention that the DUR committee will be reviewing the criteria for Synagis prophylaxis for babies 29-32 week gestation. I am a pediatrician that cares for infants that are at an increased risk for RSV. I know that there has been much controversy regarding the use of Synagis in preterm infants and don't understand why Synagis is not being utilized in such high risk infants born 29-32 week gestation. While the guidelines put forth by the AAP came out in 2014, the DHCA did not adopt them until this last RSV season. Since these changes have been made RSV hospitalizations, ICU admissions and invasive mechanical ventilations have dramatically increased since that decision to eliminate infants greater than 29 weeks gestational age. I believe there are great benefits to continue using Synagis for infants 29-32 weeks gestation and would ask that the DUR Board of Directors accept recommendations for including infants 29-32 weeks gestation.

Respectfully,

Dr Derek Landis M.D.



Appendix B



2017 Drug Utilization Review Board Meeting Dates

**Oklahoma Health Care Authority
October 2016**

Meetings are held the second Wednesday of every month at 4:00 PM

January 11, 2017

February 8, 2017

March 8, 2017

April 12, 2017

May 10, 2017

June 14, 2017

July 12, 2017

August 9, 2017

September 13, 2017

October 11, 2017

November 8, 2017

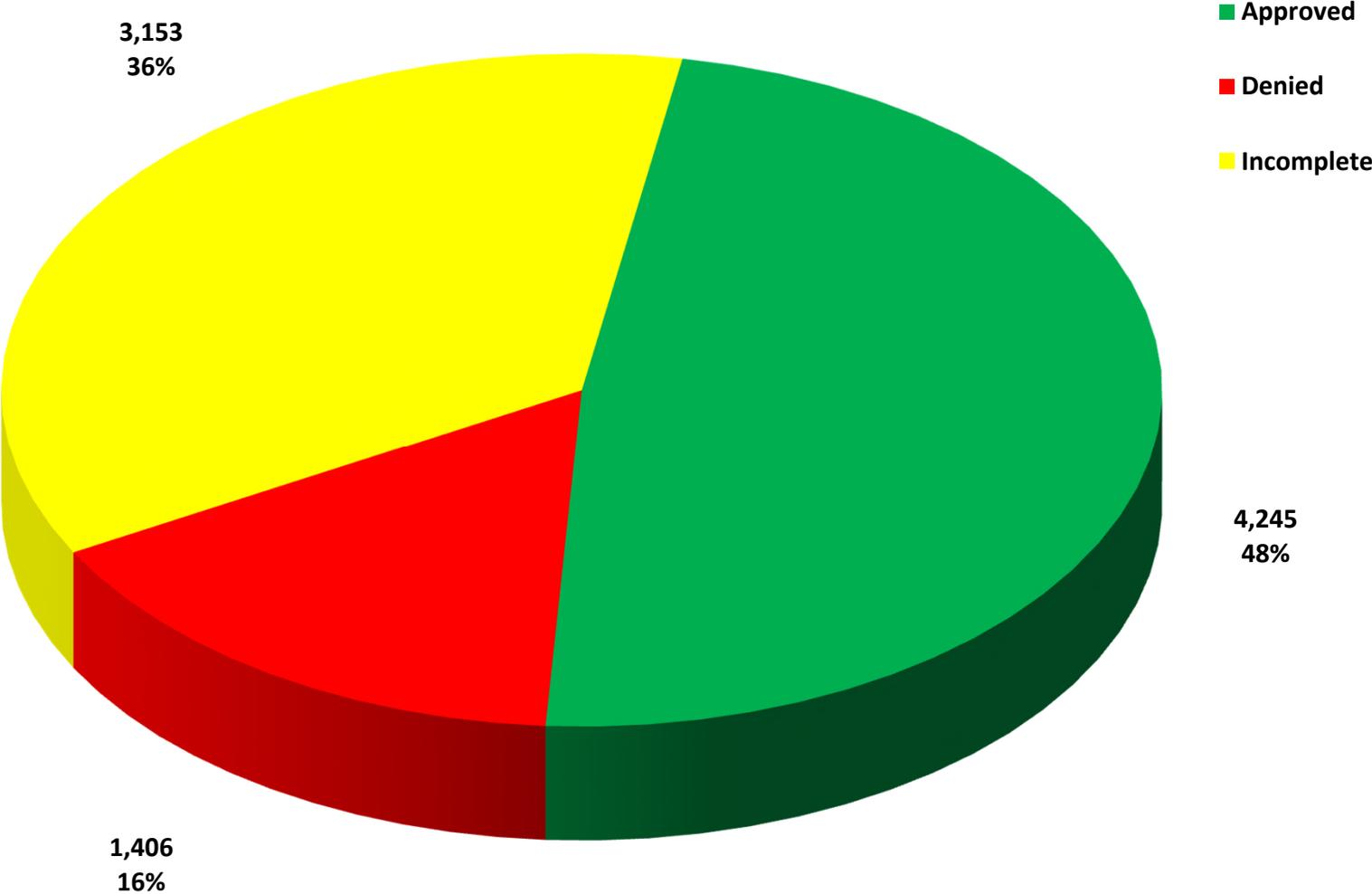
December 13, 2017



Appendix C

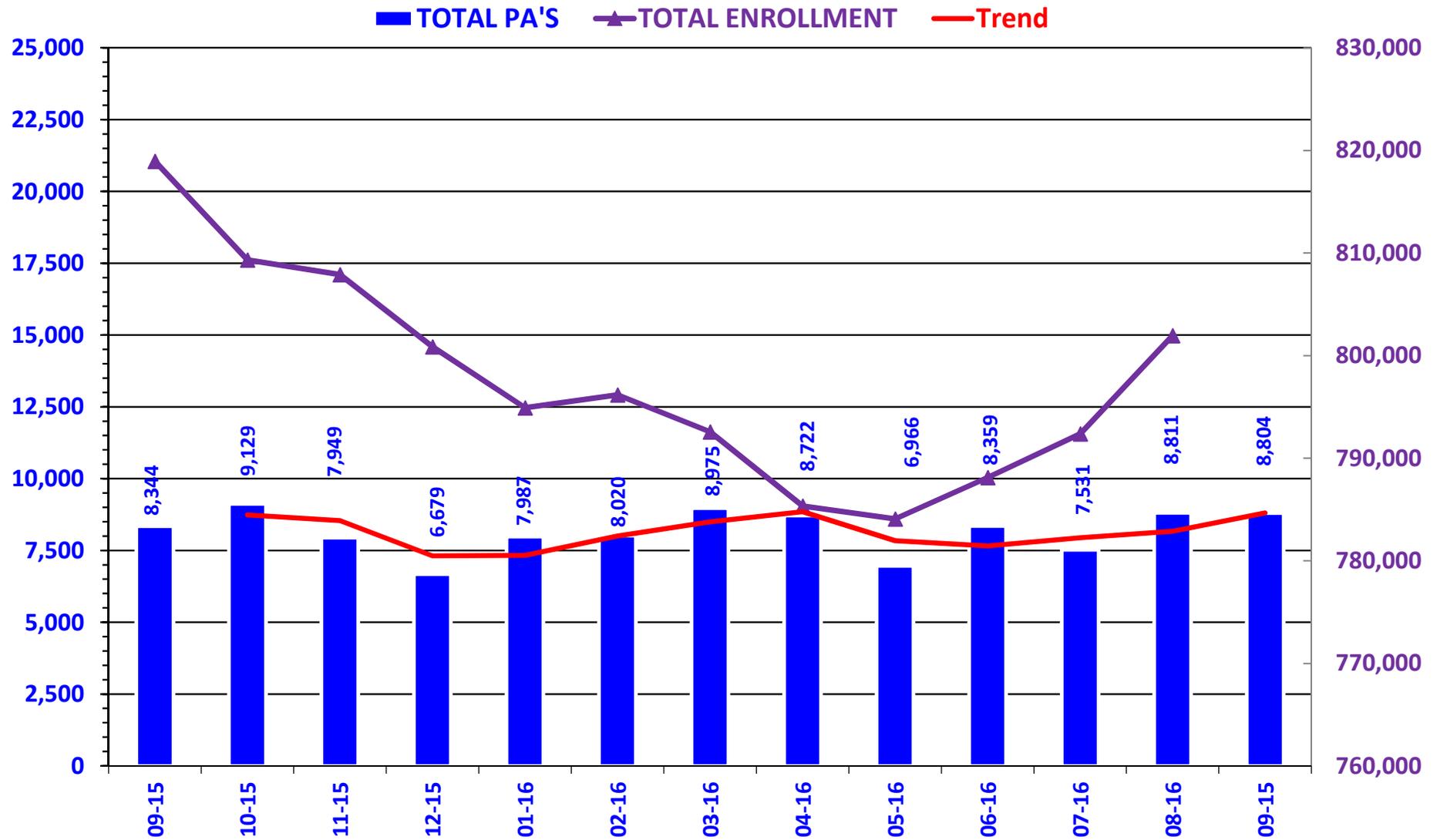


PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER 2016



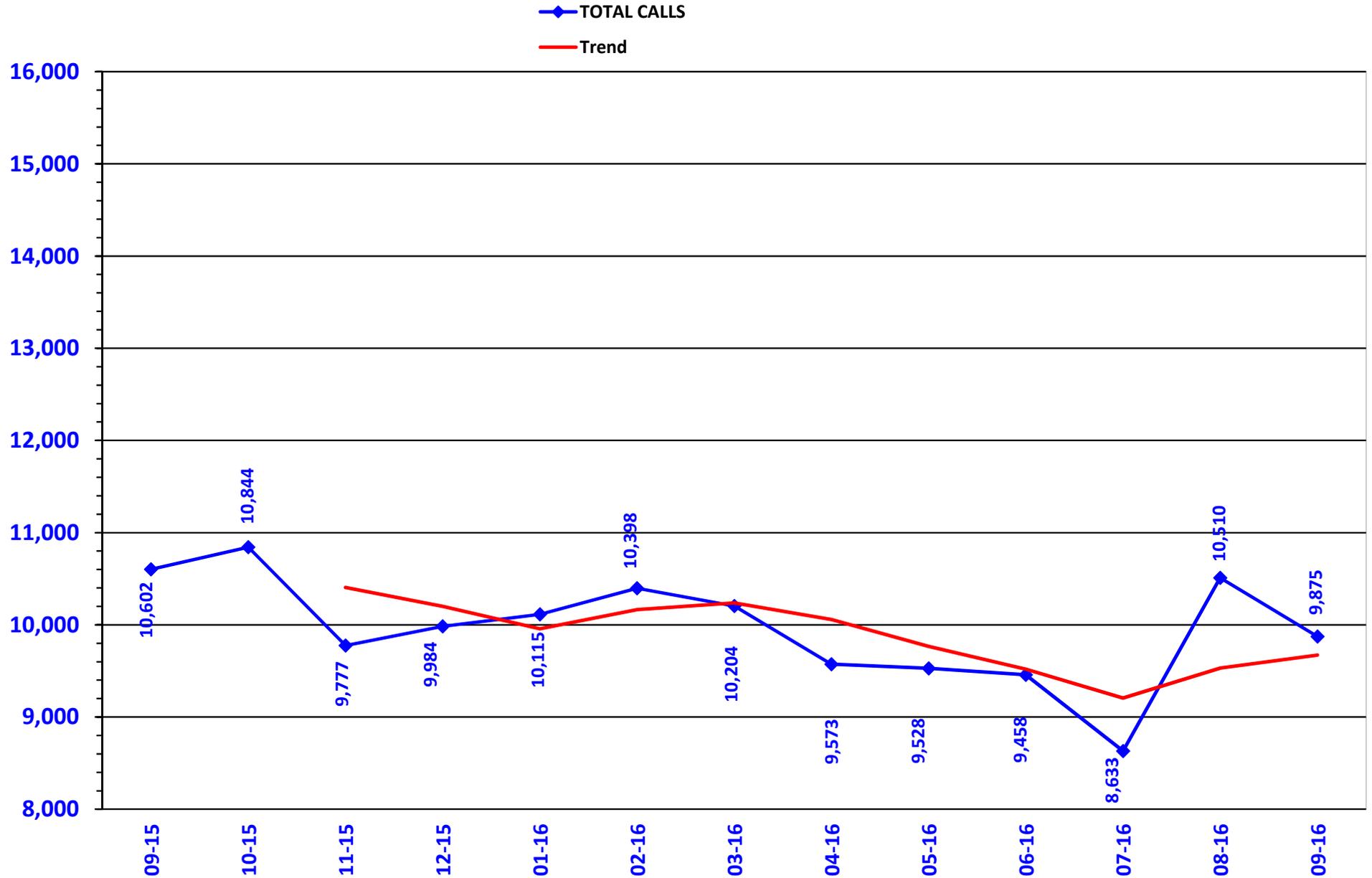
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2015 – SEPTEMBER 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: SEPTEMBER 2015 – SEPTEMBER 2016



Prior Authorization Activity
9/1/2016 Through 9/30/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	437	161	84	192	349
Analgesic - NonNarcotic	30	0	8	22	0
Analgesic - Narcotic	818	458	58	302	161
Angiotensin Receptor Antagonist	15	4	5	6	358
Antiasthma	113	38	20	55	318
Antibiotic	18	6	0	12	184
Anticonvulsant	134	61	26	47	314
Antidepressant	74	11	23	40	298
Antidiabetic	220	85	31	104	351
Antifungal	13	0	3	10	0
Antigout	16	7	0	9	270
Antihistamine	210	162	14	34	352
Antimigraine	52	8	11	33	232
Antineoplastic	20	13	0	7	167
Antiulcers	195	53	61	81	184
Antiviral	47	22	15	10	13
Anxiolytic	76	43	10	23	293
Atypical Antipsychotics	371	212	45	114	328
Biologics	97	44	21	32	297
Bladder Control	56	11	19	26	357
Blood Thinners	198	121	21	56	318
Botox	50	36	9	5	349
Buprenorphine Medications	269	199	14	56	76
Cardiovascular	66	27	11	28	283
Chronic Obstructive Pulmonary Disease	93	15	32	46	334
Constipation/Diarrhea Medications	157	28	63	66	188
Contraceptive	16	12	1	3	357
Dermatological	109	19	67	23	93
Diabetic Supplies	538	305	17	216	196
Endocrine & Metabolic Drugs	70	51	1	18	131
Erythropoietin Stimulating Agents	27	15	3	9	104
Fibromyalgia	163	25	89	49	349
Fish Oils	23	1	11	11	358
Gastrointestinal Agents	123	23	40	60	97
Growth Hormones	74	62	4	8	150
Hematopoietic Agents	38	13	11	14	43
Hepatitis C	100	59	25	16	7
HFA Rescue Inhalers	75	18	22	35	339
Insomnia	48	6	23	19	121
Insulin	76	16	21	39	334
Miscellaneous Antibiotics	26	0	3	23	0
Multiple Sclerosis	59	27	8	24	202
Muscle Relaxant	58	13	20	25	102
Nasal Allergy	73	18	16	39	251
Neurological Agents	40	33	1	6	311
NSAIDs	193	27	60	106	233
Ocular Allergy	35	10	7	18	87
Ophthalmic Anti-infectives	10	2	3	5	12
Ophthalmic NSAIDs	12	1	3	8	146
Osteoporosis	16	7	5	4	306
Other*	309	53	88	168	209
Otic Antibiotic	23	1	3	19	3
Pediculicide	15	4	2	9	13

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Prenatal Vitamins	10	0	1	9	0
Statins	41	14	8	19	337
Stimulant	953	464	112	377	338
Testosterone	56	17	15	24	354
Topical Antifungal	18	1	6	11	57
Topical Corticosteroids	133	7	40	86	166
Vitamin	47	20	16	11	357
Pharmacotherapy	81	73	0	8	271
Emergency PAs	0	0	0	0	
Total	7,533	3,242	1,356	2,935	

Overrides

Brand	60	35	6	19	311
Diabetic Supplies	3	1	0	2	357
Dosage Change	354	327	0	27	12
High Dose	7	7	0	0	232
Ingredient Duplication	44	36	0	8	9
Lost/Broken Rx	90	83	1	6	10
NDC vs Age	34	31	1	2	224
Nursing Home Issue	66	66	0	0	10
Opioid Quantity	14	11	2	1	135
Other*	39	37	1	1	19
Quantity vs. Days Supply	511	329	32	150	250
STBS/STBSM	20	16	2	2	66
Stolen	14	10	3	1	12
Temporary Unlock	1	1	0	0	9
Third Brand Request	31	25	4	2	12
Overrides Total	1,271	1,003	50	218	
Total Regular PAs + Overrides	8,804	4,245	1,406	3,153	

Denial Reasons

Unable to verify required trials.	2,503
Does not meet established criteria.	1,430
Lack required information to process request.	613

Other PA Activity

Duplicate Requests	621
Letters	8,223
No Process	6
Changes to existing PAs	860
Helpdesk Initiated Prior Authorizations	679
PAs Missing Information	33

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

Long-Acting Beta Agonist Utilization: Pediatric Members

Oklahoma Health Care Authority

October 2016

Introduction¹

The Drug Utilization Review (DUR) Board requested a review of claims for pediatric SoonerCare members utilizing single component Long-Acting Beta₂ Agonists (LABA) in late 2014. The claims analysis was conducted and presented to the DUR Board in February 2015. The following report is an update to ensure appropriate utilization is still in effect.

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

Claims Analysis

The claims analysis included members 18 years of age and younger with a paid claim for a single-component LABA. The review period was for one year and members with a single-component LABA medication claim were further evaluated for a single-component ICS medication during the same month.

Results

30

Members had a paid claim for a single-component LABA medication.*

12

Members (of the 30) did not have a paid claim for an ICS during the same month as the LABA medication. Half of the 12 members had only one paid claim for a LABA medication.

6

Members (of the 12) had more than one paid claim for a LABA medication; the maximum number of claims was eight (written by a pediatric pulmonologist).

1

Member (of the 12) had a paid claim for a LABA medication within the last 90 days (this member has had only one paid claim for a LABA medication).

*Some of the 30 members were using nebulized Perforomist® (formoterol fumarate), a single-component LABA, with nebulized Pulmicort® (budesonide), a single-component ICS, because they required nebulized therapy due to the inability to utilize a hand-held actuation device.

Recommendations

SoonerCare claims analysis of pediatric utilization of single-component LABA medications did not reveal a pressing need for intervention. The results of this analysis are similar to the number of members found in February 2015. Most pediatric members utilizing single-component LABA medications required a unique dosage formulation, had only one paid claim for a single-component LABA, or were being followed by a pulmonary specialist. Based on these findings the College of Pharmacy does not recommend any changes to the current LABA criteria at this time.

¹ U.S. Department of Health and Human Services and National Heart Lung and Blood Institute. Guidelines from the National Asthma Education and Prevention Program: Diagnosing and Managing Asthma. Available online at: https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf. Last revised 09/2011. Last accessed 09/23/2016.



Appendix D



Vote to Prior Authorize Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL)

Oklahoma Health Care Authority
October 2016

Introduction^{1,2,3,4}

- The Drug Utilization Review (DUR) board voted to prior authorize Veripred™ 20 (prednisolone sodium phosphate oral solution 20mg/5mL) and Orapred ODT® (prednisolone sodium phosphate orally disintegrating tablet) in March 2013. The prior authorization of Orapred ODT® was implemented in 2013, however the prior authorization of Veripred™ 20 was not implemented until October 2015. In March 2013, the estimated acquisition cost (EAC) of Veripred™ 20 was \$0.89 per milliliter and although higher in cost, it did not significantly differ from other prednisolone oral solutions. Since that time the price per milliliter of Veripred™ 20 has increased by 500% resulting in a cost of \$5.34 per milliliter. Similarly, the EAC of Millipred™ (prednisolone sodium phosphate oral solution 10mg/5mL) increased from \$0.35 per milliliter to \$3.75 per milliliter, an increase of 971%.
- Veripred™ 20 and Millipred™ are both alcohol-free medications. Some generic prednisolone oral solution products are alcohol-free while the remainder contain anywhere from 1.8% to 5% alcohol. If prescribers are concerned about the alcohol content of a generic prednisolone oral solution, they would have to work with their pharmacy to ensure an alcohol-free, generic formulation was selected. Despite implementation of prior authorization of two alcohol-free products, Veripred™ 20 and Millipred™, the number of claims for alcohol-free, generic prednisolone oral solution products increased significantly leading to an increase in overall alcohol-free claims (Pre: 8,327 to Post: 14,868) without a significant change in the overall percentage of alcohol-free claims (Pre: 28.12% to Post: 27.38%). The most significant change was in the cost difference of the alcohol-free claims between the two seasons (Pre: \$957,138.01 to Post: \$161,976.69).
- The poor palatability of the generic prednisolone oral solution products may reduce compliance and subsequently increase emergency room visits for asthma patients unwilling to take them. Emergency room visits were evaluated by season, October 1st to March 31st, both before and after prior authorization. Members 10 years and younger were included in the analysis if they had a paid claim for a prednisolone oral solution (brand or generic) product within 10 days prior to a claim for an emergency room visit which listed asthma in one of the first three diagnosis fields. The proportion of emergency room visits for patients receiving a prednisolone oral solution medication remained similar in the season post prior authorization implementation (Pre: 0.45% to Post: 0.43%).

Cost Comparison:

Product	Strength	Cost Per mL	Cost Per 10 Days ^Δ	Average Cost Per Claim in FY2016
Millipred™ oral solution	10mg/5mL	\$3.75⁺	\$375.00	\$151.11
Veripred™ 20 oral solution	20mg/5mL	\$5.34 ⁺	\$267.00	\$173.98
prednisolone oral solution	5mg/5mL	\$0.61 [*]	\$122.00 [◊]	\$32.84
prednisolone oral solution	15mg/5mL	\$0.11 [*]	\$7.70	\$7.62
prednisolone oral solution	25mg/5mL	\$1.02 [*]	\$40.80	\$34.69

Costs do not reflect rebated prices or net costs.

⁺Costs based on estimated acquisition cost (EAC).

^{*}Costs based on state maximum allowable cost (SMAC).

^Δ Costs based on a regimen of 20mg prednisolone per day for 10 days.

[◊]Members requiring 20mg doses would typically use a higher strength solution to limit volume of solution required.

Recommendations

The College of Pharmacy recommends the prior authorization of Millipred™ (prednisolone sodium phosphate oral solution 10mg/5mL) with criteria similar to Veripred™ 20 (prednisolone sodium phosphate oral solution 20mg/5mL). The recommended criteria can be seen below with additions noted in red.

Veripred™ 20 (Prednisolone Sodium Phosphate Oral Solution 20mg/5mL) and Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL) Approval Criteria:

1. Authorization of Veripred™ 20 **or** Millipred™ requires a patient-specific, clinically significant reason why the member cannot use a tablet or an alternative strength liquid formulation.

¹ Ishizaka T, Okada S, et al. Suppression of bitterness and improvement of palatability of commercial prednisolone powder. *Chemical and Pharmaceutical Bulletin*. 2008; 56(10):1395-9.

² Ortiz B. U.S. Food and Drug Administration (FDA). Giving Medicine to Children. Available online at: <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm291741.htm>. Last revised 10/2015. Last accessed 09/23/2016.

³ Schmitt BD. Pediatric Advisor: Medicines: Helping Children Swallow Them. RelayHealth. Available online at: http://advisor.chsys.org/crsfiles/pa/pa_swallmed_hhg.htm. Last revised 06/2010. Last accessed 09/23/2016.

⁴ Millipred™ Prescribing Information. Zylera Pharmaceuticals. Available online at: http://www.zylera.com/wp-content/uploads/2016/06/Millipred-Tablet-PI_062116.pdf. Last revised 11/2015. Last accessed 09/23/2016.



Appendix E



Vote to Prior Authorize Xiidra™ (Lifitegrast 5% Ophthalmic Solution)

Oklahoma Health Care Authority
October 2016

Introduction¹

Xiidra™ (lifitegrast ophthalmic solution) is a lymphocyte function-associated antigen-1 (LFA-1) antagonist indicated for the treatment of the signs and symptoms of dry eye disease (DED). Lifitegrast blocks the interaction of LFA-1 with its cognate ligand intercellular adhesion molecule-1 (ICAM-1). ICAM-1 may be overexpressed in corneal and conjunctival tissues in dry eye disease. LFA-1/ICAM-1 interaction can contribute to the formation of an immunological synapse resulting in T-cell activation and migration to target tissues. Lifitegrast may inhibit T-cell adhesion to ICAM-1 in a human T-cell line and may inhibit secretion of inflammatory cytokines. Lifitegrast is available as a 5% ophthalmic solution. The recommended dosing is one drop into each eye twice daily, approximately 12 hours apart. The estimated acquisition cost (EAC) of Xiidra™ and Restasis® (cyclosporine ophthalmic emulsion) is \$7.51 per vial with a 30 day supply costing \$450.60. It is important to note, however, that Restasis® has been available since 2002 resulting in a significant federal rebate. The price difference between the two products is substantial when the rebate is taken into account.

Recommendations

The College of Pharmacy recommends the prior authorization of Xiidra™ (lifitegrast ophthalmic solution) with the following criteria:

Xiidra™ (Lifitegrast Ophthalmic Solution) Approval Criteria:

1. Member must be 17 years of age or older and have an FDA approved diagnosis of dry eye disease (DED); and
2. Prescriber must verify that environmental factors (e.g. humidity, fans) have been addressed; and
3. Member must have trials with at least three over-the-counter (OTC) products for three days in the last 30 days that failed to relieve signs and symptoms of dry eyes; and
4. A patient-specific, clinically significant reason why the member cannot use Restasis® (cyclosporine ophthalmic emulsion), which is available without a prior authorization; and
5. A quantity limit of two vials per day will apply.

¹ Xiidra™ Prescribing Information. Shire US, Inc. Available online at: http://www.shirecontent.com/PI/PDFs/Xiidra_USA_ENG.pdf. Last revised 07/2016. Last accessed 09/2016.



Appendix F



Vote to Prior Authorize Allzital® (Butalbital/Acetaminophen 25mg/325mg) & Esgic® Capsules (Butalbital/Acetaminophen/Caffeine 50mg/325mg/40mg)

Oklahoma Health Care Authority
October 2016

Introduction¹

Allzital® (butalbital/acetaminophen 25mg/325mg) was approved by the U.S. Food and Drug Administration (FDA) on December 4, 2015. There are no unexpired patents for this product; however, this strength combination is only available as a brand name product. It is a combination drug product intended as a treatment for tension (or muscle contraction) headache. It consists of a fixed combination of butalbital and acetaminophen. The recommended dose is two tablets by mouth every four hours, not to exceed 12 tablets daily. The estimated acquisition cost (EAC) of Allzital® is \$12.70 per tablet with a 30 day supply costing \$457.20 (based on the recommended dosing). The state maximum allowable cost (SMAC) of similar generics is significantly less. The price of butalbital/acetaminophen (50mg/325mg) is \$1.28 per tablet and the price of butalbital/acetaminophen/caffeine (50mg/325mg/40mg) is \$0.75 per tablet. This results in a 30 day supply costing \$23.04 and \$13.50, respectively.

Based on the current SMAC, updated August 2016, the price for Esgic® capsules (butalbital/acetaminophen/caffeine 50mg/325mg/40mg) is \$1.58 per capsule. After the SMAC update in August 2016, the price of Fioricet® tablets (butalbital/acetaminophen/caffeine 50mg/325mg/40mg) is \$0.75 per tablet. This results in a price difference of 71.25% between the tablet and capsule formulation. Additionally, the capsule formulation has increased by 172.41% since September 2013.

Recommendations

The College of Pharmacy recommends the following changes to the Butalbital Products category:

1. The prior authorization of Allzital® (butalbital/acetaminophen 25mg/325mg) with criteria similar to the other butalbital containing medications.
 - a. An FDA approved indication for the treatment of tension-type headache; and
 - b. Member must be 12 years of age or older; and
 - c. Failure within the previous 60 days of the following:
 - i. All available formulations of butalbital/acetaminophen medications that do not require prior authorization (medications available without prior authorization contain butalbital/acetaminophen/caffeine in the standard 50mg/325mg/40mg dose); and

- ii. Trials of at least two nonsteroidal anti-inflammatory drugs (NSAIDs), unless contraindicated.
- 2. The prior authorization of Esgic® capsules (butalbital/acetaminophen/caffeine 50mg/325mg/40mg) based on SMAC with the following criteria:
 - a. A patient-specific, clinically significant reason why the member cannot use Fioricet® tablets (butalbital/acetaminophen/caffeine 50mg/325mg/40mg).

¹ Allzital® Prescribing Information. Larken Laboratories, Inc. Available online at: <http://medlibrary.org/lib/rx/meds/butalbital-and-acetaminophen-6/>. Last revised 12/10/2015. Last accessed 09/2016.



Appendix G



Fiscal Year 2016 Annual Review of Breast Cancer Medications

Oklahoma Health Care Authority

October 2016

Introduction^{1,2,3,4,5}

Kadcyla[®] (ado-trastuzumab), Halaven[®] (eribulin), Afinitor[®] (everolimus), Ixempra[®] (ixabepilone), Tykerb[®] (lapatinib), Ibrance[®] (palbociclib), and Perjeta[®] (pertuzumab) were voted to be prior authorized by the Drug Utilization Review (DUR) Board in October and December 2015. The prior authorization was subsequently implemented after several notifications in March 2016.

According to the National Cancer Institute, in 2016 an estimated 1,658,210 new cases of cancer will be diagnosed in the United States. Breast cancer is the most common cancer found in women with an estimated 436,660 new cases in 2016. The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Breast cancer can also begin in the cells of the lobules and in other tissues in the breast. Invasive breast cancer is breast cancer that has spread from where it began in the ducts or lobules to surrounding tissue. Traditional chemotherapy has long been used to treat breast cancer, but in more recent years targeted chemotherapy is being developed to specifically take advantage of gene changes in cells that cause cancer [e.g. drugs that target Human Epidermal Receptor Type 2 (HER2), anti-angiogenesis drugs, cyclin-dependent kinase inhibition, etc.].

These targeted cancer drugs come at a high price for many reasons. They include:

1. The high cost of drug development and performing all regulatory studies (Phase 1, 2, and 3 clinical trials);
2. The treatment paradigm for incurable cancers where patients are treated with every approved agent (sequentially or in combination), creating a virtual monopoly because the use of one drug does not automatically mean that the others are no longer needed;
3. The older (sometimes generic) version of treatment may be viewed as substandard treatment;
4. The seriousness of a cancer diagnosis leads to patients and physicians that are willing to pay higher prices for treatment, even with potentially marginal improvements in outcome;
5. The health care systems provide an incentive to administer more chemotherapy (fee-for-service);
6. There are legal barriers that prevent agencies such as the U.S. Food and Drug Administration (FDA) from taking economic and cost-effectiveness considerations into account when approving new drugs.

An article in the *Journal of the National Cancer Institute* lists the following principles to address controlling cancer care costs:

1. Low prices alone may indicate skimping on effective treatment rather than identifying high-value care. Reliable quality measures can help distinguish high-value care from inexpensive but low-value care.
2. Interventions must consider total costs for cancer care. Shifting costs, for example, away from chemotherapy and outpatient supportive care toward increased hospitalization for symptoms is not a solution.
3. Eliminating the use of services that either have no supporting evidence of superior outcomes or good evidence of similar outcomes but higher costs will reduce costs without harming patients.
4. Communication with patients about the risks, benefits, and costs of alternative therapies is critical because patients are suspicious of efforts to reduce costs, often justifiably.

Use of evidence-based expert consensus guidelines is imperative in the treatment of cancers. The National Comprehensive Cancer Network (NCCN) Compendium contains authoritative, scientifically derived information designed to support decision-making about the appropriate use of drugs and biologics in patients with cancer. These evidence-based guidelines should be used for optimal outcomes of cancer patients.

Utilization of Breast Cancer Medications: Fiscal Year 2016

Comparison of Fiscal Years: Breast Cancer Medications (Pharmacy Claims)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	38	190	\$1,724,765.14	\$9,077.71	\$310.38	9,404	5,557
2016	44	222	\$2,366,474.52	\$10,659.80	\$373.97	7,058	6,328
% Change	15.80%	16.80%	37.20%	17.40%	20.50%	-24.90%	13.90%
Change	6	32	\$641,709.38	\$1,582.09	\$63.59	-2,346	771

*Total number of unduplicated members.

Cost do not reflect rebated prices or net costs.

- Prior authorization of ado-trastuzumab, eribulin, everolimus, ixabepilone, lapatinib, palbociclib, and pertuzumab was implemented March 1, 2016. From March 1, 2016 to July 31, 2016 a total of 30 members have utilized breast cancer medications through the pharmacy benefit accounting for 92 claims costing \$1,026,314.76.

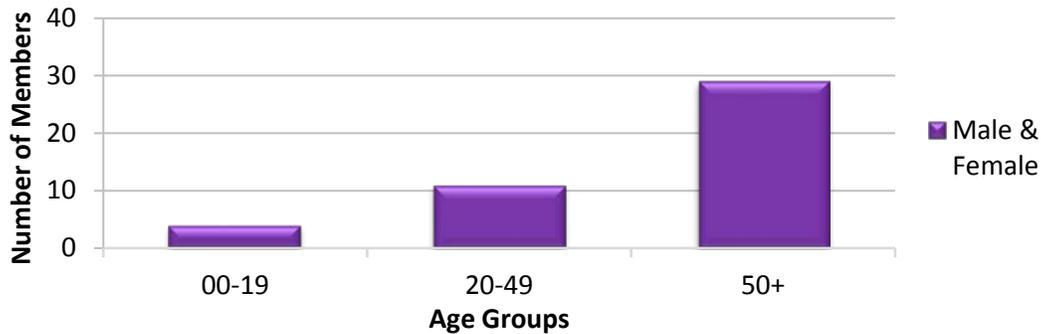
Fiscal Year 2016 Utilization of Breast Cancer Medications: Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
56	281	\$1,641,662.70	\$5,842.22	117,781

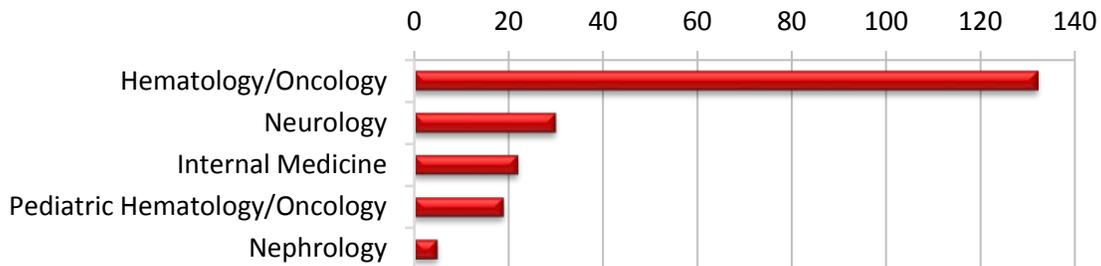
*Total number of unduplicated members.

Cost do not reflect rebated prices or net costs.

Demographics of Members Utilizing Breast Cancer Medications: Pharmacy Claims

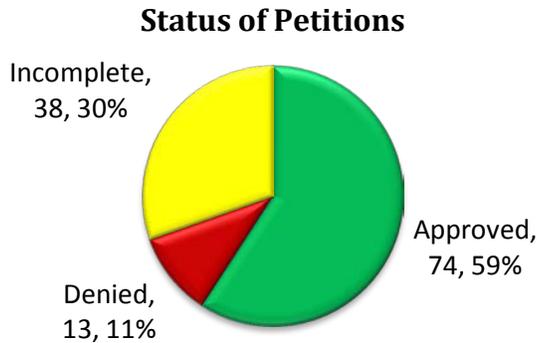


Top Prescriber Specialties of Breast Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Breast Cancer Medications

There were 132 prior authorization requests submitted for breast cancer medications during fiscal year 2016. Since the prior authorization was not implemented until March 2016, the following chart shows the status of the submitted petitions from March 1, 2016 to July 31, 2016.



Market News and Updates⁶

In the past year, eribulin gained an indication for liposarcoma, everolimus gained an indication for neuroendocrine tumors of gastrointestinal or lung origin and everolimus is now being used in combination with lenvatinib for renal cell carcinoma. There was a new drug approval for breast cancer, palbociclib, which is a first-in-class cyclin-dependent kinase (CDK) inhibitor. Cyclin-dependent kinases play a role in cell cycle progression and CDK inhibition has antitumor

activity and can be synergistic with other antitumor medications. This has been approved for hormone receptor positive, HER2-negative advanced or metastatic breast cancer either in combination with letrozole as initial endocrine-based therapy or in combination with fulvestrant in women with disease progression following endocrine therapy. Another CDK inhibitor, ribociclib, has received breakthrough therapy designation in combination with letrozole for the treatment of hormone receptor positive, HER2-negative advanced or metastatic breast cancer, but is not yet on the market. A trastuzumab biosimilar (MYL-1401O) has promising results from a Phase 3 trial and will hopefully provide a more affordable version of trastuzumab; results were presented at the American Society of Clinical Oncology Annual Meeting (ASCO) in June 2016.

Recommendations

Update the current breast cancer medication criteria with the changes noted in red (products listed in alphabetical order by generic name; all prior authorized products included even if no changes made):

Kadcyla® (Ado-Trastuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Diagnosis of metastatic breast cancer; and
3. Member has previously received trastuzumab and a taxane, separately or in combination; and
4. Members should also have either:
 - a. Received prior therapy for metastatic disease; or
 - b. Developed disease recurrence during or within six months of completing adjuvant therapy.
5. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ado-trastuzumab therapy.

Halaven® (Eribulin) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and
2. Previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on eribulin therapy.

Halaven® (Eribulin) Approval Criteria [Liposarcoma Diagnosis]:

1. Diagnosis of unresectable or metastatic liposarcoma; and
2. Previously received an anthracycline-containing chemotherapy regimen.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on eribulin therapy.

Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced breast cancer; and
2. Negative expression of Human Epidermal Receptor Type 2 (HER2); and
3. Hormone receptor-positive (ER positive); and
4. Used in combination with exemestane; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.
6. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Neuroendocrine Tumors of Pancreatic Origin (PNET) or Neuroendocrine Tumors (NET) of Gastrointestinal or Lung Origin Diagnosis]:

1. Diagnosis of unresectable, locally advanced, or metastatic neuroendocrine tumors of pancreatic (PNET), **gastrointestinal, or lung (NET) origin**; and
2. Progressive disease from a previous treatment.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Renal Cell Carcinoma Diagnosis]:

1. Diagnosis of advanced renal cell carcinoma; and
2. Failure of treatment with sunitinib or sorafenib.
3. **Everolimus may also be approved to be used in combination with lenvatinib for advanced renal cell carcinoma.**
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Renal Angiomyolipoma and Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC); and
2. Not requiring immediate surgery; and
3. Used in pediatric and adult patients with age ≥ 1 year.
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Subependymal Giant Cell Astrocytoma (SEGA) with Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC); and
2. Requires therapeutic intervention but cannot be curatively resected.

3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Ixempra® (Ixabepilone) Approval Criteria:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Usage as either:
 - a. In combination with capecitabine after failure of an anthracycline and a taxane; or
 - i. May be used in combination in taxane only resistance if anthracyclines not indicated; or
 - b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ixabepilone therapy.

Tykerb® (Lapatinib) Approval Criteria:

1. An FDA approved diagnosis of metastatic or recurrent breast cancer; and
2. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
3. Lapatinib must be used in combination with one of the following:
 - a. Herceptin® (trastuzumab); or
 - b. Xeloda® (capecitabine); or
 - c. An aromatase inhibitor [e.g. Aromasin® (exemestane), Femara® (letrozole), or Arimidex® (anastrozole)] if also estrogen receptor positive (ER positive).
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on lapatinib therapy.

Ibrance® (Palbociclib) Approval Criteria:

- ~~1. An FDA approved diagnosis of metastatic breast cancer for first-line use only; and~~
- ~~2. Member must be estrogen receptor (ER) positive; and~~
- ~~3. Member must have negative expression of Human Epidermal Receptor Type 2 (HER2); and~~
- ~~4. Ibrance® must be used in combination with letrozole (for postmenopausal women only).~~
5. A diagnosis of advanced metastatic, hormone receptor positive, Human Epidermal Receptor Type 2 (HER2)-negative breast cancer in combination with:
 - a. Letrozole as initial endocrine-based therapy in postmenopausal women; or
 - b. Fulvestrant in women with disease progression following endocrine therapy.
6. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on palbociclib therapy.

Perjeta® (Pertuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Usage for either:
 - a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease; or

- b. Neoadjuvant treatment of patients with locally advanced, inflammatory, or early stage breast cancer (either greater than 2cm in diameter or node positive); and
- 3. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents as well in addition to trastuzumab and docetaxel).
- 4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on pertuzumab therapy.

Utilization Details of Breast Cancer Medications: Fiscal Year 2016

Pharmacy Claims: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	COST/CLAIM
PALBOCICLIB PRODUCTS					
IBRANCE 125MG	51	18	\$546,190.41	2.83	\$10,709.62
IBRANCE 100MG	28	7	\$299,101.23	4	\$10,682.19
IBRANCE 75MG	14	5	\$151,374.01	2.8	\$10,812.43
SUBTOTAL	93	22	\$996,665.65	4.23	\$10,716.83
EVEROLIMUS PRODUCTS					
AFINITOR TAB 10MG	67	14	\$767,264.76	4.79	\$11,451.71
AFINITOR TAB 7.5MG	14	3	\$160,440.54	4.67	\$11,460.04
AFINITOR TAB 5MG	14	3	\$158,878.14	4.67	\$11,348.44
AFINITOR TAB 2.5MG	8	2	\$81,113.05	4	\$10,139.13
AFINITOR DIS TAB 5MG	6	1	\$71,447.14	6	\$11,907.86
AFINITOR DIS TAB 2MG	5	1	\$52,945.35	5	\$10,589.07
SUBTOTAL	114	22	\$1,292,088.98	5.18	\$11,334.11
LAPATINIB PRODUCTS					
TYKERB TAB 250MG	15	2	\$77,719.89	7.5	\$5,181.33
SUBTOTAL	15	2	\$77,719.89	7.5	\$5,181.33
TOTAL	222	44*	\$2,366,474.52	5.05	\$10,659.80

*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	COST/CLAIM
J9355 TRASTUZUMAB INJECTION	8	1	\$28,176.12	\$3,522.02
J9306 PERTUZUMAB INJECTION	196	40	\$1,056,522.60	\$5,930.42
J9354 ADO-TRASTUZUMAB INJECTION	38	5	\$374,521.80	\$9,855.84
J9179 ERIBULIN MESYLATE INJECTION	25	8	\$87,041.60	\$3,481.66
J9207 IXABEPILONE INJECTION	14	4	\$95,400.58	\$6,814.33
TOTAL	281¹	56*	\$1,641,662.70	\$5,842.22

*Total number of unduplicated claims.

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ National Cancer Institute. SEER Cancer Statistics. Retrieved September 12, 2015, from <http://www.cancer.gov/about-cancer/what-is-cancer/statistics> & <http://seer.cancer.gov/statfacts/html/breast.html>.

² American Cancer Society. *What's new in breast cancer research and treatment?* Retrieved July 20, 2015, from <http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-new-research>.

³ Siddiqui M and Rajkumar SV. The high cost of cancer drugs and what we can do about it. *Mayo Clin Proc* 2012; 87:935-943.

⁴ NCCN. *NCCN drugs & biologics compendium (NCCN Compendium)*. Retrieved August 6, 2015, from http://www.nccn.org/professionals/drug_compendium/content/contents.asp.

⁵ Ramsey SD, Ganz PA, Shankaran V, et al. Addressing the American health-care cost crisis: Role of the oncology community. *J Natl Cancer Inst* 2013; 105:1777-8.

⁶ Ehab M, Elbaz M. Profile of palbociclib in the treatment of metastatic breast cancer. *Breast Cancer* 2016; 8:83-91.



Appendix H



Fiscal Year 2016 Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), & Imlygic® (Talinogene Laherparepvec)

**Oklahoma Health Care Authority
October 2016**

Introduction

Skin cancers are commonly divided into two different types: nonmelanoma skin cancer (NMSC) and melanoma skin cancer. In general, NMSC are far more common than melanomas but result in lower mortality. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common forms of NMSC. BCC is the most common cancer diagnosed in the United States, occurring in over 2 million people annually and the incidence of BCC continues to be on the incline.¹ More people are diagnosed with BCC than all other cancers combined.¹ The incidence of SCC is approximately half of BCC.¹ Because NMSC rarely metastasize, treatment is largely focused on localized therapies including different surgical approaches and topical agents. Systemic therapy is reserved for the select number of advanced and metastatic cases. Up until 2012, there were no specific agents indicated to treat advanced cases of NMSC. Within the past 4 years, two new agents classified as Hedgehog pathway inhibitors have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of advanced BCC. Due to their novel mechanism of action, it is anticipated that the usage of these drugs will expand into other diagnoses in coming years.

According to the National Cancer Institute, in 2016 an estimated 76,380 new cases of melanoma skin cancer will be diagnosed in the U.S. accounting for 4.5% of all new cancer diagnoses.² The average lifetime risk of developing melanoma in the U.S. is 1 in 34 for women and 1 in 53 for men.² While the incidence of melanoma is far lower than NMSC, melanomas behave much more aggressively and have high rates of metastases leading to poor survival outcomes in advanced cases. Survival rates vary based on the clinical stage of the disease at diagnosis, with 5-year survival ranging from 15% to 60% in patients with distant and local metastases, respectively.² Traditional cytotoxic chemotherapy has failed to provide successful treatment outcomes in this patient population and has very little role in treating patients with melanoma.³ Surgery, immunotherapy, molecularly targeted agents and radiation are the cornerstones to the treatment of melanoma. Over the past 10 years, drug developers have focused on agents that target various immune checkpoints, specifically cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and the programmed death 1/programmed death ligand 1 (PD-1/PD-L1) pathway, which result in a tumor-specific immune response in a subset of patients. Additionally, the development of molecularly targeted therapy began after it was found that

activating BRAF mutations occur in half of all melanomas.⁴ BRAF mutations lead to activation of the mitogen-activated protein kinase (MAPK) pathway and promote tumor development.⁴ Research in these areas has led to U.S. Food and Drug Administration (FDA) approval for the following agents in the last 5 years: ipilimumab,^{5,6} vemurafenib,⁷ pembrolizumab,⁸ dabrafenib,⁹ trametinib,¹⁰ cobimetinib,¹¹ and nivolumab.¹² The National Comprehensive Cancer Network (NCCN) guidelines for melanoma treatment recommend all of these agents, some as monotherapy and others in combination, as first-line therapy.³ The development of these new drugs has produced an increase in response rates and modest improvements in survival in some melanoma cases. The cost associated with treating skin cancer, approximately \$8.1 billion, increased 5 times faster than treatments for any other cancer between 2002 and 2011.¹³

Utilization of Skin Cancer Medications: Fiscal Year 2016

Comparison of Fiscal Years: Skin Cancer Medications (Pharmacy Claims)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	11	61	\$585,495.70	\$9,598.29	\$325.82	6,612	1,797
2016	10	72	\$709,122.63	\$9,848.93	\$335.76	7,142	2,112
% Change	-9.10%	18.00%	21.10%	2.60%	3.10%	8.00%	17.50%
Change	-1	11	\$123,626.93	\$250.64	\$9.94	530	315

*Total number of unduplicated members.

Cost do not reflect rebated prices or net costs.

Fiscal Year 2016 Utilization of Skin Cancer Medications: Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
28	105	\$998,105.70	\$9,505.77	28,452

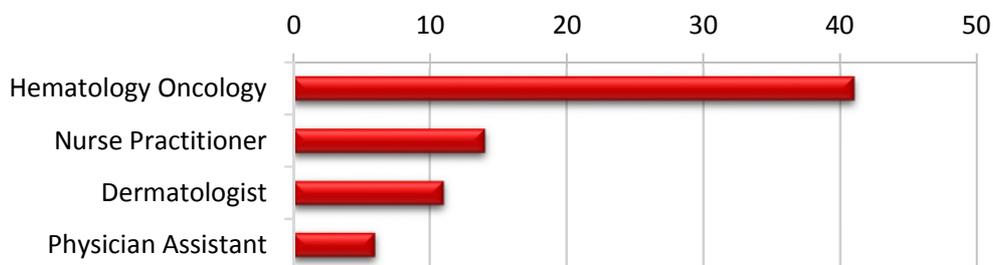
*Total number of unduplicated members.

Cost do not reflect rebated prices or net costs.

Demographics of Members Utilizing Skin Cancer Medications: Pharmacy Claims

- Due to the small number of members utilizing skin cancer medications during fiscal year 2016, detailed demographic information could not be provided.

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



Market News and Updates

The FDA Orange Book indicates the following patent expiration dates for each of the products:

- Odomzo[®] (sonidegib): 2029
- Erivedge[®] (vismodegib): 2028
- Keytruda[®] (pembrolizumab): Not applicable
- Opdivo[®] (nivolumab): Not applicable
- Yervoy[®] (ipilimumab): Not applicable
- Tafinlar[®] (dabrafenib): 2030
- Zelboraf[®] (vemurafenib): 2030
- Cotellic[®] (cobimetinib): 2027
- Mekinist[®] (trametinib): 2032
- Imlygic[®] (talimogene laherparepvec): Not applicable

Product Summaries^{6,8,11,14}

NCCN guidelines for the treatment of NMSC and melanoma skin cancer are continually updated, but the major indications are reflected in the product summaries.

Odomzo[®] (Sonidegib):

- Sonidegib is a selective Hedgehog pathway inhibitor which binds to and inhibits Smoothed homologue (SMO), the transmembrane protein involved in Hedgehog signal transduction. It is FDA approved for the following:
 - Treatment of adults with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy

Erivedge[®] (Vismodegib):

- Vismodegib is a selective Hedgehog pathway inhibitor which binds to and inhibits Smoothed homologue (SMO), the transmembrane protein involved in Hedgehog signal transduction. It is FDA approved for the following:
 - Treatment of metastatic BCC, or locally-advanced BCC that has recurred following surgery or in patients who are not candidates for surgery and not candidates for radiation therapy

Keytruda[®] (Pembrolizumab):

- Pembrolizumab is a highly selective anti-PD-1 humanized monoclonal antibody which inhibits programmed cell death-1 (PD-1) activity by binding to the PD-1 receptor on T-cells to block PD-1 ligands (PD-L1 and PD-L2) from binding. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling (Hamid 2013). This reverses T-cell suppression and induces antitumor responses (Robert 2014). It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma
 - Treatment of metastatic non-small cell lung cancer in patients with PD-L1-expressing tumors (as determined by an approved test) who have disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression (on approved EGFR- or ALK-directed therapy) prior to receiving pembrolizumab.

- Treatment of recurrent or metastatic squamous cell carcinoma of the head and neck in patients with disease progression on or after platinum-containing chemotherapy

Opdivo® (Nivolumab):

- Nivolumab is a fully human immunoglobulin-G4 (IgG4) monoclonal antibody that selectively inhibits programmed cell death-1 (PD-1) activity by binding to the PD-1 receptor to block the ligands PD-L1 and PD-L2 from binding. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling (Hamid 2013). This reverses T-cell suppression and induces antitumor responses (Robert 2014). It is FDA approved for the following:
 - Treatment of classical Hodgkin lymphoma in patients that have relapsed or progressed following autologous hematopoietic stem cell transplant and post-transplant brentuximab vedotin
 - Treatment (as a single-agent) of BRAF V600 wild-type or BRAF V600 mutation-positive unresectable or metastatic melanoma
 - Treatment of unresectable or metastatic melanoma (in combination with ipilimumab)
 - Treatment of metastatic non-small cell lung cancer (NSCLC) that has progressed on or after platinum-based chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression (on approved EGFR- or ALK-directed therapy) prior to receiving nivolumab
 - Treatment of advanced renal cell cancer in patients who have received prior anti-angiogenic therapy

Yervoy® (Ipilimumab):

- Ipilimumab is a recombinant human IgG1 immunoglobulin monoclonal antibody which binds to the cytotoxic T-lymphocyte associated antigen 4 (CTLA-4). CTLA-4 is a down-regulator of T-cell activation pathways. Blocking CTLA-4 allows for enhanced T-cell activation and proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma
 - Adjuvant treatment of cutaneous melanoma in patients with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy

Tafinlar® (Dabrafenib):

- Dabrafenib is a selective inhibitor of some mutated forms of BRAF. BRAF V600 mutations result in constitutive activation of the BRAF pathway; through BRAF inhibition, dabrafenib inhibits tumor cell growth. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E mutation (single-agent therapy)
 - Treatment of unresectable or metastatic melanoma in patients with BRAF V600E or BRAF V600K mutations (in combination with trametinib)

Zelboraf® (Vemurafenib):

- Vemurafenib is a selective inhibitor of some mutated forms of BRAF. BRAF V600 mutations result in constitutive activation of the BRAF pathway; through BRAF inhibition, vemurafenib inhibits tumor cell growth. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E mutation (as detected by an approved test)

Cotellic® (Cobimetinib):

- Cobimetinib is a potent and selective inhibitor of the mitogen-activated extracellular kinase (MEK) pathway (Larkin 2014); it reversibly inhibits MEK1 and MEK2, which are upstream regulators of the extracellular signal-related kinase (ERK) pathway. The ERK pathway promotes cellular proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E or V600K mutation (in combination with vemurafenib)

Mekinist® (Trametinib):

- Trametinib is a potent and selective inhibitor of the mitogen-activated extracellular kinase (MEK) pathway (Larkin 2014); it reversibly inhibits MEK1 and MEK2, which are upstream regulators of the extracellular signal-related kinase (ERK) pathway. The ERK pathway promotes cellular proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E or BRAF V600K mutation (as detected by an approved test), either as a single-agent or in combination with dabrafenib

Imlygic® (Talimogene Laherparepvec):

- Talimogene laherparepvec is a genetically modified attenuated herpes simplex virus 1 (HSV) oncolytic virus which selectively replicates in and lyses tumor cells (Andtbacka 2015). It is FDA approved for the following:
 - Treatment (local) of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery

Recommendations

Odomzo® (Sonidegib) Approval Criteria [Basal Cell Carcinoma Diagnosis]:

1. Either of the following criteria must be met for approval:
 - a. Diagnosis of locally advanced basal cell carcinoma (BCC) that has either:
 - i. Recurred following surgery or radiation therapy; or
 - ii. Surgery or radiation is contraindicated; or
 - b. Diagnosis of metastatic basal cell carcinoma.

Erivedge® (Vismodegib) Approval Criteria [Basal Cell Carcinoma Diagnosis]:

1. Either of the following criteria must be met for approval:
 - a. Diagnosis of locally advanced basal cell carcinoma (BCC) that has either:
 - i. Recurred following surgery or radiation therapy; or
 - ii. Surgery or radiation is contraindicated; or
 - b. Diagnosis of metastatic basal cell carcinoma.

Keytruda® (Pembrolizumab) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. Pembrolizumab must be used as a single-agent; and
 - c. Patient meets one of the following:
 - i. Pembrolizumab is being used as first-line therapy; or
 - ii. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used and patient has ECOG performance status 0 to 2; and
 - d. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)]

Keytruda® (Pembrolizumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
 - i. Exception: lymphocyte-predominant Hodgkin lymphoma
 - b. Pembrolizumab must be used as a single-agent; and
 - c. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)]

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

1. All of the following criteria must be met for approval:
 - a. Diagnosis of metastatic NSCLC; and
 - b. Tumors express PD-L1 (FDA approved test); and
 - c. Patient meets one of the following:
 - i. Disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin); or
 - ii. Patients with EGFR-mutation-positive should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations;* and
 1. Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib
 - iii. Patients with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations;* and
 1. Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib
 - d. ECOG performance status 0 to 2; and
 - e. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. All of the following criteria must be met for approval:

- a. Diagnosis of recurrent or metastatic disease; and
- b. Squamous cell histology; and
- c. Patient has received prior platinum containing regimen (cisplatin or carboplatin); and
- d. ECOG performance status 0 to 1; and
- e. Dose does not exceed 200mg every three weeks.

Opdivo® (Nivolumab) Approval Criteria [Melanoma Diagnosis]:

- 1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. Nivolumab must be used as a single-agent, or in combination with ipilimumab:
 - i. As first-line therapy for untreated melanoma; or
 - ii. As second-line or subsequent therapy for documented disease progression while receiving or since completing most recent therapy:
 - 1. If the patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)]; and
 - 2. Patient has ECOG performance status 0 to 2
 - c. Dose as follows:
 - i. Single-agent: 240mg every two weeks
 - ii. In combination with ipilimumab: 1mg/kg, followed by ipilimumab on the same day, every three weeks for four doses, then 240mg every two weeks.

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

- 1. All of the following criteria must be met for approval:
 - a. Diagnosis of metastatic NSCLC; and
 - b. Tumor histology is one of the following:
 - i. Adenocarcinoma; or
 - ii. Squamous cell; or
 - iii. Large Cell; and
 - c. Nivolumab must be used as a single-agent; and
 - d. Disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin); and
 - e. ECOG performance status 0 to 2; and
 - f. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)]; and
 - g. Dose as follows:
 - i. Single-agent: 240mg every two weeks

Opdivo® (Nivolumab) Approval Criteria [Small Cell Lung Cancer Diagnosis]:

- 1. All of the following criteria must be met for approval:
 - a. One of the following criteria is met:
 - i. Disease relapsed within six months of initial chemotherapy; or
 - ii. Disease is progressive on initial chemotherapy; and
 - b. Nivolumab must be used as a single-agent or in combination with ipilimumab; and
 - c. ECOG performance status 0 to 2

- d. The patient has not previously failed other PD-1 inhibitors (i.e. Keytruda® (pembrolizumab))

Opdivo® (Nivolumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
 - i. Exception: lymphocyte-predominant Hodgkin lymphoma
 - b. Nivolumab must be used as a single-agent; and
 - c. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Renal Cell Cancer Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or surgically unresectable stage IV disease; and
 - b. Tumor histology: predominantly clear cell; and
 - c. Failed prior therapy with one of the following medications:
 - i. Sunitinib; or
 - ii. Sorafenib; or
 - iii. Pazopanib; or
 - iv. Axitinib; and
 - d. Nivolumab must be used as a single-agent; and
 - e. ECOG performance status 0 to 2; and
 - f. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)]

Yervoy® (Ipilimumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. ECOG performance status 0 to 2; and
 - b. Ipilimumab is used in combination with nivolumab as:
 - i. First-line therapy; or
 - ii. Second-line or subsequent therapy for disease progression if nivolumab was not previously used; and
 - c. Ipilimumab is used as a single-agent for one of the following:
 - i. First-line therapy as a single course of four treatments; or
 - ii. Second-line or subsequent lines of therapy as a single course of four treatments; or
 - iii. Retreatment, consisting of a 4-dose limit, for an individual who had no significant systemic toxicity during prior ipilimumab therapy, and whose disease progressed after being stable for greater than six months following completion of a prior course of ipilimumab, and for whom no intervening therapy has been administered; and
 - d. Maximum dose of 3mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Adjuvant Treatment of Melanoma]:

1. All of the following criteria must be met for approval:

- a. Patient has complete resection of melanoma with lymphadenectomy; and
- b. Patient has Stage III disease with regional nodes of greater than 1 mm and no in-transit metastasis; and
- c. Ipilimumab must be used as a single-agent; and
- d. Maximum doses of 10mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Small Cell Lung Cancer Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. One of the following criteria is met:
 - i. Disease relapsed within six months of initial chemotherapy; or
 - ii. Disease is progressive on initial chemotherapy; and
 - b. Used in combination with nivolumab; and
 - c. ECOG performance status 0 to 2.

Tafinlar® (Dabrafenib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF melanoma
 - c. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®); and
 - d. One of the following is met:
 - i. Used as first-line therapy; or
 - ii. Used as second-line therapy or subsequent therapy and patient has an ECOG performance status of 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF NSCLC
 - b. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®)

Zelboraf® (Vemurafenib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF melanoma
 - c. Vemurafenib must be used as a single-agent or in combination with cobimetinib; and
 - d. One of the following is met:
 - i. Used as first-line therapy; or
 - ii. Used as second-line therapy or subsequent therapy and patient has an ECOG performance status of 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Vemurafenib is not indicated for wild-type BRAF NSCLC
 - b. Vemurafenib must be used as a single-agent.

Zelboraf® (Vemurafenib) Approval Criteria [Hairy-Cell Leukemia Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Vemurafenib must be used as a single-agent; and
 - b. Vemurafenib is being used to treat disease progression following failure of purine analog therapy (i.e. pentostatin, cladribine).

Cotellic® (Cobimetinib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Cobimetinib is not indicated for wild-type BRAF melanoma
 - c. One of the following is met:
 - i. Used as first-line therapy in combination with vemurafenib; or
 - ii. Used as second-line therapy or subsequent therapy with vemurafenib and patient has an ECOG performance status of 0 to 2.

Mekinist® (Trametinib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Trametinib is not indicated for wild-type BRAF melanoma.
 - c. One of the following is met:
 - i. Used as first-line therapy in combination with dabrafenib; or
 - ii. Used as second-line therapy or subsequent therapy with dabrafenib and patient has an ECOG performance status of 0 to 2; or
 - iii. Used as second-line therapy or subsequent therapy as a single-agent if:
 1. Patient was intolerant to prior BRAF inhibitor therapy (dabrafenib, vemurafenib); and
 2. No evidence of disease progression on prior BRAF inhibitor therapy (dabrafenib, vemurafenib); and
 3. ECOG performance status is 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Trametinib is not indicated for wild-type BRAF NSCLC
 - b. Trametinib must be used in combination with dabrafenib.

Imlygic® (Talimogene Laherparepvec) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Patient has unresectable cutaneous, subcutaneous, or nodal lesions that are recurrent after initial surgery; and
 - i. Talimogene laherparepvec is not indicated with visceral metastases.
 - b. The patient is not immunocompromised or pregnant.

Utilization Details of Skin Cancer Medications: Fiscal Year 2016**Pharmacy Claims: Fiscal Year 2016**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	COST/CLAIM
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	22	2	\$209,490.92	11	\$9,522.31
SUBTOTAL	22	2	\$209,490.92	11	\$9,522.31
VISMODEGIB PRODUCTS					
ERIVEDGE CAP 150MG	18	4	\$181,482.15	4.5	\$10,082.344
SUBTOTAL	18	4	\$181,482.15	4.5	\$10,082.34
TRAMETINIB PRODUCTS					
MEKINIST TAB 2MG	14	4	\$149,343.54	3.5	\$10,667.40
MEKINIST TAB 2MG	3	2	\$32,554.92	1.5	\$10,851.64
SUBTOTAL	17	4	\$181,898.46	4.25	\$10,699.91
DABRAFENIB PRODUCTS					
TAFINLAR CAP 75MG	15	4	\$136,251.10	3.75	\$9,083.41
SUBTOTAL	15	4	\$136,251.10	3.75	\$9,083.41
TOTAL	72	10*	\$709,122.63	7.2	\$9,848.93

*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	COST/CLAIM
J9228 IPILMUMAB INJECTION	8	3	\$296,002.32	\$3,700.29
J9271 PEMBROLIZUMAB INJECTION	8	3	\$69,677.25	\$8,709.66
J9299 NIVOLUMAB INJECTION	88	23	\$616,602.55	\$7,006.85
J9999 NIVOLUMAB INJECTION	5	2	\$15,823.58	\$3,164.72
TOTAL	105⁺	28*	\$998,105.70	\$9,505.77

*Total number of unduplicated claims.

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

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- ⁴ Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. *Nature* 2002; 417(6892):949–954.
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- ⁸ Hamid O, Robert C, Daud A, et al. Safety and tumor responses with Lambrolizumab (Anti-PD-1) in melanoma. *N Engl J Med* 2013; 369(2):134–144.
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- ¹⁰ Flaherty KT, Robert C, Hersey P, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. *N Engl J Med* 2012; 367(2):107–114.
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- ¹² Topalian SL, Sznol M, McDermott DF, et al. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving Nivolumab. *J Clin Oncol* 2014; 32(10):1020–1030.
- ¹³ Guy GP, Machlin S, Ekwueme DU, Yabroff KR. Prevalence and costs of skin cancer treatment in the US, 2002–2006 and 2007–2011. *Am J Prev Med*. In press 2014.
- ¹⁴ Andtbacka RHI, Kaufman HL, Collichio F, et al. Talimogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma. *J Clin Oncol* 2015; doi: 10.1200/JCO.2014.58.3377.



Appendix I



Fiscal Year 2016 Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Relistor® (Methylnaltrexone) Tablets

**Oklahoma Health Care Authority
October 2016**

Current Prior Authorization Criteria

Relistor® (Methylnaltrexone) Approval Criteria (Terminal Disease Diagnosis Receiving Palliative Care):

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in patients with severe terminal disease who are receiving only palliative care (life expectancy less than six months); and
2. Current use of opioid medications; and
3. Documented treatment attempts with a minimum of three alternate products, excluding bulk forming laxatives; and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
4. Mechanical gastrointestinal obstruction has been ruled out.
5. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
 - a. Weight range of 38kg to 62kg; and/or
 - b. Caregiver unable to draw up dose from vial.
6. A quantity limit of 30 units per month will apply.
7. Approvals will be for the duration of 16 weeks of therapy. Use of Relistor® beyond four months has not been studied in patients with severe terminal disease.

Relistor® (Methylnaltrexone) Approval Criteria (Chronic Non-Cancer Pain Diagnosis):

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of opioid-induced constipation (OIC) in patients with chronic pain unrelated to cancer; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Member must have current use of opioid medications; and
5. Documented and updated colon screening for members greater than 50 years of age; and
6. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and

- b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. Mechanical gastrointestinal obstruction has been ruled out; and
8. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik™ (naloxegol) must be provided; and
9. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
 - a. Weight range of 38kg to 62kg; and/or
 - b. Caregiver unable to draw up dose from vial.
10. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
11. A quantity limit of 30 units per month will apply.

Linzess® (Linaclotide) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) or irritable bowel syndrome characterized by constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members greater than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 capsules for a 30 day supply will apply.

Amitiza® (Lubiprostone) Approval Criteria (Chronic Idiopathic Constipation or Irritable Bowel Syndrome with Constipation Diagnosis):

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) in members 18 years of age or older, or irritable bowel syndrome with constipation (IBS-C) in female members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members greater than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90

days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and

- a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
 6. A quantity limit of 60 capsules for a 30 day supply will apply.

Amitiza® (Lubiprostone) Approval Criteria (Opioid-Induced Constipation Diagnosis):

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, except methadone; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Documented and updated colon screening for members greater than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 60 capsules for a 30 day supply will apply.

Movantik™ (Naloxegol) Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members greater than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and

6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
7. Movantik™ must be discontinued if treatment with the opioid pain medication is also discontinued.
8. A quantity limit of 30 tablets for a 30 day supply will apply.

Viberzi™ (Eluxadoline) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
2. Member must be 18 years of age or older; and
3. Documentation of trials of two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10 to 14 consecutive days at the recommended dosing). Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure.
4. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
5. A quantity limit of 60 tablets for a 30 day supply will apply.

Xifaxan® (Rifaximin) 200mg Approval Criteria:

1. An FDA approved diagnosis of traveler's diarrhea (TD); and
2. Member must be 12 years of age or older; and
3. TD must be due to noninvasive strains of *Escherichia coli*; and
4. A patient-specific, clinically significant reason why the member cannot use a fluoroquinolone antibiotic (e.g., ciprofloxacin, levofloxacin) must be provided.
5. A quantity limit of 9 tablets for a 3 day supply will apply.

Xifaxan® (Rifaximin) 550mg Approval Criteria:

1. An FDA approved indication for the reduction in risk of overt hepatic encephalopathy (HE) recurrence; or
2. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
 - a. For the diagnosis of IBS-D: Documentation of trials of two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10 to 14 consecutive days at the recommended dosing). Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure; and
 - b. For the diagnosis of IBS-D: Member must be 18 years of age or older.
3. A quantity limit of 60 tablets for a 30 day supply will apply. Patients with the diagnosis of IBS-D needing 42 tablets for a 14-day treatment regimen (550mg three times daily for 14 days) will be approved for a quantity limit override upon meeting Xifaxan® approval criteria. Patients with IBS-D who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen (550mg three times daily for 14 days).

Utilization of Constipation and Diarrhea Medications: Fiscal Year 2016

Comparison of Fiscal Years: Constipation and Diarrhea Medications

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	98	526	\$145,345.17	\$276.32	\$9.45	22,393	15,382
2016	134	528	\$185,294.43	\$350.94	\$11.64	21,430	15,922
% Change	36.70%	0.40%	27.50%	27.00%	23.20%	-4.30%	3.50%
Change	36	2	\$39,949.26	\$74.62	\$2.19	-963	540

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Please note, the above data does not include Xifaxan® (rifaximin).

Comparison of Fiscal Years: Xifaxan® (Rifaximin)

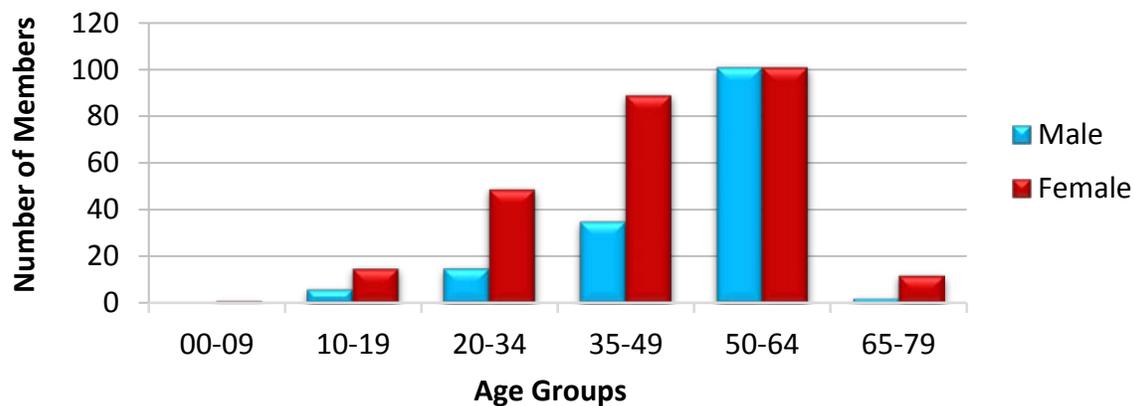
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	250	1,038	\$1,523,295.88	\$1,467.53	\$51.87	58,175	29,365
2016	294	1,208	\$2,018,187.87	\$1,670.69	\$60.55	66,473	33,329
% Change	17.60%	16.40%	32.50%	13.80%	16.70%	14.30%	13.50%
Change	44	170	\$494,891.99	\$203.16	\$8.68	8,298	3,964

*Total number of unduplicated members.

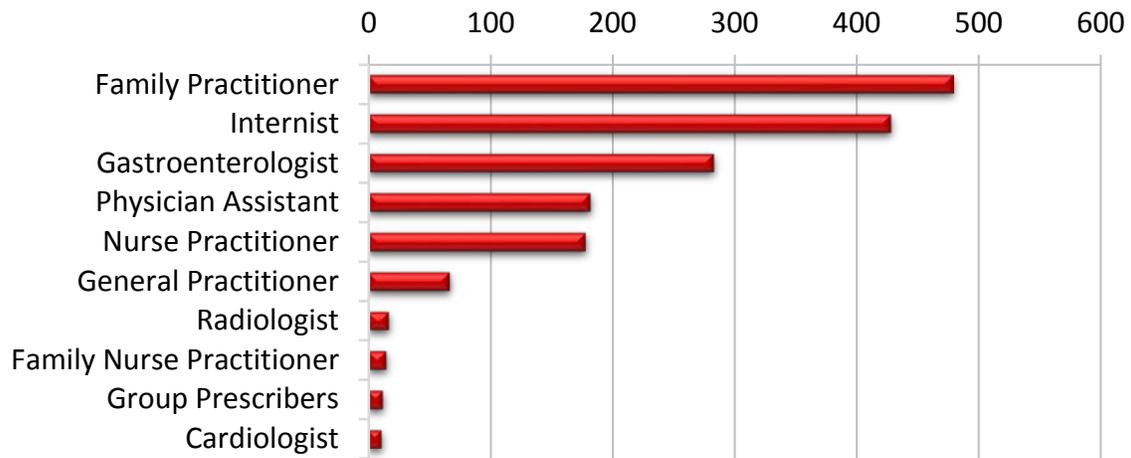
Costs do not reflect rebated prices or net costs.

Please note, the majority of utilization of rifaximin was for the 550mg strength for the reduction in risk of overt hepatic encephalopathy (HE) recurrence.

Demographics of Members Utilizing Constipation and Diarrhea Medications



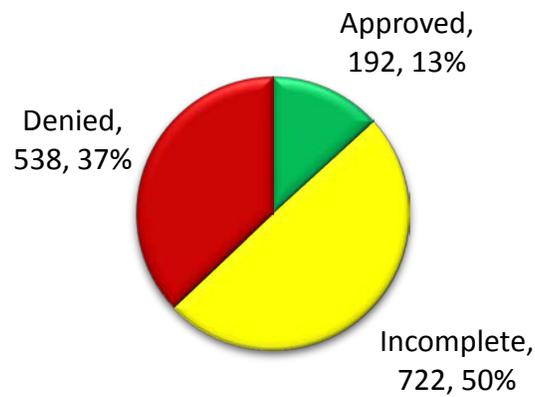
Top Prescriber Specialties of Constipation and Diarrhea Medications by Number of Claims



Prior Authorization of Constipation and Diarrhea Medications

There were 1,452 prior authorization requests submitted for constipation and diarrhea 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}

Anticipated Patent Expirations:

- Amitiza® (lubiprostone): October 2027
- Viberzi™ (eluxadoline): July 2028
- Xifaxan® (rifaximin): October 2029
- Relistor® (methylnaltrexone): December 2030
- Linzess® (linaclotide): July 2031
- Movantik™ (naloxegol): April 2032

New FDA Approvals and Indications:

- **July 2016:** The U.S. Food and Drug Administration (FDA) approved Relistor® (methylnaltrexone) tablets for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain. This is in addition to Relistor® solution for subcutaneous injection, which is FDA approved for the treatment of OIC in adults with advanced terminal illness who are receiving palliative care, when response to laxative therapy has not been sufficient, and for the treatment of OIC in adults with chronic non-cancer pain. Methylnaltrexone is a peripherally-acting mu-opioid receptor antagonist (PAMORA). Relistor® solution for subcutaneous injection was first FDA approved in 2008.
- **August 2016:** The FDA approved a Supplemental New Drug Application (sNDA) for Movantik™ (naloxegol) to update labeling information regarding the administration of crushed tablets, to add to the Warnings and Precautions section and the Adverse Reactions section, and to clarify the effects of race on pharmacokinetics. The updated labeling now states that for patients who are unable to swallow the naloxegol tablet whole, the tablet may be crushed to a powder, mixed with four ounces of water, stirred, and the contents consumed by mouth. Naloxegol can also be administered via a nasogastric (NG) tube. The Warnings and Precautions section and the Adverse Reactions section have been updated with information regarding reports of severe abdominal pain and/or diarrhea, some of which resulted in hospitalization.

Updated Guidelines:

- **April 2016:** The American College of Gastroenterology (ACG) published clinical guidelines regarding the diagnosis, treatment, and prevention of acute diarrheal infections in adults. For the treatment of traveler's diarrhea (TD), the clinical guidelines still recommend fluoroquinolones (ciprofloxacin or levofloxacin) as the primary antibiotics of choice for most destinations. SoonerCare criteria for Xifaxan® (rifaximin) for the treatment of TD is in line with the current guideline recommendations.
 - In July 2016, the FDA updated the warnings for fluoroquinolone antibiotics to include a Boxed Warning and revisions to the Warnings and Precautions section about the risk of disabling and potentially irreversible adverse reactions that can occur with the use of fluoroquinolone antibiotics. The label also contains new limitation-of-use statements to reserve fluoroquinolones for patients who do not have other available treatment options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, and uncomplicated urinary tract infections. This updated warning was issued after the ACG guidelines were published and does not specifically address fluoroquinolones used for the treatment of TD.

Medications in the Pipeline:

- **June 2016:** Shionogi has submitted a New Drug Application (NDA) to the FDA for naldemedine, a once-daily oral PAMORA for the treatment of OIC in adults with chronic non-cancer pain. The target action date under the Prescription Drug User Fee Act (PDUFA) for naldemedine is March 23, 2017.

Relistor® (Methylnaltrexone) Tablets Product Summary^{8,9}

Indications: Relistor® (methylnaltrexone tablets) is indicated for the treatment of OIC in adult patients with chronic non-cancer pain.

Dosing:

- Relistor® tablets are available as 150mg methylnaltrexone oral tablets.
- The recommended dosage of methylnaltrexone tablets is 450mg by mouth once daily in the morning.
- For patients with moderate-to-severe renal impairment or with moderate-to-severe hepatic impairment, the recommended dosage of methylnaltrexone tablets is 150mg by mouth once daily in the morning.
- All maintenance laxative therapy should be discontinued prior to initiation of methylnaltrexone. Laxatives can be used as needed if there is a suboptimal response to methylnaltrexone after three days.
- Methylnaltrexone tablets should be taken with water on an empty stomach at least 30 minutes prior to the first meal of the day.
- Methylnaltrexone should be discontinued if treatment with the opioid pain medication is also discontinued.

Mechanism of Action: Methylnaltrexone is a selective antagonist of opioid binding at the mu-opioid receptor. As a quaternary amine, the ability of methylnaltrexone to cross the blood-brain barrier is restricted. This allows methylnaltrexone to function as a peripherally-acting mu-opioid receptor antagonist (PAMORA) in tissues such as the gastrointestinal tract, thereby decreasing the constipating effects of opioids without impacting opioid-mediated analgesic effects on the central nervous system.

Contraindications:

- Patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation

Safety:

- **Gastrointestinal Perforation:** Cases of gastrointestinal perforation have been reported in adult patients with OIC and advanced illness with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies or peritoneal metastases). The overall risk-benefit profiles should be taken into account when using methylnaltrexone in patients with these conditions or other conditions which might result in impaired integrity of the gastrointestinal tract (e.g., Crohn's disease). Patients should be monitored for the development of severe, persistent, or worsening abdominal pain, and methylnaltrexone should be discontinued in patients who develop this symptom.
- **Severe or Persistent Diarrhea:** Patients should discontinue methylnaltrexone and consult with their healthcare provider if they develop severe or persistent diarrhea during treatment with methylnaltrexone.

- **Opioid Withdrawal:** Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, and yawning have occurred in patients treated with methylnaltrexone. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal and/or reduced analgesia. The overall risk-benefit profile should be taken into account when using methylnaltrexone in such patients, and such patients should be monitored for symptoms of opioid withdrawal and for adequacy of analgesia.
- **Drug-Drug Interaction(s):** Concomitant use of methylnaltrexone with other opioid antagonists should be avoided because of the potential for additive effects of opioid receptor antagonism and increased risk of opioid withdrawal.
- **Renal Impairment:** In a study of subjects with varying degrees of renal impairment receiving methylnaltrexone injection subcutaneously, there was a significant increase in the exposure to methylnaltrexone in subjects with moderate and severe renal impairment (creatinine clearance less than 60mL/min as estimated by Cockcroft-Gault) compared to healthy subjects. Therefore, a dosage reduction of methylnaltrexone tablets and injection is recommended in patients with moderate and severe renal impairment. No dosage adjustment of methylnaltrexone tablets or injection is needed in patients with mild renal impairment (creatinine clearance greater than 60mL/min as estimated by Cockcroft-Gault).
- **Hepatic Impairment:** In a study of subjects with varying degrees of hepatic impairment receiving a 450mg dose of methylnaltrexone tablets, there was a significant increase in systemic exposure of methylnaltrexone for subjects with moderate and severe hepatic impairment (Child-Pugh Class B or C) compared to healthy subjects. Therefore, a dosage reduction of methylnaltrexone tablets is recommended for patients with moderate or severe hepatic impairment. No dosage adjustment of methylnaltrexone tablets is needed in patients with mild hepatic impairment (Child-Pugh Class A).
- **Pediatric Use:** The safety and effectiveness of methylnaltrexone have not been established in pediatric patients.

Adverse Reactions: The most common adverse reactions to methylnaltrexone reported in clinical trials, occurring at an incidence of at least 2% and with a higher incidence than placebo, include abdominal pain, diarrhea, headache, abdominal distention, vomiting, hyperhidrosis, anxiety, muscle spasms, rhinorrhea, and chills. Adverse reactions of abdominal pain, diarrhea, hyperhidrosis, anxiety, rhinorrhea, and chills may reflect symptoms of opioid withdrawal.

Efficacy:

- The efficacy of methylnaltrexone tablets in the treatment of OIC in patients with chronic non-cancer pain was evaluated in a randomized, double-blind, placebo-controlled study. This study compared four-week treatment of OIC with methylnaltrexone tablets at a dosage of 450mg orally once daily with placebo.
- A total of 401 patients (200 methylnaltrexone, 201 placebo) were enrolled and treated in the double-blind period. Patients had a history of chronic non-cancer pain for which they were taking opioids. Prior to screening, patients were receiving opioid therapy for pain

for one month or longer and had OIC (median duration of OIC at baseline was 53 months).

- OIC was defined as less than three spontaneous bowel movements (SBMs) per week with at least 25% of the SBMs associated with one or more of the following conditions: straining, hard or lumpy stools, and having a sensation of incomplete evacuation.
 - A SBM was defined as a bowel movement (BM) without rescue laxative taken within the past 24 hours.
 - Patients were required to discontinue all previous laxative therapy and use only the study-permitted rescue laxative (bisacodyl tablets). If patients had not had a BM for 3 consecutive days during the study, they were permitted to use rescue medication (up to 3 bisacodyl tablets taken orally once during a 24-hour period). If rescue treatment with bisacodyl tablets did not result in a BM, a second dose of bisacodyl or an enema 24 hours after rescue was permitted (enema use was permitted after rescue with bisacodyl tablets had failed at least once).
- A responder analysis was performed which defined the proportion of patients with at least three SBMs per week, with an increase of at least one SBM per week over baseline, for at least three out of the first four weeks of the treatment period, and there was a statistically significant difference for the methylnaltrexone treatment group versus placebo (see following table).

Methylnaltrexone Tablets for OIC in Patients with Chronic Non-Cancer Pain		
	placebo (N = 201)	methylnaltrexone tablets: 450mg once daily (N = 200)
Proportion of patients responding, n (%)	77 (38%)	103 (52%)

Estimated Acquisition Cost: The estimated acquisition cost of Relistor® 150mg tablets is \$17.60 per tablet, resulting in a monthly cost of \$1,584.00 based on the recommended dosage of 450mg once daily.

Cost Comparison: Medications for OIC (Chronic Non-Cancer Pain)

Medication	Dosing Regimen	Cost/Unit*	Cost/Month
Relistor® (methylnaltrexone) 150mg tablets	450mg PO Q day	\$17.60	\$1,584.00
Amitiza® (lubiprostone) 24mcg capsules	24mcg PO BID	\$5.81	\$348.60
Movantik™ (naloxegol) 25mg tablets	25mg PO Q day	\$10.14	\$304.20
Relistor® (methylnaltrexone) 12mg/0.6mL vials or syringes	12mg subQ Q day	\$176.00	\$5,280.00

BID = Twice Daily; Q day = Once daily; PO = By mouth; SubQ = Subcutaneous

*Cost/unit based on estimated acquisition cost (EAC). Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

Recommendations

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

Relistor® (Methylnaltrexone) Tablets Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members greater than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik™ (naloxegol) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
8. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 90 tablets for a 30 day supply will apply.

Additionally the College of Pharmacy recommends updating the criteria for Relistor® injection with the changes noted in red:

Relistor® (Methylnaltrexone) Injection Approval Criteria (Chronic Non-Cancer Pain Diagnosis):

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of opioid-induced constipation (OIC) in patients with chronic pain unrelated to cancer; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Member must have current use of opioid medications; and
5. Documented and updated colon screening for members greater than 50 years of age; and
6. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and

- a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
- b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. Mechanical gastrointestinal obstruction has been ruled out; and
8. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik™ (naloxegol) must be provided; and
9. A patient-specific, clinically significant reason why member cannot use the tablet formulation of Relistor®; and
10. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
 - a. Weight range of 38kg to 62kg; and/or
 - b. Caregiver unable to draw up dose from vial.
11. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
12. A quantity limit of 30 units per month will apply.

Utilization Details of Constipation and Diarrhea Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LINACLOTIDE PRODUCTS						
LINZESS CAP 290MCG	159	30	\$49,013.43	\$10.35	\$308.26	26.45%
LINZESS CAP 145MCG	119	40	\$37,806.69	\$10.59	\$317.70	20.40%
SUBTOTAL	278	70	\$86,820.12	\$10.45	\$312.30	46.86%
LUBIPROSTONE PRODUCTS						
AMITIZA CAP 24MCG	163	36	\$51,395.78	\$10.43	\$315.31	27.74%
AMITIZA CAP 8MCG	49	16	\$16,435.19	\$10.34	\$335.41	8.87%
SUBTOTAL	212	52	\$67,830.97	\$10.41	\$319.96	36.61%
NALOXEGOL PRODUCTS						
MOVANTIK TAB 25MG	16	10	\$4,629.34	\$9.64	\$289.33	2.50%
MOVANTIK TAB 12.5MG	5	3	\$940.98	\$6.27	\$188.20	0.51%
SUBTOTAL	21	13	\$5,570.32	\$8.84	\$265.25	3.01%
METHYLNALTREXONE PRODUCTS						
RELISTOR INJ 12/0.6ML	9	3	\$16,032.94	\$61.67	\$1,781.44	8.65%
RELISTOR INJ 8/0.4ML	1	1	\$2,960.32	\$105.73	\$2,960.32	1.60%
SUBTOTAL	10	4	\$18,993.26	\$65.95	\$1,899.33	10.25%
ELUXADOLINE PRODUCTS						
VIBERZI TAB 100MG	4	2	\$3,039.68	\$33.77	\$759.92	1.64%
VIBERZI TAB 75MG	3	1	\$3,040.08	\$33.78	\$1,013.36	1.64%
SUBTOTAL	7	3	\$6,079.76	\$33.78	\$868.54	3.28%
TOTAL	528	134*	\$185,294.43	\$11.64	\$350.94	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Please note, the above data does not include Xifaxan® (rifaximin).

Utilization Details of Xifaxan® (Rifaximin): Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
RIFAXIMIN PRODUCTS						
XIFAXAN TAB 550MG	1,193	288	\$2,007,089.80	\$60.67	\$1,682.39	99.45%
XIFAXAN TAB 200MG	15	7	\$11,098.07	\$45.30	\$739.87	0.55%
TOTAL	1,208	294*	\$2,018,187.87	\$60.55	\$1,670.69	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Please note, the majority of utilization of rifaximin 550mg was for the reduction in risk of overt hepatic encephalopathy (HE) recurrence.

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 08/2016. Last accessed 09/22/2016.

² PR Newswire: Valeant and Progenics Announce FDA Approves Relistor® Tablets for the Treatment of Opioid-Induced Constipation in Adults with Chronic Non-Cancer Pain. Available online at: <http://www.prnewswire.com/news-releases/valeant-and-progenics-announce-fda-approves-relistor-tablets-for-the-treatment-of-opioid-induced-constipation-in-adults-with-chronic-non-cancer-pain-300301032.html>. Issued 07/19/2016. Last accessed 09/23/2016.

³ Hee Han D. New Warning, Administration Info Added to Labeling for OIC Drug Movantik. MPR. Available online at: <http://www.empr.com/news/new-warning-administration-info-added-to-labeling-for-oic-drug-movantik/article/518245/>. Issued 08/24/2016. Last accessed 09/23/2016.

⁴ Movantik™ Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/movantik/>. Last revised 08/22/2016. Last accessed 09/23/2016.

⁵ Riddle M, DuPont H, Connor B. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. *The American Journal of Gastroenterology*. Available online at: <http://gi.org/wp-content/uploads/2016/05/ajg2016126a.pdf>. Issued 04/12/2016. Last accessed 09/23/2016.

⁶ FDA News Release: FDA Updates Warnings for Fluoroquinolone Antibiotics. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm513183.htm>. Issued 07/26/2016. Last accessed 09/23/2016.

⁷ PR Newswire: Shionogi Announces Acceptance of New Drug Application in the U.S. for Naldemedine for the Treatment of Opioid-Induced Constipation. Available online at: <http://www.prnewswire.com/news-releases/shionogi-announces-acceptance-of-new-drug-application-in-the-us-for-naldemedine-for-the-treatment-of-opioid-induced-constipation-300279579.html>. Issued 06/06/2016. Last accessed 09/23/2016.

⁸ Relistor® Prescribing Information, Valeant Pharmaceuticals. Available online at: <https://shared.salix.com/shared/pi/relistor-pi.pdf?id=811664a>. Last revised 07/2016. Last accessed 09/23/2016.

⁹ Relistor® Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/relistor-2/>. Last revised 07/31/2016. Last accessed 09/23/2016.



Appendix J



Fiscal Year 2016 Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekezumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szszs), & Amjevita™ (Adalimumab-atto)

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

Targeted Immunomodulator Agents*		
Tier-1 (DMARDs appropriate to disease state)	Tier-2*	Tier-3+
6-mercaptopurine	adalimumab (Humira®)	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	alefacept (Amevive®)
hydroxychloroquine		anakinra (Kineret®)
leflunomide		apremilast (Otezla®)
mesalamine		canakinumab (Ilaris®)‡
methotrexate		certolizumab pegol (Cimzia®)
minocycline		golimumab (Simponi® & Simponi® Aria™)
NSAIDs		infliximab (Remicade®)
oral corticosteroids		rituximab (Rituxan®)
sulfasalazine		secukinumab (Cosentyx®)
		tocilizumab (Actemra®)
		tofacitinib (Xeljanz®)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

DMARDs = Disease modifying antirheumatic drugs; NSAIDs = Nonsteroidal anti-inflammatory drugs

*May be rebated to Tier-2 status only

‡Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS).

- Current tier trial requirements can be found in the recommendations section at the end of this report.

Utilization of Targeted Immunomodulator Agents: Fiscal Year 2016

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	684	4,275	\$15,733,399.71	\$3,680.33	\$125.10	31,775	125,768
2016	760	4,656	\$21,201,870.13	\$4,553.67	\$157.80	37,755	134,363
% Change	11.10%	8.90%	34.80%	23.70%	26.10%	18.80%	6.80%
Change	76	381	\$5,468,470.42	\$873.34	\$32.70	5,980	8,595

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

- There was a significant increase in cost seen while utilization remained relatively flat. It is important to note that several of these products are in their waning patent stages and will soon face biosimilar competition; typically when a product is close to the end of its patent life the manufacturer will raise the price. The consumer price index (CPI) penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite price increases in medications that pay the brand penalty. The cost increase in the chart does not reflect the net cost increase. Additionally, the majority of utilization was seen in Tier-2 medications which are supplementally rebated medications. The supplementally rebated prices are also not reflected in the fiscal year comparison chart.

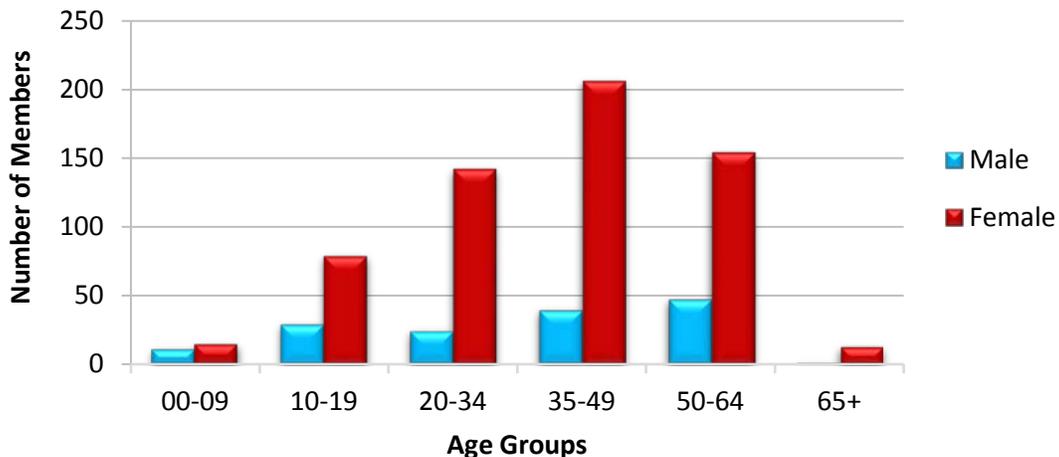
Fiscal Year 2016 Utilization of Targeted Immunomodulator Agents: Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
104	358	\$1,287,212.52	\$3,595.57	52,532

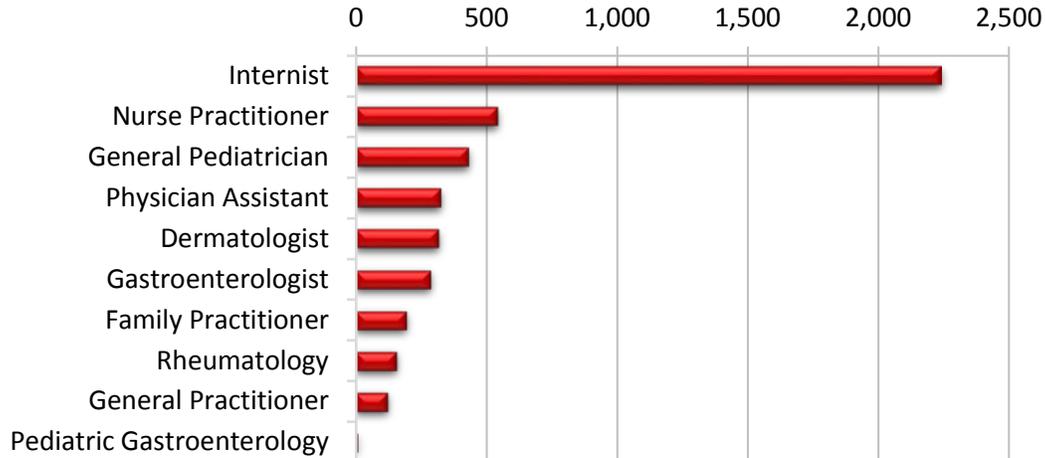
*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Targeted Immunomodulator Agents



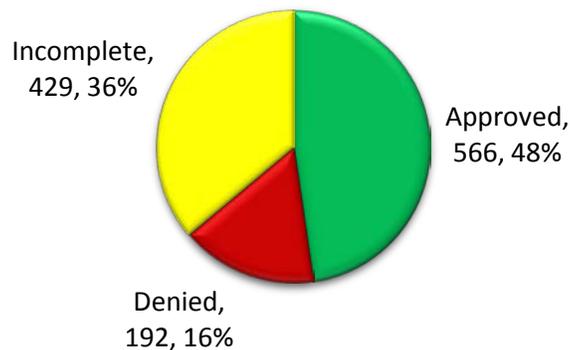
Top Prescriber Specialties of Targeted Immunomodulator Agents by Number of Claims



Prior Authorization of Targeted Immunomodulator Agents

There were 1,187 prior authorization requests submitted for targeted immunomodulator agents during fiscal year 2016.

Status of Petitions



Market News and Updates^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27}

New FDA Approval(s) and Indication(s):

- January 2016:** Novartis announced the U.S. Food and Drug Administration (FDA) approval of two new indications for Cosentyx® (secukinumab) for the treatment of adults with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). The two new indications are in addition to the indication for moderate-to-severe plaque psoriasis (PsO) which was approved in January 2015.
- February 2016:** Pfizer Inc. announced the FDA approval of 11mg once-daily Xeljanz® XR (tofacitinib extended-release) oral tablets for the treatment of moderate-to-severe rheumatoid arthritis (RA). Xeljanz® was previously approved in 2012 as a 5mg oral tablet dosed twice daily for the treatment of RA.
- March 2016:** The FDA approved Taltz® (ixekizumab) to treat adults with moderate-to-severe PsO who are candidates for systemic or phototherapy. Taltz® is a humanized

interleukin (IL)-17A antagonist. IL-17A is a cytokine that causes inflammation and immune responses; its inhibition prevents the release of proinflammatory cytokines.

- **April 2016:** The FDA approved Celltrion's Inflectra™ (infliximab-dyyb) for moderate-to-severe RA, moderate-to-severe ulcerative colitis (UC), severe PsO, PsA, AS, and adult and pediatric moderate-to-severe Crohn's disease (CD). Inflectra™ is a biosimilar to Remicade® (infliximab), which was originally approved in 1998. The FDA's approval of Inflectra™ is based on evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data that demonstrated Inflectra™ is biosimilar to Remicade®. Inflectra™ is not an interchangeable product to Remicade®.
- **July 2016:** AbbVie announced the FDA approval of Humira® (adalimumab) for the treatment of patients with noninfectious intermediate and posterior uveitis and panuveitis. Humira® is the only FDA-approved noncorticosteroid therapy for intermediate uveitis, posterior uveitis, and panuveitis. The new indication is in addition to nine other indications for use of Humira® including: PsA, AS, moderate-to-severe RA, polyarticular juvenile idiopathic arthritis (JIA), CD, hidradenitis suppurativa (HS), UC, and PsO.
- **July 2016:** Bristol-Myers Squibb Company announced the launch of Orencia® ClickJect™ (abatacept), an autoinjector that can be used for self-administration of 125mg of subcutaneous abatacept. Orencia® is also available as an intravenous (IV) infusion and prefilled syringe.
- **August 2016:** The FDA approved Erelzi™ (etanercept-szzs) for the treatment of moderate-to-severe RA, moderate-to-severe polyarticular JIA, PsA, AS, and moderate-to-severe PsO. Erelzi™ is a biosimilar to Enbrel® (etanercept), which was originally FDA approved in 1998. Erelzi™ was approved as a biosimilar and not as an interchangeable product.
- **September 2016:** The FDA approved Amjevita™ (adalimumab-atto), a biosimilar to Humira® (adalimumab), for the treatment of moderate-to-severe RA, polyarticular JIA, PsA, AS, moderate-to-severe CD, moderate-to-severe UC, and moderate-to-severe PsO. Amjevita™ is approved as a biosimilar and not as an interchangeable product.
- **September 2016:** The FDA approved Stelara® (ustekinumab), an interleukin-12/23 inhibitor, for the treatment of moderate-to-severe CD in adults who have failed or were intolerant to conventional therapy (but never failed treatment with a tumor necrosis factor (TNF)-blocker) or who have failed or were intolerant to treatment with one or more TNF-blockers. Ustekinumab was previously approved for PsO and PsA.
- **September 2016:** The FDA approved three new indications for Ilaris® (canakinumab), a interleukin-1-β inhibitor. The three new indications include tumor necrosis factor receptor-associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD), and familial Mediterranean fever (FMF). All three indications are inherited conditions characterized by intermittent attacks of fever, inflammation, and severe muscle pain. Ilaris® is the first approved therapy for TRAPS and HIDS/MKD, and was previously approved for cryopyrin-associated periodic syndromes (CAPs) and active systemic JIA.

News:

- **March 2016:** A Phase 4 superiority study of Cimzia® (certolizumab) and Humira® (adalimumab) in adults with moderate-to-severe RA showed similar efficacy between the two products at three months. The percentages of patients who achieved a 20% improvement in the symptoms of RA were 69% for certolizumab and 71% for adalimumab.
- **April 2016:** A pooled analysis of three trials found Otezla® (apremilast), a phosphodiesterase-4 inhibitor, improved enthesitis and dactylitis in patients with psoriatic arthritis. An enthesitis score and dactylitis score of zero were achieved at week 52 in 37.7% and 67.5% of patients treated with oral Otezela® twice daily.

Pipeline Update(s):

- **July 2015:** Phase 2 trial results indicated up to 45% of PsO patients taking guselkumab had completely clear skin after four months. Guselkumab is being developed by Janssen Pharmaceuticals and targets IL-23.
- **October 2015:** Eli Lilly Company and Incyte Corporation announced positive results from a Phase 3 study of baricitinib in patients with RA. The study met its primary endpoint of demonstrating superiority in ACR20 response compared to placebo after 12 weeks of treatment. Baricitinib is an oral Janus Kinase (JAK)-1 and JAK-2 inhibitor.
- **March 2016:** Celgene Corporation announced results from a Phase 2 trial of oral ozanimod, a selective S1P 1 and 5 receptor modulator, in patients with moderate-to-severe UC. Ozanimod 1mg met its primary endpoint of the proportion of patients in remission at week 8 compared to placebo.
- **March 2016:** AbbVie and Boehringer Ingelheim announced a collaboration to develop BI-655066, an IL-23 antagonist, currently in Phase 3 trials for PsO.
- **March 2016:** Regeneron Pharmaceuticals and Sanofi announced results from a Phase 3 study of sarilumab in patients with RA. Sarilumab was superior to Humira® (adalimumab) in improving signs and symptoms of RA at Week 24. Sarilumab is a human IL-6 receptor antibody.
- **March 2016:** Amgen announced that the FDA accepted a supplemental Biologics License Application (sBLA) for the use of Enbrel® (etanercept) in pediatric patients with severe PsO. The FDA has set a Prescription Drug User Fee Act (PDUFA) action date of November 5, 2016.
- **March 2016:** Phase 3 data revealed that treatment with Stelara® (ustekinumab) induced clinical response and clinical remission in patients with moderate-to-severe CD who had previously failed one or more anti-tumor necrosis factor (TNF)-alpha therapies.
- **May 2016:** Samsung Bioepis Company announced it has applied for FDA approval of its Remicade® (infliximab) biosimilar. If approved, this would be the second biosimilar approved for Remicade®.
- **May 2016:** Regeneron Pharmaceuticals announced results from its Phase 2/3 study evaluating fasinumab, a nerve growth factor antibody, for the treatment of moderate-to-severe osteoarthritis pain. Fasinumab demonstrated superior pain relief compared to placebo at week 16.
- **May 2016:** Sun Pharmaceutical Industries announced results from two Phase 3 studies of tildrakizumab, an IL-23p19 inhibitor, in patients with moderate-to-severe PsO.

Tildrakizumab showed superior efficacy to placebo in improvements in Psoriasis Area Sensitivity Index (PASI) 75 at week 12.

- **June 2016:** GlaxoSmithKline announced results from its Phase 3 study of sirukumab, an anti-IL-6 monoclonal antibody, in patients with moderate-to-severe RA. Results revealed sirukumab met its coprimary endpoints in inhibiting radiographic progression and at least a 20% improvement in RA signs and symptoms compared to placebo.
- **July 2016:** Pfizer announced positive results from a Phase 3 study of Xeljanz[®] (tofacitinib) in patients with UC. Results revealed that the proportion of patients in remission at week 52 was significantly greater in both the tofacitinib 5mg and 10mg twice daily groups compared to placebo.
- **July 2016:** The FDA's Dermatologic and Ophthalmic Drugs Advisory Committee voted to recommend approval of brodalumab, an IL-17 targeting monoclonal antibody, for the treatment of moderate-to-severe PsO. With the approval, the panel recommended strong warnings and a risk management program for the potential for suicide and self-injurious behavior.

Xeljanz[®] XR (Tofacitinib Extended-Release) Product Summary²⁸

Indications: Xeljanz[®] XR [tofacitinib extended-release (ER)] is an inhibitor of Janus kinases (JAKs) indicated for the treatment of adult patients with moderately-to-severely active RA who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).

- Limitation of Use: Use of Xeljanz[®] XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Boxed Warning:

- Serious Infections: Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving tofacitinib.
- Malignancy: Lymphoma and other malignancies have been observed in patients treated with tofacitinib. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with tofacitinib and concomitant immunosuppressive medications.

Dosing: Tofacitinib ER is available as 11mg oral tablets.

- The recommended dose of tofacitinib ER is 11mg by mouth once daily. The immediate-release formulation is dosed 5mg twice daily.
- The recommended dose in patients with moderate and severe renal impairment and moderate hepatic impairment is 5mg once daily.
- Use in patients with severe hepatic impairment is not recommended.

Mechanism of Action: Tofacitinib is a JAK inhibitor. JAKs are intracellular enzymes which transmit signals from cytokine interactions on the cellular membrane to influence immune cell function. JAKs activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity. Tofacitinib modulates the signaling pathway at the point of JAKs, preventing the activation of STATs.

Contraindications: None.

Warnings and Precautions:

- **Infections:** Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in RA patients receiving tofacitinib.
- **Malignancy and Lymphoproliferative Disorders:** Consideration should be given to the risks and benefits of tofacitinib treatment prior to initiating therapy in patients with a known malignancy or when considering continuing tofacitinib in patients who develop a malignancy. Malignancies were observed in clinical studies of tofacitinib.
- **Gastrointestinal (GI) Perforations:** Events of GI perforation have been reported in clinical studies with tofacitinib in RA patients.
- **Laboratory Abnormalities:** Lymphocyte abnormalities, neutropenia, liver enzyme elevations, and lipid elevations have all occurred with treatment with tofacitinib.
- **Vaccinations:** No data are available on the response to vaccination or on the secondary transmission of infection by live vaccines to patients receiving tofacitinib. Use of live vaccines concurrently with tofacitinib should be avoided.

Adverse Reactions: The most common adverse reactions ($\geq 2\%$ of patients & $\geq 1\%$ placebo) experienced during clinical trials with tofacitinib include the following:

- | | | |
|-------------------|---------------------|----------------|
| ▪ Diarrhea | ▪ Upper Respiratory | ▪ Headache |
| ▪ Nasopharyngitis | Tract Infection | ▪ Hypertension |

Use in Special Populations:

- **Pregnancy:** Tofacitinib is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- **Nursing Mothers:** Tofacitinib was secreted in the milk of lactating rats. It is not known whether tofacitinib is excreted in human milk.
- **Pediatric Use:** The safety and effectiveness of tofacitinib in pediatric patients have not been established.
- **Geriatric Use:** Of the 3,315 patients studied, a total of 505 RA patients were 65 years of age and older. The frequency of serious infection among tofacitinib-treated subjects 65 years of age and older was higher than among those under the age of 65.
- **Use in Diabetics:** As there is a higher incidence of infection in the diabetic population in general, caution should be used when treating patients with diabetes.
- **Hepatic Impairment:** Tofacitinib-treated patients with moderate hepatic impairment had greater tofacitinib levels than patients with normal hepatic function. Higher blood levels may increase the risk of some adverse reactions.
- **Renal Impairment:** Tofacitinib-treated patients with moderate and severe renal impairment had greater tofacitinib blood levels than tofacitinib-treated patients with normal renal function.

Efficacy: The efficacy of tofacitinib ER is based on efficacy studies of the immediate-release formulation of tofacitinib.

Cost Comparison:

Medication	EAC Per Syringe, Pen, or Tablet	EAC for 6 months of Therapy
Xeljanz® XR (tofacitinib ER) 11mg tablets	\$122.09	\$20,511.12
Xeljanz® (tofacitinib) 5mg tablets	\$61.04	\$20,509.44
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	\$1,081.80	\$25,963.20
Humira® (adalimumab) 40mg/0.8mL pen	\$2,163.25	\$25,959.00

Costs do not reflect rebated prices or net costs.

Dosing based on treatment of RA in a 70kg patient.

EAC for 6 months of therapy based on maintenance treatment dosing after initial dosing is complete.

EAC = estimated acquisition cost

Taltz® (Ixekizumab) Product Summary⁴

Indications: Taltz® (ixekizumab) is a humanized IL-17A antagonist indicated for the treatment of adults with moderate-to-severe PsO who are candidates for systemic therapy or phototherapy.

Dosing: Ixekizumab is available as 80mg/mL single-dose, prefilled autoinjectors and syringes.

- Ixekizumab is administered as a subcutaneous injection into the upper arms, thighs, or abdomen. Injection sites should be rotated.
- The recommended dosing of ixekizumab is 160mg (two 80mg injections) at Week 0, followed by 80mg at weeks 2, 4, 6, 8, 10, and 12, then 80mg every four weeks.
- Ixekizumab should be refrigerated until 30 minutes before use.

Mechanism of Action: Ixekizumab is a humanized immunoglobulin G subclass 4 (IgG4) monoclonal antibody (mAb) antibody that selectively binds with IL-17A and inhibits its interaction with the IL-17 receptor. IL-17A is a cytokine involved in normal inflammatory and immune responses. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

Contraindications: Ixekizumab is contraindicated in patients with a previous serious hypersensitivity reaction to ixekizumab or any of its excipients.

Warnings and Precautions:

- **Infections:** Ixekizumab may increase the risk of infection. In clinical trials, the ixekizumab group had a higher rate of infections than the placebo group (27% vs. 23%).
- **Pre-Treatment Evaluation for Tuberculosis:** Patients should be evaluated for tuberculosis (TB) infection prior to initiating treatment with ixekizumab. Ixekizumab should not be administered to patients with active TB infection and treatment of latent TB should be initiated prior to administering ixekizumab.
- **Hypersensitivity:** Serious hypersensitivity reactions, including angioedema and urticaria (each ≤0.1%), occurred in the ixekizumab group during clinical trials.
- **Inflammatory Bowel Disease:** CD and UC, including exacerbations, occurred at a greater frequency in the ixekizumab group (CD 0.1%, UC 0.2%) than the placebo group (0%) during clinical trials.

- **Immunizations:** Consideration should be given to all appropriate immunizations prior to initiating therapy with ixekizumab. Use of live vaccines in patients treated with ixekizumab should be avoided.

Adverse Reactions: The most commonly occurring adverse reactions reported during clinical trials ($\geq 1\%$ and more frequently than placebo) include the following:

- Injection Site Reactions
- Upper Respiratory Tract Infections
- Nausea
- Tinea Infections

Use in Special Populations:

- **Pregnancy:** There are no available data on ixekizumab use in pregnant women. Human IgG is known to cross the placental barrier; therefore, ixekizumab may be transmitted from the mother to the developing fetus.
- **Nursing Mothers:** There are no data on the presence of ixekizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Ixekizumab was detected in the milk of lactating monkeys.
- **Pediatric Use:** The safety and effectiveness of ixekizumab in pediatric patients younger than 18 years of age have not been evaluated.
- **Geriatric Use:** Of the 4,204 subjects exposed to ixekizumab, 301 were 65 years or older. Although no differences in safety or efficacy were observed in older subjects, the number of subjects aged 65 and over was not sufficient to determine whether they respond differently from younger subjects.

Efficacy: The efficacy of ixekizumab was evaluated in three randomized, double-blind, placebo-controlled trials in 3,866 adult subjects with PsO who had a minimum body surface area involvement of 10%, a static Physician Global Assessment (sPGA) score of ≥ 3 in the overall assessment (plaque thickness, erythema, and scaling) of PsO on a severity scale of 0 to 5, and a Psoriasis Area and Severity Index (PASI) score ≥ 12 . Subjects were randomized to either placebo or ixekizumab. In the two active comparator trials (Trials 2 and 3), subjects were also randomized to receive etanercept 50mg twice weekly for 12 weeks. The primary outcomes were changes from baseline to Week 12 in proportion of subjects who achieved at least a 75% reduction in PASI composite score (PASI 75), and the proportion of subjects with a sPGA of 0 or 1 and at least a 2-point improvement. Of all subjects, 44% had received prior phototherapy, 49% had received prior conventional systemic therapy, and 26% had received prior biologic therapy for the treatment of PsO. Of the subjects who had received prior biologic therapy, 15% had received at least one anti-TNF alpha agent, and 9% had received an anti-IL 12/IL23. Results at week 12 for all three trials are contained in the following table:

	Trial 1		Trial 2		Trial 3	
	Ixekizumab (N=433) n (%)	Placebo (N=431) n (%)	Ixekizumab (N=351) n (%)	Placebo (N=168) n (%)	Ixekizumab (N=385) n (%)	Placebo (N=193) n (%)
sPGA of 0 or 1	354 (82)	14 (3)	292 (83)	4 (2)	310 (81)	13 (7)
PASI 75	386 (89)	17 (4)	315 (90)	4 (2)	336 (87)	14 (7)

In an integrated analysis in the two active comparator studies using etanercept, ixekizumab demonstrated superiority to etanercept on sPGA and PASI scores during the 12 week treatment

period. The response rates for ixekizumab 80mg every two weeks and etanercept 50mg twice weekly were: sPGA of 0 or 1 (73% and 27%); PASI 75 (87% and 41%).

Cost Comparison:

Medication	EAC Per Syringe or Pen	EAC for 6 months of Therapy
Taltz® (ixekizumab) 80mg/mL autoinjector	\$4,333.45	\$26,000.70
Cosentyx® (secukinumab) 150mg/mL Sensoready® pen	\$2,146.09	\$25,753.08
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	\$1,081.80	\$25,963.20
Humira® (adalimumab) 40mg/0.8mL pen	\$2,163.25	\$25,959.00

Costs do not reflect rebated prices or net costs.

EAC for 6 months of therapy based on maintenance treatment dosing of PsO after initial dosing is complete.

EAC = estimated acquisition cost

Inflectra™ (Infliximab-dyyb) Product Summary^{5,29}

Indications: Inflectra™ (infliximab-dyyb) is a biosimilar to Remicade® (infliximab). Infliximab-dyyb is a TNF-blocker indicated for the following:

- **CD:** Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric and adult patients with moderately-to-severely active disease who have had an inadequate response to conventional therapy. Also, for adults in reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.
- **UC:** Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately-to-severely active disease who have had an inadequate response to conventional therapy.
- **RA with methotrexate:** Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately-to-severely active disease.
- **AS:** Reducing signs and symptoms in patients with active disease.
- **PsA:** Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function.
- **PsO:** Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.
- Inflectra™ is indicated for all Remicade® indications except pediatric ulcerative colitis.

Boxed Warning:

- **Serious Infections:** Patients treated with infliximab are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- **Malignancy:** Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF-blockers, including infliximab.

Dosing: Infliximab-dyyb is supplied as 100mg infliximab-dyyb in a 20mL vial intended to be administered by IV infusion over a period of not less than two hours. The recommended dosing varies by disease state. The following dosing recommendations apply:

- CD: 5mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some adult patients who initially respond to treatment may benefit from increasing the dose to 10mg/kg if they later lose their response.
- UC: 5mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- RA with methotrexate: With methotrexate, 3mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some patients may benefit from increasing the dose up to 10mg/kg or treating as often as every 4 weeks.
- AS: 5mg/kg at 0, 2, and 6 weeks, then every 6 weeks.
- PsA and PsO: 5mg/kg at 0, 2, and 6 weeks, then every 8 weeks.

Mechanism of Action: Infliximab products neutralize the biological activity of TNF α by binding with high affinity to TNF α and inhibit binding of TNF α with its receptors.

Contraindications:

- Doses >5mg/kg should not be administered to patients with moderate-to-severe heart failure.
- Infliximab-dyyb should not be readministered to patients who have experienced a severe hypersensitivity reaction to infliximab, or administered to patients with known hypersensitivity to the inactive components or to any murine proteins.

Warnings and Precautions:

- Serious Infections: Patients treated with infliximab are at increased risk for developing serious infections including reactivation of tuberculosis or new tuberculosis infections.
- Malignancies: Malignancies have been reported among children and young adults who received TNF-blockers. Approximately half of these cases were lymphomas. The other cases included malignancies that are usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents.
- Hepatitis B Virus Reactivation: Use of TNF-blockers has been associated with reactivation of hepatitis B virus (HBV).
- Hepatotoxicity: Severe hepatic reactions, including acute liver failure, jaundice, hepatitis, and cholestasis have been reported in patients receiving infliximab.
- Heart Failure: Infliximab has been associated with adverse outcomes in patients with heart failure, and should be used in patients with heart failure only after consideration of other treatment options.
- Hematologic Reactions: Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia have been reported in patients receiving infliximab.
- Hypersensitivity: Infliximab has been associated with hypersensitivity reactions.
- Neurologic Reactions: TNF-blockers have been associated with CNS manifestation of systemic vasculitis, seizure, and new onset or exacerbation of central nervous system demyelinating disorders.
- Concurrent Administration with Other Biological Therapies: There is insufficient information regarding the concomitant use of infliximab products with other biological therapeutics used to treat the same conditions as infliximab-dyyb.

- Switching Between Biological DMARDs: Care should be taken when switching biologics, since overlapping biological activity may increase the risk of infection.
- Autoimmunity: Treatment with infliximab products may result in the formation of autoantibodies and the development of a lupus-like syndrome.
- Live Vaccines/Therapeutic Infectious Agents: Limited data are available in patients receiving anti-TNF therapy and the response to live vaccines. Use of live vaccines while on infliximab-dyyb could result in clinical infections and is not recommended.

Adverse Reactions: The most common adverse reactions (≥10% of patients) experienced during clinical trials for the treatment of RA include:

- | | | |
|------------------|---------------------|--------------|
| ▪ Nausea | ▪ Upper Respiratory | ▪ Coughing |
| ▪ Abdominal Pain | Tract Infection | ▪ Bronchitis |
| ▪ Diarrhea | ▪ Sinusitis | ▪ Rash |
| ▪ Dyspepsia | ▪ Pharyngitis | ▪ Headache |

Use in Special Populations:

- Pregnancy: Infliximab-dyyb is pregnancy category B. It is not known whether infliximab can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.
- Nursing Mothers: It is not known whether infliximab is excreted in human milk.
- Pediatric Use: The safety and effectiveness of infliximab have been established in pediatric patients 6 to 17 years of age for CD. However, infliximab has not been studied in children with CD or UC <6 years of age.
- Geriatric Use: In RA and PsO clinical trials, no overall differences were observed in 256 patients aged 65 or older who received infliximab compared to younger patients – although the incidence of serious adverse reactions in patients aged 65 or older was higher in both infliximab and control groups compared to younger patients.

Efficacy: The clinical trials outlined in the infliximab-dyyb prescribing information are summaries of the clinical studies of Remicade® (infliximab). Since infliximab-dyyb is a biosimilar, it was approved by showing similarity to an already-approved reference product. The biosimilar must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. A biosimilar product can only be approved if it has the same mechanism(s) of action, route(s) of administration, dosage form(s), and strength(s) as the reference product, and only for the indication(s) and condition(s) of use that have been approved for the reference product. The FDA's approval of infliximab-dyyb is based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data.

Cost Comparison:

Medication	EAC Per Syringe, Pen, or Vial	EAC for 6 months of Therapy
Inflectra® (infliximab-dyyb) 100mg vial	Not Available	Not Available
Remicade® (infliximab) 100mg vial	\$1,131.48	\$10,183.32-\$23,761.08
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	\$1,081.80	\$25,963.20
Humira® (adalimumab) 40mg/0.8mL pen	\$2,163.25	\$25,959.00

Costs do not reflect rebated prices or net costs.

Dosing based on treatment of RA in a 70kg patient.

EAC for 6 months of therapy based on maintenance treatment dosing after initial dosing is complete.

EAC = estimated acquisition cost

Erelzi™ (Etanercept-szszs) Product Summary^{8,30}

Indications: Erelzi™ (etanercept-szszs) is a biosimilar to Enbrel® (etanercept). Etanercept-szszs is a TNF-blocker indicated for the following:

- **RA:** Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately-to-severely active RA in combination with methotrexate or used alone.
- **Polyarticular JIA:** Reducing signs and symptoms of moderately-to-severely active polyarticular JIA in patients ages 2 and older.
- **PsA:** Reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with PsA.
- **AS:** Reducing signs and symptoms in patients with active disease.
- **PsO:** Treatment of adult patients with chronic moderate-to-severe PsO who are candidates for systemic therapy or phototherapy.
- Erelzi™ is indicated for all Enbrel® indications.

Boxed Warning:

- **Serious Infections:** Patients treated with etanercept are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- **Malignancy:** Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF-blockers, including etanercept.

Dosing: Etanercept-szszs is supplied as 25mg/0.5mL and 50mg/mL prefilled syringes and 50mg/mL prefilled Sensoready® pens intended for subcutaneous injection. The recommended dosing varies by disease state. The following dosing recommendations apply:

- **Adult RA and PsA:** 50mg once weekly with or without methotrexate
- **AS:** 50mg once weekly
- **Adult PsO:** 50mg twice weekly for 3 months, followed by 50mg once weekly
- **JIA:** 0.8mg/kg weekly, with a maximum of 50mg per week

Mechanism of Action: TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Etanercept binds TNF molecules rendering TNF biologically inactive.

Contraindications: Patients with sepsis should not receive etanercept-szszs.

Warnings and Precautions:

- Serious Infections: Patients treated with etanercept are at increased risk for developing serious infections including reactivation of tuberculosis or new tuberculosis infections.
- Neurologic Events: TNF-blockers have been associated with new onset or exacerbation of central nervous system demyelinating disorders.
- Malignancies: Malignancies have been reported among children and adolescents who received TNF-blockers.
- Heart Failure: One study of etanercept in patients with heart failure suggested higher mortality in etanercept-treated patients compared to placebo. There have been postmarketing reports of worsening of congestive heart failure (CHF) in patients taking etanercept.
- Hematologic Events: Rare reports of pancytopenia, including very rare reports of aplastic anemia, have been reported in patients treated with etanercept.
- Hepatitis B Virus Reactivation: Use of TNF-blockers has been associated with reactivation of hepatitis B virus (HBV).
- Allergic Reactions: Allergic reactions associated with administration of etanercept during clinical trials have been reported in <2% of patients.
- Immunizations: Live vaccines should not be given concurrently with etanercept.
- Autoimmunity: Treatment with etanercept products may result in the formation of autoantibodies and the development of a lupus-like syndrome.
- Immunosuppression: TNF mediates inflammation and modulates cellular immune responses. TNF-blockers affect host defenses against infections.
- Use in Wegener's Granulomatosis Patients: The use of etanercept in patients with Wegener's granulomatosis receiving immunosuppressive agents is not recommended.
- Use in Patients with Moderate-to-Severe Alcoholic Hepatitis: Prescribers should use caution when using etanercept in patients with moderate-to-severe alcoholic hepatitis.

Adverse Reactions: The most common adverse reactions (≥10% of patients) experienced during clinical trials for the treatment of RA include:

- | | | |
|---------------------|-------------------|------------------|
| ▪ Infection | ▪ Non-Upper | ▪ Injection Site |
| ▪ Upper Respiratory | Respiratory Tract | Reactions |
| Tract Infection | Infection | ▪ Diarrhea |
| | | ▪ Rash |

Use in Special Populations:

- Pregnancy: Limited published data on use of etanercept in pregnant women are insufficient to inform a drug-associated risk.
- Nursing Mothers: Limited data from published literature show that etanercept is present in low levels in human milk and minimally absorbed by a breastfed infant.
- Pediatric Use: Etanercept has not been studied in children <2 years of age with JIA. The safety and efficacy of etanercept in pediatric patients with PsO have not been established.
- Geriatric Use: A total of 480 RA patients age 65 years or older have been studied in clinical trials. No overall differences in safety or effectiveness were observed between these patients and younger patients.

- **Use in Diabetics:** There have been reports of hypoglycemia following initiation of etanercept in patients receiving medication for diabetes, necessitating a reduction in anti-diabetic medication in some of these patients.

Efficacy: The clinical trials outlined in the etanercept-szszs prescribing information are summaries of the clinical studies of Enbrel® (etanercept). Since etanercept-szszs is a biosimilar, it was approved by showing similarity to an already-approved reference product. The biosimilar must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. The approval of etanercept-szszs is based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data that demonstrated etanercept-szszs was biosimilar to Enbrel®.

Cost Comparison:

Medication	EAC Per Syringe or Pen	EAC for 6 months of Therapy
Erelzi™ (etanercept-szszs) 50mg/mL Sensoready® Pen	Not Available	Not Available
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	\$1,081.80	\$25,963.20
Humira® (adalimumab) 40mg/0.8mL pen	\$2,163.25	\$25,959.00

Costs do not reflect rebated prices or net costs.

Dosing based on treatment of RA in a 70kg patient.

EAC for 6 months of therapy based on maintenance treatment dosing after initial dosing is complete.

EAC = estimated acquisition cost

Amjevita™ (Adalimumab-atto) Product Summary^{31,32}

Indications: Amjevita™ (adalimumab-atto) is a biosimilar to Humira® (adalimumab).

Adalimumab-atto is a TNF-blocker indicated for the following:

- **RA:** Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately-to-severely active RA.
- **Polyarticular JIA:** Reducing signs and symptoms of moderately-to-severely active polyarticular JIA in patients 4 years of age and older.
- **PsA:** Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
- **AS:** Reducing signs and symptoms in adult patients with active AS.
- **CD:** Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately-to-severely active CD who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.
- **UC:** Inducing and sustaining clinical remission in adult patients with moderately-to-severely active UC who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine, or 6-mercaptopurine.
- **PsO:** The treatment of adult patients with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.

- Amjevita™ is indicated for all Humira® indications except pediatric CD, polyarticular JIA in pediatric patients 2 to 4 years, hidradenitis suppurativa, and uveitis.

Boxed Warning:

- **Serious Infections:** Patients treated with adalimumab are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- **Malignancy:** Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF-blockers, including adalimumab.

Dosing: Adalimumab-atto is supplied as 40mg/0.8mL and 20mg/0.4mL prefilled syringes and 40mg/0.8mL prefilled SureClick® autoinjectors intended for subcutaneous injection. The recommended dosing varies by disease state. The following dosing recommendations apply:

- **RA, PsA, and AS:** 40mg every other week; some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40mg every week.
- **JIA:** 15kg to <30kg: 20mg every other week; ≥30kg: 40mg every other week.
- **CD and UC:** 160mg (four 40mg injections in one day or two 40mg injections per day for two consecutive days) Day 1, 80mg Day 15, maintenance dose of 40mg every other week from Day 29 forward. Patients with UC should only continue therapy if they have shown evidence of clinical remission by eight weeks.
- **PsO:** 80mg, followed by 40mg every other week starting one week after initial dose.

Mechanism of Action: Adalimumab binds to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors. Adalimumab products also lyse surface TNF expressing cells in vitro in the presence of complement. TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses.

Contraindications: None.

Warnings and Precautions:

- **Serious Infections:** Patients treated with adalimumab are at increased risk for developing serious infections including reactivation of tuberculosis or new tuberculosis infections.
- **Malignancies:** In the controlled portions of clinical trials of some TNF-blockers, including adalimumab, more cases of malignancies have been observed among TNF-blocker-treated adult patients compared to control-treated adult patients.
- **Hypersensitivity Reactions:** Anaphylaxis and angioneurotic edema have been reported following administration of adalimumab products.
- **Hepatitis B Virus Reactivation:** Use of TNF-blockers has been associated with reactivation of hepatitis B virus (HBV).
- **Neurologic Reactions:** Use of TNF-blockers has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis (MS) and optic neuritis, and peripheral demyelinating disease, including Guillain-Barré syndrome.
- **Hematologic Reactions:** Rare reports of pancytopenia, including aplastic anemia have been reported in patients treated with TNF-blockers.

- Use with Anakinra: Concurrent use of anakinra and another TNF-blocker, was associated with a greater proportion of serious infections and neutropenia and no added benefit compared with the TNF-blocker alone in patients with RA.
- Heart Failure: Cases of worsening CHF and new onset CHF have been reported with TNF-blockers. Cases of worsening CHF have also been observed with adalimumab. Adalimumab products have not been formally studied in patients with CHF.
- Autoimmunity: Treatment with adalimumab products may result in the formation of autoantibodies and the development of a lupus-like syndrome.
- Immunizations: No data are available on the secondary transmission of infection by live vaccines in patients receiving adalimumab products.
- Use with Abatacept: In controlled trials, the concurrent administration of TNF-blockers and abatacept was associated with a greater proportion of serious infections than the use of a TNF-blocker alone; the combination therapy has not demonstrated improved clinical benefit over monotherapy in the treatment of RA.

Adverse Reactions: The most common adverse reactions (≥10% of patients) experienced during clinical trials for the treatment of RA include:

- | | | |
|-------------------------------------|-------------|---------------------|
| ▪ Upper Respiratory Tract Infection | ▪ Sinusitis | ▪ Rash |
| | ▪ Headache | ▪ Accidental Injury |

Use in Special Populations:

- Pregnancy: Limited clinical data are available from a Pregnancy Registry conducted with adalimumab. Adalimumab is actively transferred across the placenta during the third trimester of pregnancy and may affect immune response in the in-utero exposed infant.
- Nursing Mothers: Limited data from case reports in the published literature describe the presence of adalimumab in human milk at infant doses of 0.1% to 1% of the maternal serum level.
- Pediatric Use: Safety and efficacy of adalimumab-atto in pediatric patients for uses other than polyarticular JIA have not been established.
- Geriatric Use: A total of 519 RA patients 65 years of age and older, received adalimumab in clinical studies. No overall difference in effectiveness was observed between these patients and younger patients.

Efficacy: The clinical trials outlined in the adalimumab-atto prescribing information are summaries of the clinical studies of Humira® (adalimumab). Since adalimumab-atto is a biosimilar, it was approved by showing similarity to an already-approved reference product. The biosimilar must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. The approval of adalimumab-atto is based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data that demonstrated adalimumab-atto was biosimilar to Humira®.

Cost Comparison:

Medication	EAC Per Syringe or Pen	EAC for 6 months of Therapy
Amjevita™ (adalimumab-atto) 40mg/0.8mL SureClick® autoinjector	Not Available	Not Available
Humira® (adalimumab) 40mg/0.8mL pen	\$2,163.25	\$25,959.00
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	\$1,081.80	\$25,963.20

Costs do not reflect rebated prices or net costs.

Dosing based on treatment of RA in a 70kg patient.

EAC for 6 months of therapy based on maintenance treatment dosing after initial dosing is complete.

EAC = estimated acquisition cost

Noninfectious Intermediate Uveitis, Posterior Uveitis, & Panuveitis Summary

6,33,34,35,36,37,38,39

Uveitis is a complex of diseases involving inflammation of the middle portion of the eye known as the uvea that can lead to vision loss and blindness. Uveitis is characterized by the location of inflammation which is classified as anterior, intermediate, posterior, and panuveitis. Posterior uveitis comprises the posterior portion of the uvea including the choroid; intermediate uveitis involves inflammation of the peripheral retina, pars plana, and vitreous. Panuveitis includes inflammation of the anterior chamber, vitreous humor, and retina or choroid. Posterior and intermediate uveitis comprise 8 to 15% of uveitis cases, and while not typically painful, often involve vision changes such as floaters, blurred vision, and reduced visual acuity.

While not well defined, the prevalence of uveitis is estimated to range from 69.0 to 114.5 per 100,000 persons annually. The etiology of uveitis can include infectious causes, systemic immune-mediated causes, uveitis syndromes restricted to the eye, or idiopathic causes. Approximately 40% of uveitis cases are associated with a systemic immune-mediated cause and approximately 30% of cases are idiopathic. Systemic causes commonly associated with intermediate and posterior uveitis include sarcoidosis, multiple sclerosis, and lyme disease.

Corticosteroids are the mainstay of treatment for uveitis. Topical corticosteroids are effective for anterior uveitis; however, topical drops are ineffective for the treatment of intermediate, posterior, or panuveitis and are not recommended in current treatment algorithms. Instead, algorithms recommend periocular corticosteroid injections. Other treatment options with some benefit include immunosuppressive agents such as cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil. In July 2016, Humira® (adalimumab) was approved by the FDA as the first noncorticosteroid therapy for noninfectious intermediate uveitis, posterior uveitis, and panuveitis. Recently, the European Commission approved adalimumab for the treatment of noninfectious intermediate uveitis, posterior uveitis, and panuveitis in patients who do not respond adequately to corticosteroids or in whom corticosteroid treatment is inappropriate.

Two randomized, double-blind, placebo-controlled studies evaluated the safety and efficacy of adalimumab in 443 adult subjects with non-infectious intermediate uveitis, posterior uveitis, and panuveitis while being treated with corticosteroids. Both studies required a mandatory taper of corticosteroids and evaluated the time to treatment failure defined as the development of new inflammatory chorioretinal or retinal vascular lesions, an increase in anterior chamber cell grade or vitreous haze grade, or a decrease in best corrected visual acuity

(BCVA). In both studies, time to treatment failure was longer in adalimumab-treated subjects compared to placebo [**Study I:** 3.0 (2.7, 3.7) *placebo* vs 5.6 (3.9, 9.2) *adalimumab*, **Study II:** 8.3 (4.8, 12.0) *placebo* vs NE (not estimable; fewer than half of at-risk subjects had an event) *adalimumab*].

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and Familial Mediterranean Fever (FMF) Summary^{11,40,41,42,43,44}

Tumor necrosis factor receptor associated periodic syndrome (TRAPS) is an autosomal dominant inherited condition characterized by periodic episodes of fever, muscle pain, and a spreading skin rash. The feverish periods typically last three weeks but can last up to several months. Additional symptoms associated with TRAPS include the following: periorbital edema, joint pain, and inflammation throughout the body including the eyes, heart muscle, throat, joints, and mucous membranes. The episodes can begin at any age, but most experience their first occurrence in childhood. TRAPS has an estimated prevalence of one per one million individuals. Prior to the approval of a TRAPS indication for Ilaris® (canakinumab) in September 2016, no other therapies were FDA approved for TRAPS and no treatment guidelines are available. Etanercept has been used successfully to manage patients with TRAPS; 15 patients with TRAPS were enrolled in a prospective, open-label study that found etanercept treatment attenuated the total symptom score, reduced the frequency of symptoms, and reduced levels of acute-phase reactants. Patients included in canakinumab clinical trials were those with chronic or recurrent disease activity defined as six flares per year.

Mevalonate kinase deficiency (MKD) is an autosomal recessive inherited condition characterized by periodic episodes of fever which typically begin during infancy. An estimated 200 cases have been reported throughout the world. The feverish periods usually last three to six days and the frequency varies with the greatest regularity occurring during childhood (as often as 25 times per year). MKD severity depends on the type of MKD: Hyperimmunoglobulin D syndrome (HIDS) or the more severe mevalonic aciduria (MVA). Symptoms associated with HIDS include: lymphadenopathy, abdominal pain, joint pain, diarrhea, skin rashes, headache, aphthous ulcers, intellectual disability, ataxia, epilepsy, and amyloidosis. Patients with HIDS typically don't have symptoms between fever episodes and have a normal life expectancy. In contrast, patients with MVA have symptoms at all times and may only live into early childhood. Symptoms associated with MVA include: developmental delay, progressive ataxia, progressive vision problems, and failure to thrive. Prior to the approval of a HIDS/MKD indication for canakinumab in September 2016 no other therapies were FDA approved for MKD. Patients included in canakinumab clinical trials were those with a confirmed diagnosis of HIDS according to known genetic MVK enzymatic findings, and a documented history of at least three febrile acute flares within a six month period.

Familial Mediterranean fever (FMF) is an autosomal recessive inherited condition characterized by periodic episodes of painful inflammation in the abdomen, chest, or joints. Most episodes are also associated with fever, rash, and headache. Other symptoms may include inflammation in the heart, testicles, and spinal cord. Episodes last 12 to 72 hours and frequency varies. The first occurrence typically occurs in childhood but may occur later in life. Patients are symptom free in between attacks, but without treatment amyloidosis, which may lead to kidney failure,

may occur. FMF affects an estimated 1 in 200 to 1,000 people of Mediterranean descent but is less common in other populations. The mainstay of attack prevention is colchicine. Patients included in canakinumab clinical trials were those with documented active disease despite colchicine therapy or documented intolerance to effective doses of colchicine.

Recommendations

The College of Pharmacy recommends the addition of Orencia® ClickJect™ (abatacept autoinjector), Xeljanz® XR (tofacitinib extended-release), Taltz® (ixekizumab), Inflectra™ (infliximab-dyyb), Erelzi™ (etanercept-szzs), and Amjevita™ (adalimumab-atto) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category.

Current Tier-3 approval criteria for this category will apply.

- If the net cost of Inflectra™ (infliximab-dyyb), Erelzi™ (etanercept-szzs), and Amjevita™ (adalimumab-atto) is determined to be greater than the net cost of the reference product formulations of Inflectra™, Erelzi™, and Amjevita™ authorization would also require a patient-specific, clinically significant reason why the member could not use the reference product formulations of Inflectra™, Erelzi™, and Amjevita™.
- If the net cost of Xeljanz® XR (tofacitinib extended-release) and Orencia® ClickJect™ (abatacept autoinjector) is determined to be greater than the net cost of the immediate-release formulation of Xeljanz® XR or the prefilled syringe formulation of Orencia® ClickJect™ authorization would also require a patient-specific, clinically significant reason why the member could not use the immediate-release formulation of Xeljanz® XR or the prefilled syringe formulation of Orencia® ClickJect™.

Additionally, the College of Pharmacy recommends the following criteria for Humira® (adalimumab) for a diagnosis of noninfectious intermediate and posterior uveitis or panuveitis:

Humira® (Adalimumab) for Noninfectious Intermediate and Posterior Uveitis or Panuveitis Approval Criteria:

1. A diagnosis of noninfectious intermediate uveitis, posterior uveitis, or panuveitis in adults; and
2. A failed trial with a corticosteroid injection or systemic steroid in which member has had an inadequate response; or
3. A patient-specific, clinically significant reason a trial of corticosteroid treatment is inappropriate for the member.

Lastly, the College of Pharmacy recommends the following criteria for Ilaris® (canakinumab) for a diagnosis of tumor necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD), or familial Mediterranean fever (FMF):

Ilaris® (Canakinumab) for Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF) Approval Criteria:

1. A diagnosis of tumor necrosis factor receptor associated periodic syndrome (TRAPS) with chronic or recurrent disease activity defined as six flares per year; or
2. A diagnosis of hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD); or

3. A diagnosis of familial Mediterranean fever (FMF) with documented active disease despite colchicine therapy or documented intolerance to effective doses of colchicine; 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.

Targeted Immunomodulator Agents*		
Tier-1 (DMARDs appropriate to disease state)	Tier-2*	Tier-3+
6-mercaptopurine	adalimumab (Humira®)	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	adalimumab-atto (Amjevita™)
hydroxychloroquine		alefacept (Amevive®)
leflunomide		anakinra (Kineret®)
mesalamine		apremilast (Otezla®)
methotrexate		canakinumab (Ilaris®)‡
minocycline		certolizumab pegol (Cimzia®)
NSAIDs		etanercept-szszs (Erelzi™)
oral corticosteroids		golimumab (Simponi® & Simponi® Aria™)
		infliximab (Remicade®)
		infliximab-dyyb (Inflectra™)
		rituximab (Rituxan®)
		secukinumab (Cosentyx®)
		tocilizumab (Actemra®)
		tofacitinib (Xeljanz® & Xeljanz® XR)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

DMARDs = Disease modifying antirheumatic drugs, NSAIDs = Nonsteroidal anti-inflammatory drugs

*May be rebated to Tier-2 status only

‡Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF).

Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least one Tier-1 medication in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. For a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) authorization of a Tier-2 product requires history of failure of a mesalamine product (does not have to be within the last 90 days) and a trial of one Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
4. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 medication and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 products.

Humira® (Adalimumab) for Hidradenitis Suppurativa Approval Criteria:

1. A diagnosis of moderate-to-severe hidradenitis suppurativa (HS); and
2. Hurley Stage II or III disease; and
3. The member must have at least 3 abscesses or inflammatory nodules; and
4. Previous failure of at least two of the following: topical or systemic antibiotics, oral or intralesional corticosteroids, dapsons, cyclosporine, antiandrogens (spironolactone or oral contraceptives), finasteride, or surgery.

Ilaris® (Canakinumab) Approval Criteria [Cryopyrin-Associated Periodic Syndromes (CAPS) Diagnosis]:

1. An FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 years of age and older; and
2. The member must not be using a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, and infliximab) or anakinra; and
3. Ilaris® should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
4. The following dosing requirements must be met:
 - a. Dosing should not be more often than once every 8 weeks; and
 - b. Dosing (requires recent weight in kilograms):
 - i. Body weight greater than 40kg: 150mg
 - ii. Body weight 15kg to 40kg: 2mg/kg. If inadequate response, may be increased to 3mg/kg.
5. Approvals will be for the duration of one year.

Utilization Details of Targeted Immunomodulator Agents: Fiscal Year 2016

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM
TIER-2 PRODUCTS					
ADALIMUMAB PRODUCTS					
HUMIRA PEN 40MG/0.8ML	1,786	328	\$7,677,557.04	\$148.63	\$4,298.74
HUMIRA SYR 40MG/0.8ML	413	77	\$1,947,088.47	\$166.79	\$4,714.50
HUMIRA CROHNS 40MG/0.8ML	48	47	\$551,099.24	\$374.13	\$11,481.23
HUMIRA PSO 40MG/0.8ML	43	42	\$324,037.50	\$262.17	\$7,535.76
HUMIRA SYR 20MG/0.4ML	29	4	\$110,312.60	\$126.22	\$3,803.88
HUMIRA SYR 10MG/0.2ML	5	1	\$20,066.70	\$143.33	\$4,013.34
HUMIRA PED CROHNS 40MG/0.8ML	2	2	\$11,094.05	\$198.11	\$5,547.03
SUBTOTAL	2,326	418	\$10,641,255.60	\$158.57	\$4,574.92
ETANERCEPT PRODUCTS					
ENBREL SRCLK INJ 50MG/ML	967	190	\$3,745,333.59	\$137.72	\$3,873.15
ENBREL INJ 50MG/ML	212	49	\$814,782.19	\$137.15	\$3,843.31
ENBREL INJ 25MG	116	19	\$221,420.41	\$67.88	\$1,908.80
ENBREL INJ 25/0.5ML	41	12	\$96,562.69	\$83.39	\$2,355.19
SUBTOTAL	1,336	260	\$4,878,098.88	\$129.89	\$3,651.27
TIER-2 SUBTOTAL	3,662	635	\$15,519,354.48	\$148.28	\$4,237.94
TIER-3 PRODUCTS					
INFLIXIMAB PRODUCTS					
REMICADE INJ 100MG	177	20	\$1,053,320.60	\$227.99	\$5,950.96
SUBTOTAL	177	20	\$1,053,320.60	\$227.99	\$5,950.96
CERTOLIZUMAB PEGOL PRODUCTS					
CIMZIA PREFL KIT 200MG/ML	144	30	\$500,336.00	\$120.50	\$3,474.56
CIMZIA KIT STARTER 200MG/ML	9	9	\$78,841.16	\$216.00	\$8,760.13
SUBTOTAL	153	33	\$579,177.16	\$128.22	\$3,785.47
ABATACEPT PRODUCTS					
ORENCIA INJ 125MG/ML	141	24	\$454,061.09	\$113.80	\$3,220.29
SUBTOTAL	141	24	\$454,061.09	\$113.80	\$3,220.29
CANAKINUMAB PRODUCTS					
ILARIS 180 MG/1.2 VIAL	86	13	\$1,820,996.15	\$660.74	\$21,174.37
SUBTOTAL	86	13	\$1,820,996.15	\$660.74	\$21,174.37
TOFACITINIB PRODUCTS					
XELJANZ TAB 5MG	79	14	\$255,982.84	\$108.01	\$3,240.29
SUBTOTAL	79	14	\$255,982.84	\$108.01	\$3,240.29
GOLIMUMAB PRODUCTS					
SIMPONI INJ 50/0.5ML	58	13	\$219,609.86	\$131.03	\$3,786.38
SIMPONI INJ 50/0.5ML	9	5	\$33,779.86	\$126.04	\$3,753.32
SIMPONI INJ 100MG/ML	5	2	\$31,353.53	\$223.95	\$6,270.71
SUBTOTAL	72	17	\$284,743.25	\$136.63	\$3,954.77
TOCILIZUMAB PRODUCTS					
ACTEMRA INJ 80MG/4ML	58	4	\$26,840.05	\$23.46	\$462.76
ACTEMRA INJ 200/10ML	49	4	\$59,023.36	\$64.09	\$1,204.56
ACTEMRA INJ 400/20ML	34	4	\$88,970.74	\$107.19	\$2,616.79
ACTEMRA INJ 162/0.9ML	31	6	\$76,161.03	\$87.74	\$2,456.81
SUBTOTAL	172	13	\$250,995.18	\$66.70	\$1,459.27

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM
USTEKINUMAB PRODUCTS					
STELARA 90 MCG	29	11	\$516,873.30	\$219.01	\$17,823.22
STELARA 45MG/0.5ML	23	9	\$206,586.14	\$146.93	\$8,982.01
SUBTOTAL	52	20	\$723,459.44	\$192.10	\$13,912.68
APREMILAST PRODUCTS					
OTEZLA TAB 30MG	28	10	\$70,823.10	\$84.31	\$2,529.40
OTEZLA TAB 10/20/30MG	3	3	\$7,409.73	\$66.75	\$2,469.91
SUBTOTAL	31	10	\$78,232.83	\$82.26	\$2,523.64
ANAKINRA PRODUCTS					
KINERET 100 MG/0.67ML	19	3	\$70,895.94	\$133.26	\$3,731.37
SUBTOTAL	19	3	\$70,895.94	\$133.26	\$3,731.37
SECUKINUMAB PRODUCTS					
COSENTYX PEN INJ 150MG/ML	8	4	\$69,644.86	\$310.91	\$8,705.61
SUBTOTAL	8	4	\$69,644.86	\$310.91	\$8,705.61
VEDOLIZUMAB PRODUCTS					
ENTYVIO INJ 300MG	2	2	\$10,203.51	\$145.46	\$5,101.76
SUBTOTAL	2	2	\$10,203.51	\$145.76	\$5,101.76
RITUXIMAB PRODUCTS					
RITUXAN INJ 500MG	2	1	\$30,802.80	\$550.05	\$15,401.40
SUBTOTAL	2	1	\$30,802.80	\$550.05	\$15,401.40
TIER-3 SUBTOTAL	994	160	\$5,682,515.65	\$191.34	\$5,716.82
TOTAL	4,656	760*	\$21,201,870.13	\$157.80	\$4,553.67

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS	COST/CLAIM
CIMZIA INJ J0717	22	3	\$40,252.00	6,200	\$1,829.64
SIMPONI ARIA IV INJ J1602	9	3	\$15,273.88	1,550	\$1,697.10
REMICADE INJ J1745	181	44	\$505,076.32	8,295	\$2,790.48
ACTEMRA INJ J3262	69	11	\$138,060.99	35,125	\$2,000.88
ENTYVIO INJ J3380	1	1	\$10,212.00	600	\$10,212.00
RITUXAN INJ J9310	76	43	\$578,337.33	762	\$7,609.70
TOTAL	358	104*	\$1,287,212.52	52,532	\$3,559.57

*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 Bladder Control Medications

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

Bladder Control Medications		
Tier-1	Tier-2	Tier-3
oxybutynin (Ditropan®)	tolterodine (Detrol®)	darifenacin (Enablex®)
oxybutynin ER (Ditropan XL®)	trospium (Sanctura™)	fesoterodine (Toviaz™)
		flavoxate (Urispas®)
		mirabegron (Myrbetriq™)
		oxybutynin gel (Gelnique™)
		oxybutynin patch (Oxytrol®)
		solifenacin (VESicare®)
		tolterodine ER (Detrol LA®)
		trospium ER (Sanctura XR™)

Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
ER = extended release

Bladder Control Medications Tier-2 Approval Criteria:

1. A trial of all Tier-1 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-1 medications lack.

Bladder Control Medications Tier-3 Approval Criteria:

1. A trial of all Tier-2 medications that yielded inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-2 medications lack.

Utilization of Bladder Control Medications: Fiscal Year 2016

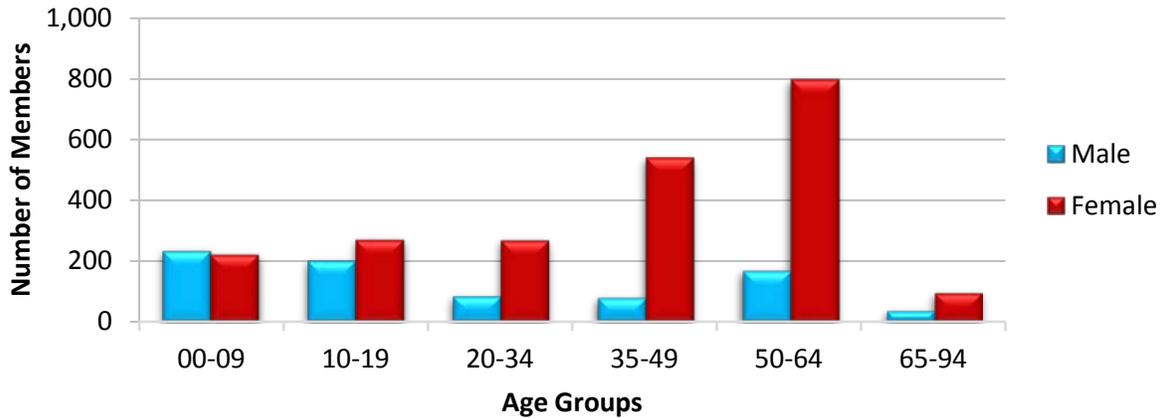
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	3,026	12,947	\$777,150.89	\$60.03	\$1.93	963,505	403,297
2016	2,999	13,211	\$699,571.07	\$52.95	\$1.66	956,922	420,414
% Change	-0.90%	2.00%	-10.00%	-11.80%	-14.00%	-0.70%	4.20%
Change	-27	264	-\$77,579.82	-\$7.08	-\$0.27	-6,583	17,117

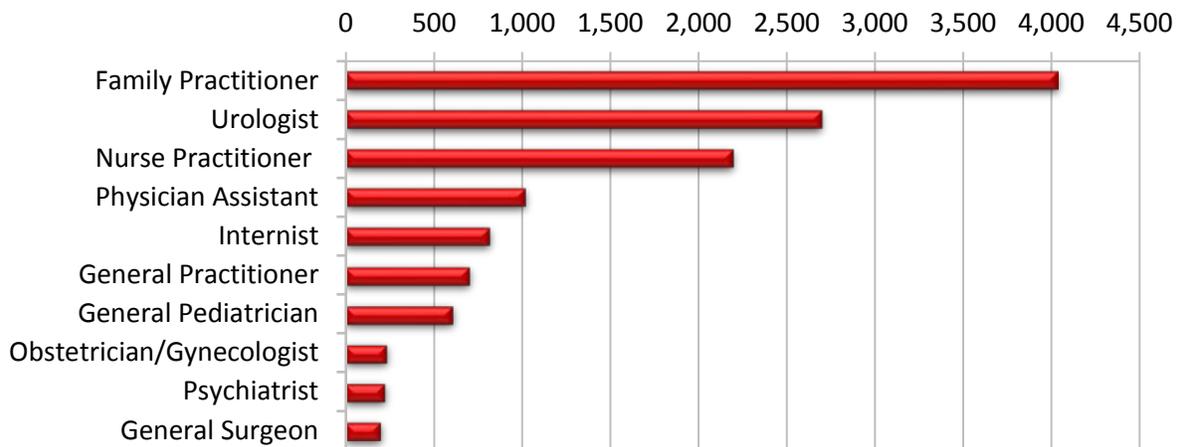
*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Bladder Control Medications

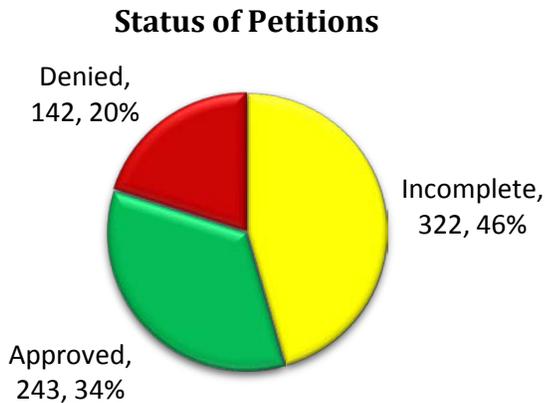


Top Prescriber Specialties of Bladder Control Medications by Number of Claims



Prior Authorization of Bladder Control Medications

There were 707 prior authorization requests submitted for the bladder control medications during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates¹

Anticipated Patent Expiration(s):

- VESIcare® (solifenacin): November 2018
- Oxytrol® (oxybutynin patch): April 2020
- Myrbetriq™ (mirabegron): November 2023
- Toviaz™ (fesoterodine): June 2027
- Gelnique™ (oxybutynin gel): March 2031

Pricing Trend(s)^{2,3,4,5}

There are several oxybutynin products available for the treatment of overactive bladder. Generic formulations, such as oxybutynin and oxybutynin extended-release tablets, provide cost-effective options for the treatment of overactive bladder. Additionally, Gelnique™ (oxybutynin 3% gel) offers a transdermal option for patients in whom an oral dosage form is not appropriate. In January 2013, the U.S. Food and Drug Administration (FDA) approved the first over-the-counter (OTC) treatment for overactive bladder in women ages 18 years and older, Oxytrol® (oxybutynin 3.9mg/day patch) for Women. The prescription product, Oxytrol®, is still available as the OTC version did not receive FDA approval for treatment of overactive bladder in men. Safety concerns regarding the possible need for physician involvement for prostate evaluation in men limited the FDA approval of the OTC version to women.

Cost Comparison:

Medication	Cost Per Unit	Cost for 30 Days of Therapy*
Oxytrol® (oxybutynin 3.9mg/day patch)	\$71.67⁺	\$573.36⁺
Gelnique™ (oxybutynin 3% gel)	\$11.12 ⁺	\$333.60 ⁺
Ditropan XL® (oxybutynin extended-release tablets)	\$0.84 ^Δ	\$25.20 ^Δ
Ditropan® (oxybutynin tablets)	\$0.34 ^Δ	\$30.60 ^Δ

*30 days of therapy based on usual dose of medication

⁺EAC = Estimated Acquisition Cost

^ΔSMAC = State Maximum Allowable Cost

Urispas® (flavoxate) has been removed from the Bladder Control Product Based Prior Authorization (PBPA) category. The FDA approved indications for flavoxate are not consistent with the other products in this category. Flavoxate is FDA approved for symptomatic relief of dysuria, urgency, nocturia, suprapubic pain, frequency and incontinence as may occur in cystitis, prostatitis, urethritis, urethrocystitis/urethrotrigonitis. Additionally, the low state maximum allowable cost (SMAC) would necessitate moving it to Tier-1. Requiring a trial of flavoxate as criteria for approval of a Tier-2 medication would not be appropriate given its unique indications.

Recommendations

The College of Pharmacy recommends the following changes to the Bladder Control Medications PBPA category:

1. The placement of Oxytrol® (oxybutynin 3.9mg/day patch) into a Special PA Tier of the Bladder Control PBPA category based on estimated acquisition cost (EAC) with the following criteria:
 - a. An FDA approved diagnosis of overactive bladder; and
 - b. A patient-specific, clinically significant reason why all lower tiered medications are not appropriate for the member; and
 - c. A quantity limit of 8 patches every 30 days will apply.

Bladder Control Medications			
Tier-1	Tier-2	Tier-3	Special PA
oxybutynin (Ditropan®)	tolterodine (Detrol®)	darifenacin (Enablex®)	oxybutynin patch (Oxytrol®)
oxybutynin ER (Ditropan XL®)	trospium (Sanctura™)	fesoterodine (Toviaz™)	
		flavoxate (Urispas®)	
		mirabegron (Myrbetriq™)	
		oxybutynin gel (Gelnique™)	
		solifenacin (VESicare®)	
		tolterodine ER (Detrol LA®)	
		trospium ER (Sanctura XR™)	

Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
ER = extended release

Utilization Details of Bladder Control Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
OXYBUTYNIN PRODUCTS					
OXYBUTYNIN TAB 5MG	6,595	1,684	\$176,618.34	\$0.87	\$26.78
OXYBUTYNIN TAB 10MG ER	1,447	424	\$59,226.60	\$1.16	\$40.93
OXYBUTYNIN TAB 5MG ER	1,130	347	\$42,331.87	\$1.16	\$37.46
OXYBUTYNIN SYP 5MG/5ML	1,103	337	\$10,913.67	\$0.35	\$9.89
OXYBUTYNIN TAB 15MG ER	751	153	\$31,807.71	\$1.16	\$42.35
SUBTOTAL	11,026	2,945	\$320,898.19	\$0.92	\$29.10
TIER-1 SUBTOTAL	11,026	2,945	\$320,898.19	\$0.92	\$29.10
TER-2 PRODUCTS					
TOLTERODINE PRODUCTS					
TOLTERODINE TAB 2MG	428	73	\$36,020.26	\$2.87	\$84.16

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TOLTERODINE TAB 1MG	101	17	\$10,415.70	\$3.45	\$103.13
SUBTOTAL	529	90	\$46,435.96	\$2.98	\$87.78
TROSPIUM PRODUCTS					
TROSPIUM CL TAB 20MG	61	22	\$5,521.72	\$2.90	\$90.52
SUBTOTAL	61	22	\$5,521.72	\$2.90	\$90.52
TIER-2 SUBTOTAL	590	112	\$51,957.68	\$2.97	\$88.06
TIER-3 PRODUCTS					
FESOTERODINE PRODUCTS					
TOVIAZ TAB 8MG	38	5	\$9,523.84	\$8.35	\$250.63
TOVIAZ TAB 4MG	9	2	\$2,307.72	\$8.55	\$256.41
SUBTOTAL	47	7	\$11,831.56	\$8.39	\$251.74
SOLIFENACIN PRODUCTS					
VESICARE TAB 5MG	104	12	\$36,392.40	\$10.58	\$349.93
VESICARE TAB 10MG	86	18	\$29,290.15	\$9.39	\$340.58
SUBTOTAL	190	30	\$65,682.55	\$10.01	\$345.70
DARIFENACIN PRODUCTS					
ENABLEX TAB 15MG	50	7	\$19,536.58	\$12.17	\$390.73
DARIFENACIN TAB 15MG ER	10	4	\$2,801.02	\$8.89	\$280.10
DARIFENACIN TAB HBR ER	3	2	\$749.84	\$8.33	\$249.95
ENABLEX TAB 7.5MG	1	1	\$294.85	\$9.83	\$294.85
SUBTOTAL	64	14	\$23,382.29	\$11.46	\$365.35
MIRABEGRON PRODUCTS					
MYRBETRIQ TAB 50MG	50	8	\$14,759.76	\$9.84	\$295.20
MYRBETRIQ TAB 25MG	37	13	\$10,428.25	\$9.58	\$281.84
SUBTOTAL	87	21	\$25,188.01	\$9.73	\$289.52
FLAVOXATE PRODUCTS					
FLAVOXATE TAB 100MG	24	4	\$1,573.07	\$2.30	\$65.54
SUBTOTAL	24	4	\$1,573.07	\$2.30	\$65.54
OXYBUTYNIN PRODUCTS					
OXYTROL DIS 3.9MG/24	6	1	\$6,001.98	\$22.23	\$1,000.33
SUBTOTAL	6	1	\$6,001.98	\$22.23	\$1,000.33
TOLTERODINE PRODUCTS					
TOLTERODINE CAP 4MG ER	302	38	\$45,876.58	\$5.09	\$151.91
TOLTERODINE CAP 2MG ER	32	3	\$4,212.94	\$4.39	\$131.65
DETROL LA CAP 4MG	11	3	\$1,668.97	\$5.06	\$151.72
SUBTOTAL	345	44	\$51,758.49	\$5.03	\$150.02
TROSPIUM PRODUCTS					
TROSPIUM CL CAP 60MG ER	832	179	\$141,297.25	\$4.87	\$169.83
SUBTOTAL	832	179	\$141,297.25	\$4.87	\$169.83
TIER-3 SUBTOTAL	1,595	300	\$326,715.20	\$6.18	\$208.84
TOTAL	13,211	2,999*	\$699,571.07	\$1.66	\$52.95

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1>. Last revised 08/2016. Last accessed 09/22/2016.

² Oxybutynin. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc. Last revised 07/2016. Last accessed 09/22/2016.

³ U.S. Food and Drug Administration (FDA): FDA News Release: FDA approves over-the-counter Oxytrol for Women to treat overactive bladder. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm336815.htm>. Issued 01/25/2013. Last accessed 09/22/2016.

⁴ U.S. Food and Drug Administration (FDA): FDA Advisory Committee Briefing Document. Available online at: <http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/nonprescriptiondrugsadvisorycommittee/ucm327162.pdf>. Last revised 01/2011. Last accessed 09/22/2016.

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Appendix L



Fiscal Year 2016 Annual Review of Lidoderm® (Lidocaine 5% Patch) and 30-Day Notice to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch)

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

Lidoderm® (Lidocaine 5% Patch) Approval Criteria:

1. A U.S. Food and Drug Administration (FDA) approved indication for the treatment of postherpetic neuralgia; and
2. Documented treatment attempts at recommended dosing or contraindication to at least one agent from two of the following drug classes:
 - a. Tricyclic antidepressants
 - b. Anticonvulsants
 - c. Topical or oral analgesics
3. A quantity limit of no more than three patches per day with a maximum of 90 patches per month will apply.

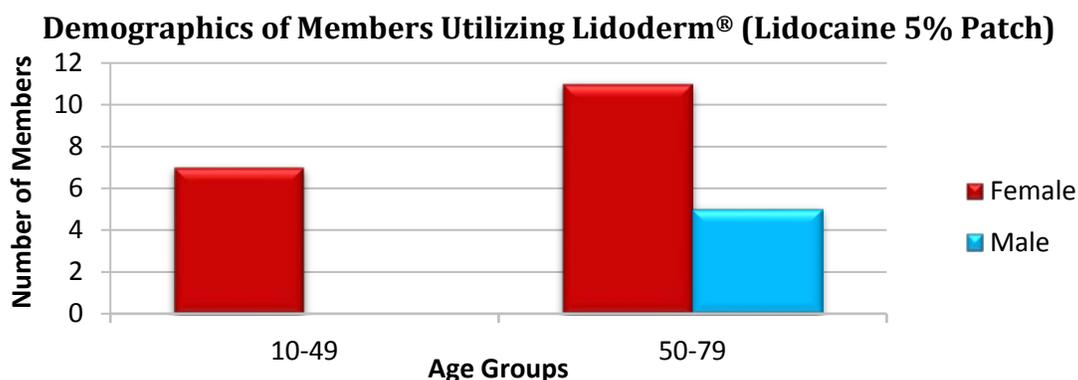
Utilization of Lidoderm® (Lidocaine 5% Patch): Fiscal Year 2016

Comparison of Fiscal Years

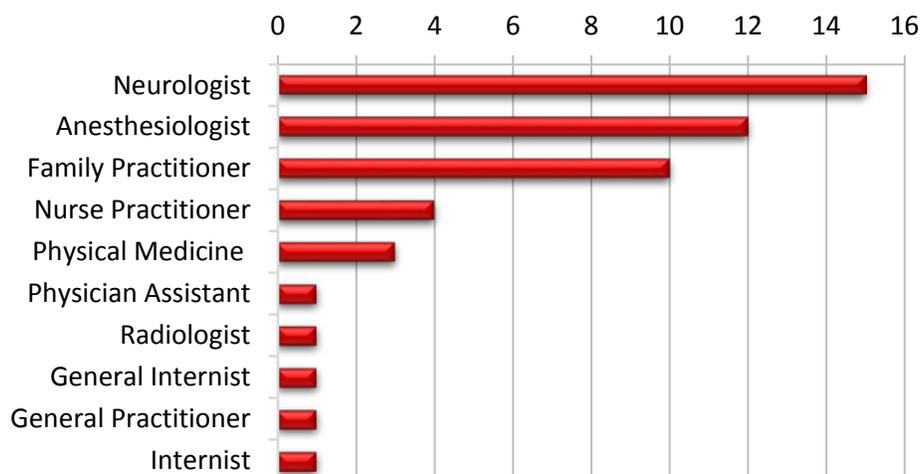
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	14	26	\$10,784.59	\$414.79	\$14.48	1,540	745
2016	23	49	\$14,436.15	\$294.62	\$10.20	2,400	1,415
% Change	64.30%	88.50%	33.90%	-29.00%	-29.60%	55.80%	89.90%
Change	9	23	\$3,651.56	-\$120.17	-\$4.28	860	670

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

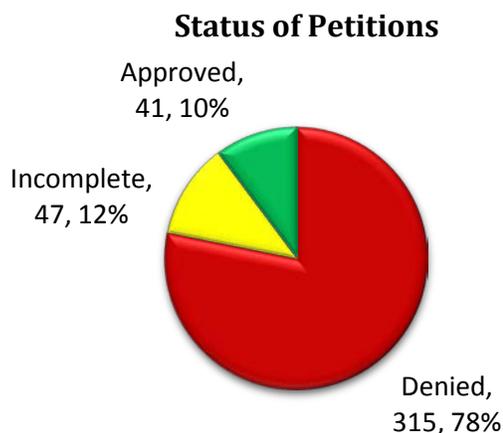


Top Prescriber Specialties of Lidoderm® (Lidocaine 5% Patch) by Number of Claims



Prior Authorization of Lidoderm® (Lidocaine 5% Patch)

There were 403 prior authorization requests submitted for Lidoderm® (lidocaine 5% patch) during fiscal year 2016. The following chart shows the status of the submitted petitions.



Synera® (Lidocaine/Tetracaine Topical Patch) Product Summary^{1,2}

FDA Approved: June 23, 2005 (previously covered as a medical benefit for SoonerCare members)

- In March 2014, the FDA approved a supplemental new drug application for labeling changes to Synera®. The patient “Instructions for Use” section of the label was revised to ensure proper use of Synera® in the home setting, and “Not for Home Use by Patient” statements were deleted from the package insert and the carton and container labels.

Indications: Synera® (lidocaine/tetracaine topical patch) is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodesiccation, and shave biopsy of skin lesions.

How Supplied:

- Synera[®] contains 70mg of lidocaine and 70mg of tetracaine supplied in a topical patch.
- The drug formulation is an emulsion in which the oil phase is a eutectic mixture of lidocaine and tetracaine with a melting point below room temperature.
- It contains an integrated, oxygen-activated heating component that is intended to enhance the delivery of the local anesthetic.
- It has an entire skin contact area of 50cm², of which 10cm² contains lidocaine and tetracaine.
- It is available as one individually packaged patch or a box of 10 individually packaged patches.

Dosing:

- One patch is applied to intact skin for 20 to 30 minutes then removed prior to venipuncture or intravenous cannulation and for 30 minutes prior to superficial dermatological procedures.
- Simultaneous or sequential application of multiple patches is not recommended.
- Application of one additional patch to a new location to facilitate venous access is acceptable after a failed attempt.

Mechanism of Action: Synera[®] provides local dermal analgesia by the release of lidocaine and tetracaine from the patch into the skin. Lidocaine is an amide-type local anesthetic agent and tetracaine is an ester-type local anesthetic agent. Both lidocaine and tetracaine block sodium ion channels required for the initiation and conduction of neuronal impulses, resulting in local anesthesia.

Contraindications:

- Known history of sensitivity to lidocaine, tetracaine, or local anesthetics of the amide or ester type.
- Known hypersensitivity to para-aminobenzoic acid (PABA).
- Known history of sensitivity to any other component of the product.

Warnings and Precautions:

- Overexposure: Application of a patch for longer duration than recommended, or the simultaneous or sequential application of multiple patches, could result in sufficient absorption of lidocaine and tetracaine to result in serious adverse effects.
- Storage and Disposal: Used patches contain a large amount of lidocaine and tetracaine (at least 90% of the initial amount). The potential exists for a child or pet to suffer serious adverse effects from chewing or ingesting a new or used patch. It is important for patients to store and dispose of Synera[®] out of the reach of children and pets.
- Avoidance of Exposure to Eyes and Mucous Membranes: Contact with the eyes should be avoided based on the findings of severe eye irritation with the use of similar products in animals. Also, the loss of protective reflexes may predispose to corneal irritation and potential abrasion. It is not recommended for use on mucous membranes or on areas with a compromised skin barrier because these uses have not been studied. Application

to broken or inflamed skin may result in toxic blood concentrations of lidocaine and tetracaine from increased absorption.

- **Magnetic Resonance Imaging:** The integrated heating component contains iron powder; therefore, the patch must be removed before a patient undergoes magnetic resonance imaging.
- **Methemoglobinemia:** Several local anesthetics, including tetracaine, have been associated with methemoglobinemia. The risk is greatest for patients with congenital or idiopathic methemoglobinemia, and infants under the age of twelve months who are receiving treatment with methemoglobin-inducing agents. Patients taking concomitant drugs associated with drug-induced methemoglobinemia such as sulfonamides, acetaminophen, acetanilide, aniline dyes, benzocaine, chloroquine, dapsone, naphthalene, nitrates and nitrites, nitrofurantoin, nitroglycerin, nitroprusside, pamaquine, para-aminosalicylic acid, phenacetin, phenobarbital, phenytoin, primaquine, and quinine are also at greater risk for developing methemoglobinemia.
- **Allergic Reactions:** Allergic reactions associated with lidocaine, tetracaine, or other components can occur. They are characterized by urticaria, angioedema, bronchospasm, and shock. If an allergic reaction occurs, it should be managed by conventional means.
- **Special Patient Populations:** It is recommended that patients who may be more sensitive to the systemic effects of lidocaine and tetracaine particularly the acutely ill or debilitated use Synera[®] with caution. Patients with severe hepatic disease or pseudocholinesterase deficiency, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations of lidocaine and tetracaine.
- **Vaccinations:** Lidocaine has been shown to inhibit viral and bacterial growth. The effect of Synera[®] on intradermal injections of live vaccines has not been determined.
- **Antiarrhythmic Drugs:** It is recommended that patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) use Synera[®] with caution since the systemic toxic effects are thought to be additive and potentially synergistic with lidocaine and tetracaine.

Adverse Reactions: The most common local adverse reactions during clinical trials (>10% of patients) include the following:

- Erythema
- Blanching
- Edema

Other adverse reactions related to application site reported in 1% or less of the patients studied include:

- Rash
- Infection
- Paresthesia
- Pruritus
- Skin Discoloration
- Urticaria
- Pain
- Allergic Reaction
- Vesiculobullous Rash
- Contact Dermatitis
- Blister

Systemic adverse reactions that occurred in 1% or less of treatment subjects include:

- Dizziness
- Nausea
- Vomiting
- Headache
- Somnolence

Efficacy: The clinical trials comparing Synera® to placebo patch for adult patients, utilized a 100-mm visual analog scale (VAS) to measure pain. A lower VAS score corresponds to less pain. In the clinical trials for pediatric patients, they were separated by age group (3 to 6 years and 7 to 17 years). Children in the younger group rated their pain using a six-point Oucher pain scale with faces. Children in the older group rated their pain using an eleven-point Oucher pain scale that contained both faces and numbers. No numerical pain scale information was reported for children in the prescribing information.

- **Superficial Venous Access in Adults:** Three randomized, double-blind, placebo controlled clinical trials in adult and geriatric subjects evaluated the degree of dermal analgesia upon venipuncture following a 20-minute treatment with Synera® or a placebo patch (patch with heating component but no drug). In each trial, subjects received Synera® on one arm and placebo patch on the other.
 - **Study 1:** There were 21 subjects with median VAS scores for Synera® and placebo treatments of 1mm and 9mm, respectively (a difference of 8mm).
 - **Study 2:** There were 40 subjects with median VAS scores of 5mm and 28mm for Synera® and placebo treatments, respectively (a difference of 23mm).
 - **Study 3:** There were 40 subjects over the age of 65 years with median VAS scores for Synera® and placebo treatments of 8mm and 14mm, respectively (a difference of 6mm).
 - Additionally, a double-blind trial of 250 adults was conducted. Subjects were randomized to receive either Synera® without a heating element or Synera® with a heating element, prior to venipuncture. Median VAS scores for the patch with the heating element and without the heating element were 17mm and 22mm, respectively.
- **Superficial Venous Access in Pediatrics:** In a randomized, double-blind, placebo controlled study, 61 pediatric patients received either Synera® or placebo for 20 minutes prior to venipuncture or IV cannulation in the antecubital fossa or dorsum of the hand. Subjects were separated by age group (3 to 6 years and 7 to 17 years). Children in the younger group reported less pain on IV cannulation, while pain scores on IV cannulation in the older children were not significantly different from pain scores in those treated with placebo.
- **Superficial Dermatological Procedures in Adults:** In one randomized, double-blind, placebo controlled study, 94 adult subjects received either Synera® or placebo patch for 30 minutes prior to a superficial dermatological procedure such as superficial excision, shave biopsy or electrodesiccation. Median VAS scores were 5mm for those receiving Synera® and 31mm for those receiving placebo. A similarly designed study included 74 subjects over the age of 65 years. Less pain was reported following Synera® treatment compared to placebo, with median VAS scores of 10mm and 23mm, respectively.
- **Superficial Dermatological Procedures in Pediatrics:** In a randomized, double-blind, placebo controlled study, 88 pediatric patients were separated by age group (3 to 6 years and 7 to 17 years) to receive a 30-minute application of either Synera® or placebo patch, prior to lidocaine injection. In the younger children, who used the Oucher pain scale with faces, those receiving Synera® reported less pain from lidocaine injection than those

receiving placebo. The older children used the numerical Oucher pain scale to report pain intensity. There was no difference between treatments observed in the older children.

Cost Comparison:

Medication	Cost Per Unit	Cost for Treatment ^Δ
Synera [®] (lidocaine/tetracaine topical patch)	\$15.79/patch ⁺	\$31.58 ⁺
EMLA [®] (lidocaine/prilocaine 2.5%/2.5%) cream	\$0.89/gram [*]	\$4.45 [*]

⁺Cost based on estimated acquisition cost (EAC)

^{*}Cost based on state maximum allowable cost (SMAC)

^ΔCost for treatment based on the maximum dose recommended for minor dermal procedures.

Recommendations

The College of Pharmacy recommends the prior authorization of Synera[®] (lidocaine/tetracaine topical patch) with the following criteria:

Synera[®] (Lidocaine/Tetracaine Topical Patch) Approval Criteria:

1. Member must be 3 years of age or older; and
2. Member must have an FDA approved need for local dermal analgesia for superficial venous access or superficial dermatological procedures; and
3. A patient-specific, clinically significant reason why the member cannot use EMLA[®] (lidocaine/prilocaine) cream, which is available without a prior authorization, must be provided; and
4. The total number of procedures must be provided on the prior authorization request; and
5. A quantity limit of two patches per day will apply.

¹ Synera[®] Prescribing Information. Galen US, Inc. Available online at: http://www.synera.com/wp-content/uploads/2015/03/SYNERA_PI.pdf. Last revised 05/2014. Last accessed 09/20/2016.

² U.S. Food and Drug Administration (FDA): Drug Databases. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/applletter/2014/021623Orig1s015_s017ltr.pdf. Issued 03/10/2014. Last accessed 09/27/2016.



Appendix M



Fiscal Year 2016 Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Ultravate® Lotion (Halobetasol Propionate 0.05%), Sernivo™ (Betamethasone Dipropionate Spray 0.05%), & Flurandrenolide 0.05% Cream and Lotion

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

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

Tier-2 Topical Corticosteroid Approval Criteria:

1. Documented trials of all Tier-1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief.
2. If Tier-1 trials are completed and do not yield adequate relief, the member must also provide a clinical reason for requesting a Tier-2 in the same potency instead of trying a higher potency.
3. When the same medication is available in Tier-1, a clinical reason must be provided for using a special dosage form of that medication in Tier-2 (foams, shampoos, sprays, kits, etc.).
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Topical Corticosteroids	
Tier-1	Tier-2
Ultra-High to High Potency	
augmented betamethasone dipropionate (Diprolene AF®) C	amcinonide C, O, L
betamethasone dipropionate (Diprosone®) O	augmented betamethasone dipropionate (Diprolene®) O, G, L
clobetasol propionate 0.05% (Temovate®) G, So	betamethasone dipropionate (Diprosone®) C
fluocinonide 0.05% C, O, So	clobetasol propionate 0.05% (Clobex®) L, Sh, Spr; (Olux®) F, (Olux-E®) F
halobetasol propionate (Ultravate®) C	clobetasol propionate 0.05% (Temovate®) C, O
	desoximetasone 0.25% (Topicort®) C, O, Spr
	desoximetasone 0.05% (Topicort®) G
	diflorasone diacetate 0.05% (Apexicon®) C; (Apexicon E®) C, O
	fluocinonide 0.05% G
	fluocinonide 0.1% (Vanos®) C
	halcinonide (Halog®) C, O
	halobetasol propionate 0.05% (Ultravate®) O

Medium-High to Medium Potency	
betamethasone dipropionate (Betanate [®]) L	betamethasone dipropionate/calcipotriene (Taclonex [®]) O, Sus, Spr
betamethasone valerate 0.1% (Beta-Val [®]) C	betamethasone valerate 0.1% (Beta-Val [®]) O, L
fluocinonide emollient (Lidex E [®]) C	betamethasone valerate 0.12% (Luxiq [®]) F
fluticasone propionate (Cutivate [®]) C, O	calcipotriene/betamethasone dipropionate (Enstilar [®]) F
hydrocortisone butyrate 0.1% So	desoximetasone 0.05% (Topicort LP [®]) C
mometasone furoate (Elocon [®]) C, L	fluocinolone acetonide 0.025% (Synalar [®]) C, O
triamcinolone acetonide C, O, L	flurandrenolide tape (Cordran [®])
	fluticasone propionate (Cutivate [®]) L
	hydrocortisone butyrate 0.1% C, O
	hydrocortisone probutate (Pandel [®]) C
	hydrocortisone valerate 0.2% C,O
	hydrocortisone valerate (Westcort [®]) C, O
	mometasone furoate 0.1% O
	prednicarbate (Dermatop [®]) O, C
	triamcinolone acetonide (Kenalog [®]) Spr
Low potency	
alclometasone dipropionate (Aclovate [®]) C, O	clocortolone pivalate (Cloderm [®]) C
fluocinolone acetonide 0.01% (Synalar [®]) C	desonide 0.05% C, O
hydrocortisone acetate 2.5% C, O, L	desonide 0.05% (Desonate [®]) G
hydrocortisone/urea (U-Cort [®]) C	desonide 0.05% (Verdeso [®]) F, L
	desonide/emollient (Desowyn [®] kit) C,O
	fluocinolone acetonide 0.01% (Capex [®]) Sh
	fluocinolone acetonide 0.01% (Synalar [®]) So, (Derma-Smooth [®] ; Derma-Smooth FS [®]) Oil
	hydrocortisone 2.5% (Texacort [®]) So
	hydrocortisone/pramoxine (Pramosone [®]) C, L

C = Cream; O = Ointment; L = Lotion; G = Gel; Sh = Shampoo; So = Solution; Spr = Spray;
Sus = Suspension; F = Foam

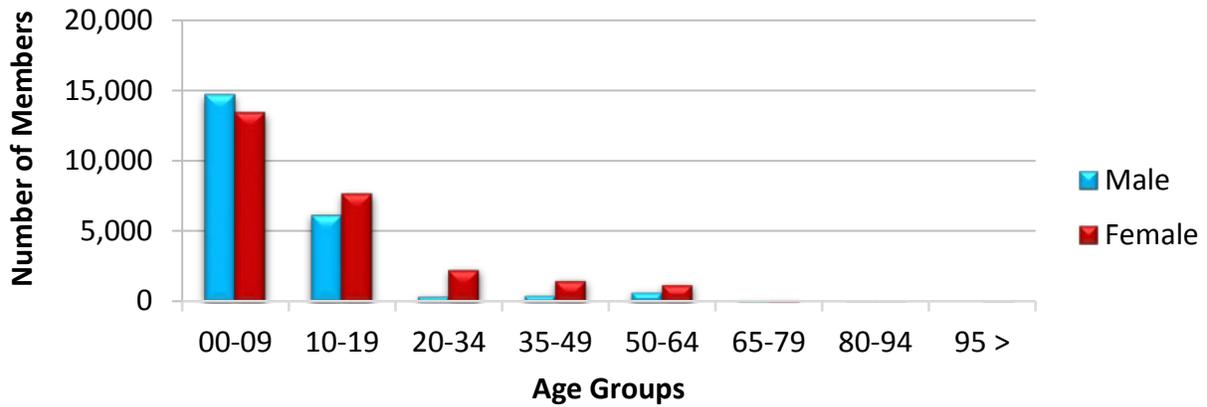
Utilization of Topical Corticosteroids: Fiscal Year 2016

Comparison of Fiscal Years

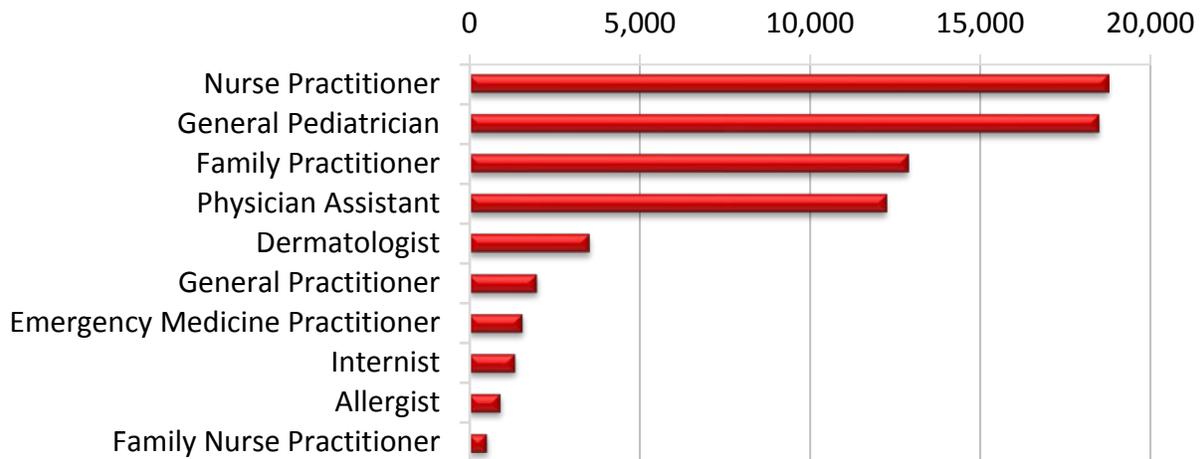
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	45,716	69,765	\$1,737,986.07	\$24.91	\$1.59	4,320,622	1,091,610
2016	48,818	74,509	\$1,612,061.86	\$21.64	\$1.34	4,604,503	1,201,718
% Change	6.80%	6.80%	-7.20%	-13.10%	-15.70%	6.60%	10.10%
Change	3,102	4,744	-\$125,924.21	-\$3.27	-\$0.25	283,881	110,108

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

Demographics of Members Utilizing Topical Corticosteroids



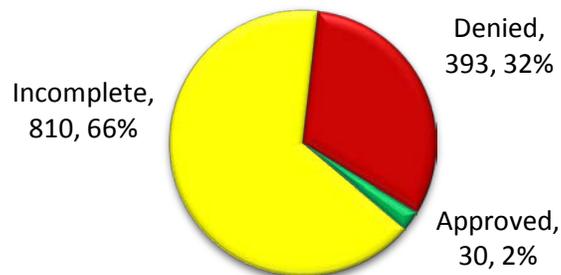
Top Prescriber Specialties of Topical Corticosteroids by Number of Claims



Prior Authorization of Topical Corticosteroids

There were 1,233 prior authorization requests submitted for the topical corticosteroid medication category during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates¹

Patent Expirations:

- Desonate[®] (desonide 0.05% gel): August 2020
- Topicort[®] (desoximetasone 0.25% spray): September 2028
- Verdeso[®] (desonide 0.05% foam): November 2028
- Capex[®] shampoo, Texacort[®] 2.5% topical solution, Halog[®], Cordran[®], Pandel[®], and U-Cort[®] are not available generically, but have no unexpired patents or exclusivities.

New Drug Approvals:

- November 2015: Ultravate[®] (halobetasol lotion 0.05%)
- February 2016: Sernivo[™] (betamethasone dipropionate topical spray 0.05%)
- April 2016: flurandrenolide 0.05% cream (first time generic approval)
- August 2016: flurandrenolide 0.05% lotion (first time generic approval)

Ultravate[®] (Halobetasol Lotion 0.05%) Product Summary^{2,3}

Indication(s): Ultravate[®] (halobetasol lotion 0.05%) is indicated for the topical treatment of plaque psoriasis in patients 18 years of age and older. Treatment beyond two weeks is not recommended, and the total dosage should not exceed 50 grams per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

Dosing:

- Ultravate[®] is available as a topical cream, ointment, and lotion.
- The recommended regimen is to apply a thin layer of Ultravate[®] to the affected skin twice daily for up to two weeks.
- Therapy should be discontinued when control is achieved. If there is no improvement seen within two weeks, reassessment of the diagnosis may be necessary.
- Treatment beyond two weeks is not recommended and the total dosage should not exceed 50 grams (50mL) per week because of the potential for the drug to suppress the HPA axis.
- Ultravate[®] should not be used with an occlusive dressing unless directed by a physician.
- Ultravate[®] is for external use only.
- Use should be avoided on the face, scalp, groin, or axillae.
- Ultravate[®] is not for ophthalmic, oral, or intravaginal use.

Mechanism of Action: Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the precise mechanism of action in plaque psoriasis is unknown.

Contraindications: None.

Warnings and Precautions:

- Effects on Endocrine System:
 - Reversible HPA axis suppression may occur, with the potential for glucocorticosteroid insufficiency during or after treatment.

- Systemic effects of topical corticosteroids may also include Cushing’s syndrome, hyperglycemia, and glucosuria.
- Systemic absorption may require evaluation for HPA axis suppression.
- **Systemic Exposure:**
 - Use of potential corticosteroids on large areas, for prolonged durations, under occlusive dressings, or on an altered skin barrier may increase systemic exposure.
 - Children may be more susceptible to systemic toxicity when treated with topical corticosteroids.
- **Local Adverse Reactions:** Local adverse reactions with topical steroids may include atrophy, striae, irritation, acneiform eruptions, hypopigmentation, and allergic contact dermatitis. Adverse reactions may be more likely to occur with occlusive use or more potent corticosteroids.
- **Concomitant Skin Infections:** Appropriate therapy should be initiated if concomitant skin infections develop.

Adverse Reactions: The most common adverse reactions experienced during clinical trials (>1%) include the following:

- Telangiectasia
- Headache
- Application Site Atrophy

Efficacy: Ultravate® was evaluated for the treatment of moderate-to-severe plaque psoriasis in two randomized, double-blind, vehicle-controlled trials involving 443 patients age 18 years and older with moderate-to-severe plaque psoriasis involving between 2% to 12% body surface area. The primary endpoint was overall treatment success, defined as the proportion of patients who were cleared or almost cleared with at least a two grade improvement from baseline at week two. The overall treatment success was 44.5% in the Ultravate® group versus 6.3% to 7.1% in the vehicle lotion groups.

Cost Comparison:

Medication	Cost Per unit	Cost for 14 Days of Therapy*
Ultravate® (halobetasol lotion 0.05%)	\$14.93/mL⁺	\$1,791.60⁺
halobetasol cream 0.05%	\$2.87/gram ^Δ	\$344.40 ^Δ
halobetasol ointment 0.05%	\$3.20/gram ^Δ	\$192.00 ^Δ

*Quantity for 14 day supply based on recommended use of a maximum of 50mLs per week and a maximum use of two weeks.

⁺EAC = Estimated Acquisition Cost

^ΔSMAC = State Maximum Allowable Cost

Sernivo™ (Betamethasone Dipropionate Topical Spray 0.05%) Product Summary^{4,5}

Indication(s): Sernivo™ (betamethasone dipropionate topical spray 0.05%) is indicated for the treatment of mild-to-moderate plaque psoriasis in patients 18 years of age and older.

Dosing:

- Sernivo™ is available as a topical spray. Each gram of Sernivo™ contains 0.643mg betamethasone dipropionate USP (equivalent to 0.5mg betamethasone) in a slightly thickened, white to off-white oil-in-water emulsion.
- Sernivo™ should be shaken well before use.
- Sernivo™ should be applied to the affected skin areas twice daily and rubbed in gently.
- Sernivo™ can be used for up to four weeks of treatment. Treatment beyond four weeks is not recommended.
- Sernivo™ should be discontinued when control is achieved.
- Sernivo™ should not be used if atrophy is present at the treatment site.
- The treated skin area should not be bandaged, covered, or wrapped unless directed by a physician.
- Use should be avoided on the face, scalp, axilla, groin, or other intertriginous areas.
- Sernivo™ is for topical use only. It is not for oral, ophthalmic, or intravaginal use.

Mechanism of Action: Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the precise mechanism of action of Sernivo™ in psoriasis is unknown.

Contraindications: None.

Warnings and Precautions:

- HPA Axis Suppression and Other Systemic Effects:
 - Sernivo™ can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency during or after treatment.
 - Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can result from systemic absorption of topical corticosteroids. Systemic absorption may require evaluation for HPA axis suppression.
 - Use of topical corticosteroids may require periodic evaluation for HPA axis suppression. Use should be modified if HPA axis suppression develops. High-potency corticosteroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure and young age may predispose patients to HPA axis suppression.
 - Pediatric patients may be more susceptible to systemic toxicity when treated with topical corticosteroids.

Adverse Reactions: The most common adverse reactions experienced during clinical trials (>1%) include the following:

- | | | |
|------------|---------------------------|-----------|
| ▪ Pruritus | ▪ Burning and/or Stinging | ▪ Pain |
| | | ▪ Atrophy |

Efficacy: The efficacy and safety of Sernivo™ were based on two randomized, double-blind, vehicle-controlled trials in adults with moderate plaque psoriasis involving 10% to 20% of the body surface area. The primary endpoint was treatment success, defined as clear or almost clear of symptoms based on the Investigator Global Assessment score and at least a 2-grade

reduction from baseline. More patients achieved greater treatment success with Sernivo™ versus the vehicle after 14 days and after 28 days of treatment (**Treatment Day 15: study 1:** 21.5% vs. 7.4%; *study 2:* 19% vs. 2.3% and **Treatment Day 29: study 1:** 42.7% vs. 11.7%, $p < 0.001$; *study 2:* 34.5% vs. 13.6%, $p < 0.001$).

Cost Comparison:

Medication	Cost Per unit	Cost per bottle* (120 mL)
Sernivo™ (betamethasone dipropionate topical spray 0.05%)	\$6.86/mL⁺	\$823.20⁺
betamethasone dipropionate 0.05% lotion	\$0.63/mL ^Δ	\$75.60 ^Δ
betamethasone dipropionate 0.05% ointment	\$1.78/gram ^Δ	\$213.60 ^Δ

*Sernivo™ is available in a 60mL and 120mL bottle.

⁺EAC = Estimated Acquisition Cost

^ΔSMAC = State Maximum Allowable Cost

Flurandrenolide 0.05% Cream and Lotion Product Summary⁶

Indication(s): Flurandrenolide 0.05% cream and lotion is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Dosing:

- Flurandrenolide 0.05% is available in several dosage forms including external tape, ointment, lotion, and cream. The ointment is a non-covered product. This review is specific to the cream and lotion formulations.
- For moist lesions, a small quantity should be rubbed gently into the affected areas two or three times a day.
- For dry, scaly lesions, flurandrenolide 0.05% should be applied to affected areas two or three times daily.
- Flurandrenolide 0.05% therapy should be discontinued when control is achieved. If no improvement is seen within two weeks, reassessment of the diagnosis may be necessary.
- Flurandrenolide 0.05% should not be used with occlusive dressings unless directed by a physician. Tight-fitting diapers or plastic pants may constitute occlusive dressings.

Mechanism of Action: The mechanism of the anti-inflammatory effect of topical corticosteroids is not completely understood. Corticosteroids with anti-inflammatory activity may stabilize cellular and lysosomal membranes. There is also the suggestion that the effect on the membranes of lysosomes prevents the release of proteolytic enzymes and, thus, plays a part in reducing inflammation.

Contraindications:

- Topical corticosteroids are contraindicated in patients with a history of hypersensitivity to any of the components of these preparations.

Warnings and Precautions:

- HPA Axis Suppression and Other Systemic Effects:

- Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing’s syndrome, hyperglycemia, and glucosuria in some patients.
- Conditions that augment systemic absorption include application of more potent corticosteroids, use over large surface areas, prolonged use, and the addition of occlusive dressings. Therefore, patients receiving a large dose of a potent topical corticosteroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression using urinary-free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent corticosteroid. Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of corticosteroid withdrawal may occur, so that supplemental systemic corticosteroids are required.
- Pediatric patients may absorb proportionately larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity.
 - Local Adverse Reactions: If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.
 - Concomitant Skin Infections: In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, flurandrenolide should be discontinued until the infection has been adequately controlled.

Adverse Reactions: The following local adverse reactions are reported infrequently with topical corticosteroids but may occur more frequently with the use of occlusive dressings:

- | | | |
|--------------|------------------|-------------------------------|
| ▪ Burning | ▪ Folliculitis | ▪ Hypopigmentation |
| ▪ Itching | ▪ Hypertrichosis | ▪ Perioral Dermatitis |
| ▪ Irritation | ▪ Acneform | ▪ Allergic Contact Dermatitis |
| ▪ Dryness | ▪ Eruptions | |

Cost Comparison:

Medication	Cost Per unit	Cost per tube* (120 grams)
flurandrenolide 0.05% cream and lotion	\$7.26/gram⁺	\$871.20⁺
fluocinonide 0.05% cream	\$1.18/gram ^Δ	\$141.60 ^Δ
halobetasol cream 0.05%	\$2.87/gram ^Δ	\$344.40 ^Δ

*Flurandrenolide is available in a 120gram tube (cream) and bottle (lotion). The 60gram tube of the cream formation is not covered due to no active Federal Drug Rate Agreement.

⁺EAC = Estimated Acquisition Cost

^ΔSMAC = State Maximum Allowable Cost

Recommendations

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

1. Placement of Ultravate® (halobetasol lotion 0.05%), flurandrenolide 0.05% cream, and flurandrenolide 0.05% lotion and into Tier-2 of the ultra-high to high-potency category; and
2. Placement of Sernivo™ (betamethasone dipropionate topical spray 0.05%) into Tier-2 of the medium-high to medium potency category; and
3. Move Beta-Val® (betamethasone valerate 0.1%) ointment and lotion to Tier-1 of the medium-high to medium potency category; and
4. Move hydrocortisone butyrate 0.1% solution and Lidex E® (fluocinonide emollient) cream to Tier-2 of the medium-high to medium potency category; and
5. Move Temovate® (clobetasol propionate 0.05%) gel and solution to Tier-2 of the ultra-high to high potency category; and
6. Move Diprolene® (augmented betamethasone dipropionate) gel to Tier-1 of the ultra-high to high potency category.

Topical Corticosteroids	
Tier-1	Tier-2
Ultra-High to High Potency	
augmented betamethasone dipropionate (Diprolene AF®) C	amcinonide C, O, L
augmented betamethasone dipropionate (Diprolene®) G	augmented betamethasone dipropionate (Diprolene®) O, L
betamethasone dipropionate (Diprosone®) O	betamethasone dipropionate (Diprosone®) C
fluocinonide 0.05% C, O, So	clobetasol propionate 0.05% (Clobex®) L, Sh, Spr; (Olux®) F, (Olux-E®) F
halobetasol propionate (Ultravate®) C	clobetasol propionate 0.05% (Temovate®) C, O
	clobetasol propionate 0.05% (Temovate®) G, So
	desoximetasone 0.25% (Topicort®) C, O, Spr
	desoximetasone 0.05% (Topicort®) G
	diflorasone diacetate 0.05% (Apexicon®) C (Apexicon E®) C, O
	fluocinonide 0.05% G
	fluocinonide 0.1% (Vanos®) C
	flurandrenolide 0.05% C, L
	halcinonide (Halog®) C, O
	halobetasol propionate 0.05% (Ultravate®) O
	halobetasol propionate 0.05% (Ultravate®) L
	halobetasol propionate/lactic acid (Ultravate® X) C
Medium-High to Medium Potency	
betamethasone dipropionate (Betanate®) L	betamethasone dipropionate 0.05% spray (Sernivo™)

betamethasone valerate 0.1% (Beta-Val®) C	betamethasone dipropionate/calcipotriene (Taclonex®) O, Sus, Spr
fluocinonide emollient (Lidex E®) C	betamethasone valerate 0.12% (Luxiq®) F
fluticasone propionate (Cutivate®) C, O	calcipotriene/betamethasone dipropionate (Enstilar®) F
mometasone furoate (Elocon®) C, L	desoximetasone 0.05% (Topicort LP®) C
betamethasone valerate 0.1% (Beta-Val®) O, L	fluocinolone acetonide 0.025% (Synalar®) C, O
	fluocinonide emollient (Lidex E®) C
	flurandrenolide tape (Cordran®)
	fluticasone propionate (Cutivate®) L
	hydrocortisone butyrate 0.1% So
	hydrocortisone butyrate 0.1% C, O
	hydrocortisone probutate (Pandel®) C
	hydrocortisone valerate 0.2% C,O
	hydrocortisone valerate (Westcort®) C, O
	mometasone furoate 0.1% O
	prednicarbate (Dermatop®) O, C
	triamcinolone acetonide (Kenalog®) Spr
Low potency	
alclometasone dipropionate (Aclovate®) C, O	clocortolone pivalate (Cloderm®) C
fluocinolone acetonide 0.01% (Synalar®) C	desonide 0.05% C,O
hydrocortisone acetate 2.5% C, O, L	desonide 0.05% (Desonate®) G
hydrocortisone/urea (U-Cort®) C	desonide 0.05% (Verdeso®) F, L
	desonide/emollient (Desowyn® kit) C, O
	fluocinolone acetonide 0.01% (Capex®) Sh
	fluocinolone acetonide 0.01% (Synalar®) So, (Derma-Smooth® ; Derma-Smooth FS®) Oil
	hydrocortisone 2.5% (Texacort®) So
	hydrocortisone/pramoxine (Pramosone®) C, L

C= Cream; O = Ointment; L = Lotion; G = Gel; Sh = Shampoo; So = Solution; Spr = Spray;
Sus = Suspension; F = Foam

Utilization Details of Topical Corticosteroids: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM	PERCENT COST
TIER-1 MEDICATIONS						
LOW-POTENCY PRODUCTS						
HYDROCORT CRE 2.5%	4,232	3,344	\$27,952.24	\$0.47	\$6.60	1.73%
HYDROCORT OIN 2.5%	2,325	1,621	\$18,260.71	\$0.60	\$7.85	1.13%
HYDROCORT CRE 1%	2,168	1,877	\$15,325.32	\$0.68	\$7.07	0.95%
HYDROCORT LOT 2.5%	487	399	\$11,209.67	\$1.33	\$23.02	0.70%
HYDROCORT OIN 1%	338	305	\$2,783.39	\$0.78	\$8.23	0.17%
ALCLOMETASON CRE 0.05%	264	215	\$21,444.01	\$3.46	\$81.23	1.33%
ALCLOMETASON OIN 0.05%	187	81	\$13,608.94	\$3.28	\$72.78	0.84%
FLUOCIN ACET CRE 0.01%	65	55	\$5,552.86	\$4.88	\$85.43	0.34%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM	PERCENT COST
HYDROCORT AC POW MICRONIZ	38	12	\$1,191.28	\$1.04	\$31.35	0.07%
HYDROCORT POW	11	8	\$192.29	\$0.70	\$17.48	0.01%
HYDROCORT AC POW	6	5	\$40.04	\$0.22	\$6.67	0.00%
HYDROCORT POW SOY	3	3	\$153.00	\$1.70	\$51.00	0.01%
HYDROCORT POW	2	2	\$42.56	\$0.61	\$21.28	0.00%
HYDROCORT AC POW SOY	1	1	\$17.61	\$0.59	\$17.61	0.00%
HYDROCORT/AB OIN 1%	1	1	\$7.67	\$0.55	\$7.67	0.00%
SUBTOTAL	10,128	7,929	\$117,781.59	\$1.39	\$29.68	7.28%
MEDIUM-HIGH TO MEDIUM POTENCY PRODUCTS						
TRIAMCINOLON CRE 0.1%	28,026	21,360	\$291,267.82	\$0.65	\$10.39	18.07%
TRIAMCINOLON OIN 0.1%	9,930	7,284	\$121,201.79	\$0.72	\$12.21	7.52%
TRIAMCINOLON CRE 0.025%	7,007	5,556	\$60,711.96	\$0.58	\$8.66	3.77%
TRIAMCINOLON CRE 0.5%	3,029	2,360	\$47,633.46	\$1.15	\$15.73	2.95%
MOMETASONE CRE 0.1%	2,340	1,650	\$48,060.41	\$1.23	\$20.54	2.98%
TRIAMCINOLON OIN 0.025%	2,240	1,785	\$23,888.36	\$0.69	\$10.66	1.48%
FLUTICASONE CRE 0.05%	1,410	1,000	\$35,671.15	\$1.49	\$25.30	2.21%
TRIAMCINOLON OIN 0.5%	1,068	782	\$19,972.43	\$1.47	\$18.70	1.24%
BETAMETH VAL CRE 0.1%	1,056	785	\$31,164.39	\$1.51	\$29.51	1.93%
TRIAMCINOLON LOT 0.1%	875	704	\$38,038.52	\$1.97	\$43.47	2.36%
TRIAMCINOLON LOT 0.025%	601	495	\$25,607.38	\$1.74	\$42.61	1.59%
FLUTICASONE OIN 0.005%	506	327	\$16,239.51	\$1.45	\$32.09	1.01%
BETAMETH DIP LOT 0.05%	161	112	\$7,520.41	\$2.22	\$46.71	0.47%
MOMETASONE SOL 0.1%	117	85	\$1,993.52	\$0.79	\$17.04	0.12%
HC BUTYRATE SOL 0.1%	58	47	\$9,221.32	\$8.04	\$158.99	0.57%
TRIAMCINOLON POW ACETONID	46	32	\$606.43	\$0.64	\$13.18	0.04%
FLUCINONIDE CRE -E 0.05%	25	19	\$1,503.04	\$3.46	\$60.12	0.09%
TRIANEX OIN 0.05%	20	18	\$520.02	\$1.13	\$26.00	0.03%
BETAMETHASON POW	2	2	\$22.32	\$0.60	\$11.16	0.00%
SUBTOTAL	58,517	44,403	\$780,844.24	\$1.66	\$31.74	48.43%
ULTRA-HIGH TO HIGH POTENCY PRODUCTS						
AUG BETAMET CRE 0.05%	1,014	744	\$19,400.00	\$1.10	\$19.13	1.20%
CLOBETASOL SOL 0.05%	936	576	\$115,903.04	\$5.90	\$123.83	7.19%
FLUCINONIDE CRE 0.05%	590	416	\$35,572.88	\$2.83	\$60.29	2.21%
FLUCINONIDE OIN 0.05%	390	260	\$32,576.20	\$4.12	\$83.53	2.02%
BETAMETH DIP OIN 0.05%	168	139	\$12,460.78	\$4.18	\$74.17	0.77%
CLOBETASOL GEL 0.05%	138	112	\$22,745.43	\$9.11	\$164.82	1.41%
HALOBETASOL CRE 0.05%	99	68	\$9,795.86	\$6.94	\$98.95	0.61%
FLUCINONIDE SOL 0.05%	63	51	\$4,780.36	\$3.18	\$75.88	0.30%
BETAMETH DIP POW MICRONIZ	8	7	\$82.27	\$0.47	\$10.28	0.01%
CLOBETASOL POW PROPIONA	2	2	\$35.18	\$0.59	\$17.59	0.00%
SUBTOTAL	3,408	2375	\$253,352.00	\$3.84	\$72.85	15.72%
TIER-1 SUBTOTAL	72,053	54,707	\$1,151,977.83	\$2.30	\$44.76	71.43%
TIER-2 MEDICATIONS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM	PERCENT COST
LOW-POTENCY PRODUCTS						
FLUOCIN ACET OIL BODY	331	243	\$54,513.38	\$6.83	\$164.69	3.38%
FLUOCIN ACET OIL 0.01% SC	142	118	\$24,957.15	\$8.21	\$175.75	1.55%
FLUOCIN ACET OIL SCALP	137	103	\$21,894.34	\$5.87	\$159.81	1.36%
FLUOCIN ACET SOL 0.01%	80	64	\$12,344.84	\$6.56	\$154.31	0.77%
DESONIDE CRE 0.05%	10	3	\$1,140.89	\$4.00	\$114.09	0.07%
DESONIDE OIN 0.05%	8	2	\$632.06	\$4.72	\$79.01	0.04%
DESONIDE LOT 0.05%	3	1	\$903.00	\$60.20	\$301.00	0.06%
CAPEX SHA 0.01%	2	1	\$814.08	\$13.57	\$407.04	0.05%
DESONATE GEL 0.05%	1	1	\$505.58	\$16.85	\$505.58	0.03%
SUBTOTAL	714	536	\$117,705.32	\$14.09	\$229.03	7.31%
MEDIUM-HIGH TO MEDIUM POTENCY PRODUCTS						
HC VALERATE CRE 0.2%	112	96	\$13,150.73	\$7.07	\$117.42	0.82%
BETAMETH VAL OIN 0.1%	5	5	\$59.10	\$0.43	\$11.82	0.00%
HC VALERATE OIN 0.2%	1	1	\$171.19	\$5.71	\$171.19	0.01%
SUBTOTAL	118	102	\$13,381.02	\$4.40	\$100.14	0.83%
ULTRA-HIGH TO HIGH POTENCY PRODUCTS						
CLOBETASOL OIN 0.05%	726	505	\$179,809.08	\$13.08	\$247.67	11.15%
CLOBETASOL CRE 0.05%	692	545	\$131,629.23	\$9.63	\$190.22	8.17%
CLOBETASOL E CRE 0.05%	140	85	\$12,256.46	\$5.00	\$87.55	0.76%
HALOBETASOL OIN 0.05%	44	30	\$3,703.14	\$4.87	\$84.16	0.23%
AUG BETAMET GEL 0.05%	12	11	\$963.59	\$4.82	\$80.30	0.06%
BETAMETH DIP CRE 0.05%	7	6	\$132.17	\$0.78	\$18.88	0.01%
DESOXIMETAS OIN 0.25%	2	1	\$369.03	\$12.30	\$184.52	0.02%
APEXICON E CRE 0.05%	1	1	\$134.99	\$4.50	\$134.99	0.01%
SUBTOTAL	1,624	1,184	\$328,997.69	\$6.87	\$128.54	20.41%
TIER-2 SUBTOTAL	2,456	1,822	\$460,084.03	\$8.45	\$152.57	28.55%
TOTAL	74,509	48,818*	\$1,612,061.86	\$1.34	\$80.73	100%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1>. Last revised 08/2016. Last accessed 09/2016.

² Ultravate® (halobetasol, 0.05%) Prescribing Information. Ranbaxy Laboratories, Inc. Available at: <http://ultravatelotion.com/pdf/ultravatelotionpi.pdf>. Last revised 11/2015. Last accessed 09/2016.

³ Ultravate® (halobetasol propionate lotion) New Formulation. Available online at: https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Ultravate_2015-1113.pdf. Last revised 11/2015. Last accessed 09/2016.

⁴ Sernivo™ (betamethasone dipropionate topical spray, 0.05%) Prescribing Information. Promius Pharma, LLC. Available online at: <http://sernivo.com/documents/sernivo-pi.pdf>. Last revised 02/2016. Last accessed 09/2016.

⁵ Sernivo™ (betamethasone dipropionate) New Formulation. Available online at https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Sernivo_2016-0210.pdf. Last revised 02/2016. Last accessed 09/2016.

⁶ Cordran® (flurandrenolide) Prescribing Information. Aqua Pharmaceuticals. Available online at: http://www.aquapharm.com/pdf/CordranPI2013Aug_CrmOintmnt.pdf. Last revised 08/2013. Last accessed 09/2016.



Appendix N



Fiscal Year 2016 Annual Review of Corlanor® (Ivabradine) and Entresto™ (Sacubitril/Valsartan)

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

Corlanor® (Ivabradine) Approval Criteria:

1. An FDA approved diagnosis of symptomatic stable, chronic worsening heart failure; and
2. The prescriber must verify that the member has left ventricular ejection fraction $\leq 35\%$; and
3. The prescriber must verify that the member is in sinus rhythm with a resting heart rate ≥ 70 beats per minute; and
4. The member must be on maximal/maximally tolerated doses of beta-blockers or have a contraindication to beta-blockers; and
5. A quantity limit of 60 tablets per 30 days will apply.

Entresto™ (Sacubitril/Valsartan) Approval Criteria:

1. An FDA approved diagnosis of chronic heart failure (NYHA Class II, III, or IV); and
2. The prescriber must verify that the member has a left ventricular ejection fraction $\leq 40\%$; and
3. The member must be on a maximally tolerated dose of a beta-blocker or have a contraindication to beta-blocker therapy; and
4. The prescriber must verify the member has been on an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) for at least four weeks; and
5. The member must not take an ACE inhibitor while taking Entresto™ as concomitant use is contraindicated; and
6. Members with a diagnosis of diabetes must not be taking aliskiren while taking Entresto™ as concomitant use is contraindicated; and
7. A quantity limit of 60 tablets per 30 days will apply.

Utilization of Corlanor® and Entresto™: Fiscal Year 2016

Comparison of Fiscal Years

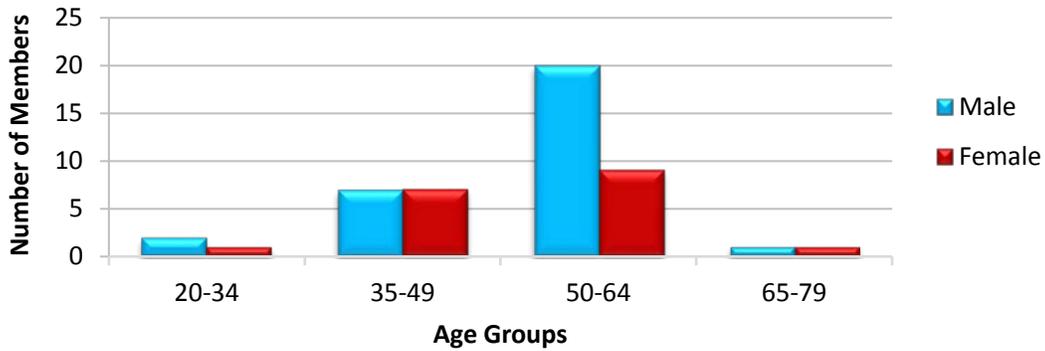
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	1	1	\$395.71	\$395.71	\$13.19	60	30
2016	48	153	\$60,697.14	\$396.71	\$13.22	9,180	4,590
% Change	4,700%	15,200%	15,238.80%	0.30%	0.20%	15,200%	15,200%
Change	47	152	\$60,301.43	\$1.00	\$0.03	9,120	4,560

*Total number of unduplicated members.

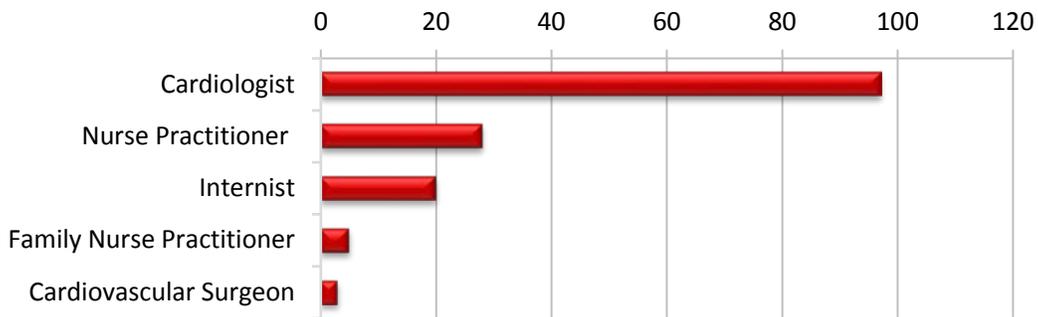
Costs do not reflect rebated prices or net costs.

- Please note: Entresto™ was FDA approved in July 2015 and had no claims during fiscal year 2015. Corlanor® was FDA approved April 2015 and had one claim during fiscal year 2015.

Demographics of Members Utilizing Corlanor® and Entresto™



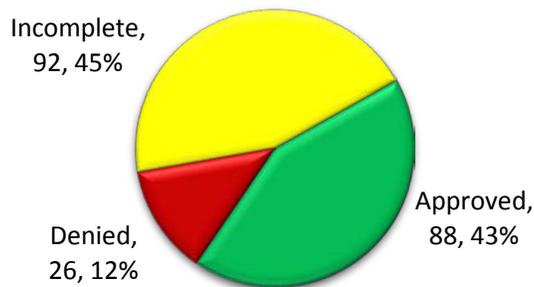
Top Prescriber Specialties of Corlanor® and Entresto™ by Number of Claims



Prior Authorization of Corlanor® and Entresto™

There were 206 prior authorization requests submitted for Corlanor® and Entresto™ during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates^{1,2,3}

Anticipated Patent Expiration(s):

- Corlanor® (ivabradine): April 2026
- Entresto™ (sacubitril/valsartan): May 2027

New Safety Information and Update(s):

- **May 2016:** The American College of Cardiology, the American Heart Association, and the Heart Failure Society of America published an update to the heart failure guidelines in the *Journal of the American College of Cardiology*. The updated guidelines gave a “Class I” recommendation to angiotensin-converting enzyme (ACE) inhibitors, or angiotensin-receptor blockers (ARBs), or angiotensin receptor-neprilysin inhibitors (ARNIs) in conjunction with evidence-based beta-blockers and aldosterone antagonists in selected patients to reduce morbidity and mortality. The societies gave ARNIs a “Class I” recommendation to replace an ACE inhibitor or ARB in selected patients with chronic symptomatic HFrEF NYHA class II or III with adequate blood pressure who are already tolerating an ACE inhibitor or an ARB. Ivabradine gained a “Class IIa” recommendation to reduce heart failure hospitalization for patients with symptomatic heart failure (NYHA class II-III) who are already receiving recommended treatments including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 beats per minute or greater at rest.
- **September 2016:** Novartis released a new analysis of PARADIGM-HF data showing that among patients who had been hospitalized for heart failure, those on Entresto™ reported higher relative health-related quality of life scores compared to those taking the ACE inhibitor enalapril.

Recommendations

The College of Pharmacy does not recommend any changes at this time.

Utilization Details of Corlanor® and Entresto™: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
IVABRADINE PRODUCTS					
CORLANOR TAB 5MG	33	13	\$13,192.22	\$13.33	\$399.76
CORLANOR TAB 7.5MG	4	2	\$1,582.62	\$13.19	\$395.66
SUBTOTAL	37	13*	\$14,774.84	\$13.26	\$397.71
SACUBITRIL/VALSARTAN PRODUCTS					
ENTRESTO TAB 24-26MG	46	21	\$18,200.48	\$13.19	\$395.66
ENTRESTO TAB 49-51MG	43	18	\$17,039.79	\$13.21	\$396.27
ENTRESTO TAB 97-103MG	27	7	\$10,682.03	\$13.19	\$395.63
SUBTOTAL	116	37*	\$45,922.30	\$13.20	\$395.86
TOTAL	153	48*	\$60,697.14	\$13.22	\$396.60

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol.* 2016;(1):. doi:10.1016/j.jacc.2016.05.011.

² Baliga R., Ragavendra, M.B.B.S., FACC. Heart Failure Focused Update on Pharmacological Therapy. Available online at: <https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2016/05/18/16/26/2016-acc-aha-hfsa-focused-update-on-new-pharmacological-therapy-for-hf>. Issued 05/2016. Last accessed 09/2016.

³ Novartis News Release: Important new analysis shows that Novartis' Entresto® is associated with higher relative health-related quality of life scores among HFrEF patients. Available online at: <https://www.novartis.com/news/media-releases/important-new-analysis-shows-novartis-entresto-associated-higher-relative>. Issued 09/2016. Last accessed 09/2016.



Appendix O



Fiscal Year 2016 Annual Review of Growth Hormone

Oklahoma Health Care Authority
October 2016

Current Prior Authorization Criteria

Growth Hormone Products	
Tier-1*	Tier-2
Genotropin® (Pfizer) - Cartridge, MiniQuick	Humatrope® (Eli Lilly) - Vials, Cartridge Kits
	Norditropin® (NovoNordisk) - FlexPro® Pens
	Nutropin® and Nutropin AQ® (Genentech) - Vials, Pen Cartridge, NuSpin®
	Omnitrope® (Sandoz) - Vials, Cartridge
	Saizen® (EMD Serono) - Vials, click.easy®
	Serostim® (EMD Serono) - Vials
	Zomacton™ and Zoma-Jet™ (Ferring) - Vials, Injection Device
	Zorbtive® (EMD Serono) - Vials

*Supplemental rebated product; tier structure based on supplemental rebate participation and/or state maximum allowable costs (SMAC).

(All products contain the identical 191 amino acid sequence found in pituitary-derived hGH.)

Growth Hormone Covered Indications (prior to epiphyseal closure):

1. Classic human growth hormone (hGH) deficiency as determined by childhood hGH stimulation tests
2. Panhypopituitarism with history of pituitary or hypothalamic injury due to tumor, trauma, surgery, whole brain radiation, irradiation, hemorrhage or infarction, or a congenital anomaly, and one of the following:
 - a. Deficiency of three or more pituitary hormones and insulin-like growth factor (IGF)-1 greater than or equal to 2.5 standard deviations (SD) below the mean for the member's age and gender; or
 - b. No deficiency or deficiency in less than three pituitary hormones and IGF-1 less than 50th percentile and failure of a growth hormone stimulation test
3. Panhypopituitarism in children with height greater than or equal to 2.25 SD below the mean for age and gender and MRI evidence of pituitary stalk agenesis, empty sella, or ectopic posterior pituitary "bright spot"
4. Short stature associated with Prader-Willi Syndrome
5. Short stature associated with chronic renal insufficiency (pre-transplantation)
6. History of intrauterine growth restriction who have not reached a normal height (greater than 2.25 SD below mean for age and gender) by age two years
7. Idiopathic short stature (ISS) who are greater than or equal to 2.25 SD below mean for height (based on age and gender) and are unlikely to catch up in height
8. Turner syndrome or 45X, 46XY mosaicism
9. Hypoglycemia with evidence for hGH deficiency

10. Short-stature homeobox-containing gene (SHOX) deficiency with genetic evidence for SHOX deficiency
11. Other evidence for hGH deficiency submitted for panel review and decision

Growth Hormone Tier-2 Approval Criteria:

1. Documented allergic reaction to non-active components of all available Tier-1 medications; or
2. A clinical exception applies to members with a diagnosis of AIDS wasting syndrome, in which case Serostim® can be used, regardless of its current Tier status.

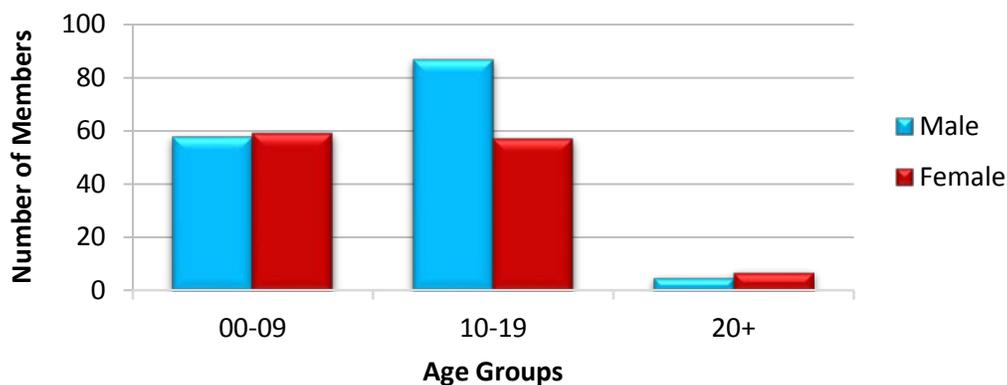
Utilization of Growth Hormone: Fiscal Year 2016

Comparison of Fiscal Years

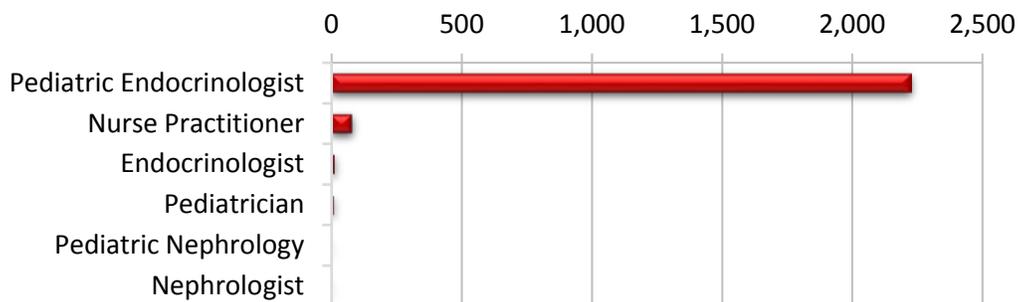
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Cost per Day	Total Units	Total Days
2015	256	2,020	\$6,255,614.17	\$3,096.84	\$107.35	23,382	58,271
2016	273	2,336	\$7,893,708.41	\$3,379.16	\$116.53	30,629	67,740
% Change	6.60%	15.60%	26.20%	9.10%	8.60%	31.00%	16.20%
Change	17	316	\$1,638,094.24	\$282.32	\$9.18	7,247	9,469

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

Demographics of Members Utilizing Growth Hormone

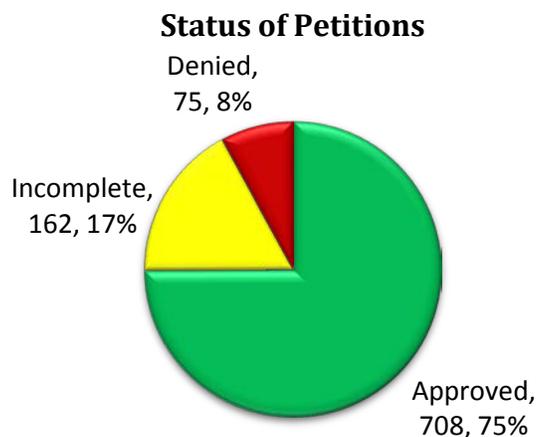


Top Prescriber Specialties of Growth Hormone by Number of Claims



Prior Authorization of Growth Hormone

There were 945 prior authorization requests submitted for growth hormone during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates^{1,2}

Anticipated Patent Expiration(s):

- Genotropin® [somatotropin (rDNA origin) for injection]: November 2018
- Norditropin® [somatotropin (rDNA origin) for injection]: August 2026

Update(s):

- **March 2015:** Ferring Pharmaceuticals Inc. announced that the U.S. Food and Drug Administration (FDA) approved a name change of Tev-Tropin® and Tjet® to Zomacton™ and Zoma-Jet™. The growth hormone Tier chart has been updated to reflect this change.

Recommendations

The College of Pharmacy does not recommend any changes at this time.

Utilization Details of Growth Hormone: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	COST/DAY	COST/CLAIM
TIER-1 PRODUCTS						
GENOTROPIN PRODUCTS						
GENOTROPIN INJ 5MG	1,027	135	\$2,695,133.24	7.61	\$89.34	\$2,624.28
GENOTROPIN INJ 12MG	390	52	\$2,357,122.56	7.5	\$204.50	\$6,043.90
GENOTROPIN INJ 0.6MG	151	23	\$285,346.22	6.57	\$67.46	\$1,889.71
GENOTROPIN INJ 0.8MG	125	19	\$322,389.10	6.58	\$91.95	\$2,579.11
GENOTROPIN INJ 1MG	124	15	\$401,755.31	8.27	\$114.98	\$3,239.96
GENOTROPIN INJ 1.2MG	97	18	\$343,982.50	5.39	\$126.65	\$3,546.21
GENOTROPIN INJ 1.6MG	74	13	\$380,273.11	5.69	\$182.12	\$5,138.83
GENOTROPIN INJ 0.4MG	72	12	\$79,008.51	6	\$38.58	\$1,097.34
GENOTROPIN INJ 1.4MG	68	13	\$309,798.44	5.23	\$162.71	\$4,555.86

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	COST/DAY	COST/CLAIM
GENOTROPIN INJ 2MG	48	8	\$303,143.35	6	\$225.55	\$6,315.49
GENOTROPIN INJ 0.2MG	46	9	\$32,005.90	5.11	\$22.70	\$695.78
GENOTROPIN INJ 1.8MG	35	7	\$195,215.69	5	\$199.20	\$5,577.59
SUBTOTAL	2,257	266	\$7,705,173.93	8.48	\$117.79	\$3,413.90
TIER-1 SUBTOTAL	2,257	266	\$7,705,173.93	8.48	\$117.79	\$3,413.90
TIER-2 PRODUCTS						
NORDITROPIN PRODUCTS						
NORDITROPIN INJ 10/1.5ML	34	6	\$101,907.71	5.67	\$94.18	\$2,997.29
NORDITROPIN INJ 5/1.5ML	15	2	\$7,502.88	7.5	\$20.01	\$500.19
NORDITROPIN INJ 15/1.5ML	10	2	\$54,954.24	5	\$180.18	\$396.28
SUBTOTAL	59	10	\$164,364.83	5.9	\$93.28	\$5,495.42
OMNITROPE PRODUCTS						
OMNITROPE INJ 5/1.5ML	10	2	\$3,962.78	5	\$14.46	396.278
OMNITROPE INJ 10/1.5ML	2	1	\$3,811.34	2	\$68.06	1905.67
SUBTOTAL	12	3	\$7,774.12	4	\$23.56	\$647.84
NUTROPIN PRODUCTS						
NUTROPIN AQ INJ 20MG/2ML	3	1	\$8,947.65	3	\$106.52	\$2,982.55
NUTROPIN AQ INJ NUSPIN 5	1	1	\$1,679.92	1	\$56.00	\$1,679.92
SUBTOTAL	4	2	\$10,627.57	2	\$93.22	\$2,656.89
HUMATROPE PRODUCTS						
HUMATROPE INJ 12MG	4	2	\$5,767.96	2	\$48.07	\$1,441.99
SUBTOTAL	4	2	\$5,767.96	2	\$48.07	\$1,441.99
TIER-2 SUBTOTAL	79	16	\$188,534.48	4.94	\$81.06	\$2,386.51
TOTAL	2,336	273*	\$7,893,708.41	8.56	\$116.53	\$3,379.16

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 08/2016. Last accessed 09/29/2016.

² Ferring Pharmaceuticals Inc. "Ferring Pharmaceuticals Receives FDA Approval for Growth Hormone Name Change, Acquires Zomacton™ [somatropin (rDNA origin)] for Injection and Needle-Free Device in the U.S." Available online at: <http://www.ferringusa.com/press/ferring-pharmaceuticals-receives-fda-approval-for-growth-hormone-name-change-acquires-zomacton-somatropin-rdna-origin-for-injection-and-needle-free-device-in-the-u-s/>. Issued 03/31/2015. Last accessed 09/29/2016.



Appendix P



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

FDA NEWS RELEASE

For Immediate Release: September 19th, 2016

FDA grants accelerated approval to first drug for Duchenne muscular dystrophy

The U.S. Food and Drug Administration approved Exondys 51 (eteplirsen) injection, the first drug approved to treat patients with Duchenne muscular dystrophy (DMD). Exondys 51 is specifically indicated for patients who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13 percent of the population with DMD.

DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. It 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 three and five 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 out 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.

Exondys 51 was approved under the accelerated approval pathway, which provides for the approval of drugs that treat serious or life-threatening diseases and generally provide a meaningful advantage over existing treatments. Approval under this pathway can be based on adequate and well-controlled studies showing the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit to patients (how a patient feels or functions or whether they survive). This pathway provides earlier patient access to promising new drugs while the company conducts clinical trials to verify the predicted clinical benefit.

The accelerated approval of Exondys 51 is based on the surrogate endpoint of dystrophin increase in skeletal muscle observed in some Exondys 51-treated patients. The FDA has concluded that the data submitted by the applicant demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in some patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. A clinical benefit of Exondys 51, including improved motor function, has not been established. In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease for these children and the lack of available therapy.

Under the accelerated approval provisions, the FDA is requiring Sarepta Therapeutics to conduct a clinical trial to confirm the drug's clinical benefit. The required study is designed to assess whether Exondys 51 improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. If the trial fails to verify clinical benefit, the FDA may initiate proceedings to withdraw approval of the drug.

The most common side effects reported by participants taking Exondys 51 in the clinical trials were balance disorder and vomiting.

The FDA granted Exondys 51 fast track designation, which is a designation to facilitate the development and expedite the review of drugs that are intended to treat serious conditions and that demonstrate the potential to address an unmet medical need. It was also granted priority review and orphan drug designation. Priority review status is granted to applications for drugs that, if approved, would be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan drug designation provides incentives such as clinical trial tax credits, user fee waiver and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.

The manufacturer received a rare pediatric disease priority review voucher, which comes from a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases. This is the seventh rare pediatric disease priority review voucher issued by the FDA since the program began.

Exondys 51 is made by Sarepta Therapeutics of Cambridge, Massachusetts.

FDA NEWS RELEASE

For Immediate Release: September 23rd, 2016

FDA approves Amjevita, a biosimilar to Humira

The U.S. Food and Drug Administration approved Amjevita (adalimumab-atto) as a biosimilar to Humira (adalimumab) for multiple inflammatory diseases.

Amjevita is approved for the following indications in adult patients:

- moderately to severely active rheumatoid arthritis;
- active psoriatic arthritis;
- active ankylosing spondylitis;
- moderately to severely active Crohn's disease;
- moderately to severely active ulcerative colitis; and
- moderate to severe plaque psoriasis.

Amjevita is also indicated for moderately to severely active polyarticular juvenile idiopathic arthritis in patients four years of age and older.

Health care professionals should review the prescribing information in the labeling for detailed information about the approved uses.

Biological products are generally derived from a living organism and can come from many sources, including humans, animals, microorganisms or yeast. A biosimilar is a biological product that is approved based on a showing that it is highly similar to an already-approved biological product and has no clinically meaningful differences in terms of safety, purity and potency (i.e., safety and effectiveness) from the reference product, in addition to meeting other criteria specified by law.

The FDA's approval of Amjevita is based on review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data and other clinical safety and effectiveness data that demonstrates Amjevita is biosimilar to Humira. It has been approved as a biosimilar, not as an interchangeable product.

The most serious known side effects with Amjevita are infections and malignancies. The most common expected adverse reactions with Amjevita are infections and injection site reactions.

Like Humira, the labeling for Amjevita contains a Boxed Warning to alert health care professionals and patients about an increased risk of serious infections leading to hospitalization or death. The Boxed Warning also notes that lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor blockers, including adalimumab products. The drug must be dispensed with a patient Medication Guide that describes important information about its uses and risks.

Amjevita is manufactured by Amgen, Inc., of Thousand Oaks, California. Humira was approved in December 2002 and is manufactured by AbbVie Inc. of North Chicago, Illinois.

FDA NEWS RELEASE

For Immediate Release: September 23rd, 2016

FDA approves expanded indications for Ilaris for three rare diseases

The U.S. Food and Drug Administration approved three new indications for Ilaris (canakinumab). The new indications are for rare and serious auto-inflammatory diseases in adult and pediatric patients:

- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS);
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD); and
- Familial Mediterranean Fever (FMF).

All three syndromes are hereditary diseases that are characterized by periodic attacks of fever and inflammation, as well as severe muscle pain. There are no previously approved therapies for TRAPS or HIDS/MKD.

Ilaris was previously approved for another periodic fever syndrome called Cryopyrin-Associated Periodic Syndromes (CAPS) and for active systemic juvenile idiopathic arthritis. Health care professionals should review the prescribing information in the labeling for detailed information about the approved uses.

Approvals for the new indications were based on clinical studies, including safety, efficacy and pharmacokinetic data. The most common adverse reactions for these indications are injection site reactions and being more susceptible to catching colds.

Ilaris can cause serious side effects, including increased risk of serious infections. Ilaris can lower the immune system's ability to fight infections. Other serious side effects include decreased ability to fight infections (immunosuppression) and allergic reactions. Patients experiencing any symptoms of an allergic reaction should call their healthcare provider, including: rash, itching and hives, difficulty breathing or swallowing, and

dizziness or feeling faint. Patients should not get live vaccines if receiving Ilaris. Patients should not receive Ilaris if they are allergic to canakinumab or any of the ingredients in Ilaris. Ilaris is manufactured and distributed by Novartis Pharmaceuticals Corporation, of East Hanover, New Jersey.

Current Drug Shortages Index (as of October 4th, 2016):

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

Acetohydroxamic Acid (Lithostat) Tablets	Currently in Shortage
Ammonium Chloride Injection	Currently in Shortage
Anagrelide Hydrochloride Capsules	Currently in Shortage
Atropine Sulfate Injection	Currently in Shortage
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
Ceftazidime and Avibactam (AVYCAZ) for Injection, 2.5g	Currently in Shortage
Chloramphenicol Sodium Succinate Injection	Currently in Shortage
Desmopressin Acetate Injection	Currently in Shortage
Dexamethasone Sodium Phosphate Injection	Currently in Shortage
Dextrose 5% Injection Bags	Currently in Shortage
Dextrose Injection USP, 70%	Currently in Shortage
Dihydroergotamine Mesylate Injection	Currently in Shortage
Disopyramide Phosphate (Norpace) Capsules	Currently in Shortage
Doxorubicin Lyophilized Powder for Injection	Currently in Shortage
Epinephrine Injection	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
Fomepizole Injection	Currently in Shortage
Gemifloxacin Mesylate (Factive) Tablets	Currently in Shortage
Imipenem and Cilastatin for Injection, USP	Currently in Shortage
Indigotindisulfonate Sodium (Indigo Carmine) Injection	Currently in Shortage
Ketoprofen Capsules	Currently in Shortage
L-Cysteine Hydrochloride Injection	Currently in Shortage
Leucovorin Calcium Lyophilized Powder for Injection	Currently in Shortage
Leuprolide Acetate Injection	Currently in Shortage
Lidocaine Hydrochloride (Xylocaine) Injection	Currently in Shortage
LifeCare PCA™ Sterile Empty Vial and Injector	Currently in Shortage
Liotrix (Thyrolar) Tablets	Currently in Shortage
Mecasermin [rDNA origin] (Increlex) Injection	Currently in Shortage
Methyldopate Hydrochloride Injection	Currently in Shortage
Methylprednisolone Sodium Succinate for Injection, USP	Currently in Shortage
Morphine Sulfate Injection, USP, CII, (Preservative-Free)(For PCA Use Only)	Currently in Shortage
Multi-Vitamin Infusion (Adult and Pediatric)	Currently in Shortage
Mupirocin Calcium Nasal Ointment	Currently in Shortage
Nimodipine (Nymalize) Oral Solution	Currently in Shortage
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
Sacrosidase (Sucraid) Oral Solution	Currently in Shortage
Scopolamine (Transderm Scop) Transdermal System Patch	Currently in Shortage
Sodium Acetate Injection, USP	Currently in Shortage
Sodium Bicarbonate Injection, USP	Currently in Shortage
Sodium Chloride 0.9% Injection Bags	Currently in Shortage
Sodium Chloride 23.4% Injection	Currently in Shortage
Sufentanil Citrate (Sufenta) Injection	Currently in Shortage
Sumatriptan (Imitrex) Nasal Spray	Currently in Shortage
Technetium Tc99m Succimer Injection (DMSA)	Currently in Shortage
Theophylline Extended Release Tablets and Capsules	Currently in Shortage
Tigecycline (Tygacil) Injection	Currently in Shortage
Tobramycin Injection	Currently in Shortage
Trimipramine Maleate (SURMONTIL) Capsules	Currently in Shortage
Water-Miscible Vitamin A Palmitate (Aquasol A Parenteral)	Currently in Shortage