Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
October 14, 2015
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 14, 2015

DATE: October 1, 2015

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 2016 Meeting Dates – Appendix B

Update on Medication Coverage Authorization Unit/Bowel Preparation Medication Post-Educational Mailing – Appendix C

Action Item – Vote to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-Trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab) – Appendix D

Action Item – Vote to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor) – Appendix E

Action Item – Vote to Prior Authorize Savaysa® (Edoxaban) – Appendix F

Action Item – Vote to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), & Repatha™ (Evolocumab) – Appendix G

Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin) – Appendix H

30-Day Notice to Prior Authorize Daraprim® (Pyrimethamine) – Appendix I

Annual Review of Allergy Immunotherapies and 30-Day Notice to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract) – Appendix J

Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Dyloject™ (Diclofenac Sodium) – Appendix K

Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Cosentyx® (Secukinumab) – Appendix L

Annual Review of Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa) and 30-Day Notice to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation) – Appendix M

Annual Review of Xolair® (Omalizumab) – Appendix N

FDA and DEA Updates – Appendix O

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – October 14, 2015 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. **Call To Order**
   A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. **Public Comment Forum**
   A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. **Action Item – Approval of DUR Board Meeting Minutes – See Appendix A**
   A. September 9, 2015 DUR Minutes – Vote
   B. September 9, 2015 DUR Recommendations Memorandum
   C. Veripred™ and Millipred™ Prior Authorization Memorandum
   D. Correspondence

Items to be presented by Dr. Muchmore, Chairman:

4. **Action Item – Vote on 2016 Meeting Dates – See Appendix B**
   A. 2016 DUR Board Meeting Dates – Vote

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

5. **Update on Medication Coverage Authorization Unit/Bowel Preparation Medication Post-Educational Mailing – See Appendix C**
   A. Medication Coverage Activity for September 2015
   B. Pharmacy Help Desk Activity for September 2015
   C. Bowel Preparation Medication Post-Educational Mailing

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

6. **Action Item – Vote to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-Trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab) – See Appendix D**
   A. Recommendations

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

7. **Action Item – Vote to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Savaysa® (Edoxaban) – See Appendix F**
   A. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), & Repatha™ (Evolocumab) – See Appendix G

A. College of Pharmacy Recommendations
B. Attachment A: Diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH)
C. Attachment B: Framingham Heart Study and Framingham Risk Score
D. Draft PCSK9 Inhibitor Prior Authorization Form

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

10. Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin) – See Appendix H

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. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Constipation and Diarrhea Medications

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

11. 30-Day Notice to Prior Authorize Daraprim® (Pyrimethamine) – See Appendix I

A. Toxoplasmosis Background Information
B. Daraprim® (Pyrimethamine) Product Summary
C. Daraprim® (Pyrimethamine) Cost Update
D. Utilization Details of Daraprim® (Pyrimethamine)
E. College of Pharmacy Recommendations

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

12. Annual Review of Allergy Immunotherapies and 30-Day Notice to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract) – See Appendix J

A. Current Prior Authorization Criteria
B. Prior Authorization of Allergy Immunotherapies
C. Oralair® (Allergen Extract) Product Summary
D. College of Pharmacy Recommendations

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

13. Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Dyloject™ (Diclofenac Sodium) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
C. Prior Authorization of NSAIDs
D. Market News and Updates
E. Dyloject™ (Diclofenac Sodium) Product Summary
F. NSAID Price Trends
G. College of Pharmacy Recommendations
H. Utilization Details of NSAIDs

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

14. Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Cosentyx® (Secukinumab) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Targeted Immunomodulator Agents
C. Prior Authorization of Targeted Immunomodulator Agents
D. Market News and Updates

E. Cosentyx® (Secukinumab) Product Summary
F. Hidradenitis Suppurativa Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Targeted Immunomodulator Agents

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

15. Annual Review of Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa) and 30-Day Notice to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation) – See Appendix M

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation
D. Prior Authorization of Inhaled Tobramycin Products and Dornase Alfa
E. Market News and Updates
F. Product Summaries
G. College of Pharmacy Recommendations
H. Utilization Details of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation

Non-Presentation, Questions Only:

16. Annual Review of Xolair® (Omalizumab) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Xolair® (Omalizumab)
C. Prior Authorization of Xolair® (Omalizumab)
D. Market News and Updates
E. College of Pharmacy Recommendations

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

17. FDA and DEA Updates – See Appendix O

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

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

A. Ophthalmic Anti-Inflammatories/Omidria™ (Phenylephrine/Ketorolac Injection)
B. Topical Corticosteroids
C. Xiaflex® (Collagenase Clostridium Histolyticum)
D. Xgeva® (Denosumab)
E. Erythropoietin Stimulating Agents
F. Prialt® (Ziconotide)
G. Tetracycline and Ofloxacin 400mg Tablets
H. Keveyis™ (Dichlorophenamide)
I. Ibrance® (Palbociclib)

**Future business subject to change.*

Items to be presented by Dr. Muchmore, Chairman:

19. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF SEPTEMBER 9, 2015

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Anetta Harrell, Pharm.D.	x	
Ashley Huddleston, Pharm.D.	x	
John Muchmore, M.D., Ph.D.; Chairman	x	
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA	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	
Michyla Adams, 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	
Grace Hsu, Pharm.D.; Clinical Pharmacist	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist		x
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Academic Detailing Pharmacist	x	
Graduate Students: Christina Bulkley, Pharm.D.	x	
David George, Pharm.D.	x	
Tammy Lambert, Pharm.D.		x
Timothy Pham, Pharm.D.	x	

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

OTHERS PRESENT:		
Sherry Crowe, Novartis	Michelle Condren, RPh, OU Tulsa	Jim Fowler, AstraZeneca
Christopher Seago, Merck	Teri Breidenbach, Pfizer Oncology	Jim Chapman, AbbVie
Desiree Gendron, BMS	Donna Erwin, Otsuka	Brian Maves, Pfizer
Debbie Berrg, OUHSC-CF Center	David Williams, Allergan	Jason Schwier, Amgen
Bob Gustafson, Lundbeck	Rick Ulasewich, DSI	Kirsten Mar, AstraZeneca
Audrey Rattan, Alkermes	Aaron Shaw, Boehringer Ingelheim	Roger Grotzinger, BMS
Eric Gardner, Vertex	Jon MaGuire, GSK	Chet Steckler, Purdue

PRESENT FOR PUBLIC COMMENT:	
Dr. Joseph Walter	Tulsa Cystic Fibrosis
Dr. Nighat Mehdi	OU Cystic Fibrosis
Jana Shardonofsky	Vertex
Drew Bernstein	AstraZeneca
Tonya Ratcliff	Integris Health

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

2A: AGENDA NO. 11 SPEAKER: DR. JOSEPH WALTER
2B: AGENDA NO. 11 SPEAKER: DR. NIGHAT MEHDI
2C: AGENDA NO. 11 SPEAKER: JANA SHARDONOFSKY
2D: AGENDA NO. 12 SPEAKER: DREW BERNSTEIN
2E: AGENDA NO. 12 SPEAKER: TONYA RATCLIFF

ACTION: NONE REQUIRED

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

3A: JULY 8, 2015 DUR MINUTES – VOTE
3B: JULY 8, 2015 DUR RECOMMENDATIONS MEMORANDUM

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR JULY 2015
4B: PHARMACY HELP DESK ACTIVITY FOR JULY 2015
4C: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2015
4D: PHARMACY HELP DESK ACTIVITY FOR AUGUST 2015
4E: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE HYSINGLA® ER (HYDROCODONE BITARTRATE EXTENDED-RELEASE)**

5A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE VARIOUS SPECIAL FORMULATIONS: SITAVIG® (ACYCLOVIR BUCCAL TABLETS), RASUVO® (METHOTREXATE INJECTION), OTREXUP™ (METHOTREXATE INJECTION), ONMEL® (ITRACONAZOLE ORAL TABLETS), & PURIXAN® (MERCAPTOPURINE ORAL SUSPENSION)**

6A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE NAMZARIC™ (MEMANTINE EXTENDED-RELEASE/DONEPEZIL)**

7A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE IRENKA™ (DULOXETINE)**

8A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE CORLANOR® (IVABRADINE)**

9A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Teel

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **30-DAY NOTICE TO PRIOR AUTHORIZE TYKERB® (LAPATINIB), HALAVEN® (ERIBULIN), IXEMPRA®(IXABEPILONE), KADCYLA® (ADO-TRASTUZUMAB), AFINITOR® (EVEROLIMUS), & PERJETA® (PERTUZUMAB)**

10A: INTRODUCTION

10B: UTILIZATION OF ONCOLOGY MEDICATIONS

10C: UTILIZATION OF BREAST CANCER MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: PRODUCT SUMMARIES

10F: RECOMMENDATIONS

10G: UTILIZATION DETAILS OF BREAST CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders, Dr. Medina

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE ORKAMBI™ (LUMACAFTOR/IVACAFTOR)

11A: INTRODUCTION

11B: ORKAMBI™ (LUMACAFTOR/IVACAFTOR) PRODUCT SUMMARY

11C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Teel

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF PALIVIZUMAB

12C: PRIOR AUTHORIZATION OF PALIVIZUMAB

12D: REFERRALS TO CARE MANAGEMENT SERVICES

12E: MARKET NEWS AND UPDATES

12F: GUIDANCE FOR PALIVIZUMAB PROPHYLAXIS

12G: PALIVIZUMAB CLAIMS ANALYSIS

12H: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF ANTIHYPERLIPIDEMICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EPANOVA® (OMEGA-3-CARBOXYLIC ACIDS), PRALUENT® (ALIROCUMAB), AND REPATHA™ (EVOLOCUMAB)

13A: CURRENT PRIOR AUTHORIZATION CRITERIA

13B: UTILIZATION OF ANTIHYPERLIPIDEMICS

13C: PRIOR AUTHORIZATION OF ANTIHYPERLIPIDEMICS

13D: MARKET NEWS AND UPDATES

13E: EPANOVA® (OMEGA-3-CARBOXYLIC ACIDS) PRODUCT SUMMARY

13F: PRALUENT® (ALIROCUMAB) PRODUCT SUMMARY

13G: REPATHA™ (EVOLOCUMAB) PRODUCT SUMMARY

13H: PLACE IN THERAPY: PCSK9 INHIBITORS

13I: COST COMPARISON: HIGH-INTENSITY STATINS AND PCSK9 INHIBITORS

13J: COLLEGE OF PHARMACY RECOMMENDATIONS

13K: UTILIZATION DETAILS OF STATINS AND ZETIA® (EZETIMIBE)

13L: UTILIZATION DETAILS OF LOVAZA® (OMEGA-3-ACID ETHYL ESTERS) AND VASCEPA® (ICOSAPENT ETHYL)

13M: UTILIZATION DETAILS OF JUXTAPID® (LOMITAPIDE) AND KYNAMRO® (MIPOMERSEN)

13N: ATTACHMENT A: DIAGNOSIS OF HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (HEFH)

13O: ATTACHMENT B: FRAMINGHAM HEART STUDY & FRAMINGHAM RISK SCORE

13P: DRAFT PCSK9 INHIBITOR PRIOR AUTHORIZATION FORM

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS AND 30-DAY NOTICE TO PRIOR AUTHORIZE SAVAYSA® (EDOXABAN)

14A: CURRENT PRIOR AUTHORIZATION CRITERIA

14B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS

14C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS

14D: ORAL ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS: UTILIZATION TRENDS
14E: MARKET NEWS AND UPDATES
14F: SAVAYSA® (EDOXABAN) PRODUCT SUMMARY
14G: COLLEGE OF PHARMACY RECOMMENDATIONS
14H: UTILIZATION DETAILS OF ANTICOAGULANTS
14I: UTILIZATION DETAILS OF PLATELET AGGREGATION INHIBITORS
Materials included in agenda packet; presented by Dr. Hsu
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ADJOURNMENT
The meeting was adjourned at 5:40 pm.

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

Memorandum

Date: September 10, 2015

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 9, 2015

Recommendation 1: Vote to Prior Authorize Hysingla® ER (Hydrocodone Bitartrate Extended-Release)

MOTION CARRIED by unanimous approval.

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

1. The addition of Hysingla® ER (hydrocodone bitartrate extended-release tablets) to Tier-3. Current criteria for this category will apply.
    a. Hysingla® ER is currently rebated to Tier-2, but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.
2. Moving Zohydro™ ER (hydrocodone bitartrate extended-release capsules) from the Special Prior Authorization (PA) category to Tier-3 based on reformulation with abuse-deterrent properties and to encourage supplemental rebate participation.

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
ASA/butalbital/caffeine/codeine (Fiorinal with Codeine®) codeine codeine/APAP hydromorphone (Dilaudid®) hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) morphine IR (MSIR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®) oxycodone IR (Oxy IR®) oxycodone/ibuprofen (Combunox™) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** buprenorphine (Butrans®) fentanyl patches (Duragesic®) **hydrocodone bitartrate ER (Hysingla® ER)** morphine ER tablets (MS Contin®) oxycodone ER (Oxycontin®) **Short-Acting:** oxymorphone IR (Opana®) tapentadol IR (Nucynta®)	**Long-Acting:** **hydrocodone bitartrate ER (Zohydro™ ER)** hydromorphone ER (Exalgo®) morphine sulfate ER (Avinza®) morphine sulfate ER (Kadian®) morphine/naltrexone (Embeda®) oxymorphone ER (Opana® ER)+ tapentadol ER (Nucynta® ER) tramadol ER (Ultram ER®, Ryzolt®) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) oxycodone (Oxecta®)	**Short-Acting:** Unique strengths of hydrocodone/APAP **Long-Acting:** oxycodone/APAP ER (Xartemis™ XR) **Oncology Only:** fentanyl (Actiq®) fentanyl (Fentora®) fentanyl (Onsolis® buccal film) fentanyl (Abstral®,Lazanda®) fentanyl (Subsys™ SL spray)

APAP: Acetaminophen, ASA: Aspirin, IBU: Ibuprofen, IR: Immediate-Release, ER: Extended-Release, SL: Sublingual
*Tier Structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications are subject to move to Tier-3.
+Brand name Opana® ER preferred. Generic oxymorphone extended-release tablets require special authorization. The generic formulation is not abuse-deterrent.

Recommendation 2: Vote to Prior Authorize Various Special Formulations: Sitavig® (Acyclovir Buccal Tablets), Rasuvo® (Methotrexate Injection), Otrexup™ (Methotrexate Injection), Onmel® (Itraconazole Oral Tablets), & Purixan® (Mercaptopurine Oral Suspension)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Sitavig® (acyclovir buccal tablets), Otrexup™ (methotrexate injection), Rasuvo® (methotrexate injection), Onmel™ (itraconazole oral tablets), & Purixan® (mercaptopurine oral suspension) with the following criteria:

1. **Sitavig® (Acyclovir Buccal Tablets) Approval Criteria:**
   a. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
   b. A patient-specific, clinically significant reason why the member cannot use acyclovir or valacyclovir oral tablets.
2. **Rasuvo® (Methotrexate Injection) & Otrexup™ (Methotrexate Injection) Approval Criteria:**
   a. An FDA approved diagnosis of one of the following:
      i. Adults with severe, active rheumatoid arthritis (RA); or
      ii. Children with active polyarticular juvenile idiopathic arthritis (pJIA); or

iii. Severe, recalcitrant, disabling psoriasis confirmed by biopsy or dermatologic consultation; and

b. Members with a diagnosis of RA or pJIA must have had an adequate trial of full dose NSAIDs; and

c. A patient-specific, clinically significant reason why the oral tablets or the generic injectable formulation cannot be used.

3. **Onmel® (Itraconazole Oral Tablets) Approval Criteria:**
   a. An FDA approved diagnosis of onychomychosis of the toenail caused by *Trichophyton rubrum* or *T. mentagrophytes;* and
   b. A patient-specific, clinically significant reason why itraconazole 100mg oral capsules cannot be used in place of Onmel® 200mg tablets.
4. **Purixan® (Mercaptopurine Oral Suspension) Approval Criteria:**
   a. An FDA approved diagnosis of acute lymphoblastic leukemia (ALL); and
   b. An age restriction on members older than 10 years of age will apply. Members 10 years of age and younger would not require prior authorization for Purixan® therapy; and
   c. Members older than 10 years of age would require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

Recommendation 3: Vote to Prior Authorize Namzaric™ (Memantine Extended-Release/Donepezil)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Namzaric™ (memantine ER/donepezil) with the following criteria:

Alzheimer's Medications Approval Criteria:

1. Special formulation products including oral solutions, transdermal patches, and other convenience formulations require prior authorization with the following approval criteria:
   a. A patient-specific, clinically significant reason why the special formulation is necessary in place of the regular formulation.
2. An age restriction for ages 0-50 years applies to all Alzheimer's medications. Members older than 50 years of age can receive regular formulations without prior authorization. Members age 50 years or younger will require prior authorization with the following criteria:
   a. An FDA approved diagnosis; or
   b. Other patient-specific, clinically significant information supporting the use of the medication.
3. Namzaric™ (Memantine ER/Donepezil) Approval Criteria:
   a. Member must have a patient-specific, clinically significant reason why the separate products cannot be used in place of this combination product; and
   b. A quantity limit of 30 capsules per 30 days will apply.

Recommendation 4: Vote to Prior Authorize Irenka™ (Duloxetine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing Irenka™ (duloxetine 40mg delayed-release capsules) into the Special Prior Authorization (PA) category of the Antidepressant Product Based Prior Authorization (PBPA) category. The existing criteria for this category will apply. Additionally, use of Irenka™ for the diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain will require a patient-specific, clinically significant reason why the member cannot use two duloxetine 20mg capsules in place of Irenka™ 40mg capsules.

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			fluoxetine 60mg tablets
escitalopram (Lexapro®)			fluoxetine DR (Prozac® Weekly™)
fluoxetine (Prozac®, Sarafem®)			fluvoxamine CR (Luvox CR®)
fluvoxamine (Luvox®)			paroxetine CR (Paxil CR®)
paroxetine (Paxil®)			paroxetine (Pexeva®)
sertraline (Zoloft®)			
Dual Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	vilazodone (Viibryd®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		desvenlafaxine (Pristiq®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron® SolTab™)		levomilnacipran (Fetzima®)	**duloxetine 40mg (Irenka™)**
trazodone (Desyrel®)		nefazodone (Serzone®)	trazodone ER (Oleptro®)
venlafaxine (Effexor®, Effexor XR® capsules)			venlafaxine ER tablets (Effexor XR® tablets)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
	vortioxetine (Brintellix®)		

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
CR = Controlled-Release DR = Delayed-Release ER = Extended-Release

Antidepressant Tier-2 Approval Criteria:

1. Member must have a documented, recent (within six months) trial of two Tier-1 medications at least four weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier-1 selection must include at least one medication from the SSRI category and one trial with duloxetine; or
2. Prior stabilization on the Tier-2 medication documented within the last 100 days. A past history of success on the Tier-2 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by Tier-1 medications or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Tier-3 Approval Criteria:

1. Member must have a documented, recent (within six months) trial with two Tier-1 medications (one medication from the SSRI category and one trial with duloxetine) and a trial of a Tier-2 medication at least four weeks in duration and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists.
3. Tier structure rules still apply.
4. When Irenka™ (Duloxetine 40mg) is being requested for non-depression related diagnoses, the criteria below will apply:
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use two duloxetine 20mg capsules in place of Irenka™ 40mg capsules; and
    c. A quantity limit of 30 capsules per 30 days will apply.

Recommendation 5: Vote to Prior Authorize Corlanor® (Ivabradine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Corlanor® (ivabradine) with the following 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 ≤ 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.

Recommendation 6: 30-Day Notice to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-Trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab)

NO ACTION REQUIRED.

Recommendation 7: 30-Day Notice to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Synagis® (Palivizumab)

MOTION CARRIED by unanimous approval.

Based on the recommendations from the American Academy of Pediatrics, the College of Pharmacy recommends updating the prior authorization criteria of Synagis® (palivizumab) to the following criteria:

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection:
   1. Infants less than 12 months old at the start of RSV season:
      a. Born before 29 weeks, 0 days gestation; or
      b. With moderate-to-severe pulmonary hypertension or with acyanotic heart disease on medications to control congestive heart failure and will require cardiac surgical procedures; or
      c. Infants with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough; or
      d. Infants who undergo cardiac transplantation during RSV season; or

e. Infants with cystic fibrosis with clinical evidence of chronic lung disease (CLD) and/or nutritionally compromised

2. Infants less than 24 months old at the start of RSV season:
    a. Born before 32 weeks, 0 days gestation and develop chronic lung disease (CLD) of prematurity (require >21% oxygen supplementation for at least 28 days after birth) and continue to require medical support (chronic corticosteroid therapy, bronchodilator therapy, or supplemental oxygen) during the 6 months before the start of the RSV season; or
    b. Infants who are profoundly immunocompromised during RSV season; or
    c. Infants less than 24 months of age with cystic fibrosis with manifestations of severe lung disease or weight for length less than the 10th percentile

B. Length of treatment: Palivizumab is approved for use only during RSV season. Approval dates will be November 1st through March 31st.

C. Units authorized: The maximum duration of therapy is five (5) doses, with a dose to be administered no more often than every 30 days. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as one of the approved total.

D. Dose-pooling: To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Recommendation 9: Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), and Repatha™ (Evolocumab)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Savaysa™ (Edoxaban)

NO ACTION REQUIRED.

Memo

To: OHCA DUR Board Members

From: Nancy Nesser, Pharmacy Director

cc: Terry Cothran

Date: October 6, 2015

Re: Veripred and Millipred Prior Authorization Letters

Dear DUR Board Members,

Many of you may remember that in February 2013 we started the process to prior authorize several special formulations of prednisolone. In March 2013 the DUR Board recommended a prior authorization and subsequently the OHCA Board of Directors approved the prior authorization at their April 2013 meeting.

Due to concern that this medication was generally used for children who were being treated for acute asthma exacerbation, the OHCA pharmacy department recommended not implementing the prior authorization at that time. The average cost of a prescription for Veripred at that time was about $53.

When Veripred was purchased by Zylera Pharmaceuticals in July 2014, the price was increased to $275 for that same prescription. This was recently brought to the attention of the OHCA pharmacy department by Representative Dr. Doug Cox. As of October 5, 2015, a prior authorization is required for Veripred and Millipred with the criteria that was approved by the DUR Board in March 2013.

Zylera Pharmaceuticals met with OHCA pharmacy staff and asked what could be done to stop the prior authorization. They were told that they could make an offer for a supplemental rebate to bring the price more in line with the cost of a generic prescription, which is about $20. They were also told that they could submit letters for the DUR packet.

These drugs are not on the agenda for this meeting and I wanted you to understand the reason these letters are included in the packet. If you have questions or concerns, please do not hesitate to let me know.

ReddyCare
Philip Watson PA-C
LMC Medical Group
932 W. Shawnee Suite A
Muskogee, OK 74401
(P)918.684.9665
(F)918.684.3206
www.reddycareclinic.com

To: SoonerCare

Re: Millipred

it is very important to have an option of a good tasting medication for younger children. You cannot explain to them how important it is to take their medication. The soar taste of unfavored steroids is a major problem in this way. Please allow us to continue to write for millipred to achieve positive outcomes for our patients.

Thank you

Philip Watson PA-C

Access MEDICAL CENTERS

URGENT CARE

I am a Physician Assistant in Urgent Care and have written for Veripred numerous times with my Soonercare patients. I have noted good compliance and low incidence of adverse drug reactions. If this medication was to stay on Medicaid formulary this would help me serve my Soonercare kids better.

Sincerely,

Adam Makin, PA-C

Access MEDICAL CENTERS

URGENT CARE

ATTENTION: Terry Cothran

September 28, 2015

I am a Physician Assistant in Urgent Care and have written for Veripred numerous times with my Soonercare patients. I have noted good compliance and low incidence of adverse drug reactions. If this medication was to stay on Medicaid formulary this would help me serve my Soonercare kids better.

Sincerely,

Tim Marlow PA-C

Access MEDICAL CENTERS

URGENT CARE

[redacted]

ATTN: Terry Cothran 9-28-15

I am a Physician Assistant in Urgent Care and have written for Veripred numerous times with my Soonercare patients. I have noted good compliance and low incidence of adverse drug reactions. If this medication was to stay on Medicaid formulary this would help me serve my Soonercare kids better.

Sincerely,

Zachary A. Robertson PA-C

BIXBY PEDIATRICS

Nidhi Koul, M.D. 8315-D East 111th Street South • Bixby, Oklahoma 74008
Ph: (918) 394-MYMD(6963) • F: (918)394-6962 • E-Fax: (855) 500-5153 • www.bixbypediatrics.com

09/30/2015

To whom it may concern
I am writing this letter to support the use of Millipred in my pedaitric population; irrespective of the insuarance coverage.

In my practice, I have seen a definite compliance to the Millipred over the generic alternative. I have seen a decrease in morbidity and hospitalisations based on that.

I also like the fact that unlike the other alternatives available, Millipred does not contain alcohol as an ingredient.

Sincerely,

CHILDREN'S CLINIC

keeping kids on track

MICHAEL F. STRATTON,
D.O.P.C., F.A.C.O.P., F.A.A.P.
CERTIFIED AMERICAN OSTEOPATHIC BOARD OF PEDIATRICS

DAVID WHATLEY, M.D.

9/30/15

Dear Terry Cothran

Please keep Millipred & Veripred on Tiers

These Meds are much better tolerated when administered to children ultimately keeping out of the Hospital.

The generic oral steroids are very nasty tasting & the children refuse to take them

Thank you

3101 CHANDLER ROAD, #101 MUSKOGEE, OK 74403 TEL (918) 687-4411 FAX (918) 687-4448

CCOM MEDICAL GROUP; PEDIATRICS
401 S YORK STREET
MUSKOGEE OK 74401 918/683-1144

ATTN: TERRY COTHRAN
DIRECTOR OF PHARMACY
PHARMACY MANAGEMENT
CONSULTANTS ORI-4403
PO BOX 26901
OKLAHOMA CITY OK 73190

OCTOBER 1, 2015

Dear Sir;

I am writing to respectfully request that Millipred and Veripred be kept on Tier 1 Soonercare.

Patient compliance is assured with Millipred and Veripred because of its pleasant taste.

Thank you,

Dr. Therese Amigo MD

CCOM Pediatrics

Houck, John J

10 E 13th Street Grove Ok 74344
Phone: 918 786 1909

«Hello Terrye»

Dear Terry Cothran, Director of Pharmacy

On behalf of my provider I am writing in regards to the taste of liquid prednisone for children. We have found that Millipred tastes much better than prednisolone and this leads to non-compliance. We would ask that you look into this and try to resolve this issue.

Thank you for your diligence in this matter.

Houck, John J
RN-CUA
Integris Express Care
9/30/2015

AXIS HEALTHCARE
WALK-IN & FAMILY PRACTICE

9/28/15

To Whom it may concern,

I am a Pediatric Nurse Practitioner in Bixby. I write Veripred frequently. My patients were not compliant when I was writing generic Prednisolone. Many of them complained of the taste or complained it was too much work to fight their children to take the medicine. I also do not like that it contains 5% alcohol. Please reconsider not covering or making a PA mandatory for Veripred and Millipred.

E Thiel, APRN
Elizabeth Thiel

MILESTONES
PEDIATRIC CARE

10-01-2015

Terry Cothran,

In regards to the recent change for Millipred and Veripred we would strongly urge you to consider keeping these products tier one.

Patient compliance is much lower when using generic medications because of taste and parents unwillingness to force children to take a medication that they themselves would not take due to the poor taste. If patient do not take their medication their illness may end up needing to be hospitalized.

Thank you for your consideration,

James Aaron Henley, DO.

3845 S 103rd E Ave, Suite 102
Tulsa, OK 74146-2452
Tel: (918) 745-0800
Fax: (918) 745-0028
www.milestonespc.com

9-30-15

Terry Cathron,

Director of Pharmacy Mgmt

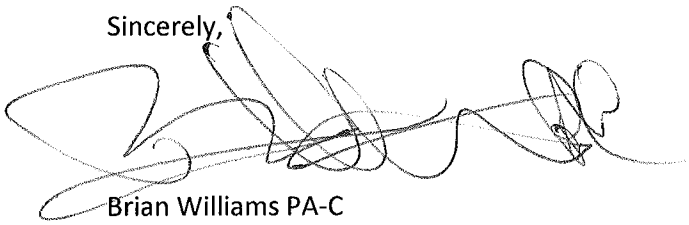
Dear Sir,

I would ask that your reconsider removing Millipred as well as Veripred. These two medications have been preferred over the bitter tasting generic Prednisone, for the treatment of Asthma, RSV, Bronchiolitis as well as other inflammatory aconditions.

The biggest issue I am concerned about dealing with, is compliance. In children who's life may actually be threatened should they refuse to take the bitter alternative, we have no more effective alternatives.

Thank you for your time and attention.

Sincerely,



Brian Williams PA-C

1306 12th NW

Ardmore, Ok. 73401

Tracy Hoos, DO
Ryan Mundy, MD

PREMIER
PEDIATRIC AND ADOLESCENT CARE

2009 N Main
Muskogee, OK 74401
Tel. 918-816-4024
Fax. 918-816-4025

9/30/15

To SoonerCare, Terri Cothran, Director of Pharmacy
Re: Millipred and Veripred

At Premier Pediatric and Adolescent Care, we are dedicated to providing our patients with superior care, especially when prescribing medications. As you may know, medication compliance is a major issue in healthcare. In pediatrics, we have discovered that palatable is one of the most important aspects in the compliance. All of our providers have prescribed Millipred and Veripred for many years without any drawbacks from parents, kids, pharmacies, or Soonercare. We have a total of 4 providers making medical decisions daily, including what medications are best for our smaller clients. We ask that you consider keeping these products tier one.

Thank you so much,

Tracy Hoos, D.O.

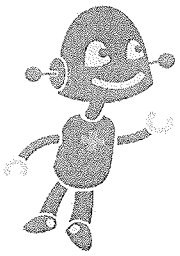
Ryan Mundy, M.D.

Amy Ceselski, APRN

Amy Ceselski, APRN, CPNP

Kelly Faltyn, APRN

Kelly Faltyn APRN-NP-C



Next Generation Pediatrics, LLC
10400 S. Western Ave. Suite 7
Oklahoma City, OK 73139

Ph: 405-378-2222 Fax: 405-378-2240

September 29, 2015

To whom it may concern,

I am a pediatric primary care provider in Oklahoma City, we have a large patient base of SoonerCare children in our practice. I am writing today asking you to reconsider taking MilliPred and VeriPred off your covered medication list. We use this medication often in children who do not tolerate the 15ml/5ml prednisilone due to flavoring. Have you ever tasted prednisilone? It is hard for even an adult to swallow, so imagine trying to get a child to tolerate that medication. The more palatable taste of MilliPred and Veripred increases medication administration compliance. Does this not therefore decrease follow-up visits and the costs associated with repeat visits? Additionally, because MilliPred and VeriPred products do not contain alcohol, I do not have to worry about the side effects associated that comes along with alcohol in my patients.

Thank you for your time,

Leslie Whisenhunt, APRN

Leslie "Jenny" Whisenhunt, APRN-CNP

Dr. Joseph Walter
Pediatric Pulmonology and Cystic Fibrosis Center of Tulsa
6151 South Yale Avenue, #1307
Tulsa, OK 74136
Phone: 918-502-2000
Fax: 918-502-2010

October 2, 2015

Terry Cothran, D.Ph
Director of Pharmacy
Pharmacy Management
Consultants ORI-4403
PO Box 26901
Oklahoma City, OK 73190

To Whom It May Concern:

I am a Pediatric Pulmonologist in Northeast Oklahoma who uses of Millipred and Veripred to dose my patients when they are ill. Compliance with medications is an issue in this population and any help, including less of a bitter aftertaste, that last a long time. It is a necessity for compliance and can decrease overall health care costs by lowering Urgent Care/ER visits and, subsequently, hospitalizations.

Unlike the cheaper alternatives, Millipred and Veripred do not contain alcohol. In my opinion, this is an ingredient that is not necessary for our patients.

Thank you for your help in taking the best care of my patients.

Sincerely,

Joseph N. Walter, MD

7512 East 91st Street
Tulsa, OK 74133

Phone: (918) 728-2000
Fax: (918) 728-2001

Dawn Mayberry, D.O.
Jerry Freed, D.O.
Christine Narrin, D.O.
Elizabeth Dunlap, D.O.

SouthTulsa Pediatrics

Attention: Terry Cothran
Director of Pharmacy
Pharmacy Management
Consultants ORI – 4403
PO Box 26901
Oklahoma City, OK 73190

To whom it may concern:

I am writing to request that Millipred and Veripred continue as a tier one medication with SoonerCare. This medication is invaluable and used regularly in pediatric primary care. The difference in taste is so significant that by choosing it as a first line medication it often prevents further office visits and quite possibly even ER visits. It is also free of alcohol which is so important when dealing with infants and children. There have been countless times when my patients have been prescribed some other form of this medication and have been unable to tolerate it due to vomiting or refusal to take because of the others offensive taste. Oral corticosteroids are such an important medication in pediatrics and knowing that with this product the likelihood of compliance is so much higher it is my first choice. Please fully review and consider all of these issues prior to removing this medication from the tier 1 list. Thank you for your attention to this matter.

Sincerely,

Erin Fleming

Erin Fleming, APRN, CPNP
Certified Pediatric Nurse Practitioner

October 2, 2015

Terry Cothran
Director of Pharmacy Consultants
ORI-4403
P.O. Box 26901
Okc, OK 73190

RE: Millipred & Veripred

Mr. Cothran:

It has been brought to my attention that Veripred and Millipred are being removed from the Soonercare formulary. I just want to voice my opinion that this is not in the best interest of our patients.

The taste and compliance with these medications are more significant than with orapred and prednisone. There is no alcohol in Veripred or Millipred which is just a added bonus.

I ask you to strongly reconsider removing these medications from the formulary.

Thanking you in advance .

Sincerely,

Robin Johnson, APRN-CNP
Mercy NW Expressway Convenient Care
8325 NW Expressway
Oklahoma City, OK 73162
(405) 470-1068

1-Oct-15

kids Pediatric & Adolescent Care

John Knippers, M.D.

Terry ...

Just wanted to encourage any acceptance of Millipred & Veripred for our patients. As a clinician, it is extremely difficult to achieve compliance with any other oral liquid steroid preparations ... Even to the point of refusal by the kids and therefore adverse results in treatment and therapy. Please help us to be able to continue to use Millipred & Veripred for the best possible treatment for our kids!

Thank-you - John Knippers MD.

7711 E. 111th St., Suite 111 · Tulsa, OK 74133 · (918) 394-KIDS (5437) · (918) 394-5440 Fax

ACCESS MEDICAL CLINIC
AFFORDABLE FAMILY HEALTH CARE

6030 S. 66th E. Ave
Tulsa, Ok 74145

Office: 918-508-7440

Fax: 918-508-7442

To : Soonercare, Terri Cothran, Dir. Of Pharmacy

September 28, 2015

RE: Millipred 10/5

Please be advised that I have used millipred for appropriate allergic reactions or acute asthma exacerbations and other common concerns when steroids are appropriate with my pediatric population with great success. The patients tolerate it and are more compliant than with other oral steroids and the ease of dosing is also helpful. A patient who needed millipred was denied from Soonercare and forced to take a generic that the mother called back and said it was increasingly difficult to get her child to complete the regimen due to the taste and complaint of 'bitterness'. Please consider keeping millipred on the tier 1 formulary as it has been very successfully utilized in my pediatric population. Please also call me with any questions or concerns.

Thank you!

Sincerely,

, CNP

Sandi Mellor, APRN, CNP

Access Medical Clinic

(918) 508 -7440

URGENT CARE of Ada

1023 Arlington • Ada, Oklahoma 74820

Office: 580-436-4400 • Fax: 580-436-4406 • urgentcareofada@cableone.net

9-30-15

Dear Sirs:

I was very disappointed to hear that Velspred was being removed from the Sooncare Formulary. As a practioner I prescribe this often & have great results with it. Please add my request to re-instate Velspred to the formulary.

Thank You —

Rebecca Poe APRN.

FAMILY
HEALTH CENTER

September 30, 2015

Attn: Terry Cothran, Director of Pharmacy
Pharmacy Management Consultants
ORI-4403
PO Box 26901
Oklahoma City, Oklahoma 73190

Dear Mr. Cothran,

I am writing to voice my concern over the change in prescription restrictions on Millipred. I understand budgetary constraints but would be hopeful that something could be renegotiated with the pharmaceutical company and not just a blatant stopping of the medication due to a couple of significant issues related to the generic medications. One is that of taste. I have a difficult time with young children, getting them to take the generic steroid preparations. In some situations when we are dealing with asthma, that is critical that they get their appropriate dosages of medications. The other concern is the alcohol content contained within the generic medications, which is significantly higher than anything over the counter and may be counterproductive with other concomitant medications they could be taking.

I would hope that there would be a reconsideration of allowing the Millipred to be prescribed and would be happy to have further discussion if one is possible or necessary.

Sincerely,

Michael Carnahan, MD

MC/mb

1104 Walnut Drive • Ardmore, Oklahoma 73401 • Phone (580) 226-0543 • Fax (580) 226-2284

FAMILY
HEALTH CENTER

September 30, 2015

To Whom It May Concern:

My name is Gina Hernandez. I am a physician assistant who works in family medicine. I am writing this letter concerning the letter that I received about the fact that Millipred will no longer be available for Soonercare patients. I am greatly disappointed to hear that we will not be able to order that for our patients anymore. It is very difficult at times to have pediatric patients take generic prednisolone due to the taste. Millipred had a great flavor, and parents never struggled to give it to their children. With prednisolone, there would be times that I would get several phone calls throughout two or three days because the child would either throw up the medication, spit out the medication, or just refuse to take it. They then would have to come in for a followup and have an injection given to them to help with their asthma exacerbation.

I as well as the patients who I take care of would greatly appreciate having Millipred available for future treatment.

Sincerely,

Gina Hernandez, PA-C

GH/mb

1104 Walnut Drive • Ardmore, Oklahoma 73401 • Phone (580) 226-0543 • Fax (580) 226-2284

Wade Pediatrics

Kevin Wade, MD

3505 W. Broadway Street
Muskogee, OK 74401

Phone 918-683-8442
Fax 918-683-8390

To: SoonerCare, Terri Cothran, Director of Pharmacy 09/30/2015

Re: Millipred and Veripred

At Wade Pediatrics, we are dedicated to providing our patients with superior care especially when prescribing medications. We have a total of 4 providers making medical decisions daily, including what medications are best for are small clients. As you may know, medication compliance is a major issue in healthcare. In pediatrics, we have discovered that TASTE is one of the most important aspects in this compliance. All of our providers have prescribed Millipred and Veripred for many years without ANY drawbacks from parents, kids, pharmacies, or SoonerCare. We ask to please keep these products tier one.

Thank you so much,

Kevin Wade, M.D.

Kristin S. Coffman, APRN, FNP-BC

Rhonda Tootill, APRN, FNP-BC

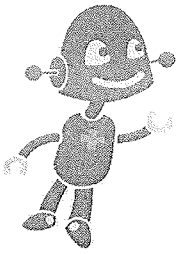
Kelli Swim, APRN, FNP-BC

Terry Cothran,

I have been informed that SoonerCare will no longer cover Veripred steroid. I understand that cost analysis often plays a major role in deciding medications that can be covered, I also find that other variables need to be considered. As a pediatric provider taste plays a major role in medication compliance. Veripred does an excellent job of masking after taste and thus makes the medication easier to take for children. When steroids are prescribed for short periods it is important that children are able to take complete doses as scheduled. I would greatly appreciate it if you would reconsider Veripred and Millipred for your formulary, or at the very least doa taste comparison of orapred vs veripred to gain a better understanding of the great difference between these two medications. Again thank you for your time.

Sincerely,

Brian J. Bauer ARNP, CPNP



Next Generation Pediatrics, LLC
10400 S. Western Ave. Suite 7
Oklahoma City, OK 73139

Ph: 405-378-2222 Fax: 405-378-2240

September 29, 2015

To whom it may concern,

I am a pediatric primary care provider in Oklahoma City, we have a large patient base of SoonerCare children in our practice. I am writing today asking you to reconsider taking MilliPred and VeriPred off your covered medication list. We use this medication often in children who do not tolerate the 15ml/5ml prednisilone due to flavoring. Have you ever tasted prednisilone? It is hard for even an adult to swallow, so imagine trying to get a child to tolerate that medication. The more palatable taste of MilliPred and Veripred increases medication administration compliance. Does this not therefore decrease follow-up visits and the costs associated with repeat visits? Additionally, because MilliPred and VeriPred products do not contain alcohol, I do not have to worry about the side effects associated that comes along with alcohol in my patients.

Thank you for your time,

Elizabeth Carlton, APRN-CNP

SOUTHERN OKLAHOMA PEDIATRICS, INC.
1214 ARLINGTON ST
ADA, OK 74820
580-436-2283 PHONE
580-436-2291 FAX

Tawfik Ramadan, M.D.
Laura Soper, P.A.

September 30, 2015

Oklahoma Health Care Authority

Dear Mr. Cothran,

We were sorry to see that Millipred and Veripred now require prior authorization on basis of cost alone.

We have been prescribing it because:

1. Better Compliance-both with patients and their parents who are reluctant to continue giving a more bitter tasting medication that the child spits out or gags and vomits.
2. Dosing is easier with 10 mg/kg and 20 mg/kg
3. More frequent return visits with other medications with no improvement. Parents just take the child for an ER visit which is much more expensive than the medication. (Prices listed in the Sooner Care Faxes are based on 10 day course. We rarely prescribe more than 6-7 days.
4. Most generic prednisolone has 5% alcohol. Millipred and Veripred are alcohol free.

Sincerely,

Tawfik Ramadan, M.D.

Laura Soper, P.A.

INTEGRIS
Grove Hospital

Grand Lake Area Clinics ~ Internal Medicine Associates

Janet Fletcher, PA-C
janet.fletcher@integrisok.com

James D. Rutter, MD
james.rutter@integrisok.com

Kelly Long, APRN-CNP
kelly.long@integrisok.com

September 29, 2015

TO: Soonercare, Terri Cothran, Dir. Of Pharmacy

RE: Millipred 10/5 Veripred 20/5

This note is to ask you to reconsider the removal of Veripred and Millipred from the tier two use for steroids. I routinely have used these products for the treatment of asthma exacerbations and allergic reactions in the pediatric population. Using these products allows me to keep from having to hospitalize children or from having them return to the ER for more emergent type care. Unfortunately when prescribing Prednisolone 15/5, the compliance rate becomes a concerns due to the bitter taste of the product. When giving Millipred or Veripred, it allows the patient to be able to stay at home and care for their child at home. Please reconsider this decision as it will allow us to provide the care we need for the children at home.

If you have any questions or concerns, please feel free to contact me. Thank you!

Sincerely,

Kelly Long APRN, CPNP

900 E 13th Street, Suite 101 • Grove, Ok 74344 • 918.786.9900 • 918.786.9904 Fax

September 30, 2015

Terry Cothran:

I am a mid-level provider who practices Urgent Care; we utilize millipred and verapred on a regular basis. Our patient population has a large amount of Oklahoma Medicaid which are pediatrics, these above medicines have been a great asset due to patients tolerating them and compliance has improved due to taste and less side effects from generic tastes. As you may know the generic steroids have a larger amount of alcohol as an ingredient compared to milliprd and verapred.

We hope that you will give these concerns careful consideration.

Thank you,

Shelby Lucas, P.A.-C

TODAY CLINIC™

(405) 631-0611 - Phone
(405) 631-0811 - Fax
www.todayclinic.com
info@todayclinic.com

DATE: 9/28/2015

Dear Mr Cothran,

This letter is in regards to millipred/veripred being taken off of Sooner Care. I ask you to please reconsider this as it will really affect my patients.
The reason why I prefer Millipred/veripred over the prednisolone is due to better taste and no alcohol content. Getting my patient to compliance with the treatment regimen is the best outcome and thus cost effective.
I have very good outcomes and compliance with Millipred/veripred.
Thank you so much for reconsideration

Sincerely,

Johnny Ng NP

OKC North
701 NE 36th
Oklahoma City, OK 73105
(405) 631-0611

OKC Buy For Less
415 SW 59th and S Walker
Oklahoma City, OK 73109
(405) 631-0611

OKC South
1317 SE 44th St
Oklahoma City, OK 73129
(405) 631-0611

Lawton
4008 Cache Road
Lawton, Ok
(580) 379-0200

September 29, 2015

To whom it may concern:

I am a Sooner Care provider in a pediatric practice at Variety Care in Del City. I am requesting OHCA to reconsider taking off prednisolone syrups that are palatable and less likely to be vomited in favor of lower cost syrups that taste awful or at such a low concentration that the dose is high.

If a patient such as a toddler has acute wheeze and/or dyspnea, early and reliable steroids will often keep them from the emergency room.

Thank you for your consideration,

Brian G Sharp PA-C

Variety Care at Middel

3851 Tinker Diagonal

Del City, OK 73115

(405) 632-6688

(405) 677-8991 fax

bgs

INTEGRIS
Express Care

21 West Central
Miami, OK 74354
918.542.3900

J. Mark Osborn, M.D.
Family Practice
Nichole Bateman, PA-C, MPAS
Family Practice

To: SoonerCare, Terri Cothran, Dir. Of Pharmacy

September 29. 2015

RE: Millipred and Veripred

One of the biggest problems I have with any medication is the matter of *compliance.* I have not had to worry about this issue with Millipred and Veripred; both are excellent products since they are palatable for my pediatric population. Medicaid patients should not have to suffer by the poor taste and effects from not taking medication that could benefit them greatly and keep them out of the ER. Please keep this in mind when deciding on keeping this medication a Tier 1 product.

Thank you!

Sincerely,

Serena Wilson, APRN-CNP

Nancy Nesser

From: Trinity Loveless <trinitymloveless@gmail.com>
Sent: Wednesday, September 09, 2015 1:07 PM
To: Nancy Nesser
Subject: [Maybe SPAM] Synagis for late preterm infants

Dear DUR Board Members, 9/9/2015

I am a pediatrician in the Yukon, Ok area. I am very concerned with the new recommendations for RSV prophylaxis. I believe that it is still very beneficial to keep protecting the late preterm infants ages 29-34 weeks gestation with synagis during RSV season. I feel that the rate of hospitalizations will greatly increase for these infants if the new recommendations are followed and the late preterm infants are no longer protected. Many of these infants are in daycare because their parents have to work. Many of them have older siblings who are in daycare or school and they are exposed to RSV in this manner.

Please continue to protect these high-risk newborns in our community with Synagis throughout the RSV season.

Respectfully,

Trinity Loveless, MD

A Place to Grow Pediatrics

812 South Mustang Road

Yukon OK 73099

(405) 265-3900

From	"Edward Co" <Edward_Co@Pediatrix.com>	Reply
To	Nancy.Nesser@okhca.org	
Subject	Letter to OK DUR regarding Synagis Guidelines	
Attachments	1	

Nancy Nesser, Pharm.D., J.D.
Pharmacy Program Director
Oklahoma Health Care Authority
4545 N Lincoln Blvd.
Oklahoma City, OK 73105-3413

Dear Ms. Nancy Nesser,

I am writing this letter to request the Drug Utilization Review Board not to change the current existing Synagis guidelines for our high risk newborns who are born less than 35 weeks gestation and admitted to our Level III and Level II NICUs. Our hospitals include Integris Baptist Medical Center, Integris Southwest Medical Center, Integris Canadian Valley Hospital, Integris Lakeside Women's Hospital, Integris Hospital Edmond and Alliance Health Deaconess Hospital. Since 2006, our Pediatrix Medical Group have developed a very successful Synagis Program at the Integris Baptist Medical Center. The readmission rate for our NICU graduates from RSV infection has been extremely low because our Synagis Program not only give the Synagis immunization to our high risk infant less than 35 week gestation at discharge, but it also provide education to all of our NICU graduates on RSV awareness and prevention prior to discharge from our NICU throughout the year. I'm very much concerned and worried that if the Synagis guidelines is changed again, this might cause a sudden resurgence and an increase in the incidence of RSV infections that may lead to an increase in the number of readmissions to our hospital and PICU as well as an increase in the rate of morbidity and even mortality in our NICU graduates.

I sincerely hope that the DUR Board would be prudent to consider not changing the current Synagis guidelines. Your kind consideration, thoughtfulness and understanding would be greatly appreciated by our patients and their families and our NICU staff.

Sincerely,

Edward Co, MD
NICU Medical Director
Pediatrix Medical Group
@Integris Health & Alliance Health Deaconess Hospital

Appendix B

2016 Drug Utilization Review Board Meeting Dates

Oklahoma Health Care Authority
October 2015

Meetings are held the second Wednesday of every month

January 13, 2016

February 10, 2016

March 9, 2016

April 13, 2016

May 11, 2016

June 8, 2016

July 13, 2016

August 10, 2016

September 14, 2016

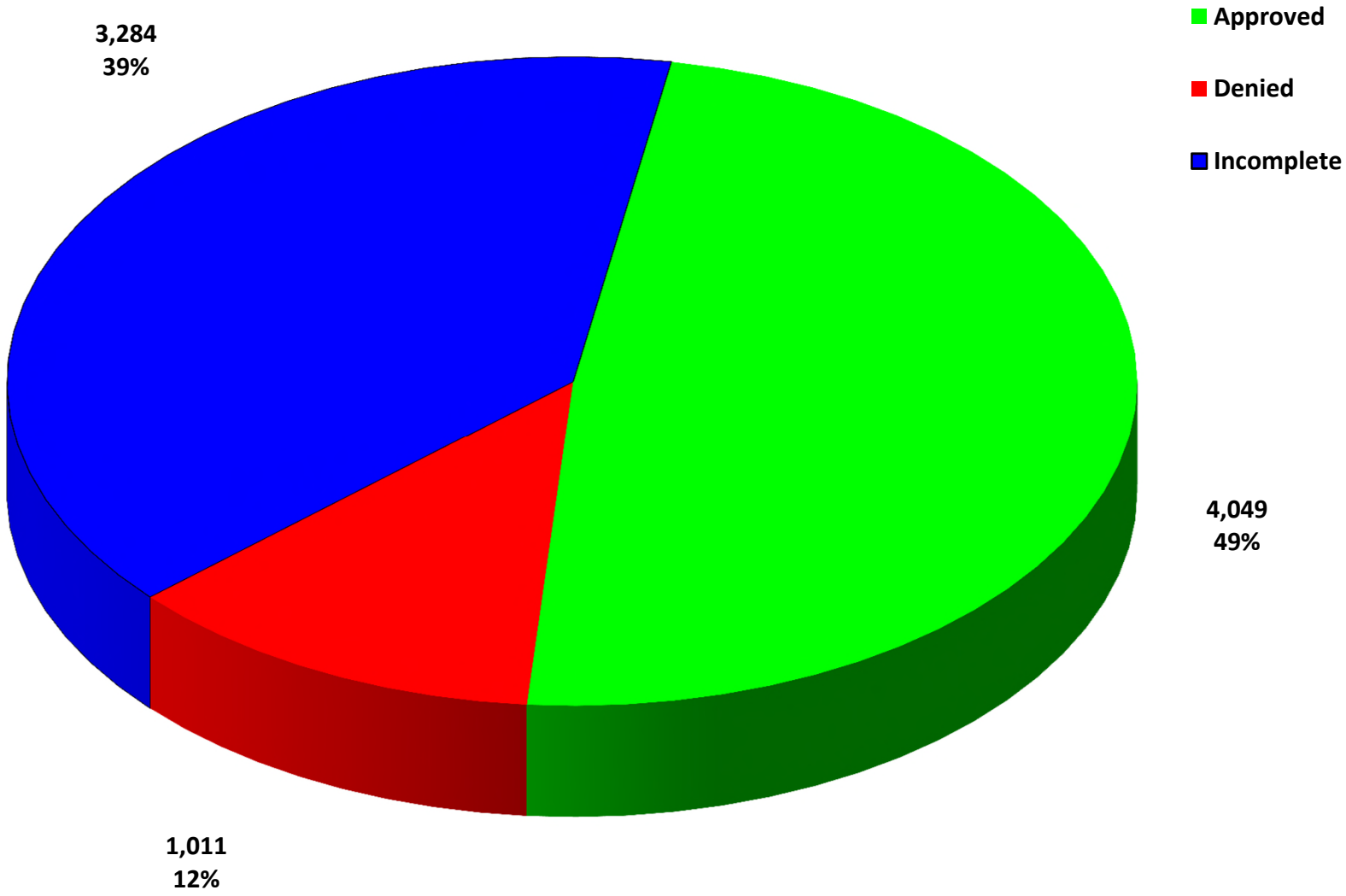
October 12, 2016

November 9, 2016

December 14, 2016

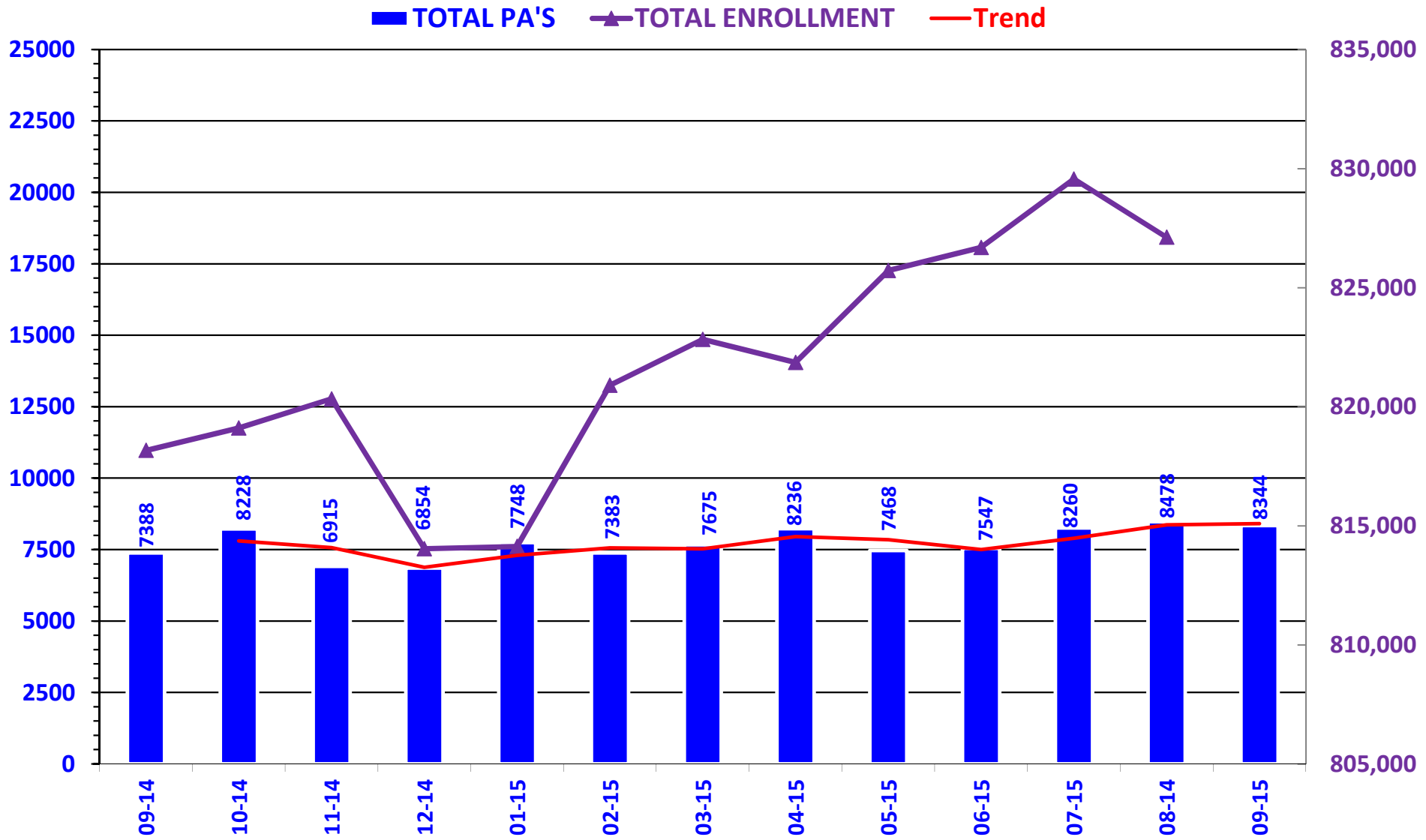
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER 2015



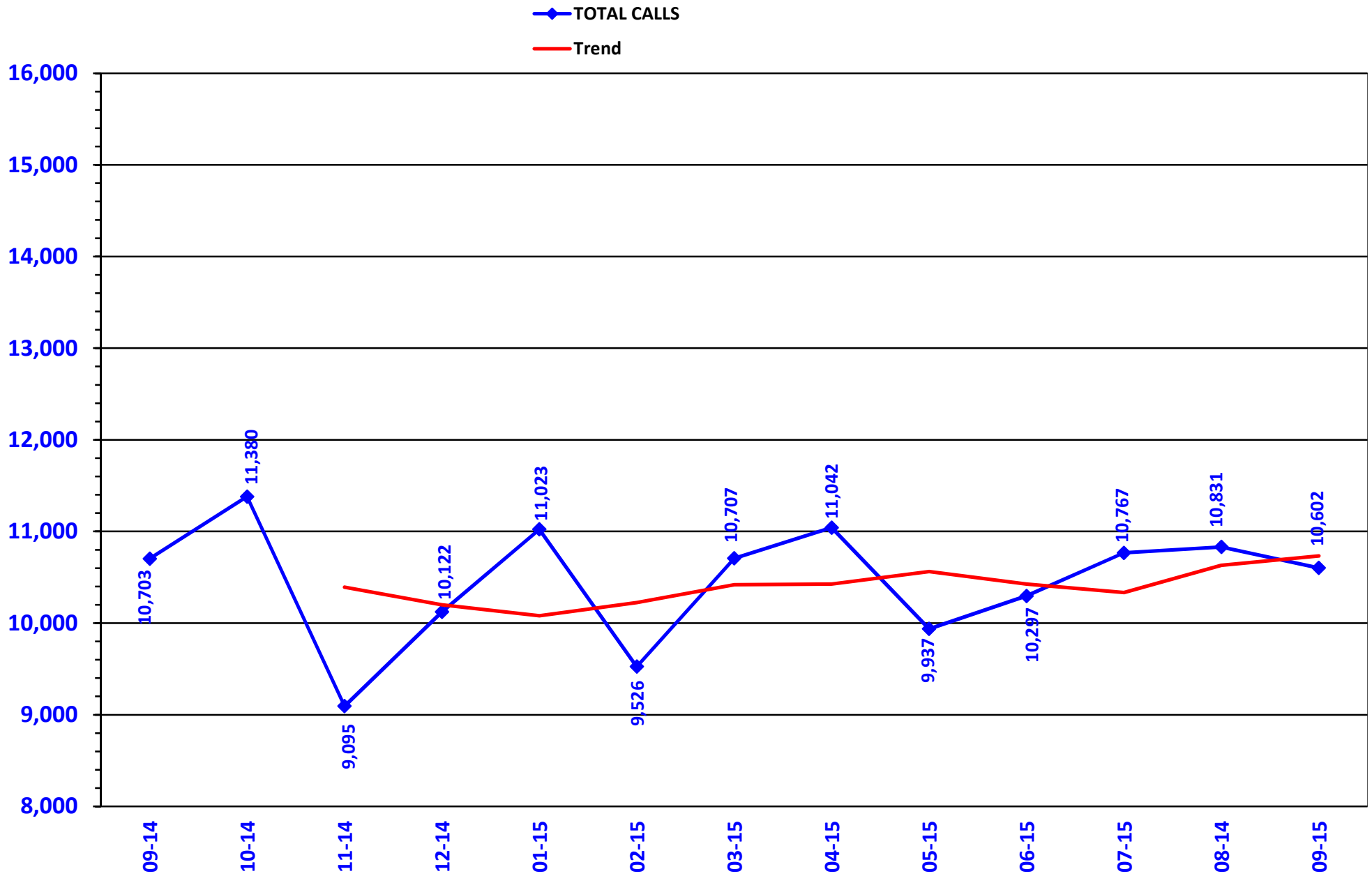
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2014 – SEPTEMBER 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
SEPTEMBER 2014 – SEPTEMBER 2015



Prior Authorization Activity

9/1/2015 Through 9/30/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	400	175	40	185	349
Analgesic - NonNarcotic	11	0	4	7	0
Analgesic - Narcotic	401	212	47	142	165
Angiotensin Receptor Antagonist	21	3	7	11	361
Antiasthma	187	71	25	91	347
Antibiotic	41	13	5	23	175
Anticonvulsant	87	36	9	42	345
Antidepressant	97	22	18	57	340
Antidiabetic	172	91	16	65	359
Antifungal	13	1	4	8	36
Antihistamine	170	147	4	19	359
Antimigraine	46	11	13	22	267
Antiulcers	170	34	41	95	174
Anxiolytic	71	49	4	18	252
Atypical Antipsychotics	522	248	29	245	345
Biologics	61	36	4	21	303
Bladder Control	55	15	6	34	359
Blood Thinners	143	98	4	41	325
Botox	25	16	7	2	298
Cardiovascular	64	30	11	23	322
Cephalosporins	21	9	2	10	7
Chronic Obstructive Pulmonary Disease	31	7	5	19	360
Contraceptive	30	27	1	2	309
Dermatological	111	16	58	37	92
Diabetic Supplies	597	309	25	263	237
Endocrine & Metabolic Drugs	64	46	8	10	125
Erythropoietin Stimulating Agents	16	11	3	2	110
Fibromyalgia	159	42	54	63	344
Fish Oils	19	2	10	7	359
Gastrointestinal Agents	98	29	22	47	83
Glaucoma	10	2	3	5	223
Growth Hormones	85	69	5	11	144
Hepatitis C	160	79	41	40	8
HFA Rescue Inhalers	68	25	5	38	345
Insomnia	66	12	15	39	163
Insulin	44	4	6	34	276
Linzess, Amitiza, and Relistor	85	12	31	42	253
Multiple Sclerosis	83	27	19	37	214
Muscle Relaxant	84	21	22	41	41
Nasal Allergy	112	18	20	74	248
Neurological Agents	56	37	8	11	355
NSAIDs	155	25	34	96	294
Ocular Allergy	41	9	5	27	176
Ophthalmic Anti-infectives	12	2	1	9	11
Osteoporosis	17	3	6	8	361
Other*	255	70	44	141	227
Otic Antibiotic	32	3	7	22	7
Pediculicide	213	93	23	97	13
Prenatal Vitamins	21	2	1	18	85
Statins	70	18	11	41	343
Stimulant	1,034	516	91	427	345
Suboxone/Subutex	202	148	5	49	78
Synagis	11	0	0	11	0
Testosterone	73	17	18	38	360
Topical Antifungal	40	1	11	28	56
Topical Corticosteroids	61	3	13	45	141

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Vitamin	65	23	34	8	335
Pharmacotherapy	49	43	1	5	323
Emergency PAs	0	0	0	0	
Total	**7,107**	**3,088**	**966**	**3,053**	
Overrides					
Brand	58	39	4	15	288
Cumulative Early Refill	5	3	0	2	180
Diabetic Supplies	4	3	0	1	361
Dosage Change	329	312	0	17	7
High Dose	3	3	0	0	129
Ingredient Duplication	36	29	0	7	17
Lost/Broken Rx	90	83	1	6	4
NDC vs Age	33	30	1	2	246
Nursing Home Issue	24	23	0	1	4
Opioid Quantity	13	9	3	1	153
Other*	31	19	4	8	6
Quantity vs. Days Supply	586	388	30	168	260
STBS/STBSM	15	14	0	1	44
Stolen	5	5	0	0	77
Third Brand Request	26	15	5	6	9
Wrong D.S. on Previous Rx	1	1	0	0	7
Overrides Total	**1,237**	**961**	**45**	**231**	
Total Regular PAs + Overrides	**8,344**	**4,049**	**1,011**	**3,284**	

Denial Reasons	
Unable to verify required trials.	2,746
Does not meet established criteria.	988
Lack required information to process request.	532

Other PA Activity	
Duplicate Requests	533
Letters	5,723
No Process	14
Changes to existing PAs	570
Help Desk Initiated Prior Authorizations	473
PAs Missing Information	46

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

Bowel Preparation Medication Post-Educational Mailing

Oklahoma Health Care Authority
October 2015

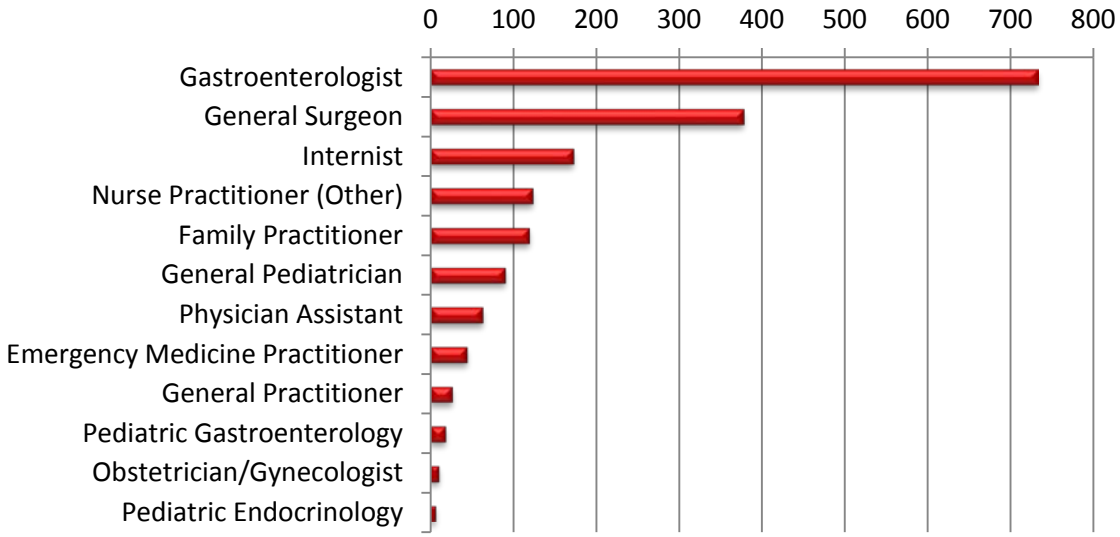
Bowel Preparation Medication Letter

The College of Pharmacy and the Oklahoma Health Care Authority are engaged in an effort to promote cost effective utilization of bowel preparation medications. In May 2015, an educational letter was sent to prescribers of bowel preparation medications in the previous six months. Examples of brand or higher cost bowel preparation medications include: MoviPrep®, SUPREP® Bowel Prep Kit, Prepopik®, and OsmoPrep®. The mailing included general cost information for brand products in comparison to generic products and suggestions to maximize the pharmacy benefit through generic and over-the-counter utilization. The mailing also included a "Preferred Bowel Preparations Change Form" that encouraged prescribers to use generic low-cost medications by simplifying the prescription writing process for preferred medications. See the attached document for an example of the letter and "Preferred Bowel Preparations Change Form".

Summary of the Mailing

Prescribers were eligible for inclusion in the mailing if they had prescribed a bowel preparation medication for a SoonerCare member from October 1, 2014 to March 31, 2015. A total of 369 prescribers were flagged for having at least one patient with a paid claim for a bowel preparation medication. These prescribers accounted for 1,547 flagged patients. All flagged prescribers were included in the mailing.

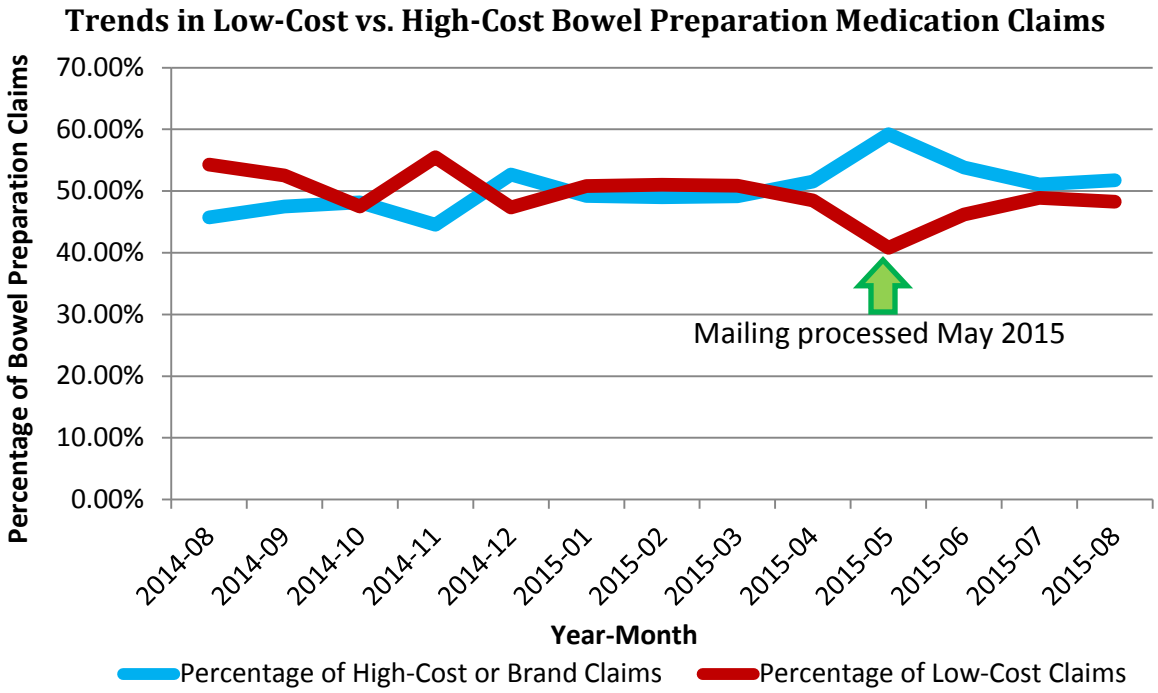
Top Prescriber Specialties Included in the Mailing by Number of Claims*



*Specialties excluded from graph if accounting for fewer than five claims for a bowel preparation medication.

Bowel Preparation Medication Trends

The chart below shows the trends in percentage of claims comparing higher cost bowel preparation medication utilization to lower cost medications. The mailing was processed in May of 2015 and is noted on the chart below. Following the mailing, an immediate decline in high cost bowel preparation medications was seen in June and July 2015 as well as a corresponding increase in utilization of generic bowel preparation medications. The purpose of the educational mailing was not to decrease overall utilization of bowel preparation medications, but to encourage cost effective utilization of lower cost bowel preparation medications.



Conclusions[1,2]

While an encouraging trend in lower cost bowel preparation medication utilization was seen following the educational mailing, further review in the bowel preparation medication class is necessary. The estimated cost savings (based on the average cost per claim) over one year if all members switched to a lower cost bowel preparation medication including possible administrative costs is $70,933.16-$108,153.16. Some consideration should be given to implementation of a Product-Based Prior Authorization (PBPA) category to encourage appropriate, cost-effective utilization of the bowel preparation medications.

There are challenges with implementing a prior authorization for products in the bowel preparation medication class. For example, many times patients will not bring their prescription to the pharmacy until the day before their procedure. A delay in processing the prescription claim could potentially result in delaying of the procedure. Another issue outlined in the American Gastroenterology Association Guidelines is that the success of the colonoscopy

procedure is linked closely to the adequacy of the preprocedure bowel cleansing. The diagnostic accuracy and therapeutic safety of colonoscopy depends, in part, on the quality of the colonic cleansing or preparation. The increased cost of a superior bowel preparation product may be negligible if an unsuccessful procedure has to be repeated due to inadequacy of preprocedure bowel cleansing. Further evaluation of the efficacy of the bowel preparation medications in relation to cost is warranted.

Additional evaluation should be considered for claims with multiple days submitted for the day supply. Some utilization could have been inappropriate if the products were used for constipation rather than bowel preparation for a procedure.

Recommendations

The College of Pharmacy recommends the following in regards to the bowel preparation medications:

1. Conduct a complete drug utilization review of the bowel preparation medication class to evaluate safety, efficacy, and cost of all products.
    a. The drug utilization review should also include claims analysis for potential inappropriate use.
2. If appropriate, consider implementation of a PBPA category.
3. Alternatives to a PBPA category include additional targeted educational mailings to encourage appropriate, cost-effective utilization of the bowel preparation medications.

[1]American Gastroenterological Association, American College of Gastroenterology, and the American Society for Gastrointestinal Endoscopy. Optimizing Adequacy of Bowel Cleansing for Colonoscopy: Recommendations From the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2014; 147:903-924.

[2] American Society for Gastrointestinal Endoscopy. Bowel Preparation Before Colonoscopy. Gastrointestinal Endoscopy 2015; 81 (4):781-794.

SoonerCare
Oklahoma Health Care Authority

Pharmacy Services

(800) 522-0114, option 4

May 15, 2015

Dear SoonerCare Prescriber,

The Oklahoma Health Care Authority is engaged in an effort to improve cost effective utilization of bowel preparation medications for procedures. The purpose of this letter is to provide information regarding generic bowel preparation medications which offer cost savings and similar therapeutic effectiveness compared to the frequently used more expensive brand-name products.

Generic bowel preparation medications generally cost $15 to $30 per container and provide similar efficacy as the more costly brand products, which range from $70 to $117 per container or kit. The following are bowel preparation products with a cost effective generic available:

- GoLYTELY®
- CoLyte®
- NuLYTELY®
- TriLyte®

SoonerCare members have a six prescription limit each month, two of which can be brand products. A brand name bowel preparation medication will count against the member's monthly two brand medication limit. Please consider use of generic medications when possible.

It is important to note that SoonerCare members pay a flat copay of $4.00 regardless of the cost of the medication. Some over-the-counter products including magnesium citrate oral solution may cost less or about the same as the member's copay and would not count against the member's prescription limit.

Thank you for the services you provide to Oklahomans insured by SoonerCare!

SoonerCare Pharmacy Services • Pharmacy Management Consultants • PO Box 26901; ORI W-4403 • Oklahoma City, Oklahoma 73126-0901 • Phone: (800) 522-0114, option 4 • Fax: (800) 224-4014

Preferred Bowel Preparations Change Form

Patient's Name: _____ **Patient's DOB:** _____
SoonerCare ID: _____

Product Name/Covered NDC	Quantity	Dosing Regimen
☐ Magnesium Citrate Oral Solution (Low Cost, over-the-counter product not covered through SoonerCare but similar to the member's copay)	Product Dependent	
☐ Polyethylene Glycol/Electrolytes (GoLYTELY®) 43386-0090-19 10572-0100-01 00378-6669-40	4000mL	
☐ Polyethylene Glycol/ Electrolytes (CoLyte®) 43386-0060-19 62175-0446-01	4000mL	
☐ Polyethylene Glycol/Electrolytes (NuLYTELY®) 43386-0050-16 10572-0400-01	4000mL	
☐ Polyethylene Glycol/Electrolytes (TriLyte®) 51525-6831-04 10572-0302-01	4000mL	

Magnesium Citrate Oral Solution would not count against the member's prescription limit.

Prescriber's Signature: _____
Date: _____
Prescriber's Name: _____
Prescriber's NPI: _____

Please Send to Patient's Pharmacy:

Pharmacy Name: _____
Pharmacy Fax: _____

Appendix D

Vote to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-Trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab)

Oklahoma Health Care Authority
October 2015

Recommendations

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. Tykerb® 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).

Halaven® (Eribulin) Approval Criteria:

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.

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.

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.

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).

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.

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

1. Diagnosis of unresectable, locally advanced, or metastatic neuroendocrine tumors of pancreatic origin (PNET); and
2. Progressive disease from a previous treatment.

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

1. Diagnosis of advanced renal cell carcinoma; and
2. Failure of treatment with sunitinib or sorafenib.

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.

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.

Appendix E

Vote to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor)

Oklahoma Health Care Authority
October 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Orkambi™ (lumacaftor/ivacaftor) with the following criteria:

Orkambi™ (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the F508del mutation in the CFTR gene detected by genetic testing; and
2. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene; and
3. Orkambi™ will not be approved for patients with CF other than those homozygous for the F508del mutation; and
4. Member must be 12 years of age or older; and
5. Members using Orkambi™ must be supervised by a pulmonary specialist; and
6. The prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi™, every three months during the first year of treatment, and annually thereafter; and
7. Members must not be taking any of the following medications concomitantly with Orkambi™: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
8. A quantity limit of four tablets per day or 112 tablets per 28 days will apply.
9. Initial approval will be for the duration of three months, after which time, compliance will be required for continued approval. After six months of utilization, compliance and information regarding efficacy, such as improvement in FEV_1, will be required for continued approval.

Appendix F

Vote to Prior Authorize Savaysa® (Edoxaban)

Oklahoma Health Care Authority
October 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Savaysa® (edoxaban) with the following criteria:

Savaysa® (Edoxaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. To reduce the risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation; or
    b. For the treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant; and
2. Requests for therapy for the treatment of DVT and PE must verify that the member has undergone 5 to 10 days of initial therapy with a parenteral anticoagulant; and
3. Member must not have a creatinine clearance (CrCl) greater than 95mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied (60mg); and
4. A quantity limit of 30 tablets per 30 days will apply.

In September 2015, the FDA approved a 60mg strength tablet of Brilinta® (ticagrelor). The 60mg dose is labeled to be used twice daily after one year of therapy with the 90mg twice daily dosage. The College of Pharmacy recommends the following changes to the prior authorization criteria for Brilinta® (ticagrelor):

Brilinta® (Ticagrelor) Approval Criteria:

1. The first 90 days of therapy with the 90mg strength tablets does not require prior authorization; and
2. Approved diagnostic criteria: acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction) with or without percutaneous coronary intervention (PCI); and
3. Approvals of the 90mg twice daily dosage will be for the duration of one year after which time the member should switch to the 60mg twice daily dosage or provide patient-specific, clinically significant reasoning for continuing the 90mg twice daily dosage; and
4. The 60mg twice daily dosage may be approved after one year of therapy with the 90mg twice daily dosage.

Appendix G

Vote to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), & Repatha™ (Evolocumab)

Oklahoma Health Care Authority
October 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Epanova® (omega-3-carboxylic acids) with the following criteria:

Lovaza® (Omega-3-Acid Ethyl Esters), Vascepa® (Icosapent Ethyl), and Epanova® (Omega-3-Carboxylic Acids) Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥ 500mg/dL), and controlled diabetes (fasting glucose < 150mg/dL at the time of triglycerides measurement and HgA1C < 7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®).

Additionally, the College of Pharmacy recommends the prior authorization of PCSK9 inhibitors, Praluent® (alirocumab) and Repatha™ (evolocumab), with the following criteria:

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 (*See Attachment A)*; 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 (*See Attachment B)*; 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® and a quantity limit of 2 syringes or autoinjectors per 28 days will apply for Repatha™. 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.
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.

Attachment A: Diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH)[1]

Simon Broome Register Criteria

A. A plasma cholesterol measurement of either:
   a. Total cholesterol >290mg/dL (adult patient) or >259mg/dL (age < 16 years); or
   b. Low-density lipoprotein cholesterol (LDL-C) > 189mg/dL (adult patient) or >155mg/dL (age <16 years)
B. Tendon xanthomas in the patient or any of the patient's first- or second-degree relatives
C. DNA-based evidence in the patient of mutation in LDLR or any other HeFH-related gene
D. Family history of myocardial infarction before the age of:
   a. 50 years in any first- or second-degree relative; or
   b. 60 years in any first-degree relative
E. Family history of plasma total cholesterol measurements >290mg/dL in any first- or second-degree relatives

Diagnosis	Criteria Required
Definite HeFH	A + B *or* C
Probable HeFH	A + D *or* A + E

Dutch Lipid Network Criteria

	Points
1. Family history: a first-degree relative with known:	
a. Premature* coronary and vascular disease	**1**
b. Plasma LDL-C concentration >95th percentile for age and sex	
i. In an adult relative	**1**
ii. In a relative <18 years of age	**2**
c. Tendon xanthomas or arcus cornealis	**2**
2. Clinical history: patient has premature*:	
a. Coronary artery disease	**2**
b. Cerebral or peripheral vascular disease	**1**
3. Physical examination of the patient:	
a. Tendon xanthomas	**6**
b. Arcus cornealis in a patient <45 years of age	**4**
4. LDL-C levels in patient's blood (mg/dL):	
a. ≥329	**8**
b. 251 – 328	**5**
c. 193 – 250	**3**
d. 155 – 192	**1**
5. DNA analysis showing a functional mutation in the LDLR or other HeFH-related gene	**8**

Diagnosis	Total Points
Definite HeFH	> 8
Probable HeFH	6 – 8
Possible HeFH	3 – 5

*Premature is defined as males <55 years of age or females <60 years of age.

[1] *CMAJ:* Heterozygous familial hypercholesterolemia: an under-recognized cause of early cardiovascular disease. Available online at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1421462/. Last revised 4/11/06. Last accessed 8/18/15.

Attachment B: Framingham Heart Study and Framingham Risk Score[1,2]

Background Information

The Framingham Heart Study is a long-term, ongoing cardiovascular study on the residents of Framingham, Massachusetts. The study began in 1948 and is now on its third generation of participants. The Framingham Heart Study is a project of the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with Boston University. The objective of the study was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke. Over the years, careful monitoring of the study population has led to the identification of major CVD risk factors (high blood pressure, high cholesterol, smoking, obesity, diabetes, and physical inactivity) as well as a great deal of valuable information on the effects of related factors such as triglyceride and HDL-C levels, age, gender, and psychosocial issues. Although the Framingham cohort is primarily Caucasian, the importance of the major CVD risk factors identified in this group have been shown in other studies to apply almost universally among racial and ethnic groups, even though the patterns of distribution may vary from group to group. The concept of CVD risk factors has become an integral part of the modern medical curriculum and has led to the development of effective treatment and preventative strategies in clinical practice.

An individual's 10-year risk of CVD, coronary heart disease (CHD), or atrial fibrillation can be estimated with the Framingham Risk Score (FRS). The FRS is based on findings of the Framingham Heart Study and uses various predictors (e.g. age, cholesterol levels, smoking) to estimate an individual's 10-year risk.

Framingham Risk Score (FRS): 10-Year Risk for Coronary Heart Disease (CHD)

Predictors for Estimating Risk of CHD in Men*	Points	Relative Risk
1. Age:		
a. 30-34 years	-1	n/a
b. 35-39 years	0	n/a
c. 40-44 years	1	n/a
d. 45-49 years	2	n/a
e. 50-54 years	3	n/a
f. 55-59 years	4	n/a
g. 60-64 years	5	n/a
h. 65-69 years	6	n/a
i. 70-74 years	7	n/a
2. LDL-C^{+}:		
a. < 100mg/dL	-3	very low risk
b. 100-129mg/dL	0	low risk
c. 130-159mg/dL	0	moderate risk
d. 160-190mg/dL	1	high risk
e. > 190mg/dL	2	very high risk
3. HDL-C:		
a. < 35mg/dL	2	very high risk
b. 35-44mg/dL	1	high risk
c. 45-49mg/dL	0	moderate risk
d. 50-59mg/dL	0	low risk

e. ≥ 60mg/dL	-1	very low risk
4. Blood Pressure[α]:		
a. < 120/80mmHg	0	very low risk
b. 120-129/80-84mmHg	0	low risk
c. 130-139/85-89mmHg	1	moderate risk
d. 140-159/90-99mmHg	2	high risk
e. ≥ 160/100mmHg	3	very high risk
5. Diabetes:		
a. Yes	2	high risk
b. No	0	low risk
6. Smoking:		
a. Yes	2	high risk
b. No	0	low risk

Total Points	FRS: 10-Year CHD Risk
≤ -3	1%
-2 to -1	2%
0	3%
1 to 2	4%
3	6%
4	7%
5	9%
6	11%
7	14%
8	18%
9	22%
10	27%
11	33%
12	40%
13	47%
≥ 14	≥ 56%

FRS	Relative Risk
< 10%	Low risk
10% - 19%	Moderate risk
≥ 20%	High risk

*Points for estimating risk of CHD vary based on sex; therefore, total points and risk score may be different for a female patient with the same predictor values and characteristics as a male patient.
[+]FRS may also be calculated using total cholesterol instead of LDL-C.
[α]When systolic and diastolic pressures provide different estimates for point scores, use the higher number.

[1] Framingham Heart Study: Coronary Heart Disease (10-year risk). Available online at: https://www.framinghamheartstudy.org/risk-functions/coronary-heart-disease/10-year-risk.php. Last accessed 8/18/15.
[2] CFP: Practical Use of the Framingham Risk Score in Primary Prevention. Available online at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3076470/. Last revised 4/2011. Last accessed 8/20/15.

State of Oklahoma: Oklahoma Health Care Authority
PCSK9 Inhibitor Prior Authorization Form

Pharmacy Section

Member Name: _____ ***Date of Birth:***_____ ***Member ID#:***_____

Pharmacy NPI:_____ ***Pharmacy Phone:*** _____ ***Pharmacy Fax:***_____

Pharmacy Name:_____ ***Pharmacist Name:***_____

Prescriber NPI: _____ ***Prescriber Name:*** _____ ***Specialty:*** _____

Prescriber Phone:_____ ***Prescriber Fax:*** _____ ***Drug Name/Strength:*** _____

NDC:_____ ***Regimen:***_____ ***Fill Quantity:***_____ ***Day Supply:***_____

Has member been trained on proper administration and storage of this medication? ___Yes ___ No

Pharmacist Signature: _____ **Date:** _____

Prescriber Section

1. Please indicate member's diagnosis:
   - ❑ Heterozygous familial hypercholesterolemia (HeFH) confirmed by one of the following:
     - ❑ Definite HeFH confirmed using the Simon Broome or the Dutch Lipid Network diagnostic criteria
       a) Please list factors leading to definite diagnosis of HeFH via Simon Broome Register criteria:
       _____ or
       b) Dutch Lipid Network criteria score: _____
     - ❑ Documented functional mutation(s) in the LDL receptor gene or other HeFH genes via genetic testing**
   - ❑ Homozygous familial hypercholesterolemia (HoFH) confirmed by one of the following:
     - ❑ Untreated total cholesterol >500mg/dL and at least one of the following:
       - ❑ Documented evidence of definite HeFH in both parents; or
       - ❑ Presence of tendinous/cutaneous xanthoma prior to age 10 years
     - ❑ Documented functional mutation(s) in both LDL receptor alleles via genetic testing**
       *(**Please note if this option is selected genetic testing results must be submitted with the prior authorization request)*
   - ❑ Clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
     - ❑ High cardiovascular risk confirmed by Framingham risk score. Please provide both the Framingham risk score and supporting diagnoses/conditions signifying this risk level: _____
       _____ or
     - ❑ Documented history of Coronary Heart Disease (CHD). Please provide supporting diagnoses/conditions and dates of occurrence signifying history of CHD: _____
       _____

2. Please specify the member's current statin therapy:
   a) Drug Name: _____ Dose:_____ Duration of Treatment:_____
   b) Has member been adherent to high-dose statin therapy for at least 12 continuous weeks? Yes___ No___
   SoonerCare claims analysis will be conducted to verify adherence compliance.
   a) If member is statin intolerant due to myalgia, provide creatine kinase (CK) labs verifying rhabdomyolysis.
   Members with myalgia not confirmed by CK labs must have at least 2 trials of lower dose statin therapy or failure of intermittent dosing.
3. Member's baseline LDL-C: _____ Current LDL-C: _____ Goal LDL-C: _____
4. How will this medication be used? _____ Monotherapy _____ Adjunct to statin therapy, diet, and exercise

Initial approvals will be for the duration of 3 months. Continued authorization will require recent LDL-C levels to demonstrate effectiveness and compliance will be checked at that time and every 6 months thereafter.

Prescriber Signature: _____ **Date:** _____

Has the member been counseled on proper administration and storage of PCSK9 therapy? Yes___ No___

Please do not send in chart notes. Specific information will be requested if necessary. Failure to complete this form in full will result in processing delays

Member (Patient) Section

Please have the member initial after each line, fill in all blanks, and sign at the bottom.

1. I understand this medicine must be injected. **Initials:**_____
2. I understand I must give myself a shot every _____ week(s). **Initials:** _____
3. I understand this medication must be kept in the refrigerator. **Initials:** _____
4. I will not leave this medication in the car or anywhere it would get hot. **Initials:** _____
5. I understand this medication will not be replaced if I leave it out of the refrigerator. **Initials:** _____

Member Signature: _____ **Date:** _____

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:

University of Oklahoma College of Pharmacy
Pharmacy Management Consultants
Product Based Prior Authorization Unit
Fax: 1-800-224-4014

Appendix H

Fiscal Year 2015 Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin)

Oklahoma Health Care Authority
October 2015

Current Prior Authorization Criteria

Relistor® (Methylnaltrexone) Approval Criteria:

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.

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 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 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.

Utilization of Constipation and Diarrhea Medications: Fiscal Year 2015

Comparison of Fiscal Years: Relistor®, Linzess®, and Amitiza®

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	143	559	$143,770.57	$257.19	$8.39	25,165	17,131
2015	98	539	$148,926.75	$276.30	$9.43	23,010	15,788
% Change	**-31.50%**	**-3.60%**	**3.60%**	**7.40%**	**12.40%**	**-8.60%**	**-7.80%**
Change	**-45**	**-20**	**$5,156.18**	**$19.11**	**$1.04**	**-2,155**	**-1,343**

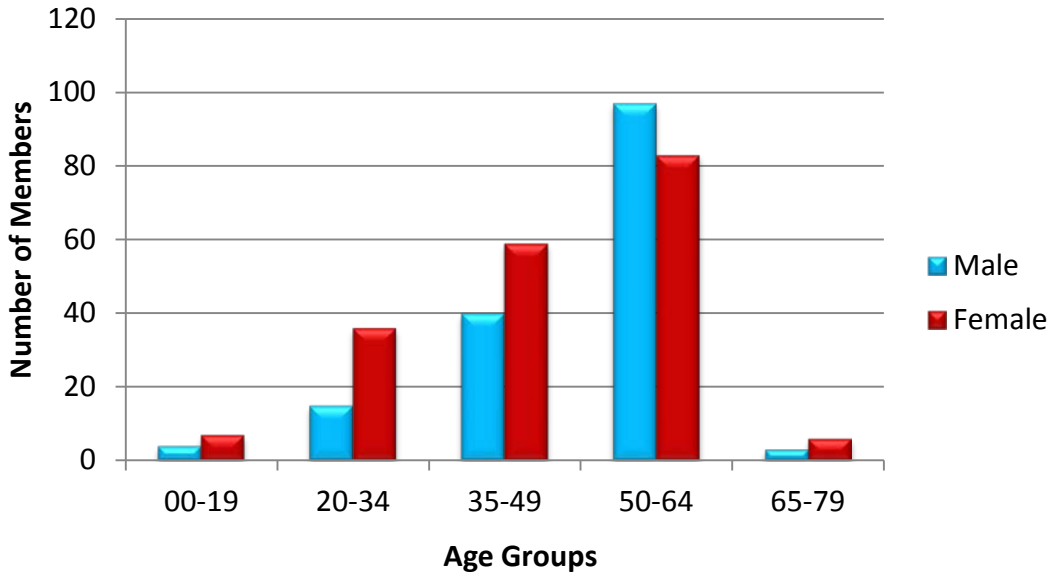
*Total number of unduplicated members.

Comparison of Fiscal Years: Xifaxan® (Rifaximin)

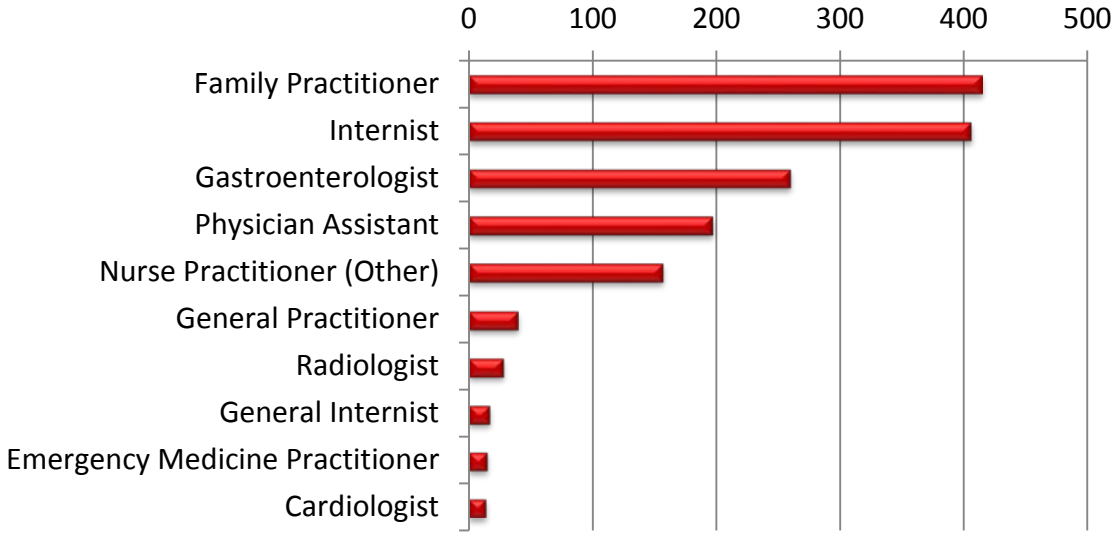
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	213	803	$1,018,410.04	$1,268.26	$45.06	45,049	22,603
2015	252	1,073	$1,570,084.55	$1,463.27	$51.65	60,063	30,399
% Change	**18.30%**	**33.60%**	**54.20%**	**15.40%**	**14.60%**	**33.30%**	**34.50%**
Change	**39**	**270**	**$551,674.51**	**$195.01**	**$6.59**	**15,014**	**7,796**

*Total number of unduplicated members.

Demographics of Members Utilizing Constipation and Diarrhea Medications



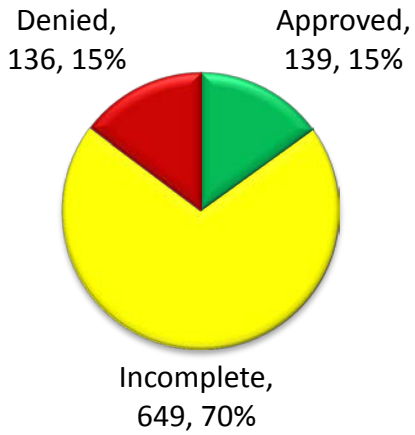
Top Prescriber Specialties of Constipation and Diarrhea Medications by Number of Claims



Prior Authorization of Constipation and Diarrhea Medications

There were 924 petitions submitted for the constipation and diarrhea medications category during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



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

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:

- In September 2014, the FDA approved Relistor® (methylnaltrexone), a peripherally-acting mu-opioid receptor antagonist (PAMORA), for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain. This is in addition to its indication 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. Relistor® was first FDA approved in 2008.
- Also in September 2014, the FDA approved Movantik™ (naloxegol), a PAMORA derivative of naloxone. Movantik™ is the first once-daily oral PAMORA indicated for the treatment of OIC in adults with chronic non-cancer pain.
- In May 2015, the FDA approved Viberzi™ (eluxadoline), a locally-acting oral mu-opioid receptor agonist that is specific to the gastrointestinal system, for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults.
- Also in May 2015, the FDA approved Xifaxan® (rifaximin), a rifamycin antibiotic, for the treatment of IBS-D in adults. This is in addition to its indications for the treatment of traveler's diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older and for hepatic encephalopathy (HE) prophylaxis in adults. Xifaxan® was first FDA approved in 2004.

Medications in the Pipeline:

- **PAMORA:** Shionogi's naldemedine, a once-daily oral PAMORA for the treatment of OIC in adults with chronic non-cancer pain, is currently in Phase III clinical trials and has shown significant improvement in symptoms of OIC.

Movantik™ (Naloxegol) Product Summary[7,8]

Indications: Movantik™ (naloxegol) is indicated for the treatment of OIC in adult patients with chronic non-cancer pain.

Dosing:

- Naloxegol is available as 12.5mg and 25mg oral tablets.
- The recommended dosing of naloxegol is 25mg once daily in the morning.
- If patients are unable to tolerate naloxegol 25mg, the dosage may be reduced to 12.5mg once daily.
- The concomitant use of naloxegol with moderate CYP3A4 inhibitors (e.g., diltiazem, erythromycin, verapamil) should be avoided. However, if concurrent use is unavoidable, the dosage of naloxegol should be reduced to 12.5mg once daily and the patient should be monitored for adverse reactions. Likewise, consumption of grapefruit or grapefruit juice should be avoided during treatment with naloxegol.
- All maintenance laxative therapy should be discontinued prior to initiation of naloxegol. Laxatives can be used as needed if there is a suboptimal response to naloxegol after three days.
- Naloxegol tablets should be taken on an empty stomach at least 1 hour prior to the first meal of the day or 2 hours after the meal, and the tablets should be swallowed whole (do not crush or chew).

- Naloxegol should be discontinued if treatment with the opioid pain medication is also discontinued.

Mechanism of Action: Naloxegol is a pegylated derivative of naloxone and when administered at recommended dose levels, is a peripherally-acting mu-opioid receptor antagonist (PAMORA) in tissues such as the gastrointestinal (GI) tract, thereby decreasing the constipating effects of opioids. Due to the presence of the PEG moiety and the P-glycoprotein substrate properties of naloxegol, the central nervous system penetration of naloxegol is expected to be negligible at the recommended dose levels, limiting the potential for interference with centrally mediated opioid analgesia.

Contraindications:

- Patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation
- Patients concomitantly using strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole) as these medications can significantly increase exposure to naloxegol which may precipitate opioid withdrawal symptoms
- Patients who have had a known serious or severe hypersensitivity reaction to naloxegol or any of its excipients

Safety:

- Gastrointestinal Perforation: Cases of gastrointestinal perforation have been reported with use of another peripherally-acting opioid antagonist in patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the GI tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative GI tract malignancies, or peritoneal metastases). The overall risk-benefit profile should be taken into account when using naloxegol in patients with these conditions or other conditions which might result in impaired integrity of the GI tract (e.g., Crohn's disease). Patients should be monitored for the development of severe, persistent, or worsening abdominal pain, and naloxegol should be discontinued in patients who develop this symptom.
- Opioid Withdrawal: Clusters of symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, irritability, and yawning have occurred in patients treated with naloxegol. In addition, patients receiving methadone as therapy for their pain condition were observed in clinical trials to have a higher frequency of GI adverse reactions that may have been related to opioid withdrawal than patients receiving other opioids. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. The overall risk-benefit profile should be taken into account when using naloxegol in such patients, and such patients should be monitored for symptoms of opioid withdrawal.
- Renal Impairment: Some patients with creatinine clearance (CrCl) less than 60mL/min (i.e., moderate, severe, or end-stage renal disease) were shown to exhibit markedly higher systemic exposure of naloxegol compared to patients with normal renal function, and the reason for these high exposures is not understood. As the risk of adverse effects increases with systemic exposure, the recommended starting dosage for patients with

CrCl less than 60mL/min is 12.5mg once daily. If this dosage is well tolerated but OIC symptoms continue, the dosage may be increased to 25mg once daily, taking into consideration the potential for markedly increased exposures in some patients with renal impairment and the increased risk of adverse reactions with higher exposures. No dosage adjustment is needed in patients with mild renal impairment.

- Hepatic Impairment: The effect of severe hepatic impairment (Child-Pugh Class C) on the pharmacokinetics of naloxegol has not been evaluated. Use of naloxegol in patients with severe hepatic impairment should be avoided, as the dosage in these patients has not been determined. No dosage adjustment is required for patients with mild or moderate hepatic impairment.
- Pediatric Use: The safety and effectiveness of naloxegol in pediatric patients have not been established.

Adverse Reactions: The most common adverse reactions to naloxegol reported in clinical trials, occurring at an incidence of at least 3% and with a higher incidence than placebo, include abdominal pain, diarrhea, nausea, flatulence, vomiting, headache, and hyperhidrosis.

Efficacy:

- The safety and efficacy of naloxegol was evaluated in two replicate, randomized, double-blind, placebo-controlled trials in 1,352 patients with OIC and non-cancer related pain.
- Patients receiving an opioid morphine equivalent daily dose of between 30mg and 1,000mg for at least four weeks before enrollment and self-reported OIC were eligible to participate.
    - OIC was confirmed through a two-week run in period and was defined as less than three spontaneous bowel movements (SBMs) per week on average 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.
    - An SBM was defined as a bowel movement (BM) without rescue laxative taken within the past 24 hours.
    - Throughout the studies, patients were prohibited from using laxatives other than bisacodyl rescue laxative (if they had not had a BM for 72 hours) and one-time use of an enema (if after 3 doses of bisacodyl, they still did not have a BM).
- The primary endpoint was defined as: at least three SBMs per week and a change from baseline of at least one BM per week for at least 9 out of the 12 study weeks and 3 out of the last 4 weeks.
- There was a statistically significant difference for the 25mg naloxegol treatment group versus placebo for the primary endpoint in both studies, and statistical significance for the 12.5mg naloxegol treatment group versus placebo was observed in one of the two studies (*see following table*).

Study 1			
	Placebo (N = 214)	**Naloxegol 12.5mg (N = 213)**	**Naloxegol 25mg (N = 214)**
Primary endpoint: patients responding, n (%)	63 (29%)	87 (41%)	95 (44%)
Study 2			
	Placebo (N = 232)	**Naloxegol 12.5mg (N = 232)**	**Naloxegol 25mg (N = 232)**
Primary endpoint: patients responding, n (%)	68 (29%)	81 (35%)	92 (40%)

Estimated Acquisition Cost: The estimated acquisition cost of Movantik™ is $8.79 per tablet, regardless of strength, resulting in a monthly cost of $263.70.

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

Medication	Dosing Regimen	Cost/Unit*	Cost/Month
Amitiza® (lubiprostone) 24mcg capsules	24mcg PO BID	$5.54	$332.40
Movantik™ (naloxegol) 25mg tablets	25mg PO Qday	$8.79	$263.70
Relistor® (methylnaltrexone) 12mg/0.6mL vials or syringes	12mg subQ Qday	$176.00	$5,280.00

*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.

Viberzi™ (Eluxadoline) Product Summary[9,10,11]

Indications: Viberzi™ (eluxadoline) is indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adult patients.

Dosing:

- Eluxadoline is available as 75mg and 100mg oral tablets.
- The recommended dosing of eluxadoline is 100mg twice daily.
- The recommended dosing of eluxadoline for patients who do not have a gallbladder, who are unable to tolerate the 100mg dose, who are receiving concomitant organic anion-transporting protein 1B1 (OATP1B1) inhibitors (e.g., cyclosporine, gemfibrozil, rifampin), or who have mild or moderate hepatic impairment is 75mg twice daily.
- Eluxadoline tablets should be taken with food, and the tablets should be swallowed whole (do not crush or chew).
- Eluxadoline should be discontinued in patients who develop severe constipation for more than four days.

Mechanism of Action: Eluxadoline is a mu- and kappa-opioid receptor agonist and delta-opioid receptor antagonist that acts locally in the enteric nervous system, possibly decreasing adverse effects on the central nervous system.

Contraindications:

- Patients with known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction
- Patients with alcoholism, alcohol abuse, alcohol addiction, or that drink more than three alcoholic beverages per day, due to the increased risk for acute pancreatitis
- Patients with a history of pancreatitis or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
- Patients with severe hepatic impairment (Child-Pugh Class C)
- Patients with severe constipation or sequelae from constipation or known or suspected mechanical GI obstruction, due to the risk for severe complications of bowel obstruction

Safety:

- Sphincter of Oddi Spasm and Pancreatitis: Given the mu-opioid receptor agonism of eluxadoline, there is an increased risk of sphincter of Oddi spasm, resulting in pancreatitis or hepatic enzyme elevation association with acute abdominal pain (e.g., biliary-type pain) with eluxadoline. Patients without a gallbladder are at an increased risk. In clinical trials, the majority of patients that developed sphincter of Oddi spasm presented within the first week of treatment and the event resolved upon discontinuation of eluxadoline. Alternative therapies should be considered before using eluxadoline and the benefits and risks of eluxadoline should be evaluated in patients without a gallbladder. Patients without a gallbladder should be monitored for new or worsening abdominal pain, with or without nausea and vomiting, or acute biliary pain with liver or pancreatic enzyme elevations. Eluxadoline should be discontinued and patients should seek medical attention if such symptoms develop. Eluxadoline should not be restarted in patients who developed biliary duct obstruction or sphincter of Oddi spasm while taking eluxadoline.
- Pancreatitis: There is a potential for increased risk of pancreatitis, not associated with sphincter of Oddi spasm, when taking eluxadoline. The majority of cases of pancreatitis not associated with sphincter of Oddi spasm that occurred in clinical trials were associated with excessive alcohol intake. All pancreatic events, whether or not associated with sphincter of Oddi spasm, resolved upon discontinuation of eluxadoline. Patients should be instructed to avoid chronic or acute excessive alcohol use while taking eluxadoline. Patients should stop eluxadoline and seek medical attention if they experience symptoms suggestive of pancreatitis such as acute abdominal or epigastric pain radiating to the back associated with elevations of pancreatic enzymes.
- Hepatic Impairment: Plasma concentrations of eluxadoline increase in patients with hepatic impairment. Eluxadoline is contraindicated in patients with severe hepatic impairment (Child-Pugh Class C) as plasma concentrations of eluxadoline increase significantly (16-fold) and there is no information to support the safety of eluxadoline in these patients. In patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class

B) hepatic impairment, plasma concentrations of eluxadoline increase to a lesser extent (4- and 6-fold, respectively). Eluxadoline should be administered at a reduced dose of 75mg twice daily to these patients. Patients with any degree of hepatic impairment should be monitored for impaired mental or physical abilities needed to perform potentially hazardous activities, such as driving a car or operating machinery, or for other eluxadoline-related adverse reactions.

- Pediatric Use: The safety and effectiveness of eluxadoline in pediatric patients have not been established.

Adverse Reactions: The most common adverse reactions to eluxadoline reported in clinical trials, occurring at an incidence greater than 2% and with a higher incidence than placebo, include constipation, nausea, abdominal pain, upper respiratory tract infection, vomiting, nasopharyngitis, abdominal distention, bronchitis, dizziness, flatulence, rash, increased ALT, fatigue, and viral gastroenteritis.

Efficacy:

- The safety and efficacy of eluxadoline was evaluated in two randomized, multi-center, multi-national, double-blind, placebo-controlled trials in 2,426 patients with IBS-D.
- All patients met Rome III criteria for IBS-D (loose [mushy] or watery stools ≥ 25% and hard or lumpy stools < 25% of bowel movements [BMs]) and were required to meet both of the following criteria over the week prior to randomization:
    - An average of worst abdominal pain scores in the past 24 hours of > 3 on a 0 to 10 scale, and
    - An average daily stool consistency score (Bristol Stool Scale or BSS) of ≥ 5.5 and at least five days with a BSS score ≥ 5 on a 1 to 7 scale.
- Throughout the studies, patients were allowed to take loperamide rescue medication for the acute treatment of uncontrolled diarrhea, but were not allowed to take any other antidiarrheal, antispasmodic agent, or rifaximin for their diarrhea. Additionally, patients were allowed to take aspirin-containing medications or nonsteroidal anti-inflammatory drugs (NSAIDs) for abdominal pain, but no narcotic or opioid-containing agents.
- The efficacy of eluxadoline was assessed in both trials using an overall composite responder primary endpoint. The primary endpoint was defined by the simultaneous improvement in daily worst abdominal pain score by at least 30% as compared to the baseline weekly average and a reduction in the BSS to less than 5 on at least 50% of the days within a 12-week time interval. Improvement in daily worst abdominal pain in the absence of a concurrent bowel movement was also considered a response day.
- The proportion of patients who were complete responders to eluxadoline was similar for male and female patients in both trials. In both trials, the proportion of patients who were composite responders to eluxadoline was statistically significantly higher than placebo for both doses (*see following table*).

Study 1			
	Placebo (N = 427)	**Eluxadoline 75mg (N = 427)**	**Eluxadoline 100mg (N = 426)**
Composite responder primary endpoint: responder rates (12 weeks)	17%	24%	25%
Composite responder primary endpoint: responder rates (26 weeks)	19%	23%	29%
Study 2			
	Placebo (N = 382)	**Eluxadoline 75mg (N = 381)**	**Eluxadoline 100mg (N = 382)**
Composite responder primary endpoint: responder rates (12 weeks)	16%	29%	30%
Composite responder primary endpoint: responder rates (26 weeks)	20%	30%	33%

Estimated Acquisition Cost: The estimated acquisition cost of eluxadoline is not yet available.

Xifaxan® (Rifaximin) Product Summary[12,13,14]

Rifaximin is a non-aminoglycoside, semi-synthetic, non-systemic antibiotic derived from rifamycin SV and is a structural analog of rifampin. Rifaximin is available as 200mg and 550mg oral tablets. Rifaximin has poor oral bioavailability, resulting in limited systemic exposure.

Rifaximin is indicated for the treatment of traveler's diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older. Rifaximin should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli.* The recommended dose of rifaximin for TD is 200mg three times daily for 3 days. Rifaximin should be discontinued if diarrhea symptoms get worse or persist for more than 24 to 48 hours, and alternative antibiotic therapy should be considered.

Rifaximin is also indicated for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults. In clinical trials of rifaximin for HE, 91% of the patients were using lactulose concomitantly. The recommended dose of rifaximin for HE prophylaxis is 550mg twice daily. There is increased systemic exposure in patients with severe (Child-Pugh Class C) hepatic impairment. No dosage adjustment is recommended because rifaximin is presumably acting locally; however, caution should be exercised when administering rifaximin to patients with severe hepatic impairment. Current treatment guidelines from the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) recommend lactulose for the prevention of recurrent episodes of HE after the initial

episode, and recommend rifaximin as an add-on to lactulose for the prevention of recurrent episodes of HE after the second episode.

Lastly, rifaximin is indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults. The recommended dose of rifaximin for IBS-D is 550mg three times daily for 14 days. Patients who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen.

Estimated Acquisition Cost:

Medication	EAC/Tablet*	Indication/Dosing	Cost/Treatment
Xifaxan® (rifaximin) 200mg tablets	$15.52	**TD:** 200mg TID for 3 days	$139.68/3-day treatment course
Xifaxan® (rifaximin) 550mg tablets	$29.59	**HE:** 550mg BID	$1,775.40/month
Xifaxan® (rifaximin) 550mg tablets	$29.59	**IBS-D:** 550mg TID for 14 days	$1,242.78/14-day treatment course

EAC = estimated acquisition cost

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

Recommendations

The College of Pharmacy recommends the following:

1. Continuing the existing criteria for Linzess® (linaclotide) and Amitiza® (lubiprostone)
2. The addition of criteria for Relistor® (methylnaltrexone) for the new indication of opioid-induced constipation (OIC) in adults with chronic non-cancer pain
3. The prior authorization of Movantik™ (naloxegol)
4. The prior authorization of Viberzi™ (eluxadoline)
5. The prior authorization of Xifaxan® (rifaximin)

New proposed criteria specific to each medication is as follows:

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

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 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.

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 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 loperamide and dicyclomine (each trial should be for at least 10-14 consecutive days at the recommended dosing) that failed to relieve diarrhea. 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. Member must be 18 years of age or older; and
2. An FDA approved indication for the reduction in risk of overt hepatic encephalopathy (HE) recurrence; or
3. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
    a. For the diagnosis of IBS-D: Documentation of trials of loperamide and dicyclomine (each trial should be for at least 10-14 consecutive days at the recommended dosing) that failed to relieve diarrhea. Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure.
4. 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 Details of Constipation and Diarrhea Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
RIFAXIMIN PRODUCTS						
XIFAXAN TAB 550MG	1,056	245	$1,566,910.92	$51.70	$1,483.82	91.15%
XIFAXAN TAB 200MG	17	8	$3,173.63	$33.76	$186.68	0.18%
SUBTOTAL	**1,073**	**253**	**$1,570,084.55**	**$51.65**	**$1,463.27**	**91.34%**
LUBIPROSTONE PRODUCTS						
AMITIZA CAP 24MCG	189	39	$55,482.00	$10.22	$293.56	3.23%
AMITIZA CAP 8MCG	95	15	$24,898.75	$9.17	$262.09	1.45%
SUBTOTAL	**284**	**54**	**$80,380.75**	**$9.87**	**$283.03**	**4.68%**
LINACLOTIDE PRODUCTS						
LINZESS CAP 290MCG	144	22	$36,469.14	$8.44	$253.26	2.12%
LINZESS CAP 145MCG	109	25	$30,409.20	$9.31	$278.98	1.77%
SUBTOTAL	**253**	**47**	**$66,878.34**	**$8.81**	**$264.34**	**3.89%**
METHYLNALTREXONE PRODUCTS						
RELISTOR INJ 12/0.6ML	2	1	$1,667.66	$29.78	$833.83	0.10%
SUBTOTAL	**2**	**1**	**$1,667.66**	**$29.78**	**$833.83**	**0.10%**
TOTAL	**1,612**	**350***	**$1,719,011.30**	**$37.22**	**$1,066.38**	**100.00%**

*Total number of unduplicated members.

Movantik™ had no utilization in fiscal year 2015.

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[3] Relistor® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/relistor-1/. Last revised 4/21/15. Last accessed 9/24/15.
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[14] Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by AASLD and EASL. Available online at: http://www.aasld.org/sites/default/files/guideline_documents/hepaticencephenhanced.pdf. Last revised December 2014. Last accessed 9/29/15.

Appendix I

30-Day Notice to Prior Authorize Daraprim® (Pyrimethamine)

Oklahoma Health Care Authority
October 2015

Toxoplasmosis Background Information[1,2]

Toxoplasmosis is a disease that results from infection with the *Toxoplasma gondii* parasite, which is one of the world's most common parasites. *Toxoplasma gondii* can survive in the soil or water for many months and can infect most animals and birds but reproduces only in cats. Toxoplasmosis is a zoonosis, an infection/disease spread from animals to humans, and humans typically become infected by ingesting the cyst form of the parasite through contamination with cat feces or undercooked meat, especially pork or lamb, or through direct inoculation via blood transfusions, transplant, laboratory accidents, or mother-to-child transmission. Once infected, the parasite can affect the brain, lungs, liver, and heart. For generally healthy individuals, symptoms of toxoplasmosis are either nonexistent or mild, consisting mainly of flu-like body aches and fever. The symptoms typically last for a few weeks and resolve with or without treatment, sometimes leaving the parasite dormant indefinitely. The infection only progresses to illness in individuals with compromised immune systems, such as Human Immunodeficiency Virus (HIV) and cancer, and in pregnant women because their immune system is unable to control the parasite. Severe toxoplasmosis can cause brain and organ damage and can result in blindness.

Daraprim® (Pyrimethamine) Product Summary[3,4]

Pyrimethamine is an antiparasitic compound that is available as 25mg oral tablets. Pyrimethamine is a folic acid antagonist that is highly selective against plasmodia and *Toxoplasma gondii*. Pyrimethamine was FDA approved in 1953; however, no generic products are available.

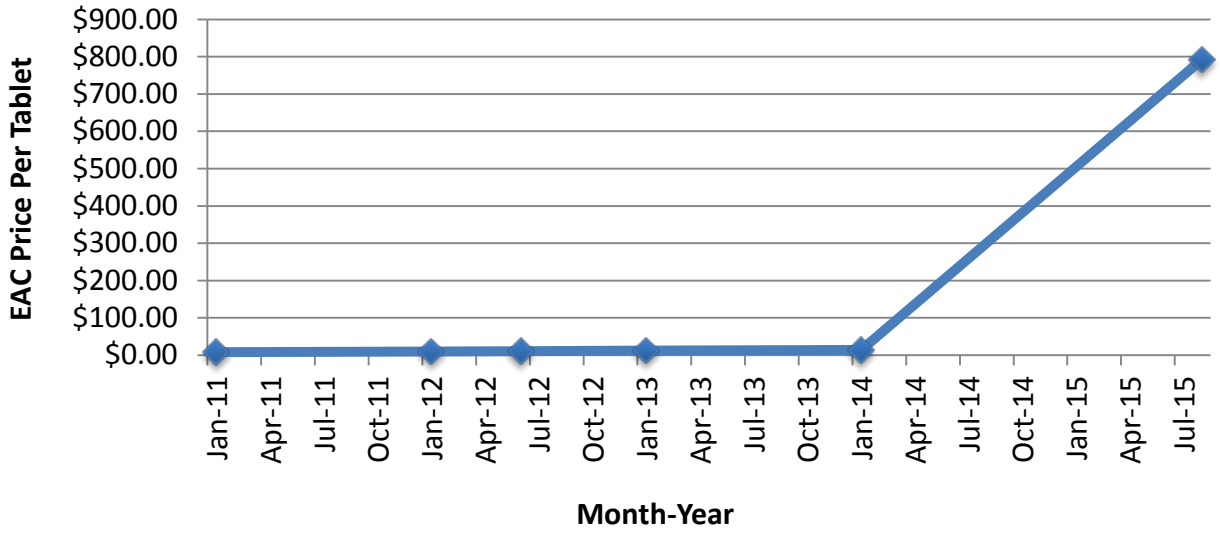
Pyrimethamine is indicated for the treatment of toxoplasmosis when used concomitantly with a sulfonamide, as synergism exists with this combination. Pyrimethamine is the only FDA approved medication for the treatment of toxoplasmosis. The dosage of pyrimethamine for the treatment of toxoplasmosis must be carefully adjusted so as to provide maximum therapeutic effect and a minimum of side effects. Concurrent administration of folic acid is strongly recommended in all patients. The adult starting dose for toxoplasmosis is 50mg to 75mg daily, together with 1g to 4g daily of a sulfonamide of the sulfapyrimidine type (e.g., sulfadiazine). This dosage is ordinarily continued for one to three weeks, depending on the response of the patient and tolerance to therapy. The dosage may then be reduced to about one-half that previously given for each drug and continued for an additional four to five weeks.

Pyrimethamine is also indicated for the treatment of acute malaria, but should not be used as monotherapy. Fast-acting schizonticides such as chloroquine or quinine are indicated and preferable for the treatment of acute malaria. However, concurrent use of pyrimethamine with

a sulfonamide will initiate transmission control and suppression of susceptible strains of plasmodia. Lastly, pyrimethamine is indicated for the chemoprophylaxis of malaria due to susceptible strains of plasmodia. However, resistance to pyrimethamine is prevalent worldwide; therefore, it is not suitable as a prophylactic agent for travelers to most areas.

Daraprim® (Pyrimethamine) Cost Update[5,6,7]

Daraprim® (pyrimethamine) has recently increased in price by more than 5,000%. The increase in price is a result of acquisition of Daraprim® by Turing Pharmaceuticals in August of 2015. After much objection from the Infectious Disease Society of America and the HIV Medicine Association to the drastic price increase, the CEO of Turing Pharmaceuticals has agreed to lower the price of Daraprim®, but has not revealed how much or when the price will be lowered. The graph below outlines the estimated acquisition cost (EAC) price trend for Daraprim® since January 2011.



The most recent EAC price updated in August 2015 is $792.00 per tablet, significantly greater than the previous EAC price of $14.31 per tablet. Daraprim® tablets cost only about $1.00 per tablet several years ago, but the drug's price rose sharply after CorePharma acquired it in 2010 from GlaxoSmithKline, who received the original FDA approval for the drug in 1953 and had manufactured it for over 50 years.

Utilization Details of Daraprim® (Pyrimethamine): Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
DARAPRIM TAB 25MG	8	2*	$1,406.92	$3.47	$175.87	100.00%

*Total number of unduplicated members.

Recommendations

The College of Pharmacy recommends the prior authorization of Daraprim® (pyrimethamine) with the following criteria:

Daraprim® (Pyrimethamine) Approval Criteria:

1. An FDA approved indication for the treatment of toxoplasmosis; or
2. An FDA approved indication for the treatment of susceptible strains of acute malaria; and
3. Member must take Daraprim® concomitantly with a sulfonamide; and
4. Approval length will be based on recommended dosing regimen specific to the member's diagnosis.

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Appendix J

Fiscal Year 2015 Annual Review of Allergy Immunotherapies and 30-Day Notice to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract)

Oklahoma Health Care Authority
October 2015

Current Prior Authorization Criteria

Grastek® (Timothy Grass Pollen Allergen Extract) Approval Criteria:

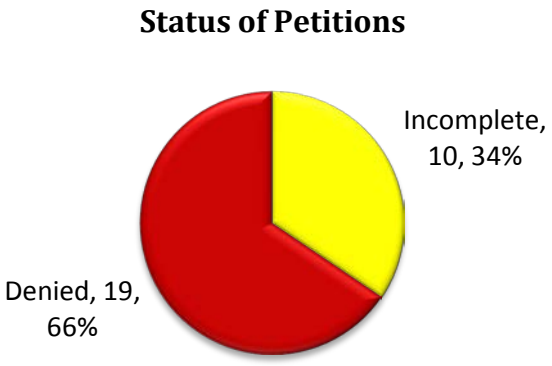
1. Member must be 5 years of age or older; and
2. Member must have a positive skin test (labs required) or in vitro testing for pollen specific IgE antibodies for Timothy grass or cross-reactive grass pollen (cool season grasses); and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of the grass pollen season (November 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Ragwitek™ (Short Ragweed Pollen Allergen Extract) Approval Criteria:

1. Member must be 18 years of age or older; and
2. Member must have a positive skin test or in vitro testing for pollen specific IgE antibodies to short ragweed pollen; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis symptoms; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of ragweed pollen season (May 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Prior Authorization of Allergy Immunotherapies: Fiscal Year 2015

There were a total of 29 petitions submitted for allergy immunotherapy products during fiscal year 2015. The following chart shows the status of the submitted petitions



Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) Product Summary[1]

Indications: Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy and Kentucky Blue Grass Mixed Pollens Allergen Extract) is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in this product.

Dosing:

- Oralair® is available as 100 IR (index of reactivity) and 300 IR sublingual tablets.
- For adults 18 years through 65 years of age, the recommended dose is 300 IR daily.
- For children and adolescents 10 years through 17 years of age, the recommended dose is increased over the first three days. The recommended dose day one is 100 IR, day two is (2) 100 IR tablets, and day three and thereafter is 300 IR.
- Treatment should be initiated four months before the expected onset of each grass pollen season and continued throughout the season.
- The tablet should be placed under the tongue for at least one minute until complete dissolution.
- The first dose should be administered under the supervision of a physician with experience in the diagnosis and treatment of severe allergic reactions. The patient should be observed for at least 30 minutes.

Contraindications:

- Severe, unstable, or uncontrolled asthma
- History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy
- History of eosinophilic esophagitis
- Hypersensitivity to any of the inactive ingredients contained in Oralair®

Safety:

- Severe Allergic Reactions: Oralair® can cause systemic allergic reactions including anaphylaxis which may be life-threatening. In addition, Oralair® can cause severe local reactions, including laryngopharyngeal swelling, which can compromise breathing and be life-threatening.
- Epinephrine: Auto-injectable epinephrine should be prescribed to patients receiving Oralair®.
- Eosinophilic Esophagitis: Eosinophilic esophagitis has been reported in association with sublingual tablet immunotherapy. Discontinue Oralair® and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastro-esophageal symptoms including dysphagia or chest pain.
- Asthma: Oralair® has not been studied in subjects with moderate or severe asthma or any subjects who required daily medication for asthma. Immunotherapy with Oralair® should be withheld if the patient is experiencing an acute asthma exacerbation.

Reevaluate patients who have recurrent asthma exacerbations and consider discontinuation of Oralair®.

- Concomitant Allergen Immunotherapy: Oralair® has not been studied in subjects receiving concomitant allergen immunotherapy. Concomitant dosing with other allergen immunotherapy may increase the likelihood of local or systemic adverse reactions to either subcutaneous or sublingual allergen immunotherapy.
- Oral Inflammation: Stop treatment with Oralair® to allow complete healing of the oral cavity in patients with oral inflammation (e.g., oral lichen planus, mouth ulcers, or thrush) or oral wounds, such as those following oral surgery or dental procedures.
- Initiation of Oralair® during grass pollen season: The risk of Oralair® may be increased when treatment is initiated during the grass pollen season.

Adverse Reactions: The most common adverse reactions to Oralair® reported in clinical trials, occurring at an incidence of at least 5%, include oral pruritus, throat irritation, ear pruritus, mouth edema, tongue pruritus, cough, and oropharyngeal pain.

Efficacy:

- The effectiveness of Oralair® as a treatment for grass pollen-induced allergic rhinoconjunctivitis was assessed in five double-blind, placebo-controlled clinical trials.
- Study participants reported a history of rhinoconjunctivitis symptoms occurring in at least two grass pollen seasons. For the European studies, subjects had a positive skin prick test to 5-grass pollen extract and positive in vitro testing for Timothy grass-specific serum IgE. For the US study, subjects had a positive skin prick test to Timothy grass pollen extract.
- With the exception of those with mild intermittent asthma, patients with asthma were excluded.
- Efficacy was established by self-reporting of rhinoconjunctivitis total symptom scores (RTSS), daily combined scores (CS), and daily rescue medication scores (RMS).
- Subjects treated with Oralair® had a decrease in the CS, RTSS, and RMS throughout the grass pollen season compared to placebo-treated subjects. The difference in CS for the entire season relative to placebo was -28% for the adult US study, -29% for the adult European study, and -30% for the pediatric study.

Cost Comparison:

Medication	Dose	Cost per Unit	Cost for 24 Weeks of Therapy
Oralair® Sublingual Tablets	One tablet daily	$11.60+	$1,948.80
Grastek® Sublingual Tablets	One tablet daily	$8.71+	$1,463.28
Fluticasone 50mcg Nasal	2 sprays daily	$0.75*	$72.00
Cetirizine 10mg Tablets	10mg daily	$0.10*	$16.80
Loratadine 10mg Tablets	10mg daily	$0.10*	$16.80
Montelukast 10mg Tablets	10mg daily	$0.24*	$40.32

*SMAC = state maximum allowable cost.
+Estimated acquisition cost (EAC)

Recommendations

Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) Approval Criteria:

1. Member must be 10 years of age or older; and
2. Member must have a positive skin test or in vitro testing for pollen specific IgE antibodies to one of the five grass pollens contained in Oralair®; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 16 weeks prior to the start of the grass pollen season (October 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 16 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

[1] Oralair® Product Information. Greer Laboratories, Inc. Available online at: http://oralair.com/docs/ORALAIR%20Prescribing%20Information-Med%20Guide.pdf. Last revised 06/2015. Last accessed 09/30/2015.

Appendix K

Fiscal Year 2015 Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Dyloject™ (Diclofenac Sodium)

Oklahoma Health Care Authority
October 2015

Current Prior Authorization Criteria

Non-Steroidal 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®)	fenoprofen (Nalfon®)	diclofenac potassium (Cambia® powder pack)
etodolac (Lodine®)		diclofenac potassium (Zipsor® capsule)
etodolac ER (Lodine® XL)		diclofenac sodium (Pennsaid® top drops)
flurbiprofen (Ansaid®)		diclofenac sodium (Voltaren Gel®)
ibuprofen (Motrin®)		ibuprofen/famotidine (Duexis®)
ketoprofen (Orudis®)		indomethacin (Indocin®)
meclofenamate (Meclomen®)		indomethacin (Tivorbex™)
meloxicam (Mobic®)		ketoprofen ER (Oruvail®)
nabumetone (Relafen®)		mefenamic acid (Ponstel®)
naproxen (Naprosyn®)		naproxen sodium (Naprelan®)
naproxen EC (Naprosyn®)		naproxen/esomeprazole (Vimovo®)
oxaprozin (Daypro®)		piroxicam (Feldene®)
sulindac (Clinoril®)		
tolmetin (Tolectin®)		

ER= Extended-Release, EC= Enteric Coated

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 Approval Criteria:

1. A unique indication for which a Tier-1 or Tier-2 medication is not appropriate, such as the diagnosis of gout for indomethacin; 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.

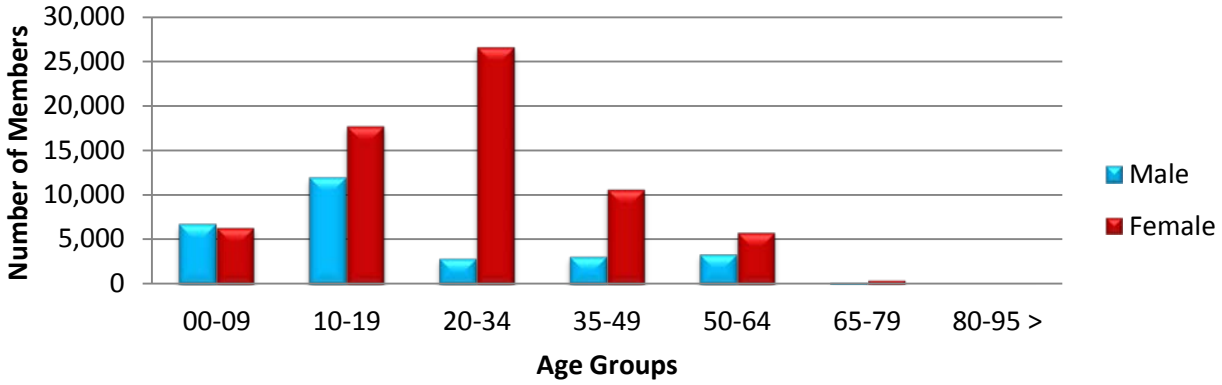
Utilization of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): Fiscal Year 2015

Comparison of Fiscal Years

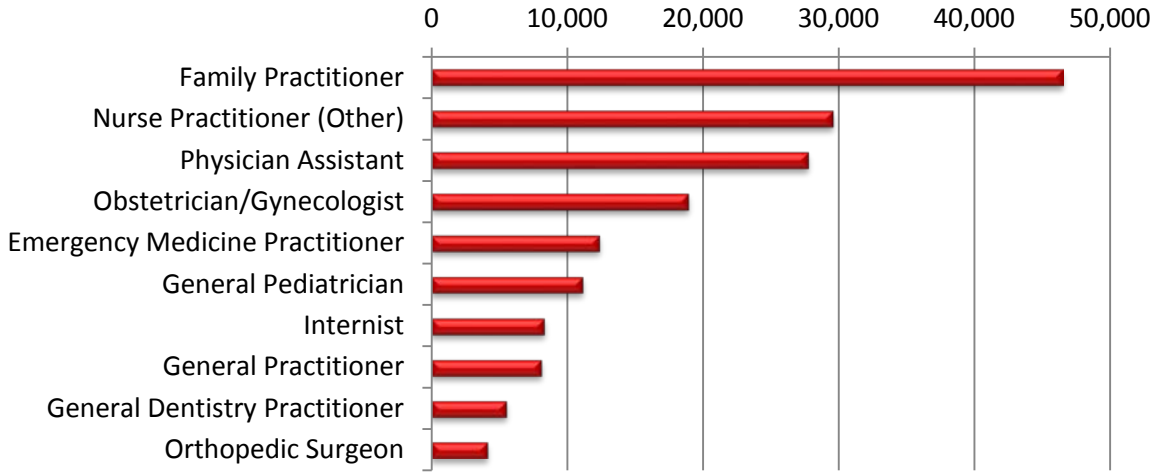
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	103,485	192,429	$2,274,299.47	$11.82	$0.54	10,487,260	4,190,368
2015	96,112	181,282	$1,793,363.16	$9.89	$0.46	10,034,046	3,849,019
% Change	**-7.12%**	**-5.79%**	**-21.15%**	**-16.33%**	**-14.80%**	**-4.32%**	**-8.15%**
Change	**-7,373**	**-11,147**	**-$480,936.31**	**-$1.93**	**-$0.08**	**-453,214**	**-341,349**

*Total number of unduplicated members.

Demographics of Members Utilizing NSAIDs

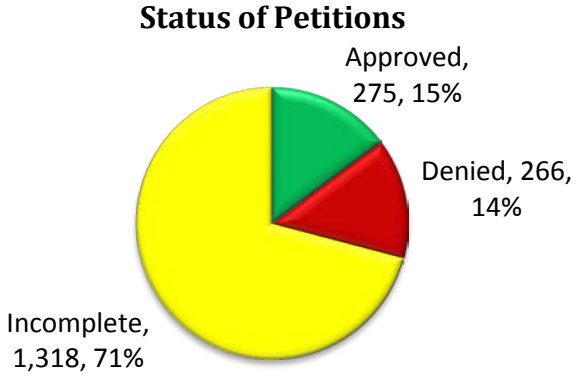


Top Prescriber Specialties of NSAIDs by Number of Claims



Prior Authorization of NSAIDs

There were 1,859 prior authorizations submitted for NSAIDs during fiscal year 2015. The following chart shows the status of the submitted petitions.



Market News and Updates[1, 2, 3]

Anticipated Patent Expirations:

- Flector® (diclofenac epolamine) patch: April 2019
- Cambia® (diclofenac potassium) powder pack: June 2026
- Duexis® (ibuprofen/famotidine): July 2026
- Zipsor® (diclofenac potassium) capsule: February 2029
- Pennsaid® (diclofenac sodium) topical solution: August 2030
- Tivorbex™ (indomethacin): April 2030
- Zorvolex® (diclofenac): April 2030
- Vimovo® (naproxen/esomeprazole): October 2031

FDA Safety Updates:

- **July 2015**: The FDA released a safety announcement strengthening the warning that non-aspirin NSAIDs can cause heart attacks or strokes. Drug labels of all prescription NSAIDs are required to be updated. The FDA also requested that the Drug Facts labels of over-the-counter (OTC) non-aspirin NSAIDs be updated as well.
- **August 2015**: The results of the Standard Care vs. Celecoxib Outcome Trial (SCOT) presented at the European Society of Cardiology (ESC) 2015 Congress showed that NSAIDs did not increase the risk of heart attack or stroke in patients with no history of cardiovascular disease. There was a similar adverse cardiovascular event rate between non-selective NSAIDs and celecoxib.

FDA Approvals and New Indications:

- In December 2014, the FDA approved Dyloject™ (diclofenac sodium), an injectable NSAID that can be administered over 15 seconds in a small volume intravenous bolus. Other injectable non-opioid analgesics are formulated in large volumes or need to be diluted and infused over 15 to 30 minutes, such as Ofirmev® (acetaminophen) and Caldolor® (ibuprofen).

Dyloject™ (Diclofenac Sodium) Product Summary[4]

FDA Approved: December 2014

Indications: Dyloject™ (diclofenac sodium) is indicated for the management of mild-to-moderate pain. Dyloject™ is also indicated for the management of moderate-to-severe pain alone or in combination with opioid analgesics.

Dosing:

- Dyloject™ is available for injection as a single use vial containing 37.5mg/mL.
- The recommended dose is 37.5mg administered by intravenous bolus injection over 15 seconds. Treatment may be repeated every six hours, with a maximum dose of 150mg/day.
- Patients must be well hydrated before administration.

Mechanism of Action: Dyloject™ inhibits cyclooxygenase (COX-1 and COX-2) pathways and may also inhibit prostaglandin synthetase.

Contraindications:

- Known hypersensitivity to diclofenac
- History of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs
- Perioperative pain in the setting of coronary artery bypass graft (CABG) surgery
- Moderate-to-severe renal insufficiency in the perioperative period and who are at risk for volume depletion

Warnings and Precautions:

- Serious and potentially fatal cardiovascular (CV) thrombotic events, myocardial infarction, and stroke
  - Risk may increase with duration of use
  - Greater risk for patients with cardiovascular disease or risk factors for cardiovascular disease
- Serious gastrointestinal (GI) adverse events, including bleeding, ulceration, and perforation
  - Dyloject™ should be used with caution in patients with prior history of ulcer disease or GI bleeding
- Renal papillary necrosis and other renal injury with long-term administration of NSAIDs
- Abnormal elevation of liver tests
  - Discontinue Dyloject™ immediately if abnormal elevation liver tests persists or worsen or if symptoms of liver disease develop
- New onset or worsening of hypertension
- Fluid retention and edema
- Anaphylactic reactions
- Serious skin reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN)

Adverse Reactions: The most common adverse reactions (>5%) during clinical trials were nausea, constipation, headache, infusion site pain, dizziness, flatulence, vomiting, and insomnia.

Special Populations:

- Pregnancy: Dyloject™ is Pregnancy Category C prior to 30 weeks gestation and Category D starting at 30 weeks gestation. Dyloject™ should be avoided starting at 30 weeks gestation, since premature closure of the ductus arteriosus can occur. There are no adequate and well-controlled studies in pregnant women. Prior to 30 weeks gestation, Dyloject™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Pediatric Use: The safety and effectiveness of Dyloject™ in pediatric patients have not been established.
- Geriatric Use: Caution should be used in elderly patients since this population has a greater frequency of decreased cardiac, hepatic, or renal function. This population also has a greater frequency of concomitant diseases or other drug therapy.
- Renal Impairment: For patients with moderate-to-severe renal insufficiency, Dyloject™ is not recommended. Dyloject™ is contraindicated in patients with moderate-to-severe renal insufficiency in the perioperative period and who are at risk for volume depletion.
- Hepatic Impairment: Dosing adjustments are not necessary in patients with mild hepatic impairment. Dyloject™ was not studied in patients with moderate or severe hepatic impairment and use is not recommended in this population.
- Body Weight: Adjusting the dose based on body weight is not recommended since the effect of body weight on clinical efficacy and safety of Dyloject™ has not been fully studied.

Efficacy: The efficacy of Dyloject™ for short-term treatment of acute pain was evaluated in two double-blind, placebo and active-controlled, multiple-dose clinical trials in patients with postoperative pain. Intravenous morphine was allowed as rescue medication for pain management in both trials.

- The first study included 245 adult patients with postoperative pain who had undergone elective abdominal or pelvic surgery. The mean age was 43 years (range 18 to 65 years) and patients had a minimum pain intensity of 50mm on a 100mm visual analog scale (VAS) at baseline. The mean baseline pain intensity was 68mm on the VAS. Patients were treated with Dyloject™, a positive NSAID control (ketorolac tromethamine), or placebo starting within six hours after surgery. Treatments were administered every six hours and for up to five days. Efficacy was determined by a reduction in pain intensity and was measured by the sum of the pain intensity differences over 0 to 48 hours. Within the first 48 hours of the treatment phase, about 63% of the Dyloject™ group took rescue medication compared to about 92% of the placebo group.
- The second study included 277 adult patients with postoperative pain who had undergone elective orthopedic surgery. The mean age was 55 years (range 19 to 84 years) and patients had a minimum pain intensity of 50mm on a 100mm VAS at baseline. The mean baseline pain intensity was 69mm on the VAS. The treatment arms

and determination of efficacy were the same as the first study. Within the first 48 hours of the treatment phase, about 74% of the Dyloject™ group took rescue medication compared to about 92% of the placebo group.

Utilization: There has been no utilization of Dyloject™ since it was FDA approved in December 2014.

Cost Comparison:

Medication Name	Cost Per Unit	Cost for 30 days of Therapy
Dyloject™ (diclofenac sodium) injection 37.5mg/mL	**$16.63[+]**	**$1,995.60**
Voltaren® (diclofenac sodium) gel 1%	$0.48[+]	$480.00
Voltaren XR® (diclofenac sodium ER) 100mg tablet	$0.40[*]	$24.00

+EAC= estimated acquisition cost
*State Maximum Allowable Cost (SMAC)

NSAID Price Trends

Several of the generic Tier-1 NSAIDs have increased in price significantly in recent months. Anaprox® (naproxen sodium) 275mg tablets increased from $0.12 to $1.17, a price increase of more than 875%. Similarly Anaprox® (naproxen sodium) 550mg tablets increased approximately 1,100%. The following table contains products that are now significantly more costly than other current Tier-1 medications. The estimated average monthly cost for the products listed below is around $250.00 compared to an average monthly cost of $27.54 for other Tier-1 products.

NSAIDs	Cost/ Unit	Cost/ Day	Cost/ 30 Days	Claims	Members
diclofenac sodium (Voltaren®) 25mg tab	$1.09	$8.72	$261.60	79	52
etodolac ER (Lodine® XL) 400mg tab	$2.27	$6.81	$204.30	59	38
etodolac ER (Lodine® XL) 500mg tab	$2.48	$4.96	$148.80	67	28
etodolac ER (Lodine® XL) 600mg tab	$2.73	$5.46	$163.80	27	17
etodolac (Lodine®) 300mg cap	$1.25	$5.00	$150.00	576	376
etodolac (Lodine®) 200mg cap	$1.03	$6.18	$185.40	290	246
meclofenamate (Meclomen®) 50mg cap	$1.77	$14.16	$424.80	8	3
meclofenamate (Meclomen®) 100mg cap	$6.81*	$27.24	$817.20	10	7
naproxen sodium (Anaprox®) 275mg tab	$1.17	$7.02	$210.60	335	255
naproxen sodium (Anaprox®) 550mg tab	$1.86	$5.58	$167.40	2,622	2,110
oxaprozin (Daypro®) 600mg tab	$2.41	$7.23	$216.90	110	51
tolmetin (Tolectin®) 200mg tab	$0.97	$8.73	$261.90	8	2
tolmetin (Tolectin®) 400mg cap	$1.71	$6.84	$205.20	16	5
tolmetin (Tolectin®) 600mg tab	$2.54	$7.62	$228.60	1	1
Total	**N/A**	**N/A**	**N/A**	**4,208**	**3,191**

All costs are state maximum allowable costs (SMAC) unless otherwise specified.
*Cost based on estimated acquisition cost (EAC).

Recommendations

The College of Pharmacy recommends the following changes to the Non-Steroidal Anti-Inflammatory Drugs Product Based Prior Authorization (PBPA) category:

1. The addition of Dyloject™ to the Special Prior Authorization (PA) category. The current criteria for this category will apply.
2. Move the following medications to Tier-2 based on recent increases in State Maximum Allowable Costs (SMAC). The existing criteria for this category will apply. All products listed below now exceed a SMAC cost of $100.00 per month for a 30-day supply.
    a. Lodine® (etodolac) 200mg and 300mg capsules
    b. Lodine XL® (etodolac extended-release) 400mg, 500mg, and 600mg tablets
    c. Meclomen® (meclofenamate) 50mg and 100mg capsules
    d. Anaprox® (naproxen sodium) 275mg and 550mg tablets
    e. Daypro® (oxaprozin) 600mg tablets
    f. Tolectin® (tolmetin) 200mg and 600mg tablets; 400mg capsules
3. Place a quantity limit of 60 tablets per 30 days on Voltaren® (diclofenac sodium) 25mg tablets.
4. Initiate an educational mailing to prescribers with patients who have cardiovascular co-morbidities and are on NSAID therapy regarding the FDA Safety Alert of NSAIDs and cardiovascular risk.

Non-Steroidal 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® top drops)
ketoprofen (Orudis®)	**meclofenamate (Meclomen®)**	diclofenac sodium (Voltaren Gel®)
meloxicam (Mobic®)	**naproxen sodium (Anaprox®) 275mg and 550mg tablets**	ibuprofen/famotidine (Duexis®)
nabumetone (Relafen®)	**oxaprozin (Daypro®)**	indomethacin (Indocin®)
naproxen (Naprosyn®)	**tolmetin (Tolectin®)**	indomethacin (Tivorbex™)
naproxen EC (Naprosyn®)		ketoprofen ER (Oruvail®)
sulindac (Clinoril®)		mefenamic acid (Ponstel®)
		naproxen sodium (Naprelan®)
		naproxen/esomeprazole (Vimovo®)
		piroxicam (Feldene®)

ER= Extended-Release, EC= Enteric Coated

Utilization Details of NSAIDs: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
TIER-1 UTILIZATION						
DICLOFENAC ORAL PRODUCTS						
DICLOFEN POT TAB 50MG	1,213	739	$24,880.75	$0.88	1.64	$20.51
DICLOFENAC TAB 25MG DR	79	52	$5,580.11	$2.13	1.52	$70.63
DICLOFENAC TAB 50MG DR	1,316	787	$21,813.40	$0.65	1.67	$16.58
DICLOFENAC TAB 75MG DR	5,883	3,202	$74,381.95	$0.46	1.84	$12.64
DICLOFENAC TAB 100MG ER	383	161	$6,223.89	$0.50	2.38	$16.25
SUBTOTAL	**8,874**	**4,941**	**$132,880.10**	**$0.56**	**1.80**	**$14.97**
ETODOLAC PRODUCTS						
ETODOLAC CAP 200MG	290	246	$10,596.31	$2.74	1.18	$36.54
ETODOLAC CAP 300MG	576	376	$32,995.68	$2.96	1.53	$57.28
ETODOLAC TAB 400MG	1,907	1,107	$80,333.50	$1.73	1.72	$42.13
ETODOLAC TAB 500MG	764	368	$36,034.70	$1.70	2.08	$47.17
ETODOLAC ER TAB 400MG	59	38	$5,204.46	$3.32	1.55	$88.21
ETODOLAC ER TAB 500MG	67	28	$7,346.71	$3.36	2.39	$109.65
ETODOLAC ER TAB 600MG	27	17	$3,261.50	$2.53	1.59	$120.80
SUBTOTAL	**3,690**	**2,180**	**$175,772.86**	**$2.00**	**1.69**	**$47.63**
FLURBIPROFEN PRODUCTS						
FLURBIPROFEN TAB 100MG	94	27	$1,434.11	$0.61	3.48	$15.26
FLURBIPROFEN TAB 50MG	2	1	$20.83	$0.69	2.00	$10.42
SUBTOTAL	**96**	**28**	**$1,454.94**	**$0.61**	**3.43**	**$15.16**
IBUPROFEN PRODUCTS						
IBUPROFEN SUS 100/5ML	17,527	13,573	$163,765.28	$0.80	1.29	$9.34
ADVIL CHILD SUS 100/5ML	260	235	$1,861.41	$0.52	1.11	$7.16
IBUPROFEN DRO 50/1.25	99	95	$1,015.02	$0.80	1.04	$10.25
INFANT ADVIL DRO 50/1.25	21	19	$185.19	$0.45	1.11	$8.82
CHLD IBUPRFN DRO 40MG/ML	10	9	$98.16	$1.13	1.11	$9.82
IBU-DROPS DRO 50/1.25	3	3	$29.81	$1.36	1.00	$9.94
IBU-DROPS DRO 40MG/ML	3	3	$25.62	$0.66	1.00	$8.54
IBUPROFEN TAB 400MG	8,305	5,389	$55,201.86	$0.47	1.54	$6.65
IBUPROFEN TAB 600MG	14,540	11,478	$96,198.00	$0.48	1.27	$6.62
IBUPROFEN TAB 800MG	53,718	34,406	$338,831.42	$0.34	1.56	$6.31
SUBTOTAL	**94,486**	**65,210**	**$657,211.77**	**$0.43**	**1.45**	**$6.96**
KETOPROFEN PRODUCTS						
KETOPROFEN CAP 50MG	674	588	$6,299.05	$0.92	1.15	$9.35
KETOPROFEN CAP 75MG	1,961	1,664	$18,668.05	$0.88	1.18	$9.52
SUBTOTAL	**2,635**	**2,252**	**$24,967.10**	**$0.89**	**1.17**	**$9.48**
KETOROLAC PRODUCTS						
KETOROLAC TAB 10MG	2,318	2,019	$29,711.01	$1.85	1.15	$12.82
KETOROLAC INJ 30MG/ML	249	216	$1,614.73	$4.45	1.15	$6.48
KETOROLAC INJ 60MG/2ML	103	74	$521.51	$2.67	1.39	$5.06
SUBTOTAL	**2,670**	**2,275**	**$31,847.25**	**$1.92**	**1.17**	**$11.73**
MECLOFENAMATE PRODUCTS						
MECLOFEN SOD CAP 100MG	10	7	$1,605.76	$12.35	1.43	$160.58
MECLOFEN SOD CAP 50MG	8	3	$1,203.23	$5.47	2.67	$150.40
SUBTOTAL	**18**	**10**	**$2,808.99**	**$8.03**	**1.80**	**$156.06**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
MELOXICAM PRODUCTS						
MELOXICAM SUS 7.5/5ML	235	79	$22,481.02	$3.24	2.97	$95.66
MOBIC SUS 7.5/5ML	24	10	$3,440.47	$4.34	2.40	$143.35
MELOXICAM TAB 15MG	22,036	9,970	$64,886.40	$0.08	2.21	$2.94
MELOXICAM TAB 7.5MG	11,088	5,718	$37,545.46	$0.11	1.94	$3.39
MOBIC TAB 7.5MG	1	1	$6.16	$0.21	1.00	$6.16
SUBTOTAL	**33,384**	**15,778**	**$128,359.51**	**$0.11**	**2.12**	**$3.84**
NABUMETONE PRODUCTS						
NABUMETONE TAB 500MG	1,679	866	$27,444.14	$0.61	1.94	$16.35
NABUMETONE TAB 750MG	1,537	645	$24,900.27	$0.56	2.38	$16.20
SUBTOTAL	**3,216**	**1,511**	**$52,344.41**	**$0.59**	**2.13**	**$16.28**
NAPROXEN PRODUCTS						
NAPROXEN SOD TAB 275MG	335	255	$2,633.31	$0.53	1.31	$7.86
NAPROXEN SOD TAB 550MG	2,622	2,110	$20,345.57	$0.45	1.24	$7.76
NAPROXEN SUS 125/5ML	329	231	$8,350.89	$1.80	1.42	$25.38
NAPROXEN TAB 250MG	1,429	1,009	$9,378.63	$0.35	1.42	$6.56
NAPROXEN TAB 375MG	2,956	1,809	$16,370.80	$0.24	1.63	$5.54
NAPROXEN TAB 500MG	21,353	13,212	$121,903.07	$0.25	1.62	$5.71
NAPROXEN DR TAB 375MG	97	61	$1,109.04	$0.50	1.59	$11.43
NAPROXEN DR TAB 500MG	758	419	$9,190.81	$0.45	1.81	$12.13
SUBTOTAL	**29,879**	**19,106**	**$189,282.12**	**$0.28**	**1.56**	**$6.33**
OXAPROZIN PRODUCTS						
OXAPROZIN TAB 600MG	110	51	$13,231.83	$4.09	2.16	$120.29
SUBTOTAL	**110**	**51**	**$13,231.83**	**$4.09**	**2.16**	**$120.29**
SULINDAC PRODUCTS						
SULINDAC TAB 150MG	87	35	$1,021.69	$0.38	2.49	$11.74
SULINDAC TAB 200MG	168	85	$2,211.28	$0.45	1.98	$13.16
SUBTOTAL	**255**	**120**	**$3,232.97**	**$0.43**	**2.13**	**$12.68**
TOLMETIN PRODUCTS						
TOLMETIN SOD CAP 400MG	16	5	$1,132.56	$2.77	3.20	$70.79
TOLMETIN SOD TAB 200MG	8	2	$804.93	$3.59	4.00	$100.62
TOLMETIN SOD TAB 600MG	1	1	$205.19	$6.84	1.00	$205.19
SUBTOTAL	**25**	**8**	**$2,142.68**	**$3.23**	**3.13**	**$85.71**
TIER-1 SUBTOTAL	**179,338**	**97,045**	**$1,415,536.53**	**$0.37**	**1.85**	**$7.89**
TIER-2 UTILIZATION						
CELECOXIB PRODUCTS						
CELEBREX CAP 100MG	93	32	$20,601.39	$7.18	2.91	$221.52
CELEBREX CAP 200MG	640	189	$202,075.28	$9.31	3.39	$315.74
CELEBREX CAP 50MG	3	2	$315.95	$3.51	1.50	$105.32
CELECOXIB CAP 100MG	85	33	$6,208.14	$2.29	2.58	$73.04
CELECOXIB CAP 200MG	604	194	$72,462.45	$3.31	3.11	$119.97
CELECOXIB CAP 400MG	6	1	$671.82	$3.73	6.00	$111.97
CELECOXIB CAP 50MG	3	2	$189.74	$1.26	1.50	$63.25
SUBTOTAL	**1,434**	**453**	**$302,524.77**	**$6.10**	**3.17**	**$210.97**
DICLOFENAC/MISOPROSTOL COMBINATION PRODUCTS						
DICLO/MISOPR TAB 50-0.2MG	25	7	$4,506.64	$5.54	3.57	$180.27
DICLO/MISOPR TAB 75-0.2MG	41	12	$6,740.09	$4.92	3.42	$164.39

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
SUBTOTAL	**66**	**19**	**$11,246.73**	**$5.15**	**3.47**	**$170.41**
FENOPROFEN PRODUCTS						
NALFON CAP 400MG	2	2	$412.87	$10.32	1.00	$206.44
SUBTOTAL	**2**	**2**	**$412.87**	**$10.32**	**1.00**	**$206.44**
TIER-2 SUBTOTAL	**1,502**	**322**	**$314,184.37**	**$6.06**	**4.66**	**$209.18**
SPECIAL PA UTILIZATION						
DICLOFENAC PRODUCTS						
CAMBIA POW 50MG	1	1	$317.42	$35.27	1.00	$317.42
VOLTAREN GEL 1%	115	59	$16,349.39	$6.21	1.95	$142.17
SUBTOTAL	**116**	**60**	**$16,666.81**	**$6.31**	**1.93**	**$143.68**
INDOMETHACIN PRODUCTS						
INDOCIN SUS 25MG/5ML	26	3	$6,210.48	$8.02	8.67	$238.86
INDOMETHACIN CAP 25MG	35	13	$612.53	$0.51	2.69	$17.50
INDOMETHACIN CAP 50MG	108	47	$1,350.83	$0.52	2.30	$12.51
INDOMETHACIN CAP 75MG ER	6	3	$736.04	$1.60	2.00	$122.67
SUBTOTAL	**175**	**66**	**$8,909.88**	**$1.77**	**2.65**	**$50.91**
KETOPROFEN PRODUCTS						
SPRIX SPR 15.75MG	4	4	$1,579.67	$13.16	1.00	$394.92
KETOPROFEN CAP 200MG ER	3	2	$837.39	$6.98	1.50	$2.79.13
KETOPROFEN POW	104	79	$8,342.61	$3.24	1.32	$80.22
KETOPROFEN POW	1	1	$562.70	$18.76	1.00	$562.70
SUBTOTAL	**112**	**86**	**$11,322.37**	**$10.53**	**1.30**	**$101.09**
NAPROXEN PRODUCTS						
NAPRELAN TAB 375MG CR	5	5	$3,256.56	$24.30	1.00	$651.31
NAPRELAN TAB 500MG CR	24	12	$22,802.75	$34.50	2.00	$950.11
SUBTOTAL	**29**	**17**	**$26,059.31**	**$32.78**	**1.71**	**$898.60**
PIROXICAM PRODUCTS						
PIROXICAM CAP 20MG	10	4	$683.89	$1.63	2.50	$68.39
SUBTOTAL	**10**	**4**	**$683.89**	**$1.63**	**2.50**	**$68.39**
SPECIAL PA SUBTOTAL	**442**	**233**	**$63,642.26**	**$10.60**	**1.90**	**$143.99**
TOTAL	**181,282**	**96,112***	**$1,793,363.16**	**$0.46**	**1.89**	**$9.89**

*Total number of unduplicated members.

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[1]FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 9/14/15. Last accessed 9/14/15.

[2]FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm. Last revised 7/17/15. Last accessed 9/15/15.

[3]European Society of Cardiology Press Release: SCOT study quells concerns about NSAID safety. Available online at: http://www.escardio.org/The-ESC/Press-Office/Press-releases/ESC-Press-Releases. Last revised 8/31/15. Last accessed 9/23/15.

[4]Dyloject™ Package Insert. Hospira, Inc. Available online at: http://medlibrary.org/lib/rx/meds/dyloject/. Last revised 1/14/2015. Last accessed 9/15/15.

Appendix L

Fiscal Year 2015 Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Cosentyx® (Secukinumab)

Oklahoma Health Care Authority
October 2015

Current Prior Authorization Criteria

Targeted Immunomodulator Agents*		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3+**
Methotrexate	Adalimumab (Humira®)	Abatacept (Orencia®)
Hydroxychloroquine	Certolizumab pegol (Cimzia®)	Alefacept (Amevive®)
Sulfasalazine	Etanercept (Enbrel®)	Anakinra (Kineret®)
Minocycline		Apremilast (Otezla®)
Oral Corticosteroids		Canakinumab (Ilaris®)¥
Leflunomide		Golimumab (Simponi® and Simponi® Aria™)
Mesalamine		Infliximab (Remicade®)
6-Mercaptopurine		Rituximab (Rituxan®)
Azathioprine		Tocilizumab (Actemra®)
NSAIDs		Tofacitinib (Xeljanz®)
		Ustekinumab (Stelara®)
		Vedolizumab (Entyvio™)

*Tier structure based on supplemental rebate participation. 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= Non-steroidal 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

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	685	4,003	$12,905,953.36	$3,224.07	$107.93	26,684	119,580
2015	700	4,455	$16,360,246.62	$3,672.33	$125.16	33,326	130,710
% Change	**2.19%**	**11.29%**	**26.77%**	**13.90%**	**15.97%**	**24.89%**	**9.31%**
Change	**15**	**452**	**$3,454,293.26**	**$448.26**	**$17.24**	**6,642**	**11,130**

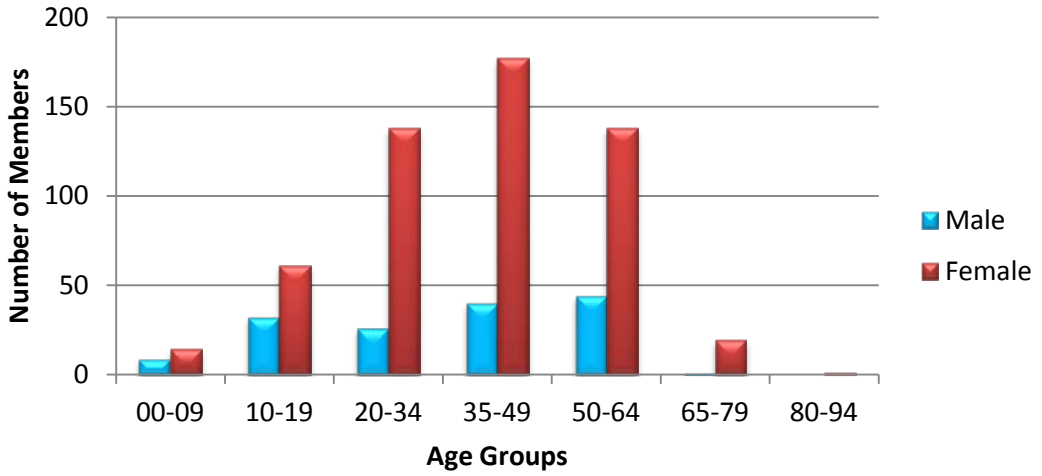
*Total number of unduplicated members.

Fiscal Year 2015 Utilization of Targeted Immunomodulator Agents: Medical Claims

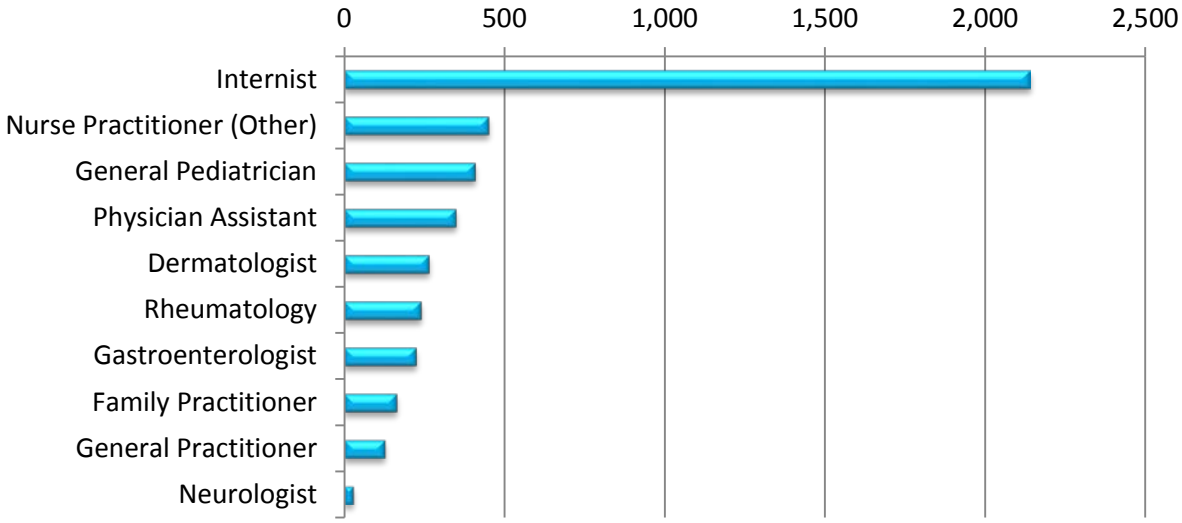
*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
79	280	$912,886.69	$3,260.31	47,662

*Total number of unduplicated members.
Totals exclude rituximab oncology claims and natalizumab multiple sclerosis claims.

Demographics of Members Utilizing Targeted Immunomodulator Agents

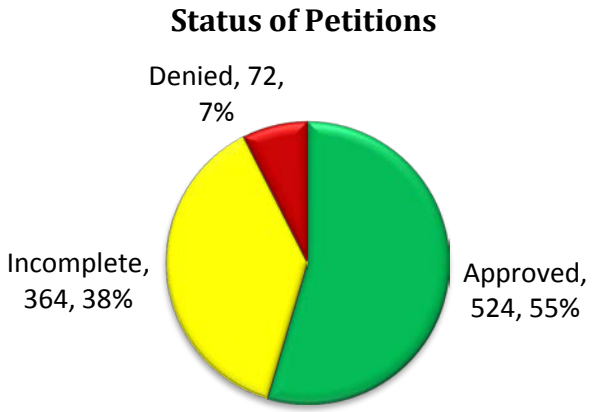


Top Prescriber Specialties of Targeted Immunomodulator Agents by Number of Claims



Prior Authorization of Targeted Immunomodulator Agents

There were 960 prior authorization requests submitted for targeted immunomodulator agents during fiscal year 2015. The following chart shows the status of the submitted prior authorization requests.



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

Biosimilars: The Affordable Care Act amended the Public Health Service Act (PHS Act) to create an abbreviated licensure pathway for biological products that are demonstrated to be "biosimilar" to or "interchangeable" with an FDA-licensed biological product. A *biosimilar* product is a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product. An *interchangeable* biological product is biosimilar to an FDA-approved reference product and meets additional standards for interchangeability. An interchangeable biological product may be substituted for the reference product by a pharmacist without the intervention of the health care provider who prescribed the reference product.

- **August 2014:** Celltrion, Inc. submitted a biologics license application (BLA) to the FDA under the biosimilar regulatory approval pathway for Remsima®. If approved, Remsima® would be a biosimilar for Remicade® (infliximab). Celltrion has already obtained approval for its biosimilar infliximab product, in over 50 countries.
- **June 2015:** Merck announced that pivotal Phase 3 clinical studies of an investigational biosimilar of Enbrel® (etanercept) and an investigational biosimilar of Remicade® (infliximab) met their primary endpoints demonstrating equivalence to the originator medicine in patients with moderate-to-severe rheumatoid arthritis (RA) despite methotrexate therapy.
- **August 2015:** The FDA released guidance for the industry regarding nonproprietary naming of biological products. The draft guidance and proposed rule calls for biologics, including reference products and biosimilars, to bear a nonproprietary name with an FDA-designated suffix.

New FDA Approvals and Indications:

- **September 2014:** The FDA approved Humira® (adalimumab) to treat moderate-to-severe Crohn's disease in pediatric patients 6 years and older who have had an inadequate response to corticosteroids or immunomodulators. Adalimumab has previously been FDA approved for Crohn's disease in adults along with six other indications (rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, ulcerative colitis, and plaque psoriasis).
- **January 2015:** The FDA approved Cosentyx® (secukinumab) for treatment of adults with moderate-to-severe plaque psoriasis.
- **September 2015:** The FDA approved Humira® (adalimumab) for the treatment of moderate-to-severe hidradenitis suppurativa (HS) making it the first and only FDA-approved treatment for HS.

Pipeline Updates:

- **July 2015:** Janssen Pharmaceuticals' anti-interleukin-23 monoclonal antibody, guselkumab, showed promising results for treatment of plaque psoriasis in a Phase II randomized, placebo-controlled trial. The results of the trial were published in the July issue of the *New England Journal of Medicine*. However, experts caution that more data are needed to evaluate the safety profile.
- **July 2015:** Pfizer announced that the FDA has accepted for review their new drug application (NDA) for Xeljanz® (tofacitinib) 11mg once daily. Tofacitinib is currently available as a 5mg oral tablet dosed twice daily.
- **September 2015:** Pfizer's Xeljanz® (tofacitinib) met its primary endpoints in two Phase III placebo-controlled studies in patients with moderate-to-severe ulcerative colitis.
- **September 2015:** AbbVie's investigational oral Janus Kinase inhibitor (JAK-1) was found effective for refractory moderate-to-severe rheumatoid arthritis in two Phase II studies.
- **September 2015:** Cosentyx® (secukinumab) was found significantly more effective than placebo in the treatment of psoriatic arthritis in a Phase III study.
- **September 2015:** The safety and efficacy of baricitinb (Lilly/Incyte), a once-daily, oral JAK-1 and JAK2 inhibitor, for patients with moderate-to-severe rheumatoid arthritis (RA) was found superior to methotrexate in a Phase III study.

Cosentyx® (Secukinumab) Product Summary[14,15,16]

FDA Approved: January 2015

Indications: Cosentyx® (secukinumab) is a human interleukin-17A antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Dosing:

- Secukinumab is available as 150mg/mL solution in a single-use Sensoready® pen, a single-use prefilled syringe, and as a lyophilized powder in a single-use vial for reconstitution.
- All dosage forms must be refrigerated. Secukinumab should be administered within one hour after removal from the refrigerator.

- The recommended dose of secukinumab is 300mg by subcutaneous injection weekly for five doses followed by 300mg every four weeks.
- Each 300mg dose is given as two subcutaneous injections of 150mg.
- Patients may self-inject after proper training in subcutaneous injection technique using the Sensoready® pen or prefilled syringe. The lyophilized powder for reconstitution is for healthcare provider use only.
- Secukinumab can be administered in the upper arms, thighs, or any quadrant of the abdomen; injection sites should be rotated.

Mechanism of Action: Secukinumab is a human IgG1 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Secukinumab inhibits the release of pro-inflammatory cytokines and chemokines.

Contraindications: Secukinumab is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the product's excipients.

Warnings and Precautions:

- Infections: Secukinumab may increase the risk of infections. In clinical trials, a higher rate of infections was observed in secukinumab-treated patients compared to placebo-treated patients. The incidence of some types of infections appeared to be dose-dependent in clinical studies.
- Pre-Treatment Evaluation for Tuberculosis (TB): Patients should be evaluated for TB infection prior to initiating treatment with secukinumab. Secukinumab should not be administered to patients with active TB infection. Treatment of latent TB should be initiated prior to administering secukinumab. Anti-TB therapy should be considered prior to initiation of secukinumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving secukinumab should be monitored for signs and symptoms of active TB during and after treatment.
- Exacerbations of Crohn's Disease: Caution should be exercised when prescribing secukinumab to patients with active Crohn's disease, as exacerbations of Crohn's disease, in some cases serious, were observed in secukinumab-treated patients during clinical trials. Patients who are treated with secukinumab and have active Crohn's disease should be monitored closely.
- Hypersensitivity Reactions: Anaphylaxis and cases of urticaria occurred in secukinumab-treated patients during clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.
- Risk of Hypersensitivity in Latex-Sensitive Individuals: The removable cap of the secukinumab Sensoready® pen and prefilled syringe contains natural rubber latex which may cause an allergic reaction in latex-sensitive individuals.

- Vaccinations: Prior to initiating therapy with secukinumab, consideration should be given to completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with secukinumab should not receive live vaccinations, and non-live vaccinations received during a course of secukinumab may not elicit an immune response sufficient to prevent disease.

Adverse Reactions: The most common adverse reactions (≥1% and greater than placebo) reported during secukinumab clinical trials include the following:

- Nasopharyngitis
- Diarrhea
- Upper respiratory tract infection
- Rhinitis
- Oral herpes
- Pharyngitis
- Urticaria
- Rhinorrhea

Drug Interactions: The formation of CYP450 enzymes can be altered by increased levels of certain cytokines during chronic inflammation. Thus, secukinumab, an antagonist of IL-17A, could normalize the formation of CYP450 enzymes. Upon initiation or discontinuation of secukinumab in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, monitoring of therapeutic effect (warfarin) or drug concentration (cyclosporine) should be considered. Dosage modification of the CYP450 substrate may be necessary.

Use in Special Populations:

- Pregnancy: Secukinumab is pregnancy category B. There are no adequate and well-controlled trials of secukinumab in pregnant women. Secukinumab should be used during pregnancy only if the potential benefit justifies the potential harm to the fetus.
- Nursing Mothers: It is not known whether secukinumab is excreted in human milk or absorbed systemically after injection. Because many drugs are excreted in human milk, caution should be exercised when secukinumab is administered to a nursing woman.
- Pediatric Use: The safety and effectiveness of secukinumab in pediatric patients have not been evaluated.
- Geriatric Use: Of the 3,430 plaque psoriasis patients exposed to secukinumab in clinical trials, a total of 230 were 65 years or older, and 32 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects age 65 years and older was not sufficient to determine whether they responded differently from younger subjects.

Efficacy: The efficacy of secukinumab was evaluated in four multicenter, randomized, double-blind, placebo-controlled trials. The four trials enrolled a total of 2,403 subjects who were 18 years of age or older, had a minimum body surface area involvement of 10%, a Psoriasis Area and Severity Index (PSAI) score greater than or equal to 12, and who were candidates for photo therapy or systemic therapy. Subjects were randomized to receive secukinumab 300mg, secukinumab 150mg, placebo, or a biologic active control.

- In all trials, the endpoints were the proportion of patients who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline to Week 12 and treatment success (clear or almost clear) on the Investigator's Global Assessment modified 2011 (IGA).

Clinical Outcomes at Week 12 in Adults with Plaque Psoriasis		
	PASI 75 Response n (%)	**IGA of Clear or Almost Clear n (%)**
Trial 1	300mg: 200 (82) 150mg: 174 (71) Placebo: 11 (4)	300mg: 160 (65) 150mg: 125 (51) Placebo: 6 (2)
Trial 2	300mg: 249 (76) 150mg: 219 (67) Placebo: 16 (5)	300mg: 202 (62) 150mg: 167 (51) Placebo: 9 (3)
Trial 3	300mg: 44 (75) 150mg: 41 (69) Placebo: 0(0)	300mg: 40 (68) 150mg: 31 (53) Placebo: 0 (0)
Trial 4	300mg: 52 (87) 150mg: 43 (70) Placebo: 2(3)	300mg: 44 (73) 150mg: 32 (52) Placebo: 0 (0)

Additional Efficacy Studies: Two additional studies supported by Novartis Pharmaceuticals compared the efficacy of secukinumab to currently available etanercept (Enbrel®) and ustekinumab (Stelara®).

- Full Year Investigative Examination of Secukinumab vs. Etanercept Using Two Dosing Regimens to Determine Efficacy in Psoriasis (FIXTURE): A phase-3, double-blind, 52-week trial evaluated the efficacy of secukinumab 300mg or 150mg in comparison to placebo or etanercept. The objective of the study was to show the superiority of secukinumab over placebo at week 12 with respect to the proportion of patients who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline and a score of clear or almost clear on the IGA.
    - Proportion of patients who met PASI 75: secukinumab 300mg 77.1%, secukinumab 150mg 67.0%, etanercept 50mg twice weekly 44.0%, and placebo 4.9% (P<0.001 for each secukinumab dose vs. comparators)
    - Proportion of patients who met clear or almost clear on the IGA: secukinumab 300mg 62.5%, secukinumab 150mg 51.1%, etanercept 50mg twice weekly 27.2%, and placebo 2.8% (P<0.001 for each secukinumab dose vs. comparators)
    - The rates of infection were higher with secukinumab than with placebo in both studies and were similar to those with etanercept.
- Secukinumab is Superior to Ustekinumab in Clearing of Subjects with Moderate to Severe Plaque Psoriasis: CLEAR, a Randomized Controlled Trial: A double-blind, 52-week trial evaluated the efficacy of secukinumab 300mg in comparison to ustekinumab per label. The primary endpoint was 90% or more improvement from baseline PASI score (PASI 90) at week 16.
    - PASI 90 response at week 16: secukinumab 300mg 79.0% vs. ustekinumab 57.6% (P<0.001)
    - The safety profile of secukinumab was comparable with ustekinumab.

Cost Comparison:

Medication	EAC Per mL or Tablet	EAC for 28 Days of Therapy
Cosentyx® (secukinumab) 150mg Pen	**$1,930.36**	**$3,860.71**
Methotrexate Oral Tablet 2.5mg	$1.51 +	$60.40
Enbrel® (entanercept) 50mg	$930.92	$3,723.68

Costs do not reflect supplemental rebated prices or net costs.
Dosing is based on maintenance treatment after initial dosing is complete.
EAC= estimated acquisition cost
+ State maximum allowable cost (SMAC) pricing
Dosing based on recommended target dose of methotrexate 25mg per week.

Hidradenitis Suppurativa Summary[17,18,19,20,21,22,23]

Hidradenitis Suppurativa (HS), or acne inversa, is a chronic, relapsing, inflammatory skin disease characterized by inflamed nodules typically located in the apocrine gland-bearing regions (armpits, genital area, groin, breasts, and buttocks). The nodules can progress to abscesses and scarring and are frequently characterized by chronic drainage.

The etiology of HS involves both genetic and environmental factors. The central pathogenic event in HS is believed to be the occlusion of the upper parts of the hair follicle leading to perifollicular inflammation. The inflammation triggers an influx of inflammatory cells and overexpression of pro-inflammatory cytokines [interleukin and tumor necrosis factor (TNF)-alpha].

HS typically develops after puberty and severity is described according to three Hurley stages. Stage I is most common (68% of patients), while stage II occurs in 28% or patients, and 4% of patients have stage III.

- Stage I: Abscess formation, single or multiple, without sinus tracts and cicatrisation.
- Stage II: Recurrent abscesses with tract formation and cicatrisation, single or multiple, widely separated lesions.
- Stage III: Diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area.

The estimated world-wide prevalence of HS is 1-4% and HS is three times more common in women than men. Risk factors include smoking, obesity, and family history. Comorbidities include inflammatory bowel disease and spondyloarthropathies.

There are no current US guidelines for the treatment and management of HS. The European treatment guidelines and several systematic reviews suggest topical or systemic antibiotics, oral or intralesional corticosteroids, dapsone, cyclosporine, antiandrogens (spironolactone or oral contraceptives), finasteride, and surgery. In September 2015, the FDA approved Humira® (adalimumab) for the treatment of moderate-to-severe HS making it the first and only FDA-approved treatment for HS. The European Commission approved adalimumab for treatment of active moderate-to-severe HS in adults with an inadequate response to conventional systemic HS treatment in July.

Two randomized, double-blind, placebo-controlled studies evaluated the safety and efficacy of adalimumab in 633 adult subjects with moderate-to-severe HS with Hurley Stage II or III disease

and with at least 3 abscesses or inflammatory nodules. Both studies evaluated Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12. HiSCR was defined as at least a 50% reduction in total abscess and inflammatory nodule count with no increase in abscess count and no increase in draining fistula count relative to baseline. In both studies, a higher proportion of adalimumab-treated subjects achieved HiSCR (Study I: 26% placebo vs 42% adalimumab, Study II: 28% placebo vs 59% adalimumab).

Recommendations

The College of Pharmacy recommends the addition of Cosentyx® (secukinumab) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization category. Current approval criteria for this category will apply.

Additionally, the College of Pharmacy recommends the following criteria for Humira® (adalimumab) for a diagnosis of hidradenitis suppurativa:

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, dapsone, cyclosporine, antiandrogens (spironolactone or oral contraceptives), finasteride, or surgery.

Targeted Immunomodulator Agents*		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3+**
Methotrexate	Adalimumab (Humira®)	Abatacept (Orencia®)
Hydroxychloroquine	Certolizumab pegol (Cimzia®)	Alefacept (Amevive®)
Sulfasalazine	Etanercept (Enbrel®)	Anakinra (Kineret®)
Minocycline		Apremilast (Otezla®)
Oral Corticosteroids		Canakinumab (Ilaris®)¥
Leflunomide		Golimumab (Simponi® and Simponi® Aria™)
Mesalamine		Infliximab (Remicade®)
6-Mercaptopurine		Rituximab (Rituxan®)
Azathioprine		**Secukinumab (Cosentyx®)**
NSAIDs		Tocilizumab (Actemra®)
		Tofacitinib (Xeljanz®)
		Ustekinumab (Stelara®)
		Vedolizumab (Entyvio™)

*Tier structure based on supplemental rebate participation. 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= Non-steroidal anti-inflammatory drugs
+ May be rebated to Tier-2 status only
¥ Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS).

Tier-2 A pproval 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.

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.

Tysabri® (Natalizumab) Approval Criteria (Crohn's Disease Diagnosis):

1. An FDA approved diagnosis of Crohn's disease; and
2. Treatment with at least two different first line therapeutic categories for Crohn's disease that have failed to yield an adequate clinical response, or a patient specific, clinically significant reason why the member cannot use all available first and second line alternatives; and
3. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

Utilization Details of Targeted Immunomodulator Agents: Fiscal Year 2015

Pharmacy Claims

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Adalimumab Products					
HUMIRA PEN INJ 40MG/0.8ML	1,626	308	$5,543,812.30	$114.87	$3,409.48
HUMIRA SYRINGE INJ 40MG/0.8ML	349	75	$1,304,000.37	$130.88	$3,736.39
HUMIRA PEN INJ 40MG/0.8ML PS	43	35	$262,660.53	$193.13	$6,108.38
HUMIRA KIT 20MG/0.4mL	30	7	$97,747.72	$101.61	$3,258.26
HUMIRA PEN INJ 40MG/0.8ML CD	30	28	$275,460.80	$264.36	$9,182.03
HUMIRA INJ 40MG/0.8ML PED-CD	1	1	$10,147.95	$362.43	$10,147.95
Subtotal	**2,079**	**371**	**$7,493,829.67**	**$121.62**	**$3,604.54**
Certolizumab Pegol Products					
CIMZIA INJ KIT (2) 200MG/ML	281	55	$935,860.65	$118.98	$3,330.46
CIMZIA INJ KIT (6) STARTER 200MG/ML	32	32	$270,395.55	$189.35	$8,449.86
Subtotal	**313**	**65**	**$1,206,256.20**	**$129.79**	**$3,853.85**
Etanercept Products					
ENBREL SRCLK INJ 50MG/ML	894	176	$2,851,271.22	$113.02	$3,189.34
ENBREL INJ 50MG/ML	253	55	$773,250.41	$108.12	$3,056.33
ENBREL INJ KIT 25MG	142	24	$223,538.54	$55.77	$1,574.22
ENBREL INJ 25mg/0.5ML	60	13	$120,504.87	$69.42	$2,008.41
Subtotal	**1,349**	**176**	**$3,968,565.04**	**$104.10**	**$2,941.86**
Tier-2 Subtotal	**3,741**	**612**	**$12,668,650.91**	**$116.19**	**$3,386.43**
Abatacept Products					
ORENCIA INJ 125MG/ML	131	20	$364,356.49	$98.55	$2,781.35
ORENCIA INJ 250MG	1	1	$2,426.31	$86.65	$2,426.31
Subtotal	**132**	**21**	**$366,782.80**	**$98.47**	**$2,778.66**
Anakinra Products					
KINERET INJ 100MG/0.67ML	24	6	$67,066.26	$112.72	$2,794.43
Subtotal	**24**	**6**	**$67,066.26**	**$112.72**	**$2,794.43**
Infliximab Products					
REMICADE INJ 100MG	158	23	$724,881.40	$147.66	$4,587.86
Subtotal	**158**	**23**	**$724,881.40**	**$147.66**	**$4,587.86**
Rituximab Products					
RITUXAN INJ 500MG	11	5	$212,687.96	$837.35	$19,335.27
RITUXAN INJ 100MG	6	4	$63,723.61	$558.98	$10,620.60
Subtotal	**17**	**6**	**$276,411.57**	**$751.12**	**$16,259.50**
Tocilizumab Products					
ACTEMRA INJ 80MG/4ML	55	4	$34,735.42	$43.97	$631.55
ACTEMRA INJ 400/20ML	50	6	$130,661.14	$132.52	$2,613.22
ACTEMRA INJ 200/10ML	33	2	$45,976.18	$84.21	$1,393.22
ACTEMRA INJ 162MG/0.9ML	17	6	$39,284.01	$82.53	$2,310.82
Subtotal	**155**	**12**	**$250,656.75**	**$89.58**	**$1,617.14**
Canakinumab Products					
ILARIS 180MG/1.2ML VIAL	44	9	$901,307.91	$522.19	$20,484.27
Subtotal	**44**	**9**	**$901,307.91**	**$522.19**	**$20,484.27**
Tofacitinib Products					
XELJANZ TAB 5MG	35	8	$90,800.11	$86.48	$2,594.29
Subtotal	**35**	**8**	**$90,800.11**	**$86.48**	**$2,594.29**

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Ustekinumab Products					
STELARA 90 MCG	27	10	$470,462.53	$226.18	$17,424.54
STELARA 45MG/0.5ML	21	7	$167,745.51	$98.21	$7,987.88
Subtotal	**48**	**16**	**$638,208.04**	**$168.48**	**$13,296.00**
Golimumab Products					
SIMPONI INJ 50MG/0.5ML	33	6	$105,194.02	$106.47	$3,187.70
SIMPONI INJ 50MG/0.5ML	15	3	$48,182.06	$107.07	$3,212.14
SIMPONI INJ 100MG/ML	2	1	$7,950.86	$141.98	$3,975.43
Subtotal	**90**	**9**	**$161,326.94**	**$107.98**	**$3,226.54**
Vedolizumab Products					
ENTYVIO INJ 300MG	12	3	$71,240.58	$201.81	$5,936.72
Subtotal	**12**	**3**	**$71,240.58**	**$201.81**	**$5,936.72**
Apremilast Products					
OTEZLA TAB 30MG	10	5	$24,856.59	$69.80	$2,094.00
OTEZLA STARTER 10/20/30MG	3	3	$3,916.56	$69.94	$1,305.52
Subtotal	**13**	**5**	**$24,856.59**	**$69.82**	**$1,912.05**
Tier-3 Subtotal	**688**	**111**	**$3,573,538.95**	**$168.87**	**$5,194.10**
Natalizumab Products					
TYSABRI INJ 300/15ML	26	4	$118,056.76	$229.68	$4,540.64
Subtotal	**26**	**4**	**$118,056.76**	**$229.68**	**$4,540.64**
Total	**4,455**	**700***	**$16,360,246.62**	**$125.16**	**$3,672.33**

*Total number of unduplicated members.

Medical Claims

Product Utilized	Total Claims	Total Members	Total Cost	Units	Cost/ Claim
CIMZIA INJ J0717	20	1	$28,448.00	4,400	$1,422.40
ORENCIA INJ J0129	11	5	$26,260.75	875	$2,387.34
SIMPONI ARIA IV INJ J1602	6	2	$26,465.66	1,103	$4,410.94
REMICADE INJ J1745	102	31	$299,120.33	5,127	$2,932.55
TYSABRI INJ J2323	1	1	$4,485.00	300	$4,485.00
ACTEMRA INJ J3262	73	8	$130,709.68	35,294	$1,790.54
RITUXAN INJ J9310	67	31	$397,397.27	563	$5,931.30
Total	**280**	**79***	**$912,886.69**	**47,662**	**$3,260.31**

*Total number of unduplicated members.

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Appendix M

Fiscal Year 2015 Annual Review of Inhaled Tobramycin Products & Pulmozyme® (Dornase Alfa) and 30-Day Notice to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation)

Oklahoma Health Care Authority
October 2015

Introduction

The inhaled tobramycin products (Bethkis®, Tobi®, and Tobi® Podhaler™) and Pulmozyme® (dornase alfa) were voted to be prior authorized by the drug utilization review (DUR) board in February 2014. After several educational interventions were completed, the prior authorization of the aforementioned products was implemented April 30, 2014.

Current Prior Authorization Criteria

Inhaled Tobramycin Products (Bethkis®, Tobi® and Tobi® Podhaler™) & Pulmozyme® (Dornase Alfa) Approval Criteria:

1. Use of inhaled tobramycin products and Pulmozyme® (dornase alfa) is reserved for members who have a diagnosis of cystic fibrosis.
    a. These medications will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 12 months of claims history.
    b. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Use of inhaled tobramycin products is restricted to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy.
    a. Use outside of this recommended regimen may be considered for coverage via a manual prior authorization submission with a patient-specific, clinically significant reason why the member would need treatment outside of the FDA approved dosing.
    b. Pharmacies should process the prescription claim with a 56 day supply.

Utilization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation

Comparison of Fiscal Years: Inhaled Tobramycin Products & Dornase Alfa

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	234	1,355	$5,180,812.17	$3,823.48	$126.33	183,836	41,009
2015	204	1,171	$4,331,777.80	$3,699.21	$102.49	145,005	42,265
% Change	**-12.80%**	**-13.60%**	**-16.40%**	**-3.30%**	**-18.90%**	**-21.10%**	**3.10%**
Change	**-30**	**-184**	**-$849,034.37**	**-$124.27**	**-$23.84**	**-38,831**	**1,256**

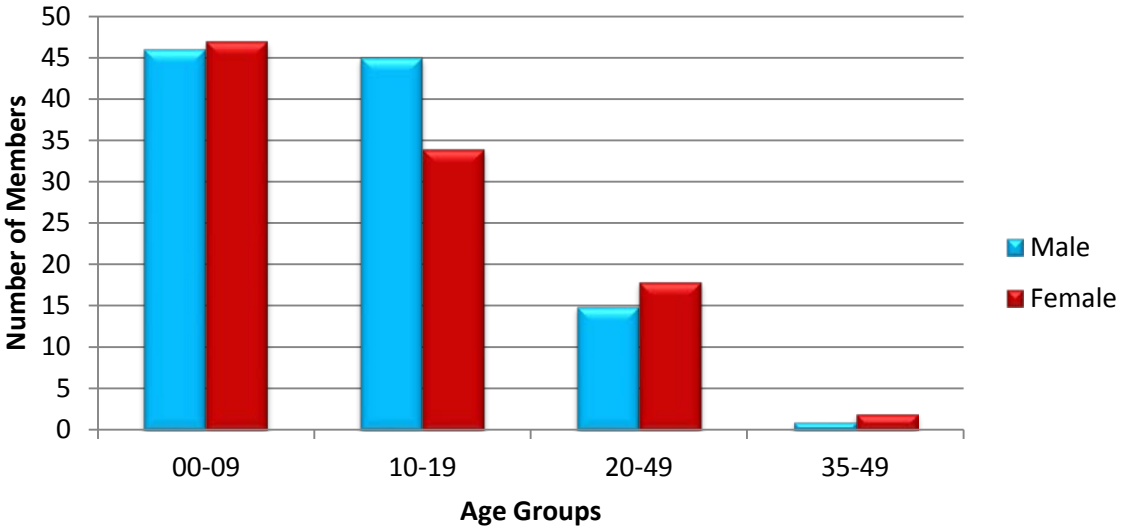
*Total number of unduplicated members.

Comparison of Fiscal Years: Aztreonam Inhalation

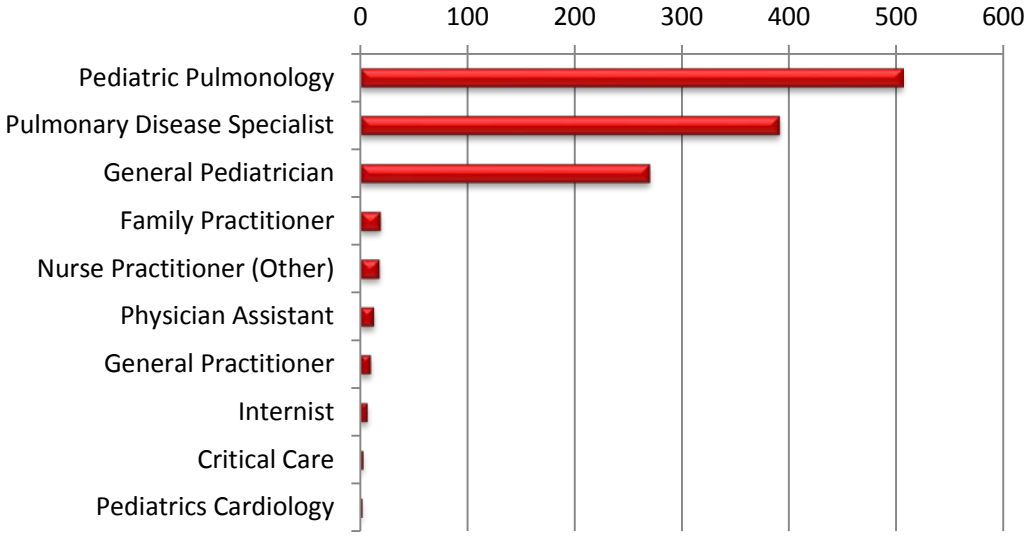
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	28	79	$472,473.03	$5,980.67	$213.60	6,636	2,212
2015	27	71	$401,610.31	$5,656.48	$202.02	5,964	1,988
% Change	**-3.60%**	**-10.10%**	**-15.00%**	**-5.40%**	**-5.40%**	**-10.10%**	**-10.10%**
Change	**-1**	**-8**	**-$70,862.72**	**-$324.19**	**-$11.58**	**-672**	**-224**

*Total number of unduplicated members.

Demographics of Members Utilizing Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation



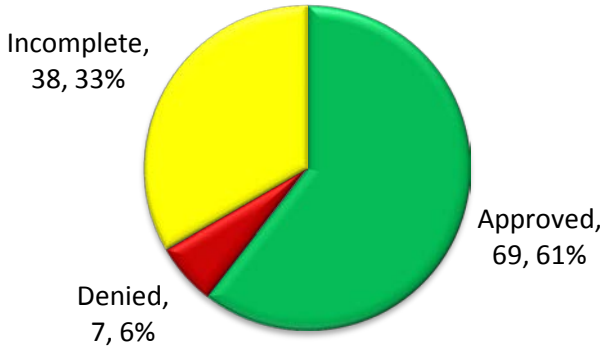
Top Prescriber Specialties of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation by Number of Claims



Prior Authorization of Inhaled Tobramycin Products and Dornase Alfa

There were 114 prior authorization requests submitted for inhaled tobramycin products and dornase alfa during fiscal year 2015. Computer edits are in place to detect a cystic fibrosis diagnosis in the member's recent diagnosis claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1, 2]

Anticipated Patent Expirations:

- Cayston® (aztreonam inhalation): December 2021
- Bethkis® (tobramycin solution inhalation): March 2023
- Tobi® Podhaler™ (tobramycin powder inhalation): October 2025

New FDA Approvals and Indications:

- **December 2014:** The FDA approved Kitabis™ Pak (tobramycin inhalation solution) for the management of cystic fibrosis in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*. Kitabis™ Pak is a co-packaged product containing tobramycin inhalation solution with a PARI LC Plus® reusable nebulizer. Similar products include Bethkis® and TOBI®, both of which are nebulized tobramycin products.

Cayston® (Aztreonam Inhalation) Product Summary[3]

Indications: Cayston® (aztreonam inhalation) is a monobactam antibacterial indicated to improve respiratory symptoms in CF patients with *Pseudomonas aeruginosa* in the lungs. The safety and effectiveness of aztreonam inhalation have not been established in pediatric patients below the age of 7 years, patients with forced expiratory volume in 1 second (FEV_1) less than 25% of predicted or greater than 75% of predicted, or patients colonized with *Burkholderia cepacia*.

Dosing:

- Aztreonam inhalation is available in a single-use vial containing 75mg of lyophilized aztreonam.

- The recommended dose of aztreonam inhalation is one single-use vial (75mg of aztreonam) reconstituted with 1mL of sterile diluent administered three times daily for a 28-day course (followed by 28 days off aztreonam inhalation therapy).
- The recommended dose is the same for both pediatric and adult patients.
- Aztreonam inhalation is administered by inhalation using an Altera Nebulizer System. Aztreonam inhalation should not be administered with any other nebulizer.
- Aztreonam inhalation should be administered immediately after reconstitution.

Mechanism of Action: Aztreonam exhibits activity *in vitro* against Gram-negative aerobic pathogens including *P. aeruginosa*. Aztreonam binds to penicillin-binding proteins of susceptible bacteria, which leads to inhibition of bacterial cell wall synthesis and death of the cell. Aztreonam activity is not decreased in the presence of CF lung secretions.

Contraindications: Contraindicated in patients with a known allergy to aztreonam.

Warnings and Precautions:
- Allergic Reactions: Severe allergic reactions have been reported following administration of aztreonam for injection to patients with no known history of exposure to aztreonam. In addition, allergic reactions with facial swelling and throat tightness were reported with aztreonam inhalation in clinical trials. Caution is advised when administering aztreonam inhalation to patients if they have a history of beta-lactam allergy since cross-reactivity may occur.
- Bronchospasm: Bronchospasm is a complication associated with nebulized therapies, including aztreonam inhalation. Reduction of 15% or more in FEV_1 immediately following administration of aztreonam inhalation after pretreatment with a bronchodilator was observed in 3% of patients.
- Reductions in FEV_1 After 28-Day Treatment Cycle: In clinical trials, patients with increases in FEV_1 during a 28-day course of aztreonam inhalation were sometimes treated for pulmonary exacerbations when FEV_1 declined after the treatment period.
- Development of Drug-Resistant Bacteria: Prescribing aztreonam inhalation in the absence of known *P. aeruginosa* infection in patients with CF is unlikely to provide benefit and increases the risk of development of drug-resistant bacteria.

Adverse Reactions: The most common adverse reactions (≥5% and greater than placebo) reported during aztreonam inhalation clinical trials include the following:
- Cough
- Nasal congestion
- Wheezing
- Pharyngolaryngeal pain
- Pyrexia
- Chest discomfort
- Abdominal pain
- Vomiting

Use in Special Populations:
- Pregnancy: Aztreonam inhalation is pregnancy category B. There are no adequate and well-controlled studies of aztreonam inhalation in pregnant women. Aztreonam inhalation should be used during pregnancy only if the potential benefit justifies the potential harm to the fetus.
- Nursing Mothers: Following administration of aztreonam for injection, aztreonam is excreted in human milk at concentrations that are less than one percent of those

determined in simultaneously obtained maternal serum. Use of aztreonam inhalation during breastfeeding is unlikely to pose a risk to infants.

- Pediatric Use: Patients 7 years and older were included in clinical trials with aztreonam inhalation. Fifty-five patients under 18 years of age received aztreonam inhalation in placebo-controlled trials. No dose adjustments were made for pediatric patients. Pyrexia was more commonly reported in pediatric patients than in adult patients. The safety and effectiveness of aztreonam inhalation in pediatric patients younger than 7 years of age have not been established.
- Geriatric Use: Clinical trials of aztreonam inhalation did not include patients aged 65 years of age and older to determine whether they respond differently from younger patients.
- Patients with Renal Impairment: Aztreonam is known to be excreted by the kidney. Placebo-controlled trials with aztreonam inhalation excluded patients with abnormal baseline renal function. Given the low systemic exposure of aztreonam following administration of aztreonam inhalation, clinically relevant accumulation of aztreonam is unlikely to occur in patients with renal impairment. Aztreonam inhalation may be administered to patients with mild, moderate, and severe renal impairment.

Efficacy: The efficacy of aztreonam inhalation was evaluated over a period of 28 days of treatment in a randomized, double-blind, placebo-controlled, multicenter trial that enrolled 164 patients with CF and *P. aeruginosa*.

- The primary efficacy endpoint was improvement in respiratory symptoms on the last day of treatment.
- Patients 7 years of age and older with FEV_1 of 25% to 75% predicted were enrolled. All patients were required to take a dose of an inhaled bronchodilator (beta-agonist) prior to taking a dose of aztreonam inhalation or placebo. Patients were receiving standard care for CF, including drugs for obstructive airway diseases.
- Pulmonary function, as measured by FEV_1 increased from baseline in patients treated with aztreonam inhalation. The treatment difference at Day 28 between aztreonam-treated and placebo-treated patients for percent change in FEV_1 was statistically significant at 10% (95% CI: 6%, 14%). Improvements in FEV_1 were comparable between adult and pediatric patients. Two weeks after completion of drug treatment, the difference in FEV_1 between aztreonam inhalation and placebo groups had decreased to 6% (95% CI: 2%, 9%).

Cost Comparison:

Medication	EAC Per mL or Capsule	EAC for 28 Days of Therapy
Cayston® (aztreonam inhalation) 75mg Vial	**$83.19**	**$6,987.96**
Tobi® (tobramycin inhalation solution) 300mg/5mL	$27.67	$7,747.60
Tobi® (tobramycin inhalation powder) 28mg Capsules	$38.02	$8,516.48
Bethkis® (tobramycin inhalation solution) 300mg/4mL	$26.75	$5,992.00

Costs do not reflect supplemental rebated prices or net costs.
EAC= estimated acquisition cost

Kitabis™ Pak (Tobramycin Inhalation) Product Summary[2]

Indications: Kitabis™ Pak (tobramycin inhalation) is an aminoglycoside antibacterial drug indicated for the management of CF in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*. The safety and efficacy of Kitabis™ Pak have not been demonstrated in patients under the age of 6 years, patients with FEV_1 less than 25% or greater than 75% predicted, or patients colonized with *Burkholderia cepacia*.

Dosing:

- Kitabis™ Pak is a co-packaging of tobramycin inhalation solution ampules (300mg/5mL) with a PARI LC PLUS® reusable nebulizer.
- The recommended dose is one single-use ampule (300mg/5mL) twice daily via oral inhalation in alternating periods of 28 days on drug, followed by 28 days off drug.
- The recommended dose is the same for all patients regardless of age or weight.
- Each dose of tobramycin inhalation solution is administered by oral inhalation using only the co-packaged PARI LC PLUS® reusable nebulizer included in the Kitabis™ Pak.
- The entire tobramycin inhalation solution treatment should take approximately 15 minutes to complete.
- Tobramycin inhalation solution should not be diluted or mixed with other drugs in the nebulizer.

Mechanism of Action: Tobramycin is an aminoglycoside antibacterial produced by *Streptomyces tenebrarius.* It acts primarily by disrupting protein synthesis, leading to altered cell membrane permeability, progressive disruption of the cell envelope, and eventual cell death. Tobramycin has *in vitro* activity against Gram-negative bacteria including *P. aeruginosa*. It is bactericidal *in vitro* at peak concentrations equal to or slightly greater than the minimum inhibitory concentration.

Contraindications: Tobramycin inhalation solution is contraindicated in patients with a known hypersensitivity to any aminoglycoside.

Warnings and Precautions:

- Bronchospasm: Bronchospasm can occur with inhalation of tobramycin inhalation solution. In clinical studies, changes in FEV_1 measured after the inhaled doses were similar in tobramycin and placebo groups.
- Ototoxicity: Transient tinnitus occurred in some patients treated with tobramycin inhalation in the clinical studies. In post marketing experience, patients receiving tobramycin inhalation have reported hearing loss.
- Nephrotoxicity: Nephrotoxicity was not seen during clinical studies with tobramycin inhalation solution but has been seen with aminoglycosides as a class.
- Neuromuscular Disorders: Aminoglycosides, including tobramycin, may aggravate muscle weakness because of a potential curare-like effect on neuromuscular function. Neuromuscular blockade, respiratory failure, and prolonged respiratory paralysis may occur more commonly in patients with underlying neuromuscular disorders, such as myasthenia gravis or Parkinson's disease. Prolonged respiratory paralysis may also occur in patients receiving neuromuscular blocking agents. If neuromuscular blockade occurs,

it may be reversed by the administration of calcium salts but mechanical assistance may be necessary.

- Embryo-Fetal Toxicity: Aminoglycosides can cause fetal harm when administered to pregnant women. Aminoglycosides cross the placenta had have been associated with reports of deafness in pediatric patients exposed in utero.
- Concomitant Use of Systemic Aminoglycosides: Patients receiving concomitant tobramycin inhalation and parenteral aminoglycoside therapy should be monitored as clinically appropriate for toxicities associated with aminoglycosides as a class.

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

- Increased cough
- Pharyngitis
- Increased Sputum
- Dyspnea
- Hemoptysis
- Decreased lung function
- Voice Alteration
- Taste Perversion
- Rash

Use in Special Populations:

- Pregnancy: Tobramycin inhalation is pregnancy category D. There are no adequate and well-controlled studies of tobramycin in pregnant women. If tobramycin inhalation solution is used during pregnancy, or if the patient becomes pregnant while taking tobramycin inhalation solution, the patient should be apprised of the potential hazard to the fetus.
- Nursing Mothers: It is not known if tobramycin inhalation will reach sufficient concentrations to be excreted in human breast milk. Because of the potential for ototoxicity and nephrotoxicity in nursing infants from tobramycin inhalation, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- Pediatric Use: The safety and efficacy of tobramycin inhalation have not been studied in pediatric patients younger than 6 years of age.
- Geriatric Use: Clinical studies of tobramycin inhalation did not include patients aged 65 years and over. Tobramycin is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function.

Efficacy: The safety and effectiveness of tobramycin inhalation was evaluated in two, double-blind, randomized, placebo-controlled, 24-week clinical studies (Study 1 and Study 2). The studies were conducted in CF patients with *P. aeruginosa* who had baseline FEV_1 % predicted between 25% and 75%. All patients received either tobramycin inhalation solution or placebo in addition to standard treatment recommended for CF patients. In each study, tobramycin inhalation-treated patients experienced significant improvement in pulmonary function. Improvement was demonstrated in the tobramycin inhalation group in Study 1 by an average increase in FEV_1 % predicted of about 11% relative to baseline during 24 weeks compared to no average change in placebo patients. In Study 2, tobramycin inhalation-treated patients had an average increase of about 7% compared to an average decrease of about 1% in the placebo group.

Cost Comparison:

Medication	EAC Per mL or Capsule	EAC for 28 Days of Therapy
Kitabis™ Pak (tobramycin inhalation) 300mg/5mL	**$16.97**	**$4,751.60**
Tobi® (tobramycin inhalation solution) 300mg/5mL	$27.67	$7,747.60
Tobi® (tobramycin inhalation powder) 28mg Capsules	$38.02	$8,516.48
Bethkis® (tobramycin inhalation solution) 300mg/4mL	$26.75	$5,992.00

Costs do not reflect supplemental rebated prices or net costs.
EAC= estimated acquisition cost

Recommendations

The College of Pharmacy recommends the addition of Kitabis™ Pak (tobramycin inhalation) and Cayston® (aztreonam) to the inhaled tobramycin and Pulmozyme® (Dornase Alfa) category. Current criteria for this category will apply.

Inhaled Tobramycin Products (Bethkis®, Tobi®, Tobi® Podhaler™, and Kitabis™ Pak), Pulmozyme® (Dornase Alfa), & Cayston® (Aztreonam) Approval Criteria:

1. Use of inhaled tobramycin products, Pulmozyme® (dornase alfa), and Cayston® (aztreonam) is reserved for members who have a diagnosis of cystic fibrosis.
    a. These medications will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 12 months of claims history.
    b. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Use of inhaled tobramycin products and Cayston® (aztreonam) is restricted to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy.
    a. Use outside of this recommended regimen may be considered for coverage via a manual prior authorization submission with a patient-specific, clinically significant reason why the member would need treatment outside of the FDA approved dosing.
    b. Pharmacies should process the prescription claim with a 56 day supply.

Utilization Details of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Dornase Alfa Products					
PULMOZYME SOL 1MG/ML	874	159	$2,561,292.44	$96.96	$2,930.54
Subtotal	**874**	**159**	**$2,561,292.44**	**$96.96**	**$2,930.54**
Tobramycin Nebulized Products					
TOBRAMYCIN NEB 300/5ML	197	71	$1,035,557.26	$99.17	$5,256.64
TOBI NEB 300/5ML	12	3	$77,513.26	$152.59	$6,459.44
BETHKIS NEB 300/4ML	7	4	$41,971.57	$107.07	$5,995.94
KITABIS PAK NEB 300/5ML	1	1	$4,755.71	$84.92	$4,755.71
Subtotal	**217**	**76**	**$1,159,797.80**	**$101.75**	**$5,344.69**
Tobramycin Powder Products					
TOBI PODHALR CAP 28MG	80	33	$610,687.56	$137.17	$7,633.59
Subtotal	**80**	**33**	**$610,687.56**	**$137.17**	**$7,633.59**
Aztreonam Products					
CAYSTON INH 75MG	71	27	$401,610.31	$202.02	$5,656.48
Subtotal	**71**	**27**	**$401,610.31**	**$202.02**	**$5,656.48**
Total	**1,242**	**205***	**$4,733,388.11**	**$106.96**	**$3,811.10**

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 09/25/15. Last accessed 09/29/15.

[2] Kitabis Pak Product Information. Catalent Pharma Solutions, LLC and PARI Respiratory Equipment, Inc. Available online at: http://kitabis.com/wp-content/uploads/pdfs/Kitabis-Pak-Full-Prescribing-Information.pdf . Last revised 11/2014. Last accessed 09/2015.

[3] Cayston Product Information. Gilead Science Inc. Available online at: http://www.gilead.com/~/media/files/pdfs/medicines/respiratory/cayston/cayston_pi.pdf?la=en. Last revised 05/2014. Last accessed 09/2015.

Appendix N

Annual Review of Xolair® (Omalizumab)

Oklahoma Health Care Authority
October 2015

Current Prior Authorization Criteria

Xolair® (Omalizumab) for Asthma Approval Criteria:

1. Member must be between 12 and 75 years of age; and
2. Member must have a diagnosis of severe persistent asthma (as per NAEPP guidelines); and
3. Member must have a positive skin test to at least one perennial aeroallergen. Positive perennial allergens must be listed on the prior authorization request; and
4. Member must have a pretreatment serum IgE level between 30 and 700 IU/mL; and
5. Member's weight must be between 30kg and 150kg; and
6. Member must have been on high dose inhaled corticosteroids (ICS) (as per NAEPP Guidelines) for at minimum the past three months; and
7. Medication must be prescribed by either a pulmonary or an allergy/asthma specialist; and
8. Member must have been in the emergency room (ER) or hospitalized, due to an asthma exacerbation, twice in the past six months (date of visits must be listed on the prior authorization request), or member must have been determined to be dependent on systemic steroids to prevent serious exacerbations; and
9. Both the prior authorization request form and statement of medical necessity form must be submitted for processing.

Xolair® (Omalizumab) for Chronic Idiopathic Urticaria Approval Criteria:

1. Member must be 12 years of age or older; and
2. Other forms of urticaria must be ruled out; and
3. Other potential causes of urticaria must be ruled out; and
4. Member must have an Urticaria Activity Score (UAS) greater than or equal to 16; and
5. Prescriber must be an allergist, immunologist, dermatologist, or be an advanced care practitioner with a supervising physician that is an allergist, immunologist, or dermatologist; and
6. Member has tried and failed to obtain relief from other treatments including the following trials within the last six months (member must fail all classes unless contraindicated):
    a. At least two different H1-antihistamine trials for a minimum duration of two weeks each:
        i. One trial must be a second generation antihistamine dosed four times the maximum FDA dose; and
        ii. One trial must be tried in combination with an H2-antihistamine; and

b. A 4-week trial of a leukotriene receptor antagonist in combination with a 4-week trial of doxepin dosed 10mg to 50mg daily; and

7. Initial dosing will only be approved at a dose of 150mg every four weeks. If the 150mg dose yields inadequate results, then the dose may be increased to 300mg every four weeks.

Utilization of Xolair® (Omalizumab): Fiscal Year 2015

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	15	72	$203,305.20	$2,823.68	$100.35	265	2,026
2015	13	82	$274,689.70	$3,349.87	$119.43	330	2,300
% Change	**-13.30%**	**13.90%**	**35.10%**	**18.60%**	**19.00%**	**24.50%**	**13.50%**
Change	**-2**	**10**	**$71,384.50**	**$526.19**	**$19.08**	**65**	**274**

*Total number of unduplicated members.

Fiscal Year 2015 Utilization of Xolair® (Omalizumab): Medical Claims

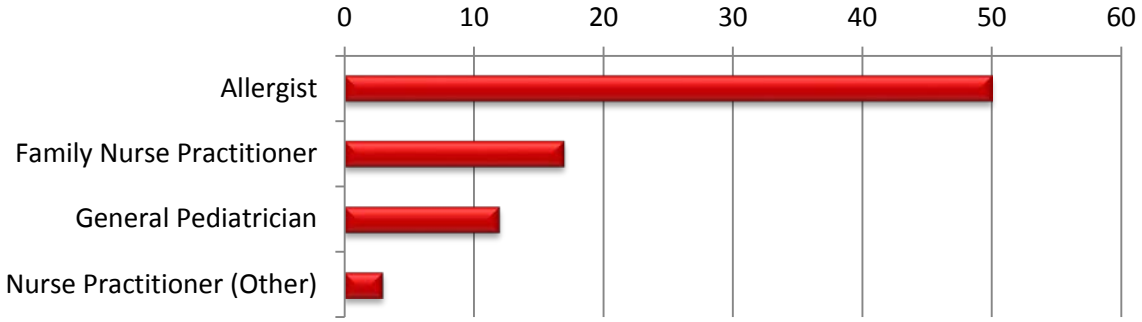
*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
9	71	$194,494.50	$2,739.36	7,050

*Total number of unduplicated members.

Demographics of Members Utilizing Xolair® (Omalizumab)

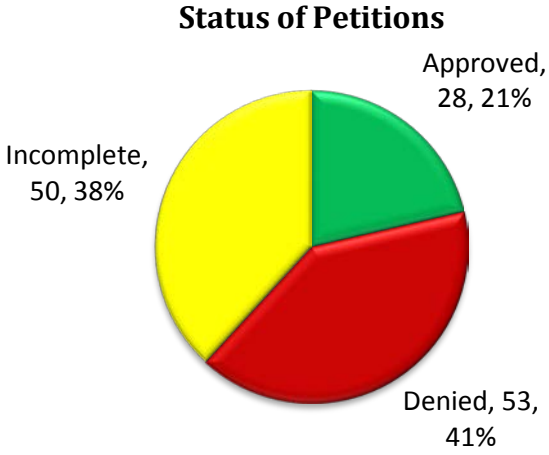
Demographics could not be provided due to the small number of members utizilizing Xolair® (omalizumab).

Top Prescriber Specialties of Xolair® (Omalizumab) by Number of Claims



Prior Authorization of Xolair® (Omalizumab)

There were 131 prior authorizations submitted for Xolair® (omalizumab) during fiscal year 2015. The following chart shows the status of the submitted petitions.



Market News and Updates[1]

Medication in the Pipeline:

- **Nucala® (Mepolizumab):** In June 2015, the FDA Pulmonary Allergy Drugs Advisory Committee voted unanimously to support approval for GlaxoSmithKline's mepolizumab for add-on maintenance treatment in patients aged 18 years or older with severe eosinophilic asthma. Mepolizumab is a humanized monoclonal antibody that prevents IL-5 from binding to receptors on eosinophils. This leads to a decrease in eosinophil levels in blood, tissue, and sputum. The dosing is 100mg given via a subcutaneous injection every four weeks. GlaxoSmithKline is anticipating a final decision on approval by the FDA in late 2015.

Recommendations

The College of Pharmacy does not recommend any changes to the current prior authorization criteria of Xolair® (omalizumab) at this time.

[1]GlaxoSmithKline PLC Press Release: GSK announces outcome of US FDA Advisory Committee recommending approval of mepolizumab for the treatment of adults with severe asthma. Available online at: https://www.gsk.com/en-gb/media/press-releases/2015/gsk-announces-outcome-of-us-fda-advisory-committee-recommending-approval-of-mepolizumab-for-the-treatment-of-adults-with-severe-asthma/. Last revised 6/11/2015. Last accessed 9/23/15.

Appendix O

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

FDA NEWS RELEASE

For Immediate Release: September 17th, 2015

FDA approves new drug to treat schizophrenia and bipolar disorder

The U.S. Food and Drug Administration today approved Vraylar (cariprazine) capsules to treat schizophrenia and bipolar disorder in adults.

Schizophrenia is a chronic, severe and disabling brain disorder affecting about one percent of Americans. Typically, symptoms are first seen in adults younger than 30 years of age and include hearing voices or seeing things that are not there, believing other people are reading their minds or controlling their thoughts, and being suspicious or withdrawn.

Bipolar disorder, also known as manic-depressive illness, is another brain disorder that causes unusual shifts in mood, energy, activity levels and the ability to carry out day-to-day tasks. The symptoms of bipolar disorder include alternating periods of depression and high, irritable mood, increased activity and restlessness, racing thoughts, talking fast, impulsive behavior and a decreased need for sleep.

The efficacy of Vraylar in treating schizophrenia was demonstrated in 1,754 participants in three six-week clinical trials. In each of the trials, Vraylar was shown to reduce the symptoms of schizophrenia compared to placebo.

The efficacy of Vraylar in treating bipolar disorder was shown in three three-week clinical trials of 1,037 participants. Vraylar was shown to reduce symptoms of bipolar disorder in each of the trials.

Vraylar and all other FDA-approved drugs used to treat schizophrenia and bipolar disorder have a Boxed Warning alerting health care professionals about an increased risk of death associated with the use of these drugs in older people with dementia-related psychosis. Neither Vraylar nor any other drug in this class is approved to treat such patients.

The most common side effects reported by participants receiving Vraylar in the clinical trials for schizophrenia were extrapyramidal symptoms, such as tremor, slurred speech, and involuntary muscle movements. The most common side effects reported by trial participants receiving Vraylar for bipolar disorder were extrapyramidal symptoms, the urge to move (akathisia), indigestion (dyspepsia), vomiting, drowsiness (somnolence) and restlessness.

Vraylar is manufactured by Forest Laboratories LLC of Jersey City, New Jersey and distributed by Actavis Pharma Inc. of Parsippany, New Jersey.

FDA NEWS RELEASE

For Immediate Release:September 22nd, 2015

FDA approves new oral medication to treat patients with advanced colorectal cancer

The U.S. Food and Drug Administration approved Lonsurf (a pill that combines two drugs, trifluridine and tipiracil) for patients with an advanced form of colorectal cancer who are no longer responding to other therapies.

Colorectal cancer is the third most common non-skin cancer in men and women in the U.S., according to the National Cancer Institute. While still the second leading cause of cancer-related death in the U.S., over the past 10 years the number of colorectal cancer cases and related deaths have decreased, due in part to screenings, such as colonoscopies.

Lonsurf is an oral medication intended to treat patients with advanced (metastatic) colorectal cancer who have been previously treated with chemotherapy and biological therapy.

The efficacy and safety of Lonsurf were evaluated in an international, randomized, double-blind study involving 800 patients with previously treated metastatic colorectal cancer.

Study participants received Lonsurf plus best supportive care, or placebo plus best supportive care until their disease worsened or side effects became intolerable. The primary endpoint of the study was overall survival and the secondary endpoint was progression-free survival. Patients treated with Lonsurf lived an average of 7.1 months compared to 5.3 months for those treated with placebo. On average, the time to disease progression was two months for patients on Lonsurf compared to 1.7 months for patients receiving placebo.

The most common side effects of treatment with Lonsurf are anemia, a decrease in infection-fighting white blood cells (neutropenia) or blood platelets (thrombocytopenia), physical weakness, extreme tiredness and lack of energy (fatigue), nausea, decreased appetite, diarrhea, vomiting, abdominal pain and fever.

The FDA recommends that health care providers obtain complete blood counts prior to starting each treatment cycle of Lonsurf and monitor patients throughout treatment, as Lonsurf may cause a severe decrease in blood cell and platelet production (myelosuppression).
Healthcare providers are also encouraged to advise women of potential risks to developing fetuses when taking Lonsurf. Women who are taking Lonsurf should not breastfeed.
Lonsurf is manufactured by Taiho Oncology Inc. in Princeton, New Jersey.

FDA NEWS RELEASE

For Immediate Release: September 25th, 2015

FDA approves two new drug treatments for diabetes mellitus

The U.S. Food and Drug Administration approved Tresiba (insulin degludec injection) and Ryzodeg 70/30 (insulin degludec/insulin aspart injection) to improve blood sugar (glucose) control in adults with diabetes mellitus.
According to the Centers for Disease Control and Prevention, approximately 21 million people in the United States have been diagnosed with diabetes. Over time, diabetes increases the risk of serious health complications, including heart disease, blindness, nerve and kidney damage. Improvement in blood sugar control can reduce the risk of some of these long-term complications.
Tresiba is a long-acting insulin analog indicated to improve glycemic control in adults with type 1 and 2 diabetes mellitus. Dosing of Tresiba should be individualized based on the patient's needs. Tresiba is administered subcutaneously once daily at any time of day.
The efficacy and safety of Tresiba used in combination with mealtime insulin for the treatment of patients with type-1 diabetes were evaluated in two 26-week and one 52-week active-controlled clinical trials involving 1,102 participants exposed to Tresiba. The efficacy and safety of Tresiba used in combination with mealtime insulin or used as add-on to common background oral antidiabetic drugs for the treatment of patients with type-2 diabetes were evaluated in four 26-week and two 52-week active-controlled clinical trials involving 2,702 participants exposed to Tresiba. In participants with type 1 and 2 diabetes who had inadequate blood sugar control at trial entry, treatment with Tresiba provided reductions in HbA1c in line with reductions achieved with other, previously approved long-acting insulin.
Ryzodeg 70/30 is a mixture of insulin degludec, a long-acting insulin analog, and insulin aspart, a rapid-acting human insulin analog. It is indicated to improve glycemic control in adults with diabetes mellitus.
The efficacy and safety of Ryzodeg 70/30 used in combination with mealtime insulin for the treatment of patients with type 1 diabetes were evaluated in one 26-week active controlled clinical trial involving 362 participants exposed to Ryzodeg 70/30. The efficacy and safety of Ryzodeg 70/30 administered once or twice daily for the treatment of patients with type 2 diabetes were evaluated in four active controlled 26-week clinical trials involving 998 participants exposed to Ryzodeg 70/30. In participants with type 1 and 2 diabetes who had inadequate blood sugar control at trial entry, treatment with Ryzodeg 70/30 provided reductions in HbA1c equivalent to reductions achieved with other, previously approved long-acting or pre-mixed insulin.
Tresiba and Ryzodeg should not be used in those who have increased ketones in their blood or urine (diabetic ketoacidosis). Patients or caregivers should monitor blood glucose in all patients treated with insulin. Insulin regimens should be modified cautiously and only under medical supervision. Tresiba and Ryzodeg may cause hypoglycemia, which can be life-threatening. Patients should be monitored more closely with changes to insulin dosage, co-administration of other glucose-lowering medications, meal pattern, physical activity, and in patients with renal impairment or hepatic impairment or hypoglycemia unawareness.
Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin.
The most common adverse reactions associated with Tresiba and Ryzodeg in clinical trials were hypoglycemia, allergic reactions, injection site reactions, pitting at the injection site (lipodystrophy), itching, rash, edema, and weight gain.
Tresiba and Ryzodeg are manufactured by Novo Nordisk in Plainsboro, New Jersey.

FDA NEWS RELEASE

For Immediate Release: October 2nd, 2015

FDA approves Keytruda for advanced non-small cell lung cancer

First drug approved in lung cancer for patients whose tumors express PD-L1

The U.S. Food and Drug Administration granted accelerated approval for Keytruda (pembrolizumab) to treat patients with advanced (metastatic) non-small cell lung cancer (NSCLC) whose disease has progressed after other treatments and with tumors that express a protein called PD-L1. Keytruda is approved for use with a companion diagnostic, the PD-L1 IHC 22C3 pharmDx test, the first test designed to detect PD-L1 expression in non-small cell lung tumors.

Lung cancer is the leading cause of cancer death in the United States, with an estimated 221,200 new diagnoses and 158,040 deaths in 2015, according to the National Cancer Institute. NSCLC is the most common type of lung cancer.

Keytruda works by targeting the cellular pathway known as PD-1/PD-L1 (proteins found on the body's immune cells and some cancer cells). By blocking this pathway, Keytruda may help the body's immune system fight the cancer cells. In 2014, Keytruda was approved to treat patients with advanced melanoma following treatment with ipilimumab, a type of immunotherapy. Another drug, Opdivo (nivolumab), manufactured by Bristol-Meyers Squibb, also targets the PD-1/PD-L1 pathway and was approved to treat squamous non-small cell lung cancer (a certain kind of NSCLC) in 2015.

The safety of Keytruda was studied in 550 patients with advanced NSCLC. The most common side effects of Keytruda included fatigue, decreased appetite, shortness of breath or impaired breathing (dyspnea) and cough. Keytruda also has the potential to cause severe side effects that result from the immune system effect of Keytruda (known as "immune-mediated side effects").

The effectiveness of Keytruda for this use was demonstrated in a subgroup of 61 patients enrolled within a larger multicenter, open-label, multi-part study. The subgroup consisted of patients with advanced NSCLC that progressed following platinum-based chemotherapy or, if appropriate, targeted therapy for certain genetic mutations (ALK or EGFR). This subgroup also had PD-L1 positive tumors based on the results of the 22C3 pharmDx diagnostic test. Study participants received 10 mg/kg of Keytruda every two or three weeks. The major outcome measure was overall response rate (percentage of patients who experienced complete and partial shrinkage of their tumors). Tumors shrank in 41 percent of patients treated with Keytruda and the effect lasted between 2.1 and 9.1
months.

In the 550 study participants with advanced NSCLC, severe immune-mediated side effects occurred involving the lungs, colon and hormone-producing glands. Other uncommon immune-mediated side effects were rash and inflammation of blood vessels (vasculitis). Women who are pregnant or breastfeeding should not take Keytruda because it may cause harm to a developing fetus or newborn baby. Across clinical studies, a disorder in which the body's immune system attacks part of the peripheral nervous system (Guillain-Barre Syndrome) also occurred.

The FDA granted Keytruda breakthrough therapy designation for this indication because Merck demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies. The drug also received priority review status, which is granted to drugs that, at the time the application was submitted, have the potential to be a significant improvement in safety or effectiveness in the treatment of a serious condition.

Keytruda was approved under the agency's accelerated approval program, which allows the approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials. An improvement in survival or disease-related symptoms in patients being treated with Keytruda has not yet been established.

Keytruda is marketed by Merck & Co., based in Whitehouse Station, New Jersey and the PD-L1 IHC 22C3 pharmDx diagnostic test is marketed by Dako North America Inc. in Carpinteria, California.

Safety Announcements

FDA Drug Safety Communication: FDA revises label of diabetes drug canagliflozin (Invokana, Invokamet) to include updates on bone fracture risk and new information on decreased bone mineral density

[9-10-15] The FDA has strengthened the warning for the type 2 diabetes medicine canagliflozin (Invokana, Invokamet) related to the increased risk of bone fractures and added new information about decreased bone mineral density. Bone mineral density relates to the strength of a person's bones. To address these safety concerns, they added a new Warning and Precaution and revised the Adverse Reactions section of the Invokana and Invokamet drug labels.

Health care professionals should consider factors that contribute to fracture risk prior to starting patients on canagliflozin. Patients should talk to their health care professionals about factors that may increase their risk for bone fracture. Patients should not stop or change their diabetes medicines without first talking to their health care professional.
Canagliflozin is a prescription medicine used with diet and exercise to lower blood sugar in adults with type 2 diabetes. It belongs to a class of drugs called sodium-glucose cotransporter-2 (SGLT2) inhibitors. Untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. Canagliflozin lowers blood sugar by causing the kidneys to remove sugar from the body through the urine. It is available as a single-ingredient product under the brand name Invokana and also in combination with the diabetes medicine metformin under the brand name Invokamet.
Information about the risk of bone fractures was already in the Adverse Reactions section of the drug label at the time of canagliflozin's approval. Based on updated information about bone fractures from several clinical trials, we revised the drug label and added a new Warning and Precaution. The additional data confirm the finding that fractures occur more frequently with canagliflozin than placebo, which is an inactive treatment. Fractures can occur as early as 12 weeks after starting the drug. In the clinical trials, when trauma occurred prior to a fracture, it was usually minor, such as falling from no more than standing height.
In addition, we have added new information about the risk of decreased bone mineral density to the canagliflozin label. A clinical trial that we required the manufacturer of canagliflozin to conduct evaluated changes to bone mineral density over two years in 714 elderly individuals and showed that canagliflozin caused greater loss of bone mineral density at the hip and lower spine than a placebo. This new safety information has been added to the Adverse Reactions section of the drug label.
We are continuing to evaluate the risk of bone fractures with other drugs in the SGLT2 inhibitor class, including dapagliflozin (Farxiga, Xigduo XR) and empagliflozin (Jardiance, Glyxambi, Synjardy), to determine if additional label changes or studies are needed. We urge health care professionals and patients to report side effects involving canagliflozin or other SGLT2 inhibitors to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA modifies monitoring for neutropenia associated with schizophrenia medicine clozapine; approves new shared REMS program for all clozapine medicines

[9-15-15] The FDA is making changes to the requirements for monitoring, prescribing, dispensing, and receiving the schizophrenia medicine clozapine, to address continuing safety concerns and current knowledge about a serious blood condition called severe neutropenia. Severe neutropenia is a dangerously low number of neutrophils, white blood cells that help fight infections. Severe neutropenia can be life-threatening.
Treatment with clozapine may improve the symptoms of schizophrenia in patients who do not respond adequately to standard antipsychotic treatments. Symptoms of schizophrenia include hearing voices, seeing things that are not there, and being suspicious or withdrawn. Clozapine is also effective in reducing the risk of repeated suicidal behavior in patients with schizophrenia or schizoaffective disorder. We previously communicated safety information associated with clozapine in February 2011.
There are two parts to the changes in the requirements for treating patients with clozapine. First, we have clarified and enhanced the prescribing information for clozapine that explains how to monitor patients for neutropenia and manage clozapine treatment. Second, we approved a new, shared risk evaluation and mitigation strategy (REMS) called the Clozapine REMS Program. The revised prescribing information and the Clozapine REMS Program will improve monitoring and management of patients with severe neutropenia. The shared REMS is also expected to reduce the burden and possible confusion related to having separate registries for individual clozapine medicines. The requirements to monitor, prescribe, dispense, and receive all clozapine medicines are now incorporated into the Clozapine REMS Program. The Clozapine REMS Program replaces the six existing clozapine registries maintained by individual clozapine manufacturers. The shared REMS requires prescribers, pharmacies, and patients to enroll in a single centralized program. Patients who are currently treated with clozapine will be automatically transferred to the Clozapine REMS Program. In order to prescribe and dispense clozapine, prescribers and pharmacies will be required to be certified in the Clozapine REMS Program according to a specific transition schedule starting *October 12, 2015*.
The monitoring recommendations for neutropenia caused by clozapine treatment have changed. Clozapine can decrease the number of neutrophils in the blood, in some cases causing severe neutropenia. As described in the revised clozapine prescribing information, and in the Clozapine REMS Program,

neutropenia will be monitored by the absolute neutrophil count (ANC) only, rather than in conjunction with the white blood cell count. Moreover, in the Clozapine REMS Program, the requirements for ANC are being modified so that patients will be able to continue on clozapine treatment with a lower ANC, a change that will allow continued treatment for a greater number of patients. In addition, patients with benign ethnic neutropenia (BEN), who previously were not eligible for clozapine treatment, will now be able to receive the medicine. The revised prescribing information facilitates prescribers' ability to make individualized treatment decisions if they determine that the risk of psychiatric illness is greater than the risk of recurrent severe neutropenia, especially in patients for whom clozapine may be the antipsychotic of last resort.
We urge health care professionals, patients, and caregivers to report side effects involving clozapine medicines to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA evaluating the risks of using the pain medicine tramadol in children aged 17 and younger

[9-21-15] The U.S. Food and Drug Administration (FDA) is investigating the use of the pain medicine tramadol in children aged 17 years and younger, because of the rare but serious risk of slowed or difficult breathing. This risk may be increased in children treated with tramadol for pain after surgery to remove their tonsils and/or adenoids. We are evaluating all available information and will communicate our final conclusions and recommendations to the public when our review is complete.
Tramadol is not FDA-approved for use in children; however, data show it is being used "off-label" in the pediatric population. Health care professionals should be aware of this and consider prescribing alternative FDA-approved pain medicines for children.
Parents and caregivers of children taking tramadol who notice any signs of slow or shallow breathing, difficult or noisy breathing, confusion, or unusual sleepiness should stop tramadol and seek medical attention immediately by taking their child to the emergency room or calling 911. Parents and caregivers should talk with their child's health care professional if they have any questions or concerns about tramadol or other pain medicines their child is taking.
Treating pain in children is important because it can lead to faster recoveries and fewer complications. Untreated pain can potentially result in long-term physical and psychological consequences. There are other pain medicines available that do not have this side effect of slowed or difficult breathing associated with tramadol and are FDA-approved for use in children.
Tramadol is a specific type of narcotic medicine called an opioid that is approved to treat moderate to moderately severe pain in adults. It is available under the brand names Ultram, Ultram ER, Conzip, and also as generics. Tramadol is also available in combination with the pain reliever acetaminophen under the brand name Ultracet and as generics.
In the body, tramadol is converted in the liver to the active form of the opioid, called O-desmethyltramadol. Some people have genetic variations that cause tramadol to be converted to the active form of the opioid faster and more completely than usual. These people, called ultra-rapid metabolizers, are more likely to have higher-than-normal amounts of the active form of the opioid in their blood after taking tramadol, which can result in breathing difficulty that may lead to death. Recently, a 5-year-old child in France experienced severely slowed and difficult breathing requiring emergency intervention and hospitalization after taking a single prescribed dose of tramadol oral solution for pain relief following surgery to remove his tonsils and adenoids. The child was later found to be an ultra-rapid metabolizer and had high levels of O-desmethyltramadol in his body.
We urge health care professionals, parents, and caregivers to report side effects involving tramadol to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA cautions about dose confusion and medication error with antibacterial drug Avycaz (ceftazidime and avibactam)

[9-22-15] The FDA is warning health care professionals about the risk for dosing errors with the intravenous antibacterial drug Avycaz (ceftazidime and avibactam) due to confusion about the drug strength displayed on the vial and carton labels. Avycaz was initially approved with the vial and carton labels displaying the individual strengths of the two active ingredients (i.e., 2 gram/0.5 gram); however, the product is dosed based on the sum of the active ingredients (i.e., 2.5 gram). To prevent medication errors, we have

revised the labels to indicate that each vial contains Avycaz 2.5 gram, equivalent to ceftazidime 2 gram and avibactam 0.5 gram.
Avycaz is approved for intravenous administration to treat complicated infections in the urinary tract, or in combination with the antibacterial drug metronidazole to treat complicated infections in the abdomen in patients with limited or no alternative treatment options. Antibacterial drugs work by killing or stopping the growth of bacteria that can cause illness.
Since Avycaz's approval in February 2015, we have received reports of three medication error cases related to confusion on how the strength was displayed on the Avycaz vial and carton labels. Two cases stated that the errors occurred during preparation of the dose in the pharmacy. The third case described concern about the potential for confusion because the strength displayed for Avycaz differs from how the strength is displayed for other beta-lactam/beta-lactamase antibacterial drugs. Based on the information provided in the reports, we are aware that at least one of the patients received a higher-than-intended dose of Avycaz. No adverse events were reported.
We urge health care professionals and patients to report side effects and medication errors involving Avycaz to the FDA MedWatch program.

Current Drug Shortages Index (as of October 5th, 2015):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Aprepitant (Emend) Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluoxymesterone (Androxy) Tablets, USP	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***

L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam (Keppra) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Memantine Hydrochloride (Namenda) XR Capsules	***Currently in Shortage***
Meropenem for Injection, USP	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets	***Currently in Shortage***
Metoprolol Injection	***Currently in Shortage***
Mometasone Furoate Monohydrate (Nasonex)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nebivolol (BYSTOLIC) Tablets	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***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***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trace Elements	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***