Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday
January 13, 2016
4 pm

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

# *The University of Oklahoma*

*Health Sciences Center*

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS


MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

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

DATE: January 4, 2016

Note: The DUR Board will meet at 4:00p.m. The meeting will be held at 4345 N Lincoln Blvd.

*Enclosed are the following items related to the January meeting.*
*Material is arranged in order of the agenda.*

**Call to Order**

**Public Comment Forum**

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

**Update on Medication Coverage Authorization Unit/SoonerPsych Program Update – Appendix B**

**Action Item – Vote to Prior Authorize Daklinza™ (Daclatasvir) and Technivie™ (Ombitasvir/Paritaprevir/ Ritonavir) – Appendix C**

**Action Item – Vote to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate) – Appendix D**

**Action Item – Vote to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-filgrastim), and Zarxio™ (Filgrastim-sndz) – Appendix E**

**Action Item – Vote to Prior Authorize Aggrenox® (Aspirin/Dipyridamole Extended-Release) – Appendix F**

**Action Item – Vote to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) – Appendix G**

**Action Item – Vote to Prior Authorize Stiolto™ Respimat® (Tiotropium Bromide/Olodaterol), Arnuity™ Ellipta® (Fluticasone Furoate), Utibron™ Neohaler® (Indacaterol/Glycopyrrolate), Seebri™ Neohaler® (Glycopyrrolate), & Nucala® (Mepolizumab) – Appendix H**

**Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Migranal® (Dihydroergotamine Mesylate Nasal Spray) – Appendix I**

**30-Day Notice to Prior Authorize Strensiq™ (Asfotase Alfa) – Appendix J**

**Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Varubi™ (Rolapitant) – Appendix K**

**30-Day Notice to Prior Authorize Cortisporin® and Pediotic® (Neomycin/Polymyxin B/Hydrocortisone Otic) – Appendix L**

**Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Duopa™**

**(Carbidopa/Levodopa Enteral Suspension) and Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) – Appendix M**

**30-Day Notice to Prior Authorize Xuriden™ (Uridine Triacetate) – Appendix N**

**Annual Review of Testosterone Products – Appendix O**

**Action Item – Election of the Drug Utilization Review Board 2016-2017 Officers – Appendix P**

**FDA and DEA Updates – Appendix Q**

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

**Adjournment**

# Oklahoma Health Care Authority

**Drug Utilization Review Board**
**(DUR Board)**
**Meeting – January 13, 2016 @ 4:00 p.m.**

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

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## 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. December 16, 2015 DUR Minutes – Vote
B. December 16, 2015 DUR Recommendations Memorandum

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:
**4. Update on Medication Coverage Authorization Unit/SoonerPsych Program Update – See Appendix B**
A. Medication Coverage Activity for December 2015
B. Pharmacy Help Desk Activity for December 2015
C. SoonerPsych Program Update

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:
**5. Action Item – Vote to Prior Authorize Daklinza™ (Daclatasvir) and Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) – See Appendix C**
A. Indication(s)
B. College of Pharmacy Recommendations

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:
**6. Action Item – Vote to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate) – See Appendix D**
A. Indication(s)
B. College of Pharmacy Recommendations

Items to be presented by Dr. Adams, Dr. Muchmore, Chairman:
**7. Action Item – Vote to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-filgrastim), and Zarxio™ (Filgrastim-sndz) – See Appendix E**
A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Adams, Dr. Muchmore, Chairman:
**8. Action Item – Vote to Prior Authorize Aggrenox® (Aspirin/Dipyridamole Extended-Release) – See Appendix F**
A. Introduction
B. College of Pharmacy Recommendations

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

**9. Action Item – Vote to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) – See Appendix G**

A. Indication(s)
B. College of Pharmacy Recommendations

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

**10. Action Item – Vote to Prior Authorize Stiolto™ Respimat® (Tiotropium Bromide/Olodaterol), Arnuity™ Ellipta® (Fluticasone Furoate), Utibron™ Neohaler® (Indacaterol/Glycopyrrolate), Seebri™ Neohaler® (Glycopyrrolate), & Nucala® (Mepolizumab) – See Appendix H**

A. Introduction
B. College of Pharmacy Recommendations

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

**11. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Migranal® (Dihydroergotamine Mesylate Nasal Spray) – See Appendix I**

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Migranal® (dihydroergotamine mesylate nasal spray) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Migraine Medications
H. Utilization Details of Dihydroergotamine Products

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

**12. 30-Day Notice to Prior Authorize Strensiq™ (Asfotase Alfa) – See Appendix J**

A. Overview
B. Strensiq™ (asfotase alfa) Product Summary
C. College of Pharmacy Recommendations

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

**13. Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Varubi™ (Rolapitant) – See Appendix K**

A. Current Prior Authorization Criteria
B. Utilization of Anti-Emetic Medications
C. Prior Authorization of Anti-Emetic Medications
D. Market News and Updates
E. Varubi™ (rolapitant) Product Summary
F. Cost Comparison
G. College of Pharmacy Recommendations
H. Utilization Details of Anti-Emetic Medications

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

**14. 30-Day Notice to Prior Authorize Cortisporin® and Pediotic® (Neomycin/Polymyxin B/ Hydrocortisone Otic) – See Appendix L**

A. Current Prior Authorization Criteria
B. Utilization of Cortisporin® and Pediotic® Otic
C. Market News and Updates
D. College of Pharmacy Recommendations

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

**15. Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Duopa™ (Carbidopa/Levodopa Enteral Suspension) and Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) – See Appendix M**

A. Current Prior Authorization Criteria
B. Utilization of Parkinson's Disease Medications
C. Prior Authorization of Parkinson's Disease Medications
D. Market News and Updates
E. Duopa™ (carbidopa/levodopa enteral suspension) Product Summary
F. Rytary™ (carbidopa/levodopa extended-release capsules) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Parkinson's Disease Medications

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

**16. 30-Day Notice to Prior Authorize Xuriden™ (Uridine Triacetate) – See Appendix N**

A. Overview
B. Xuriden™ (uridine triacetate) Product Summary
C. College of Pharmacy Recommendations

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

**17. Annual Review of Testosterone Products – See Appendix O**

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

Items to be presented by Dr. Muchmore, Chairman:

**18. Action Item – Election of the Drug Utilization Review Board 2016-2017 Officers – See Appendix P**

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

**19. FDA and DEA Updates – See Appendix Q**

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

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

A. Growth Hormone
B. Makena® (hydroxyprogesterone caproate)
C. Gout Medications/Mitigare™ (colchicine capsules)/Zurampic® (lesinurad)
D. Gonadotropin Releasing Hormones
E. Multiple Sclerosis Medications
F. Northera™ (droxidopa)
G. Seizure Medications/Spritam® (levetiracetam)
H. Solaraze® (diclofenac gel)
I. Ulcerative Colitis and Crohn's Disease Oral Medications

***Future business subject to change.**

**21. Adjournment**

# Appendix A

**OKLAHOMA HEALTH CARE AUTHORITY**
**DRUG UTILIZATION REVIEW BOARD MEETING**
**MINUTES OF MEETING OF DECEMBER 16, 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 |
| Tammy Lambert, Ph.D.; Postdoctoral Research Fellow | | x |
| Carol Moore, Pharm.D.; Clinical Pharmacist | | x |
| Brandy Nawaz, Pharm.D.; Clinical Pharmacist | x | |
| Leslie Robinson, D.Ph.; PA Coordinator | | x |
| Ashley Teel, Pharm.D.; Clinical Pharmacist | x | |
| Jacquelyn Travers, Pharm.D.; Academic Detailing Pharmacist | | x |
| Graduate Students: Christina Bulkley, Pharm.D. | | x |
| David George, Pharm.D. | | x |
| Timothy Pham, Pharm.D. | x | |

| OKLAHOMA HEALTH CARE AUTHORITY STAFF: | PRESENT | ABSENT |
|---|---|---|
| Marlene Asmussen, R.N.; Population Care Management Director | | x |
| Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm | x | |
| Kelli Brodersen, Marketing Coordinator | | x |
| Nico Gomez, Chief Executive Officer | x | |
| Ed Long, Chief Communications Officer | x | |
| Sylvia Lopez, M.D.; FAAP; Chief Medical Officer | | x |
| Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director | x | |
| Rebecca Pasternik-Ikard, 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: | | |
|---|---|---|
| Melvin Nwamadi, Abbott | Jim McKay, Sandoz | John Michael Thomas, BMS |
| Reginald Lavendar, Abbott | Clint Degner, Novatis | Rick Ulasewich, DSI |
| Gay Thomas, BMS | Mai Duong, Novartis | Ken Skipmore, Alexion |
| Erica Brumleve, GSK | David Williams, Allergan | Nima Nabavi, Novo Nordisk |
| Jason Schweir, Amgen | Desiree Gendron, BMS | Toby Thompson, Pfizer |
| Doug Wood, Viiv | M Patty Laster, Astellas | Kyle Nettlingham, Family Discount |
| John Zaiger, Sandoz | Quynh Chau Doan, AbbVie | Donna Erwin, Otsuka |
| Jeff Knappen, Allergan | Jim Chapman, AbbVie | Jeffrey Stewart, Foster Corner Drug |
| Jon Maguire, GSK | Ron Cain, Pfizer | Terry McCurren, Otsuka |
| David Large, Supernus Pharma | Avani Patel, Pfizer | Patrick Harvey, Walgreens |
| Dave Hibbard, Teva | Sean Seago, Merck | Brent Hilderbrand, Gilead |
| Jonathan Cramer, Teva | Marc Parker, Sunovion | Aaron Shaw, BI |
| Brian Maves, Pfizer | Jim Fowler, AstraZeneca | Eric Leonard, Astellas |
| Sherry Crowe, Novartis | Michele Puyear, Gilead | |

| PRESENT FOR PUBLIC COMMENT: | |
|---|---|
| Jim McKay | Sandoz |
| Mai Duong | Novartis |
| Quynh Chau Doan | AbbVie |
| Dave Hibbard | Teva |
| John Michael Thomas | BMS |
| Michele Puyear | Gilead Sciences |

**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. 19 SPEAKER: JIM MCKAY**
**2B: AGENDA NO. 15 & 22 SPEAKER: MAI DUONG**
**2C: AGENDA NO. 15 & 18 SPEAKER: QUYNH CHAU DOAN**
**2D: AGENDA NO. 21 SPEAKER: DAVE HIBBARD**
**2E: AGENDA NO. 18 SPEAKER: JOHN MICHAEL THOMAS**
**2F: AGENDA NO. 18 SPEAKER: MICHELE PUYEAR**

**ACTION: NONE REQUIRED**

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

**3A: OCTOBER 14, 2015 DUR MINUTES – VOTE**
**3B: OCTOBER 14, 2015 DUR RECOMMENDATIONS MEMORANDUM**
**3C: NOVEMBER 11, 2015 DUR RECOMMENDATIONS MEMORANDUM**

Materials included in agenda packet; presented by Dr. Muchmore

Ms. Varalli-Claypool requested agenda item number 5 be updated to reflect she did not make a motion for approval.

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

**ACTION: NONE REQUIRED**

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

**4A: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2015**

**4B: PHARMACY HELP DESK ACTIVITY FOR OCTOBER 2015**

**4C: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2015**

**4D: PHARMACY HELP DESK ACTIVITY FOR NOVEMBER 2015**

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NO ACTION REQUIRED**

**AGENDA ITEM NO. 5:** **VOTE TO PRIOR AUTHORIZE IBRANCE® (PALBOCICLIB)**

**5A: INTRODUCTION**

**5B: COLLEGE OF PHARMACY RECOMMENDATIONS**

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

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 6:** **VOTE TO PRIOR AUTHORIZE ORALAIR® (SWEET VERNAL, ORCHARD, PERENNIAL RYE, TIMOTHY, & KENTUCKY BLUE GRASS MIXED POLLENS ALLERGEN EXTRACT)**

**6A: INDICATION(S)**

**6B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented Dr. Teel

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 7:** **VOTE TO PRIOR AUTHORIZE DYLOJECT™ (DICLOFENAC SODIUM)**

**7A: INTRODUCTION**

**7B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Hsu

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 8:** **VOTE TO PRIOR AUTHORIZE OMIDRIA® (PHENYLEPHRINE/KETOROLAC INJECTION)**

**8A: INDICATION(S)**

**8B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Hsu

Dr. Muchmore recommends expanding criteria

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 9:** **VOTE TO UPDATE CRITERIA FOR XGEVA® (DENOSUMAB)**

**9A: INDICATION(S)**

**9B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Hsu

D. Hardzog-Britt moved to approve; seconded by Ms. Varalli-Claypool

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 10:** **VOTE TO PRIOR AUTHORIZE DARAPRIM® (PYRIMETHAMINE)**

**10A: INTRODUCTION**

**10B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Adams

Dr. Rhymer moved to approve; seconded by Dr. Garton
**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE MOVANTIK™ (NALOXEGOL), VIBERZI™ (ELUXADOLINE), & XIFAXAN® (RIFAXIMIN)**
**11A: INDICATION(S)**
**11B: COLLEGE OF PHARMACY RECOMMENDATIONS**
Materials included in agenda packet; presented by Dr. Adams
Dr. Rhymer moved to approve; seconded by Dr. Garton
**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 12: VOTE TO PRIOR AUTHORIZE KEVEYIS™ (DICHLORPHENAMIDE)**
**12A: INDICATION(S)**
**12B: COLLEGE OF PHARMACY RECOMMENDATIONS**
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Winegardner moved to approve; seconded by Dr. Harrell
**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 13: VOTE TO PRIOR AUTHORIZE PRAMOSONE® (HYDROCORTISONE/PRAMOXINE TOPICAL CREAM AND LOTION) & ENSTILAR® (CALCIPOTRIENE/BETAMETHASONE DIPROPIONATE FOAM)**
**13A: INDICATION(S)**
**13B: COLLEGE OF PHARMACY RECOMMENDATIONS**
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Varalli-Claypool
**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 14: VOTE TO PRIOR AUTHORIZE CAYSTON® (AZTREONAM INHALATION) & KITABIS™ PAK (TOBRAMYCIN INHALATION)**
**14A: INDICATION(S)**
**14B: 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. 15: VOTE TO PRIOR AUTHORIZE COSENTYX® (SECUKINUMAB)**
**15A: INDICATION(S)**
**15B: COLLEGE OF PHARMACY RECOMMENDATIONS**
Materials included in agenda packet; presented by Dr. Holderread
Dr. Winegardner moved to approve; seconded by Dr. Rhymer
**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 16: VOTE TO PRIOR AUTHORIZE TETRACYCLINE CAPSULES, MINOCYCLINE TABLETS, OFLOXACIN TABLETS, & MOXIFLOXACIN TABLETS**
**16A: INTRODUCTION**
**16B: COLLEGE OF PHARMACY RECOMMENDATIONS**
Materials included in agenda packet; presented by Dr. Holderread
Dr. Harrell moved to approve; seconded by Dr. Rhymer
**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 17:</u> VOTE TO UPDATE CRITERIA FOR XIAFLEX® (COLLAGENASE CLOSTRIDIUM HISTOLYTICUM)**

**17A: INDICATION(S)**

**17B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Holderread

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

**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 18:</u> ANNUAL REVIEW OF HEPATITIS C MEDICATIONS & 30-DAY NOTICE TO PRIOR AUTHORIZE DAKLINZA™ (DACLATASVIR) & TECHNIVIE™ (OMBITASVIR/PARITAPREVIR/ RITONAVIR)**

**18A: INTRODUCTION**

**18B: CURRENT PRIOR AUTHORIZATION CRITERIA**

**18C: UTILIZATION OF HEPATITIS C MEDICATIONS**

**18D: PRIOR AUTHORIZATION OF HEPATITIS C MEDICATIONS**

**18E: MARKET NEWS AND UPDATES**

**18F: REGIMEN COMPARISON**

**18G: OTHER STATES' COVERAGE OF DIRECT ACTING ANTIVIRALS**

**18H: PRODUCT SUMMARIES**

**18I: COLLEGE OF PHARMACY RECOMMENDATIONS**

**18J: UTILIZATION DETAILS OF HEPATITIS C MEDICATIONS**

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**<u>AGENDA ITEM NO. 19:</u> ANNUAL REVIEW OF GRANULOCYTE COLONY-STIMULATING FACTORS (G-CSFs) & 30-DAY NOTICE TO PRIOR AUTHORIZE NEULASTA® (PEGFILGRASTIM), GRANIX® (TBO-FILGRASTIM), & ZARXIO™ (FILGRASTIM-SNDZ)**

**19A: INTRODUCTION**

**19B: UTILIZATION OF G-CSFs**

**19C: PRIOR AUTHORIZTION OF G-CSFs**

**19D: MARKET NEWS AND UPDATES**

**19E: PRODUCT SUMMARIES**

**19F: COST COMPARISON RATIOS: G-CSFs**

**19G: COLLEGE OF PHARMACY RECOMMENDATIONS**

**19H: UTILIZATION DETAILS OF G-CSFs**

Materials included in agenda packet; presented by Dr. Adams

**ACTION: NONE REQUIRED**

**<u>AGENDA ITEM NO. 20:</u> 30-DAY NOTICE TO PRIOR AUTHORIZE AGGRENOX® (ASPIRIN/ DIPYRIDAMOLE EXTENDED-RELEASE)**

**20A: AGGRENOX® (ASPIRIN/DIPYRIDAMOLE ER) PRODUCT SUMMARY**

**20B: AGGRENOX® (ASPIRIN/DIPYRIDAMOLE ER) COST UPDATE**

**20C: AGGRENOX® (ASPIRIN/DIPYRIDAMOLE ER) COST COMPARISON**

**20D: UTILIZATION DETAILS OF AGGRENOX® (ASPIRIN/DIPYRIDAMOLE ER)**

**20E: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Adams

**ACTION: NONE REQUIRED**

**<u>AGENDA ITEM NO. 21:</u> ANNUAL REVIEW OF HFA RESCUE INHALERS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PROAIR® RESPICLICK (ALBUTEROL SULFATE INHALATION POWDER)**

**21A: CURRENT PRIOR AUTHORIZATION CRITERIA**

**21B: UTILIZATION OF HFA RESCUE INHALERS**
**21C: PRIOR AUTHORIZATION OF HFA RESCUE INHALERS**
**21D: MARKET NEWS AND UPDATES**
**21E: PROAIR® RESPICLICK (ALBUTEROL SULFATE INHALATION POWDER) PRODUCT SUMMARY**
**21F: COLLEGE OF PHARMACY RECOMMENDATIONS**
**21G: UTILIZATION DETAILS OF HFA RESCUE INHALERS**
Materials included in agenda packet; presented by Dr. Nawaz
**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 22: ANNUAL REVIEW OF MAINTENANCE ASTHMA & CHRONIC OBSTRUCTIVE PULMONARY DISEASE MEDICATIONS & 30-DAY NOTICE TO PRIOR AUTHORIZE STIOLTO™ RESPIMAT® (TIOTROPIUM BROMIDE/OLODATEROL), ARNUITY™ ELLIPTA® (FLUTICASONE FUROATE), UTIBRON™ NEOHALER® (INDACATEROL/GLYCOPYRROLATE), SEEBRI™ NEOHALER® (GLYCOPYRROLATE), & NUCALA® (MEPOLIZUMAB)**
**22A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**22B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS**
**22C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS**
**22D: MARKET NEWS AND UPDATES**
**22E: PRODUCT SUMMARIES**
**22F: NEW INDICATIONS**
**22G: COLLEGE OF PHARMACY RECOMMENDATIONS**
**22H: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS**
Materials included in agenda packet; presented by Dr. Nawaz
**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 23: ANNUAL REVIEW OF ORAL ANTI-FUNGAL MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NOXAFIL® (POSACONAZOLE) AND CRESEMBA® (ISAVUCONAZONIUM SULFATE)**
**23A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**23B: UTILIZATION OF ORAL ANTI-FUNGALS**
**23C: PRIOR AUTHORIZATION OF ORAL ANTI-FUNGALS**
**23D: MARKET NEWS AND UPDATES**
**23E: PRODUCT SUMMARIES**
**23F: COLLEGE OF PHARMACY RECOMMENDATIONS**
**23G: UTILIZATION DETAILS OF ORAL ANTI-FUNGALS**
Materials included in agenda packet; presented by Dr. Hsu
**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 24: ANNUAL REVIEW OF FIBROMYALGIA MEDICATIONS**
**24A: CURRENT PRIOR AUTHORIZATION CRITERIA**
**24B: UTILIZATION OF FIBROMYALGIA MEDICATIONS**
**24C: PRIOR AUTHORIZATION OF FIBROMYALGIA MEDICATIONS**
**24D: MARKET NEWS AND UPDATES**
**24E: COLLEGE OF PHARMACY RECOMMENDATIONS**
**24F: UTILIZATION DETAILS OF FIBROMYALGIA MEDICATIONS**
Materials included in agenda packet; presented by Dr. Hsu
Dr. Muchmore requested members also try gabapentin in addition to duloxetine before approval of pregabalin for diabetic neuropathy.
Dr. Winegardner moved to approve; seconded by Dr. Rhymer
**ACTION: MOTION CARRIED**

**<u>AGENDA ITEM NO. 25:</u>** **FDA AND DEA UPDATES**
Materials included in agenda packet; presented by Dr. Cothran
**ACTION:** **NONE REQUIRED**

**<u>AGENDA ITEM NO. 26:</u>** **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**
**26A: ANTI-MIGRAINE MEDICATIONS/MIGRANAL® (DIHYDROERGOTAMINE NASAL SPRAY)**
**26B: ANTI-EMETIC MEDICATIONS/VARUBI™ (ROLAPITANT)**
**26C: GROWTH HORMONE**
**26D: RYTARY™ (CARBIDOPA/LEVODOPA EXTENDED-RELEASE CAPSULES) & DUOPA™ (CARBIDOPA/LEVODOPA ENTERAL SUSPENSION)**
**26E: TESTOSTERONE PRODUCTS**
**26F: XURIDEN™ (URIDINE TRIACETATE)**
**26G: STRENSIQ™ (ASFOTASE ALFA)**
**26H: CORTISPORIN® (NEOMYCIN/POLYMYXIN B/HYDROCORTISONE OTIC SUSPENSION)**
***FUTURE BUSINESS SUBJECT TO CHANGE.**
Materials included in agenda packet; presented by Dr. Holderread
**ACTION:** **NONE REQUIRED**

**<u>AGENDA ITEM NO. 27:</u>** **ADJOURNMENT**
The meeting was adjourned at 5:56 pm.

*The University of Oklahoma*

*Health Sciences Center*

**COLLEGE OF PHARMACY**

**PHARMACY MANAGEMENT CONSULTANTS**

# Memorandum

**Date:** December 17, 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 December 16, 2015

## Recommendation 1: Vote to Prior Authorize Ibrance® (Palbociclib)

MOTION CARRIED by unanimous approval.

**Ibrance® (Palbociclib) Approval Criteria:**

1. An FDA approved diagnosis of metastatic breast cancer for first-line use only; and
2. Member must be estrogen receptor (ER)-positive; and
3. Member must have negative expression of Human Epidermal Receptor Type 2 (HER2); and
4. Ibrance® must be used in combination with letrozole (for postmenopausal women only).

## Recommendation 2: Vote to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) with the following criteria:

**Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & 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.

## Recommendation 3: Vote to Prior Authorize Dyloject™ (Diclofenac Injection)

MOTION CARRIED by unanimous approval.

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 injection (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

## Recommendation 4: Vote to Prior Authorize Omidria® (Phenylephrine/ Ketorolac) Injection

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Omidria® (phenylephrine/ketorolac) with the following criteria:

**Omidria® (Phenylephrine/Ketorolac) Approval Criteria:**

1. An FDA approved diagnosis of preventing intraoperative miosis and reducing postoperative pain in patients undergoing cataract surgery or intraocular lens replacement; and
2. Prescriber must be an ophthalmologist.

## Recommendation 5: Vote to Update Criteria for Xgeva® (Denosumab) for Hypercalcemia of Malignancy

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of the criteria below for Xgeva® (denosumab) for the indication of hypercalcemia of malignancy.

**Xgeva® (Denosumab) Approval Criteria**:

1. An FDA approved indication of one of the following:
    a. Prevention of skeletal-related events in patients with bone metastases from solid tumors; or
    b. Treatment of adults and skeletally mature adolescents with giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity; or
        i. Prescriber must document that tumor is unresectable or that surgical resection is likely to result in severe morbidity.
    c. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.
        i. Member must have albumin-corrected calcium of greater than 12.5 mg/dL (3.1 mmol/L) despite treatment with intravenous bisphosphonate therapy in the last 30 days prior to initiation of Xgeva® therapy.

## Recommendation 6: Vote to Prior Authorize Daraprim® (Pyrimethamine)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 7: Vote to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), and Xifaxan® (Rifaximin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The addition of criteria for Relistor® (methylnaltrexone) for the new indication of opioid-induced constipation (OIC) in adults with chronic non-cancer pain
2. The prior authorization of Movantik™ (naloxegol)
3. The prior authorization of Viberzi™ (eluxadoline)
4. 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 two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10-14 consecutive days at the recommended dosing). Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure.
4. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
5. A quantity limit of 60 tablets for a 30 day supply will apply.

**Xifaxan® (Rifaximin) 200mg Approval Criteria:**

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

**Xifaxan® (Rifaximin) 550mg Approval Criteria:**

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

## Recommendation 8: Vote to Prior Authorize Keveyis™ (Dichlorphenamide)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Keveyis™ (dichlorphenamide) with the following criteria:

**Keveyis™ (Dichlorphenamide) Approval Criteria:**

1. An FDA approved indication for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, or related variants; and
2. Prescriber documentation that all non-pharmacological treatments failed including the following:
    a. Hyperkalemic periodic paralysis:
        i. Acute attacks can be aborted with sugar or mild exercise
        ii. Avoiding foods rich in potassium
        iii. Avoiding fasting
        iv. High-carbohydrate diet
        v. Avoiding strenuous activity
        vi. Avoiding prolonged cold exposure
    b. Hypokalemic periodic paralysis:
        i. Low-carbohydrate diet (avoiding carbohydrate loading)
        ii. Avoiding vigorous exercise (some mild attacks can be aborted by low level exercise)
3. Prescriber documentation of frequent and severe attacks requiring pharmacological treatment (at least one attack per week but no more than three attacks per day); and
4. A four-week trial within the last 90 days of acetazolamide in combination with
    a. Spironolactone or triamterene in hypokalemic periodic paralysis; or
    b. Hydrochlorothiazide in hyperkalemic periodic paralysis
5. A quantity limit of four tablets per day will apply.
6. Initial approvals will be for the duration of three months after which time compliance will be required for continued approval. Additionally, for continuation the prescriber must include information regarding reduced frequency or severity of attacks.

## Recommendation 9: Vote to Prior Authorize Pramosone® (Hydrocortisone/ Pramoxine Topical Cream and Lotion) and Enstilar® (Calcipotriene/ Betamethasone Dipropionate Foam)

MOTION CARRIED by unanimous approval.

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

1. Placement of Pramosone® (hydrocortisone acetate/pramoxine HCL) cream and lotion into Tier-2 of the low-potency category; and
2. Placement of Enstilar® foam (calcipotriene/betamethasone dipropionate foam) into Tier-2 of the medium/high to medium potency category; and
3. Move fluocinonide 0.05% solution and betamethasone dipropionate 0.05% (Diprosone®) ointment from Tier-2 to Tier-1 of the ultra-high to high potency category; and
4. Move diflorasone diacetate 0.05% (Apexicon®, Apexicon E®) cream and ointment, halobetasol propionate (Ultravate®) ointment, and clobetasol propionate 0.05%

(Temovate®) cream and ointment from Tier-1 to Tier-2 of the ultra-high to high potency category; and

5. Move hydrocortisone valerate 0.2% cream from Tier-1 to Tier-2 of the medium/high to high potency category; and
6. Move fluocinolone acetonide 0.01% (Synalar®, Derma-Smooth®, Derma-Smooth FS®) solution and oil from Tier-1 to Tier-2 of the low-potency category.

## Recommendation 10: Vote to Prior Authorize Cayston® (Aztreonam Inhalation) and Kitabis™ Pak (Tobramycin Inhalation)

MOTION CARRIED by unanimous approval.

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.

## Recommendation 11: Vote to Prior Authorize Cosentyx® (Secukinumab)

MOTION CARRIED by unanimous approval.

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.

| 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).

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.

**Tier-2 Approval Criteria:**

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

**Tier-3 Approval Criteria:**

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 medication and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or

3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 products.

**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.

## Recommendation 12: Vote to Prior Authorize Tetracycline Capsules, Minocycline Tablets, Ofloxacin Tablets, & Moxifloxacin Tablets

MOTION CARRIED by unanimous approval.

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

1. Remove the prior authorization on doxycycline monohydrate immediate-release capsules and tablets except on the 75mg capsules, 150mg capsules, and the 150mg tablets.
2. Prior authorize tetracycline 250mg and 500mg capsules with the following criteria:
   **Tetracycline 250mg and 500mg Oral Capsules Approval Criteria:**
    a. Approval requires a patient-specific, clinically significant reason why the member requires tetracycline and cannot use doxycycline or minocycline capsules and/or other cost effective therapeutic equivalent medication(s).
3. Prior authorize minocycline immediate-release tablets with the following criteria:
   **Minocycline Tablets Approval Criteria:**
    a. Approval requires a patient-specific, clinically significant reason why the member requires the immediate-release tablet formulation and cannot use the

immediate-release capsule formulation and/or other cost effective therapeutic equivalent medication(s).

Additionally, the College of Pharmacy recommends the following changes to the fluoroquinolone antibiotics category:

1. Place an age restriction of six years and younger on levofloxacin 25mg/mL oral solution, ciprofloxacin 250mg/mL oral suspension, and ciprofloxacin 500mg/mL oral suspension. Members older than six years of age would require a patient-specific, clinically significant reason why the oral tablet formulations cannot be used.
2. Prior authorize ofloxacin 400mg and moxifloxacin 400mg tablets with the following criteria:
   **Ofloxacin 400mg and Moxifloxacin 400mg Oral Tablets Approval Criteria:**
   a. Approval requires a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, and/or other cost effective therapeutic equivalent medication(s).
3. Prior authorize ciprofloxacin 100mg tablets with the following criteria:
   **Ciprofloxacin 100mg Oral Tablets Approval Criteria:**
   a. Approval requires a patient-specific, clinically significant reason why the member cannot use alternative strengths of ciprofloxacin tablets or levofloxacin tablets and/or other cost effective therapeutic equivalent medication(s).
4. Prior authorize ciprofloxacin 500mg and 1000mg extended-release tablets with the following criteria:
   **Ciprofloxacin 500mg and 1000mg Extended-Release Tablets Approval Criteria:**
   a. Approval requires a patient-specific, clinically significant reason why the member cannot use the immediate-release formulation of ciprofloxacin tablets, levofloxacin tablets, and/or other cost effective therapeutic equivalent medication(s).

## Recommendation 13: Vote to Update Criteria for Xiaflex® (Collagenase Clostridium Histolyticum)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following criteria for Xiaflex® (collagenase clostridium histolyticum) for the diagnosis of Peyronie's Disease:

**Xiaflex® (Collagenase Clostridium Histolyticum) Approval Criteria (Peyronie's Disease):**

1. A diagnosis of stable Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees and less than 90 degrees at the start of therapy; and
2. Member must be 18 years or older; and
3. Member must have pain outside the circumstances of intercourse that is refractory to other available treatments; and
4. Peyronie's plaques must not involve the penile urethra; and
5. Member must have intact erectile function (with or without the use of medications); and
6. Prescriber must be certified to administer Xiaflex® through the Xiaflex® REMS program; and
7. A maximum of 8 injection procedures will be approved.

**Recommendation 14: Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Daklinza™ (Daclatasvir) and Technivie™ (Ombitasvir/ Paritaprevir/Ritonavir)**

NO ACTION REQUIRED.

**Recommendation 15: Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) and 30-Day Notice to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-filgrastim), and Zarxio™ (Filgrastim-sndz)**

NO ACTION REQUIRED.

**Recommendation 16: 30-Day Notice to Prior Authorize Aggrenox® (Aspirin/Dipyridamole Extended-Release)**

NO ACTION REQUIRED.

**Recommendation 17: Annual Review of HFA Rescue Inhalers and 30-Day Notice to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder)**

NO ACTION REQUIRED.

**Recommendation 18: Annual Review of Maintenance Asthma & Chronic Obstructive Pulmonary Disease Medications & 30-Day Notice to Prior Authorize Stiolto™ Respimat® (Tiotropium Bromide/Olodaterol), Arnuity™ Ellipta® (Fluticasone Furoate), Utibron™ Neohaler® (Indacaterol/Glycopyrrolate), Seebri™ Neohaler® (Glycopyrrolate), & Nucala® (Mepolizumab)**

NO ACTION REQUIRED.

**Recommendation 19: Annual Review of Oral Anti-Fungals and 30-Day Notice to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate)**

NO ACTION REQUIRED.

**Recommendation 20: Annual Review of Fibromyalgia Medications**

MOTION CARRIED by unanimous approval.

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

**Lyrica® (Pregabalin) Approval Criteria (Diabetic Neuropathy Diagnosis):**

1. For the diagnosis of diabetic neuropathy, a trial of duloxetine and a trial of gabapentin or a patient-specific, clinically significant reason why duloxetine or gabapentin cannot be used must be provided.
2. Other criteria for Lyrica® (pregabalin) will continue to apply.
3. Clinical exceptions for Lyrica® (pregabalin) include:
    a. Diagnosis of seizures or postherpetic neuralgia

| Fibromyalgia Medications | | |
|---|---|---|
| **Tier-1** | **Tier-2*** | **Tier-3** |
| amitriptyline (Elavil®) | | milnacipran (Savella®) |
| cyclobenzaprine (Flexeril®) | | pregabalin (Lyrica®) |
| duloxetine (Cymbalta®) | | |
| fluoxetine (Prozac®) | | |
| tramadol (Ultram®) | | |

*Tier-2 will include supplemental rebated products. If no products rebate to Tier-2, Tier-2 will include the lowest cost Tier-3 product(s).

**Fibromyalgia Medications Tier-2 Approval Criteria**:

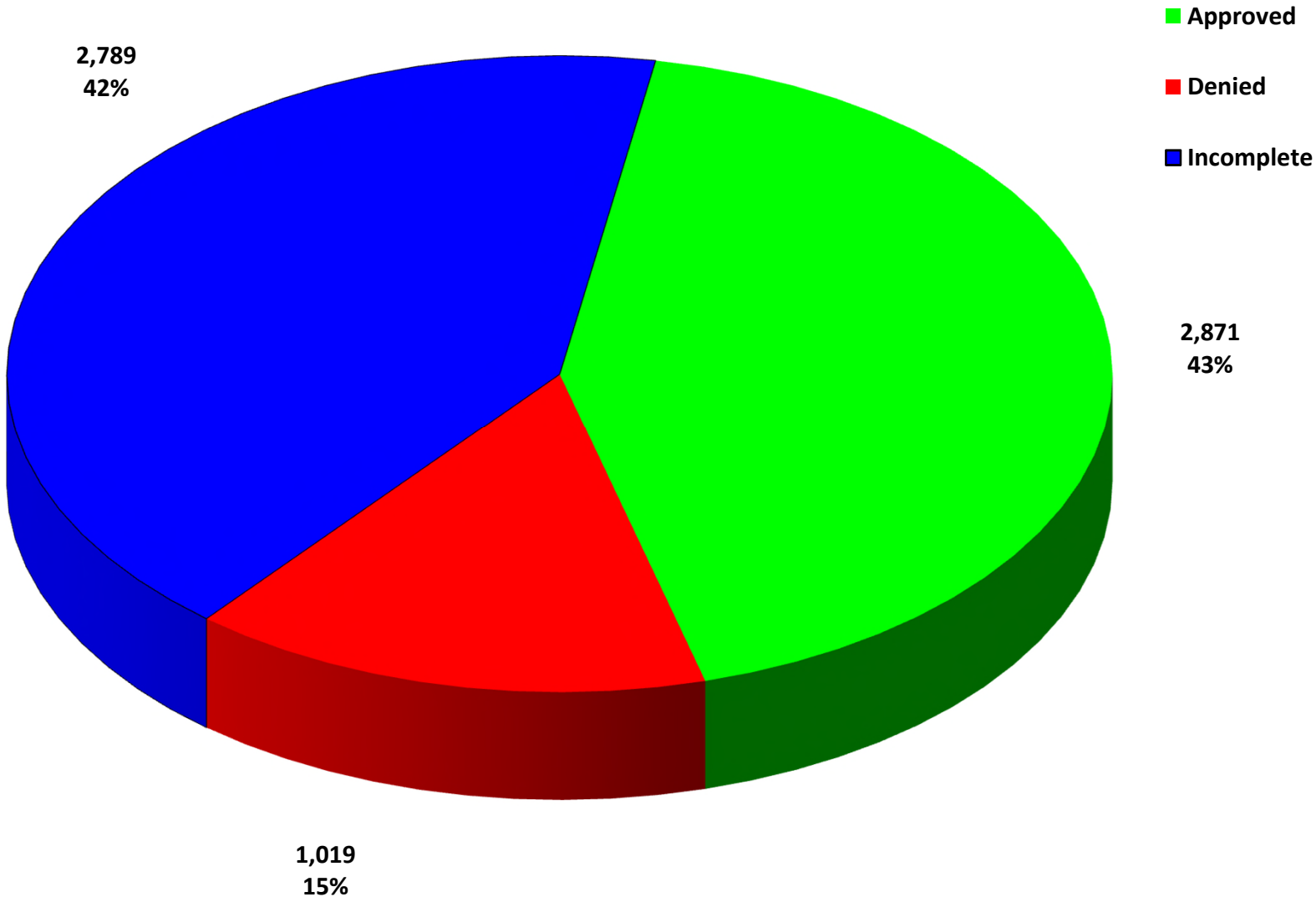
1. A documented, recent (within the last six months) trial of two Tier-1 medications (must include one trial with duloxetine) at least three weeks in duration that did not provide an adequate response or resulted in intolerable adverse effects; or
2. Contraindication(s) to all available lower tiered medications; or
3. Current stabilization on a Tier-2 medication.

**Fibromyalgia Medications Tier-3 Approval Criteria:**

1. A documented, recent (within the last six months) trial of two Tier-1 medications (must include one trial with duloxetine) and all available Tier-2 medications at least three weeks in duration that did not provide an adequate response or resulted in intolerable adverse effects; or
2. Contraindication(s) to all available lower tiered medications; or
3. Current stabilization on a Tier-3 medication.

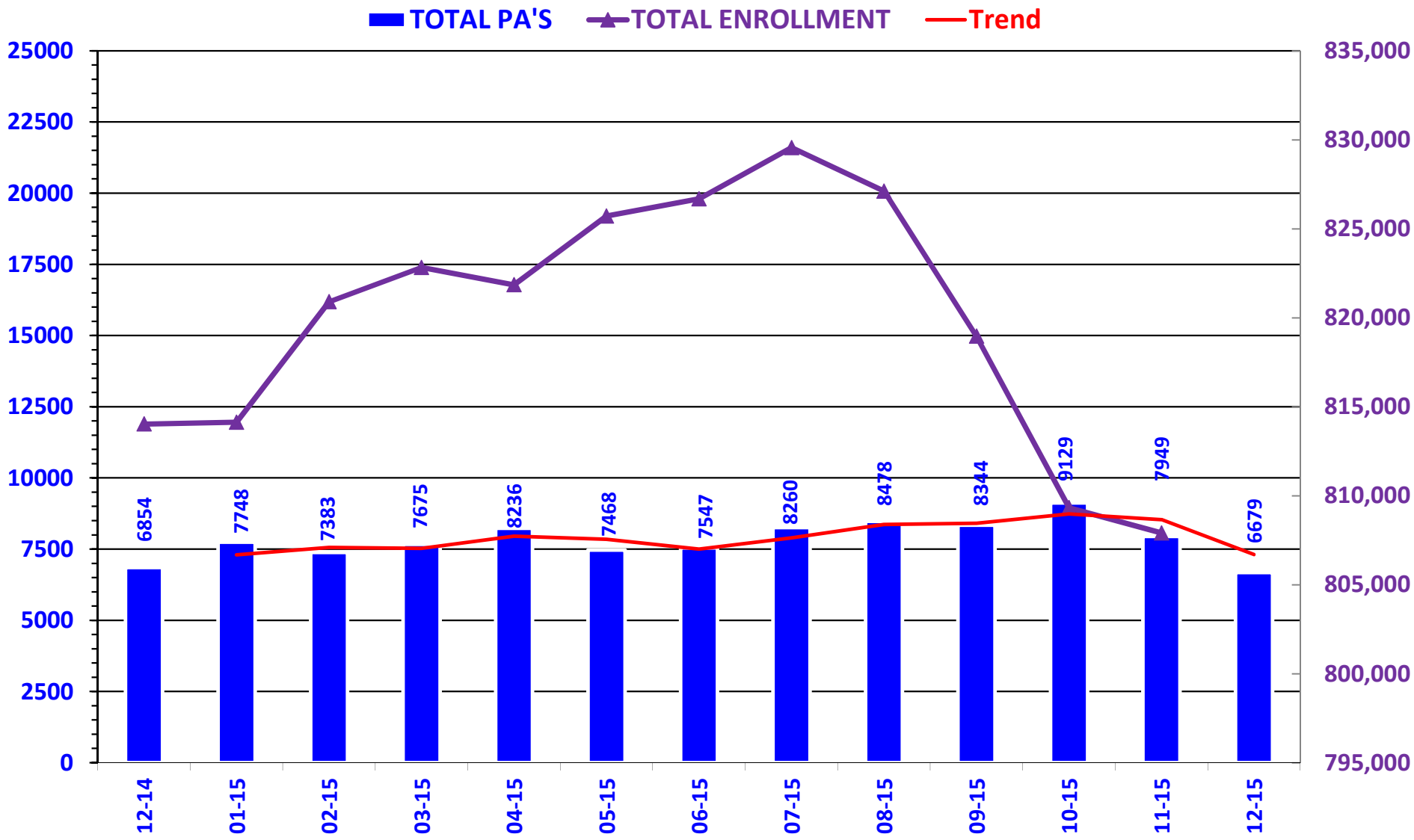
# Appendix B

# PRIOR AUTHORIZATION ACTIVITY REPORT: DECEMBER 2015



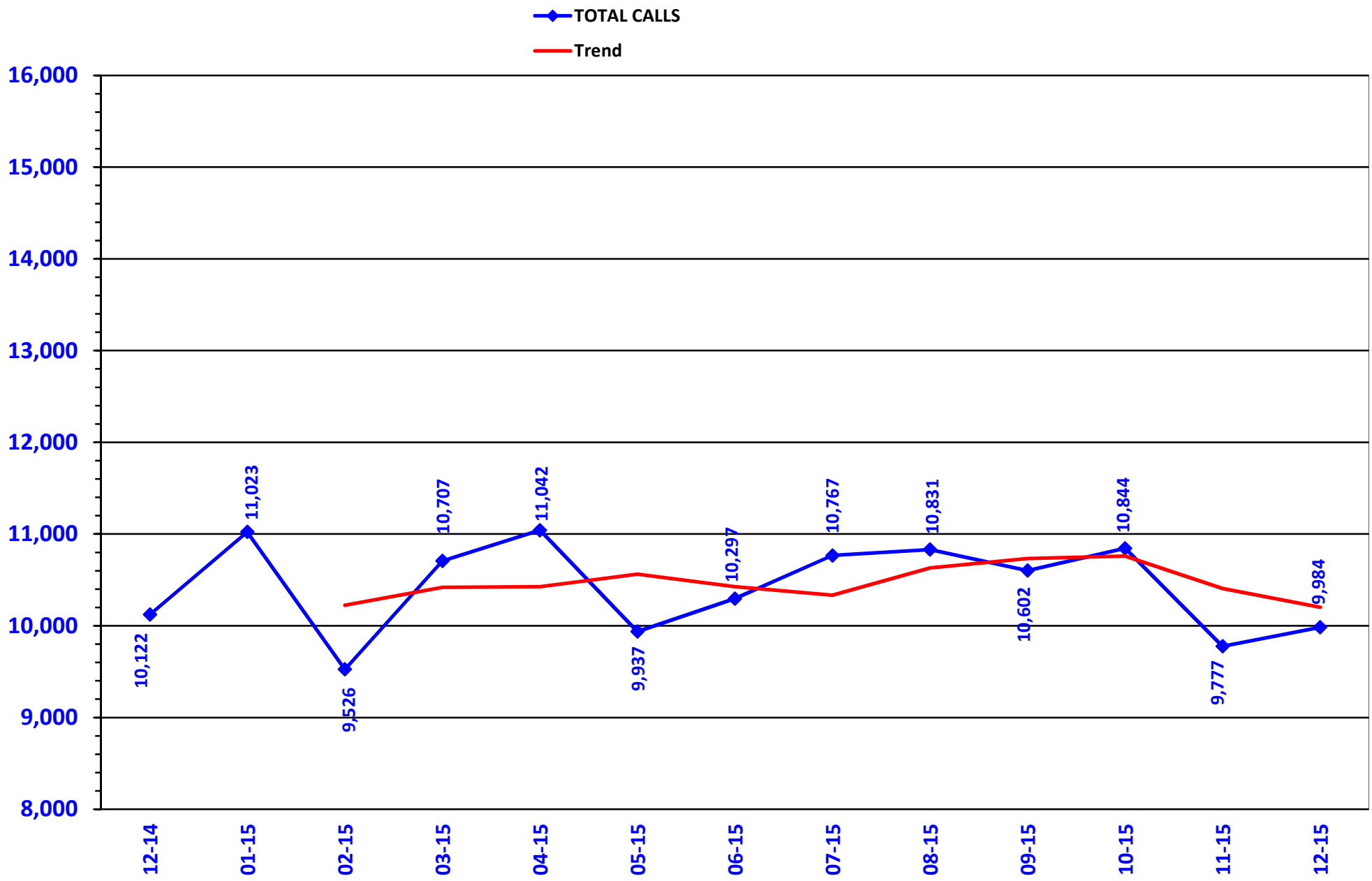

*PA totals include approved/denied/incomplete/overrides*

# PRIOR AUTHORIZATION REPORT: DECEMBER 2014 – DECEMBER 2015




*PA totals include approved/denied/incomplete/overrides*

# CALL VOLUME MONTHLY REPORT:
# DECEMBER 2014 – DECEMBER 2015



# Prior Authorization Activity

## 12/1/2015 Through 12/31/2015

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Advair/Symbicort/Dulera | 352 | 150 | 36 | 166 | 357 |
| Analgesic - NonNarcotic | 25 | 0 | 7 | 18 | 0 |
| Analgesic, Narcotic | 394 | 232 | 27 | 135 | 155 |
| Angiotensin Receptor Antagonist | 21 | 6 | 3 | 12 | 360 |
| Antiasthma | 102 | 30 | 22 | 50 | 333 |
| Antibiotic | 35 | 8 | 3 | 24 | 87 |
| Anticonvulsant | 78 | 26 | 12 | 40 | 359 |
| Antidepressant | 103 | 19 | 23 | 61 | 323 |
| Antidiabetic | 143 | 64 | 19 | 60 | 356 |
| Antifungal | 19 | 3 | 3 | 13 | 29 |
| Antihistamine | 185 | 154 | 6 | 25 | 357 |
| Antimigraine | 48 | 4 | 16 | 28 | 312 |
| Antiulcers | 193 | 41 | 61 | 91 | 120 |
| Anxiolytic | 66 | 40 | 6 | 20 | 267 |
| Atypical Antipsychotics | 532 | 234 | 53 | 245 | 335 |
| Biologics | 91 | 39 | 12 | 40 | 302 |
| Bladder Control | 38 | 9 | 12 | 17 | 333 |
| Blood Thinners | 140 | 89 | 10 | 41 | 329 |
| Botox | 26 | 21 | 2 | 3 | 319 |
| Calcium Channel Blockers | 10 | 5 | 0 | 5 | 99 |
| Cardiovascular | 71 | 33 | 9 | 29 | 348 |
| Cephalosporins | 10 | 5 | 0 | 5 | 10 |
| Chronic Obstructive Pulmonary Disease | 50 | 11 | 11 | 28 | 334 |
| Contraceptive | 19 | 16 | 1 | 2 | 316 |
| Dermatological | 93 | 20 | 45 | 28 | 116 |
| Diabetic Supplies | 447 | 220 | 24 | 203 | 225 |
| Endocrine & Metabolic Drugs | 72 | 55 | 3 | 14 | 132 |
| Erythropoietin Stimulating Agents | 24 | 15 | 2 | 7 | 113 |
| Fibromyalgia | 157 | 29 | 60 | 68 | 326 |
| Fish Oils | 12 | 4 | 2 | 6 | 361 |
| Gastrointestinal Agents | 112 | 24 | 35 | 53 | 129 |
| Glaucoma | 11 | 1 | 4 | 6 | 354 |
| Growth Hormones | 60 | 44 | 3 | 13 | 155 |
| Hepatitis C | 175 | 113 | 24 | 38 | 8 |
| HFA Rescue Inhalers | 41 | 18 | 2 | 21 | 360 |
| Insomnia | 56 | 11 | 15 | 30 | 145 |
| Insulin | 47 | 10 | 14 | 23 | 360 |
| Linzess, Amitiza, and Relistor | 86 | 14 | 31 | 41 | 214 |
| Multiple Sclerosis | 39 | 19 | 5 | 15 | 219 |
| Muscle Relaxant | 72 | 15 | 28 | 29 | 60 |
| Nasal Allergy | 105 | 11 | 23 | 71 | 265 |
| Neurological Agents | 80 | 55 | 7 | 18 | 358 |
| Nsaids | 171 | 23 | 54 | 94 | 307 |
| Ocular Allergy | 30 | 8 | 6 | 16 | 154 |
| Ophthalmic Anti-infectives | 21 | 3 | 5 | 13 | 11 |
| Osteoporosis | 18 | 5 | 7 | 6 | 357 |
| Other* | 242 | 49 | 58 | 135 | 249 |

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

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Otic Antibiotic | 31 | 3 | 4 | 24 | 7 |
| Pediculicide | 115 | 62 | 9 | 44 | 17 |
| Prenatal Vitamins | 15 | 1 | 0 | 14 | 178 |
| Statins | 48 | 10 | 7 | 31 | 360 |
| Stimulant | 883 | 436 | 78 | 369 | 337 |
| Suboxone/Subutex | 201 | 151 | 9 | 41 | 75 |
| Synagis | 127 | 47 | 42 | 38 | 105 |
| Testosterone | 45 | 14 | 14 | 17 | 346 |
| Topical Antifungal | 48 | 5 | 7 | 36 | 85 |
| Topical Corticosteroids | 60 | 0 | 13 | 47 | 0 |
| Vitamin | 69 | 28 | 25 | 16 | 315 |
| Pharmacotherapy | 115 | 109 | 0 | 6 | 267 |
| Emergency PAs | 0 | 0 | 0 | 0 | |
| **Total** | **6,679** | **2,871** | **1,019** | **2,789** | |
| | | | | | |
| **Overrides** | | | | | |
| Brand | 40 | 26 | 4 | 10 | 299 |
| Cumulative Early Refill | 3 | 2 | 1 | 0 | 180 |
| Diabetic Supplies | 3 | 3 | 0 | 0 | 138 |
| Dosage Change | 309 | 290 | 0 | 19 | 12 |
| High Dose | 1 | 1 | 0 | 0 | 54 |
| Ingredient Duplication | 30 | 22 | 0 | 8 | 8 |
| Lost/Broken Rx | 122 | 110 | 7 | 5 | 12 |
| NDC vs Age | 39 | 39 | 0 | 0 | 227 |
| Nursing Home Issue | 41 | 36 | 0 | 5 | 13 |
| Opioid Quantity | 8 | 7 | 1 | 0 | 131 |
| Other* | 14 | 13 | 1 | 0 | 11 |
| Quantity vs. Days Supply | 552 | 373 | 46 | 133 | 243 |
| STBS/STBSM | 13 | 12 | 0 | 1 | 50 |
| Stolen | 7 | 4 | 1 | 2 | 13 |
| Third Brand Request | 25 | 14 | 8 | 3 | 15 |
| **Overrides Total** | **1,193** | **940** | **67** | **186** | |
| **Total Regular PAs + Overrides** | **7,872** | **3,811** | **1,086** | **2,975** | |

| **Denial Reasons** | |
|---|---|
| Unable to verify required trials. | 2,440 |
| Does not meet established criteria. | 1,029 |
| Lack required information to process request. | 573 |

| **Other PA Activity** | |
|---|---|
| Duplicate Requests | 522 |
| Letters | 5,707 |
| No Process | 9 |
| Changes to existing PAs | 551 |
| Helpdesk Initiated Prior Authorizations | 671 |
| PAs Missing Information | 39 |

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

# SoonerPsych Program Update

**Oklahoma Health Care Authority**
**January 2016**

## Prescriber Mailing Summaries

The SoonerPsych program is an educational quarterly mailing to prescribers with members on atypical antipsychotic medications. Each mailing includes a gauge showing prescribers how their prescriptions compare to those of other SoonerCare prescribers of atypical antipsychotic medications regarding potential differences from evidence-based prescribing practices. Each mailing also includes an informational page with evidence-based material related to the mailing topic.

The SoonerPsych program has been using a "report card" format since April 2014. The following list includes details of previous SoonerPsych mailings processed during 2015 in the "report card" format.

- **Metabolic Monitoring: January 2015**
  - Inclusion Criteria: Prescribers were eligible if they had prescribed atypical antipsychotic medications for members whose recent twelve-month medical claims history lacked glucose testing. Prescribers were also eligible for inclusion if they had prescribed atypical antipsychotics for members with a diagnosis of hyperlipidemia whose recent twelve-month medical claims history lacked lipid testing.
  - Number of Prescribers and Patients Flagged: A total of 1,222 prescribers were flagged for having at least one member with missing metabolic monitoring while on atypical antipsychotic medications. These prescribers accounted for 8,238 flagged patients for missing metabolic monitoring.
  - Number of Prescribers and Members Included in the Mailing: A total of 200 prescribers were included in the mailing which included 1,308 patients flagged for missing metabolic monitoring.

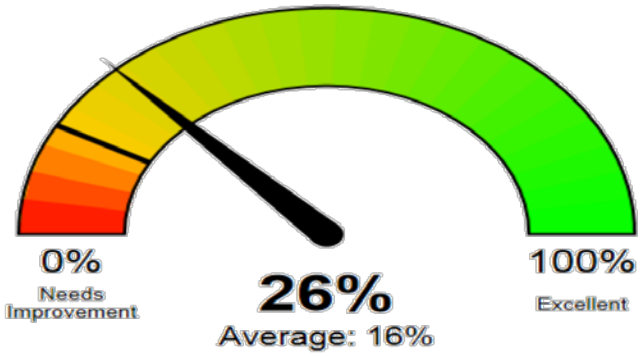
- **Diagnosis: April 2015**
  - Inclusion Criteria: Prescribers were eligible if they had prescribed atypical antipsychotic medications for members whose recent twelve-month medical claims history lacked a diagnosis with a strong indication for prescribing an antipsychotic medication.
  - Number of Prescribers and Patients Flagged: A total of 1,691 prescribers were flagged for having at least one patient without a target diagnosis. These prescribers had 16,416 flagged patients without a target diagnosis.
  - Number of Prescribers and Members Included in the Mailing: A total of 200 prescribers were included in the mailing which included 1,962 flagged patients without a target diagnosis.

- **Polypharmacy: July 2015**
  - Inclusion Criteria: Prescribers were eligible if they had prescribed atypical antipsychotics for members whose pharmacy claims history indicated concurrent use of two or more atypical antipsychotic medications for more than 90 days.
  - Number of Prescribers and Patients Flagged: A total of 1,309 prescribers were flagged for having at least one patient with polypharmacy. These prescribers had 10,282 patients flagged for polypharmacy.
  - Number of Prescribers and Members Included in the Mailing: A total of 200 prescribers were included in the mailing which included 5,062 patients flagged for polypharmacy.

- **Adherence: October 2015**
  - Inclusion Criteria: Prescribers were eligible if they had prescribed atypical antipsychotic medications for members whose proportion of days covered (PDC) or adherence was calculated as less than 80%.
  - Number of Prescribers and Patients Flagged: A total of 1,533 prescribers were flagged for having at least one member using an atypical antipsychotic medication and considered non-adherent. These prescribers accounted for 12,473 flagged patients considered non-adherent.
  - Number of Prescribers and Members Included in the Mailing: A total of 200 prescribers were included in the mailing which included 1,325 patients flagged for non-adherence.

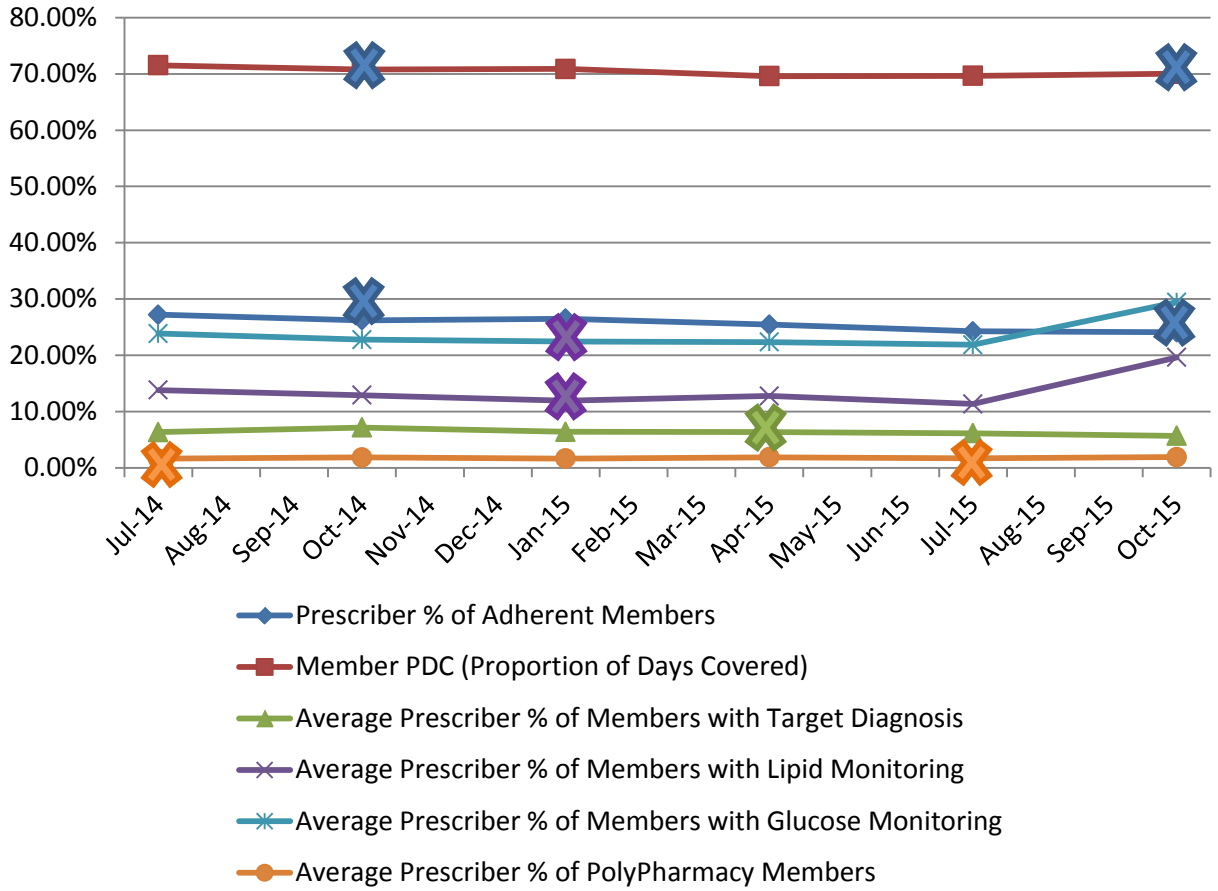
## Example Gauge

Each gauge includes the individual prescriber's performance in relation to the specific mailing topic as well as the average of other SoonerCare prescribers for comparison.



## SoonerPsych Trends

Each time a mailing is processed all modules or topics are tracked. The line graph below shows prescriber trends for each topic. Markers indicate when a mailing was processed. The line graph below depicts the percentage for all atypical antipsychotic SoonerCare prescribers and does not differentiate those prescribers who received a mailing and prescribers who did not receive a mailing.




The prescriber percent of adherent members and the member PDC experienced a slight increase after the adherence mailing was processed in October 2014 but has since declined.

The diagnosis mailing was first processed in April 2014 and again in April 2015. The average prescriber percent of members with a target diagnosis increased slightly in October 2014, but has declined.

The metabolic mailing was processed in January 2015. An increase was seen in the average prescriber percentage of members with lipid monitoring, however no increase was seen in the average prescriber percentage of members with glucose monitoring. Recently, a significant increase can be seen in both lipid and glucose monitoring as of October 2015.

The polypharmacy mailing was processed in July 2014 and again in July 2015. The average prescriber percent of members with polypharmacy increased slightly in October 2014 and again in October 2015 following the polypharmacy mailings.

## Conclusions

Most mailings appear to be effective in improving evidence-based care in the quarter immediately following the initial mailing for each topic, but then the effect of the intervention appears to decline over time. Educational mailings may be most effective in their initial round, with subsequent mailings having less effect on improvement in potential differences from generally accepted evidence-based prescribing practices. Consistently receiving evidence-based educational mailings reminds providers of evidence-based practices, and averts some potentially inappropriate prescribing.

The substantial increase in October 2015 in metabolic monitoring in SoonerCare members receiving antipsychotic medications does not correlate with a recent mailing. This increase may be a result of repeated mailing interventions, as well as prescribers being more aware of the need for metabolic monitoring in patients receiving atypical antipsychotic medications. The College of Pharmacy will continue to work with the Oklahoma Health Care Authority to improve educational mailings with the goal of improving the quality of care for SoonerCare members utilizing atypical antipsychotic medications.

# Appendix C

# Vote to Prior Authorize Daklinza™ (Daclatasvir) and Technivie™ (Ombitasvir/Paritaprevir/Ritonavir)

**Oklahoma Health Care Authority**
**January 2016**

## Indication(s)[1,2]

- Daklinza™ (daclatasvir) is a hepatitis C virus (HCV) NS5A inhibitor indicated for use with sofosbuvir for the treatment of chronic HCV genotype-3 infection.
  - Limitation of Use: Sustained virologic response (SVR) rates are reduced in patients with cirrhosis.
- Technivie™ (ombitasvir/paritaprevir/ritonavir) is a fixed dose combination of ombitasvir, a HCV NS5A inhibitor, paritaprevir, a HCV NS3/4A protease inhibitor, and ritonavir, a CYP3A inhibitor. Ombitasvir/paritaprevir/ritonavir is indicated in combination with ribavirin for the treatment of patients with genotype-4 chronic HCV infection without cirrhosis.

## Recommendations

The College of Pharmacy recommends the prior authorization of Daklinza™ (daclatasvir) and Technivie™ (ombitasvir/paritaprevir/ritonavir) with criteria similar to the other prior authorized hepatitis C medications (see criteria noted in red). Additionally, the College of Pharmacy recommends the changes noted in red to the Hepatitis C medications prior authorization category. The following table highlights the preferred regimens for each genotype in treatment-naïve members (alphabetical order).

| Genotype | Patient Factors | Preferred Regimen(s) |
|---|---|---|
| **Genotype-1** | | |
| **1** | Treatment naïve, non-cirrhotic | Harvoni® for 8 or 12 weeks<br>Sovaldi® + RBV + PEG IFN for 12 weeks<br>1a: Viekira Pak™ + RBV for 12 weeks<br>1b: Viekira Pak™ for 12 weeks |
| **1** | Treatment naïve, cirrhotic | Harvoni® for 12 weeks<br>Sovaldi® + RBV + PEG IFN for 12 weeks<br>1a: Viekira Pak™ + RBV for 24 weeks<br>1b: Viekira Pak™ + RBV for 12 weeks |
| **1** | Treatment experienced, non-cirrhotic | Harvoni® for 12 weeks<br>Sovaldi® + RBV + PEG IFN for 12 weeks<br>1a: Viekira Pak™ + RBV for 12 weeks<br>1b: Viekira Pak™ for 12 weeks |
| **1** | Treatment experienced, cirrhotic | Harvoni® + RBV for 12 weeks<br>Harvoni® for 24 weeks<br>Sovaldi® + RBV + PEG IFN for 12 weeks<br>1a: Viekira Pak™ + RBV for 24 weeks<br>1b: Viekira Pak™ + RBV for 12 weeks |

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

Not all regimens included are FDA approved.
All regimens are either FDA approved, recommended in AASLD/IDSA treatment guidance, or have study data indicating efficacy
RBV = Ribavirin PEG IFN = peginterferon alfa

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Harvoni® (sofosbuvir/ledipasvir), and Sovaldi® (sofosbuvir) are the preferred direct-acting antivirals for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination or Olysio® (simeprevir) alone for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira Pak™, Harvoni®, or Sovaldi® with peginterferon and ribavirin is not appropriate for the member.

**Daklinza™ (Daclatasvir) Approval Criteria:**

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-3**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Daklinza™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype and concomitant drug therapy will apply:
    a. **Genotype-3, treatment-naïve or treatment-experienced, without cirrhosis:**
        i. Daklinza™ 60mg with Sovaldi® for 12 weeks
    b. **Genotype-3, treatment-naïve or treatment-experienced, with cirrhosis:**
        i. Daklinza™ 60mg with Sovaldi® in combination with weight-based ribavirin for 12 weeks
    c. **Genotype-3, without cirrhosis, and concomitant use of moderate CYP3A inducer(s):**
        i. Daklinza™ 90mg with Sovaldi® 400mg for 12 weeks
        ii. Moderate Inducers: bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, and rifapentine
    d. **Genotype-3, without cirrhosis, and concomitant use of strong CYP3A inhibitors:**
        i. Daklinza™ 30mg with Sovaldi® for 12 weeks
        ii. Strong CYP3A inhibitors include the following: atazanavir/ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, and voriconazole
    e. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have decompensated cirrhosis; and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms

of non-hormonal birth control while on therapy and for six months after therapy completion; and

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

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

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-4**; and
3. Member must have a METAVIR fibrosis score of **F2** or **F3** (Technivie™ is not indicated in cirrhotic patients) or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Technivie™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype, cirrhosis status, and prior treatment status will apply:
    a. **Genotype-4, treatment-naïve and experienced, non-cirrhotic:**
        i. Technivie™ in combination with weight-based ribavirin for 12 weeks
    b. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and

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

**Harvoni® (Ledipasvir/Sofosbuvir) Approval Criteria:**

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

6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
   a. **Genotype-1:**
      i. **Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA less than 6 million IU/mL:**
         1. Harvoni® for 8 weeks
      ii. **Treatment-naïve with or without cirrhosis:**
         1. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA greater than 6 million IU/mL
         2. Harvoni® for 12 weeks
      iii. **Treatment-experienced without cirrhosis**
         1. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
         2. Harvoni® for 12 weeks
      iv. **Treatment-experienced with cirrhosis**
         1. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
         2. Harvoni® with weight-based ribavirin for 12 weeks
   b. **Genotype-4, Genotype-5, or Genotype-6:**
      i. **Treatment-naïve and treatment-experienced, with or without cirrhosis:**
         1. Harvoni® for 12 weeks
   c. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have decompensated cirrhosis; and
14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m$^2$); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for those on ribavirin); and
16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or

elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and

17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

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

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Viekira Pak™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, genotypic subtype, and cirrhosis will apply:
   a. **Genotype 1a, without cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 12 weeks
   b. **Genotype 1a, with cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 24 weeks
      ii. Viekira Pak™ with weight-based ribavirin for 12 weeks may be considered for some patients based on prior treatment history.
   c. **Genotype 1b, without cirrhosis:**
      i. Viekira Pak™ for 12 weeks
   d. **Genotype 1b, with cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 12 weeks
   e. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and

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

**Sovaldi™ (Sofosbuvir) Approval Criteria:**

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

6. Member must be eligible for ribavirin (RBV) or daclatasvir therapy. Approvals will not be granted for regimens without RBV or daclatasvir; and
7. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
8. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
9. The following regimens and requirements based on genotype, prior treatment experience, and cirrhosis status will apply:
    a. **Genotype 1:**
        i. **Treatment-naïve or experienced, non-cirrhotic or cirrhotic:**
            1. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
    b. **Genotype 2:**
        i. **Treatment-naïve, non-cirrhotic:**
            1. Sovaldi™ with weight-based ribavirin for 12 weeks
        ii. **Treatment-naïve, cirrhotic:**
            1. Sovaldi® with weight-based ribavirin for 12 or 16 weeks
        iii. **Treatment-experienced, non-cirrhotic or cirrhotic:**
            1. Sovaldi® with weight-based ribavirin for 16 weeks
            2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
    c. **Genotype 3:**
        i. **Treatment-naïve, non-cirrhotic**
            1. Daklinza™ with Sovaldi® for 12 weeks
            2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
            3. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)
        ii. **Treatment-naïve, cirrhotic**
            1. Daklinza™ with Sovaldi® and weight based ribavirin for 12 weeks
            2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
            3. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)
        iii. **Treatment-experienced, non-cirrhotic**
            1. Daklinza™ with Sovaldi® for 12 weeks
            2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
            3. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)
        iv. **Treatment-experienced, cirrhotic**
            1. Daklinza™ with Sovaldi® and weight based ribavirin for 12 weeks
            2. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
            3. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)
    d. **Genotype 4:**
        i. **Treatment-naïve or experienced, non-cirrhotic or cirrhotic:**
            1. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
    e. New regimens will apply as approved by the FDA. For regimens containing Olysio™ with Sovaldi® please refer to Olysio™ criteria.
10. Member must sign and submit the Hepatitis C Intent to Treat contract; and
11. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and

12. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
13. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
14. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
15. Member must not have decompensated cirrhosis; and
16. Female members must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin members); and
17. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, phenytoin, oxcarbazepine, tipranavir/ritonavir, didanosine or St. John's wort; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease.
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

**Olysio™ (Simeprevir) Approval Criteria:**

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic Hepatitis C genotype 1; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
5. Members with genotype 1a must be screened for the NS3 Q80K polymorphism prior to initiation of therapy. Approvals will not be granted for members with this polymorphism; and
6. Olysio™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
7. Olysio™ must be used as a component of a combination regimen. Olysio™ will be approved for combination therapy only.
8. The following regimens and requirements based on genotype, prior treatment experience, and cirrhosis status will apply
    a. **Genotype 1a and 1b:**

i. **Treatment-naïve, non-cirrhotic:**
    1. Olysio™ with Sovaldi™ +/- weight-based ribavirin for 12 weeks
ii. **Treatment-naïve, cirrhotic:**
    1. Olysio™ with Sovaldi™ +/- weight-based ribavirin for 24 weeks
iii. **Treatment-experienced, non-cirrhotic:**
    1. Olysio™ with Sovaldi™ +/- weight-based ribavirin for 12 weeks
iv. **Treatment-experienced, cirrhotic:**
    1. Olysio™ with Sovaldi™ +/- weight-based ribavirin for 24 weeks

b. New regimens will apply as approved by the FDA

9. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
10. Member must sign and submit the Hepatitis C Intent to Treat Contract; and
11. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
12. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
13. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
14. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
15. Member must not have decompensated cirrhosis; and
16. Female members must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin members); and
17. Member must not be taking the following medications: efavirenz, delavirdine, etravirine, nevirapine, ritanovir and any HIV protease inhibitor (boosted or not by ritanovir), rifampin, rifabutin, rifapentine, erythromycin, clarithromycin, telithromycin, carbamazepine, oxcarbazepine, phenobarbital, phenytoin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, dexamethasone, cisapride, didanosine, milk thistle, or St. John's wort; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity weight management, severe concurrent medical diseases such as but not limited to retinal disease or autoimmune thyroid disease.
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

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[1] Daklinza™ Product Information. Bristol-Myers Squibb Company. Available online at: http://packageinserts.bms.com/pi/pi_daklinza.pdf. Last revised 07/2015. Last accessed 01/06/2016.

[2] Technivie™ Product Information. AbbVie Inc. Available online at http://www.rxabbvie.com/pdf/technivie_pi.pdf. Last revised: 10/2015. Last accessed 01/06/2016.

# Appendix D

# Vote to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate)

**Oklahoma Health Care Authority**
**January 2016**

## Indication(s)[1,2]

**Noxafil® (Posaconazole)**

- The injection, delayed-release tablets, and oral suspension are indicated for prophylaxis of invasive Aspergillus and Candida infections in high-risk patients due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.
- The oral suspension is indicated for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole

**Cresemba® (Isavuconazonium Sulfate)**

- Invasive mucormycosis and invasive aspergillosis

## Recommendations

The College of Pharmacy recommends the prior authorization of Noxafil® (posaconazole) and Cresemba® (isavuconazonium sulfate) with the following criteria:

**Noxafil® (Posaconazole) Approval Criteria:**

1. An FDA approved diagnosis of one of the following:
    a. Prophylaxis of invasive *Aspergillus* and *Candida* infections in high-risk patients due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy; or
    b. Treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole; or
2. Treatment of invasive mucormycosis; or
3. Other appropriate diagnoses for which Noxafil® is not FDA approved may be considered with submission of a manual prior authorization; and
4. For the diagnosis of OPC, only the oral suspension may be used.

**Cresemba® (Isavuconazonium Sulfate) Approval Criteria:**

1. An FDA approved diagnosis of one of the following:
    a. Invasive aspergillosis
    b. Invasive mucormycosis
2. For the treatment of invasive aspergillosis, a patient-specific, clinically significant reason why voriconazole cannot be used must be provided.

[1] Noxafil® Package Insert. Merck Sharp & Dohme Corp. Available online at: http://medlibrary.org/lib/rx/meds/noxafil-1/. Last revised 7/28/2015. Last accessed 11/9/15.
[2] Cresemba® Package Insert. Astellas Pharma US, Inc. Available online at: http://medlibrary.org/lib/rx/meds/cresemba-1/. Last revised 8/27/2015. Last accessed 11/10/15.

# Appendix E

# Vote to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-filgrastim), and Zarxio™ (Filgrastim-sndz)

**Oklahoma Health Care Authority**
**January 2016**

## Introduction[1,2,3]

- **Neulasta® (pegfilgrastim)** is a pegylated derivative of Neupogen® (filgrastim). Pegfilgrastim is indicated for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy and for radiation injury of bone marrow following acute exposure of myelosuppressive radiation doses.
- **Granix® (tbo-filgrastim)** was approved prior to the abbreviated licensure pathway for biosimilar products and is only indicated for prophylaxis of severe neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy.
- **Zarxio™ (filgrastim-sndz)** is a biosimilar product for filgrastim and is indicated for prophylaxis of febrile neutropenia in patients with acute myeloid leukemia receiving induction or consolidation chemotherapy and in patients with non-myeloid malignancies who receive myeloablative chemotherapy followed by bone marrow transplantation or who receive myelosuppressive chemotherapy, for harvesting of peripheral blood stem cells, and for symptomatic chronic (severe) neutropenic disorder.

## Recommendations

The College of Pharmacy recommends the prior authorization of Neulasta® (pegfilgrastim), Granix® (tbo-filgrastim), and Zarxio™ (filgrastim-sndz) with the following criteria:

**Neulasta® (Pegfilgrastim), Granix® (Tbo-filgrastim), and Zarxio™ (Filgrastim-sndz) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Neupogen® (filgrastim).
3. Additional consideration for Neulasta® will be given for caregivers or members who cannot self-inject at home. The prescriber must provide specific documentation of the reason the caregiver or member cannot self-inject at home.

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[1] Neulasta® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/neulasta-1/. Last revised 12/1/14. Last accessed 10/27/15.
[2] Granix® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/granix/. Last revised 12/19/14. Last accessed 10/27/15.
[3] Zarxio™ Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/zarxio/. Last revised 8/11/15. Last accessed 10/27/15.

# Appendix F

# Vote to Prior Authorize Aggrenox®
# (Aspirin/Dipyridamole Extended-Release)

**Oklahoma Health Care Authority**
**January 2016**

## Introduction[1]

Aggrenox® is a combination antiplatelet agent that contains aspirin (25mg immediate-release (IR) sugar-coated tablet) and dipyridamole (200mg extended-release (ER) pellets) in each hard gelatin capsule. Aspirin/dipyridamole ER was FDA approved in 1999 and is indicated for the prophylaxis of recurrent thromboembolic stroke.

## Recommendations

The College of Pharmacy recommends the prior authorization of Aggrenox® (aspirin/dipyridamole ER) with the following criteria:

**Aggrenox® (Aspirin/Dipyridamole ER) Approval Criteria:**

1. An FDA approved indication for the prophylaxis of recurrent thromboembolic stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why member cannot use immediate-release dipyridamole and over-the-counter (OTC) aspirin in place of Aggrenox® must be provided.
4. A quantity limit of 60 capsules for a 30 day supply will apply.

[1] Aggrenox® Prescribing Information, Boehringer Ingelheim Pharmaceuticals, Inc. Available online at: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Aggrenox%20Caps/Aggrenox.pdf. Last revised 9/2012. Last accessed 11/12/15.

# Appendix G

# Vote to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder)

**Oklahoma Health Care Authority**
**January 2016**

## Indication(s)[1]

ProAir® RespiClick (albuterol sulfate inhalation powder) is a beta$_2$-adrenergic agonist indicated for treatment or prevention of bronchospasm in patients 12 years of age and older with reversible obstructive airway disease and prevention of exercise-induced bronchospasm in patients 12 years of age and older.

## Recommendations

The College of Pharmacy recommends the placement of ProAir® RespiClick (albuterol sulfate inhalation powder) into Tier-2 of the HFA Rescue Inhalers Product Based Prior Authorization (PBPA) category. Current criteria for this category will apply.

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

**Tier-2 HFA Rescue Inhalers Approval Criteria:**

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member cannot use all available Tier-1 medications.

| HFA Rescue Inhalers | |
|---|---|
| **Tier-1** | **Tier-2** |
| albuterol HFA (ProAir® HFA) | albuterol HFA (Ventolin® HFA) |
| albuterol HFA (Proventil® HFA) | levalbuterol HFA (Xopenex® HFA) |
| | **albuterol sulfate inhalation powder (ProAir® RespiClick)*** |

*FDA approved for ages 12 years and older.

[1] ProAir® RespiClick Prescribing Information, Teva Respiratory, LLC. Available online at: http://www.myproair.com/respiclick/library/docs/PI.pdf . Last revised: 03/2015. Last accessed 11/2015.

# Appendix H

# Vote to Prior Authorize Stiolto™ Respimat® (Tiotropium Bromide/Olodaterol), Arnuity™ Ellipta® (Fluticasone Furoate), Utibron™ Neohaler® (Indacaterol/Glycopyrrolate), Seebri™ Neohaler® (Glycopyrrolate), & Nucala® (Mepolizumab)

**Oklahoma Health Care Authority**
**January 2016**

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

- **Stiolto™ Respimat® (tiotropium/olodaterol)** is a combination of tiotropium, an anticholinergic, and olodaterol, a long-acting beta$_2$-adrenergic agonist (LABA), that is indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
- **Arnuity™ Ellipta® (fluticasone furoate)** is an inhaled corticosteroid (ICS) indicated for once-daily, maintenance treatment of asthma as prophylactic therapy in patients aged 12 years and older.
- **Breo® Ellipta® (fluticasone furoate /vilanterol)** is a combination of fluticasone furoate, an ICS, and vilanterol, a LABA, indicated for long-term, once-daily, maintenance treatment of airflow obstruction and reducing exacerbations in patients with COPD and asthma in patients aged 18 years and older.
- **Spiriva® Respimat® (tiotropium bromide soft mist inhaler)** is an anticholinergic, for the long-term, once-daily, maintenance treatment of asthma in patients 12 years of age and older.
- **Nucala® (mepolizumab injection)** is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.
- **Utibron™ Neohaler® (indacaterol/glycopyrrolate)** is a combination of indacaterol, a LABA, and glycopyrrolate, an anticholinergic, indicated for the long-term, maintenance treatment of airflow obstruction in patients with COPD.
- **Seebri™ Neohaler® (glycopyrrolate)** is an anticholinergic indicated for the long-term, maintenance treatment of airflow obstruction in patients with COPD.

## Recommendations

The College of Pharmacy recommends the following criteria and updates to the maintenance asthma and COPD Product Based Prior Authorization (PBPA) category:

**Stiolto™ Respimat® (Tiotropium/Olodaterol) Approval Criteria:**

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and

3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components.

**Arnuity™ Ellipta® (Fluticasone Furoate) Approval Criteria:**

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) is not an option for the member.

**Breo® Ellipta® (Fluticasone Furoate/Vilanterol) Approval Criteria:**

1. An FDA approved diagnosis of COPD or chronic bronchitis and/or emphysema associated with COPD; or
2. An FDA approved diagnosis of asthma in patients 18 years and older; and
3. Trials of Advair® and Symbicort®, consisting of at least 30 days each within the last 90 days that did not adequately control COPD or asthma symptoms.

**Spiriva® Respimat® (Tiotropium Bromide Soft Mist Inhaler) Approval Criteria for Asthma Diagnosis:**

1. Member must have an FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. Member must have used a high-dose inhaled corticosteroid and long-acting beta$_2$ agonist (ICS/LABA) product for at least one month immediately prior to request for authorization; and
4. Member must have had a trial of a leukotriene receptor antagonist for at least one month in the last 90 days; and
5. Member must have a history of exacerbations despite required trials; and
6. Member must remain on an ICS or ICS/LABA while on tiotropium therapy; and
    a. Member's asthma must be considered uncontrolled by prescriber:
        i. Member requires rescue inhaler more than two days per week for reasons other than prevention of exercise induced bronchospasms; or
        ii. Member requires oral systemic corticosteroids; or
    b. Clinical situation warranting initiation of tiotropium therapy in addition to an ICS/LABA due to severity of asthma; and
7. A clinically significant reason the member is unable to use Spiriva® Handihaler® (tiotropium) which does not require prior authorization.

**Nucala® (Mepolizumab Injection) Approval Criteria:**

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be age 12 years or older; and
3. Member must have a baseline blood eosinophil count of 150 cell/mcL or greater within the last six weeks of initiation of dosing; and
4. Member must have had at least two asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids

despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least one additional controller medication; and

5. Member must have failed a high-dose ICS (≥ 880 mcg/day fluticasone propionate or equivalent daily dose or ≥ 440 mcg/day in ages 12 to 17) used compliantly for at least the past 12 months (for ICS/LABA combination products, the highest approved dose meets this criteria); and
6. Member must have failed at least one other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past three months; and
7. Nucala® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last twelve months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
8. Initial approvals will be for the duration of six months after which time compliance will be evaluated for continued approval; and
9. A quantity limit of 1 vial per 28 days will apply.

**Utibron™ Neohaler® (Indacaterol/Glycopyrrolate) Approval Criteria:**

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

**Seebri™ Neohaler® (Glycopyrrolate) Approval Criteria:**

1. The college of pharmacy recommends placement of Seebri™ Neohaler® (glycopyrrolate) into Tier-2 of the Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Anticholinergics (LAMA) product based prior authorization category. The current criteria for this category will apply.

| Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Anticholinergics (LAMA) | |
|---|---|
| **Tier-1** | **Tier-2** |
| **Long Acting Beta$_2$ Agonists* (LABA)** | |
| Serevent® (salmeterol inhalation powder) | Perforomist® (formoterol nebulizer solution) |
| Foradil® (formoterol aerosolized powder) | Brovana® (arformoterol nebulizer solution) |
| | Arcapta® (indacaterol inhalation powder |
| | Striverdi® Respimat® (olodaterol inhalation spray) |
| **Long Acting Anticholinergics (LAMA)** | |
| Spiriva® (tiotropium inhalation powder) | Tudorza® (aclidinium inhalation powder) |
| | Spiriva® Respimat® (tiotropium soft mist inhaler)* |
| | Incruse™ Ellipta®(umeclidinium inhalation powder) |
| | **Seebri™ Neohaler® (glycopyrrolate)** |

*See Spiriva® Respimat® (tiotropium soft mist inhaler) Approval Criteria for Asthma.

[1] Stiolto™ Respimat® Prescribing Information, Boehringer Ingelheim Pharmaceuticals, Inc. Available online at: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Stiolto%20Respimat/stiolto.pdf . Last revised 06/2015. Last accessed 11/15.

[2] Arnuity™ Ellipta® (fluticasone furoate) Prescribing information. GlaxoSmithKline. Available online at: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Arnuity_Ellipta/pdf/ARNUITY-ELLIPTA-PI-PIL.PDF. Last updated 11/2014. Last accessed 11/15.

[3] Breo® Ellipta® Updated Indication, Safety Updates. Available at: https://www.optumrx.com/vgnlive/HCP/Assets/RxNews/Clinical%20Updates_Breo%20Ellipta_2015-0501.pdf. Last accessed 11/2015.

[4] Spiriva® Respimat® (tiotropium) New Indication. Available online at: https://www.optumrx.com/vgnlive/HCP/Assets/RxNews/Clinical%20Updates_Spiriva%20Respimat_2015-0916.pdf. Last accessed 11/15.

[5] Nucala® (mepolizumab) Prescribing Information. GlaxoSmithKline. Available online at: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL.PDF. Last accessed 11/15.

[6] Utibron™ Neohaler® Prescribing Information, Novartis Pharmaceuticals Corporation. Available online at: http://www.pharma.us.novartis.com/product/pi/pdf/utibron.pdf. Last revised 10/2015. Last accessed 11/15.

[7] Seebri™ Neohaler ® Prescribing Information, Novartis Pharmaceuticals Corporation. Available online at: http://www.pharma.us.novartis.com/product/pi/pdf/seebri.pdf. Last revised 10/2015. Last accessed 11/15.

# Appendix I

# Fiscal Year 2015 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Migranal® (Dihydroergotamine Mesylate Nasal Spray)

**Oklahoma Health Care Authority**
**January 2016**

## Current Prior Authorization Criteria

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

**Anti-Migraine Medications Tier-2 Approval Criteria:**

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

**Anti-Migraine Medications Tier-3 Approval Criteria:**

1. A trial of all available Tier-1 and Tier-2 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days.
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.
5. Additionally, Zecuity® will require a patient-specific, clinically significant reason why member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection).

| Anti-Migraine Medications | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Tier-3** |
| sumatriptan (Imitrex®)<br>rizatriptan (Maxalt®, Maxalt MLT®) | naratriptan (Amerge®)<br>zolmitriptan (Zomig®, Zomig-ZMT®) | almotriptan (Axert®)<br>eletriptan (Relpax®)<br>frovatriptan (Frova®)<br>sumatriptan (Sumavel® DosePro®)*<br>sumatriptan (Zecuity®)*<br>sumatriptan injection (Imitrex®)*<br>sumatriptan/naproxen (Treximet®)<br>sumatriptan nasal spray (Imitrex®)*<br>zolmitriptan nasal spray (Zomig®) |

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

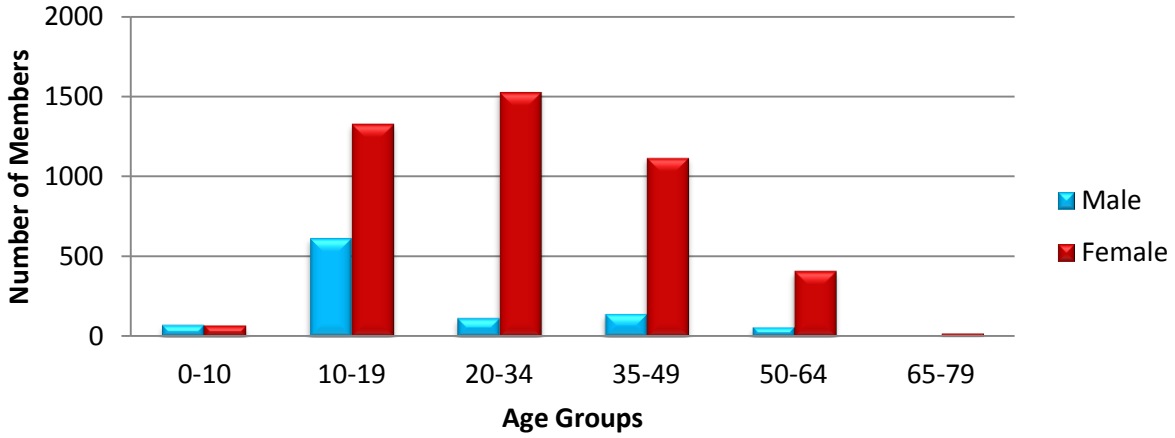
## Utilization of Anti-Migraine Medications: Fiscal Year 2015

### Comparison of Fiscal Years

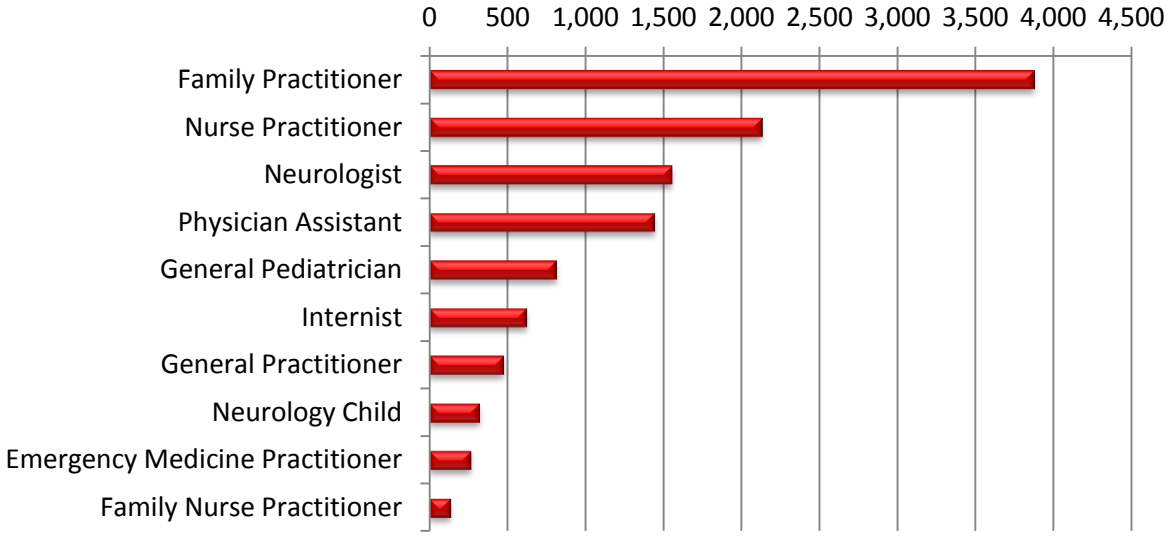
| Fiscal Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2014** | 5,729 | 12,288 | $463,887.19 | $37.75 | $2.32 | 123,615 | 199,728 |
| **2015** | 5,495 | 12,251 | $278,661.81 | $22.75 | $1.35 | 126,748 | 206,305 |
| **% Change** | **-4.10%** | **-0.30%** | **-39.90%** | **-39.70%** | **-41.80%** | **2.50%** | **3.30%** |
| **Change** | **-234** | **-37** | **-$185,225.38** | **-$15.00** | **-$0.97** | **3,133** | **6,577** |

*Total number of unduplicated members.

### Demographics of Members Utilizing Anti-Migraine Medications



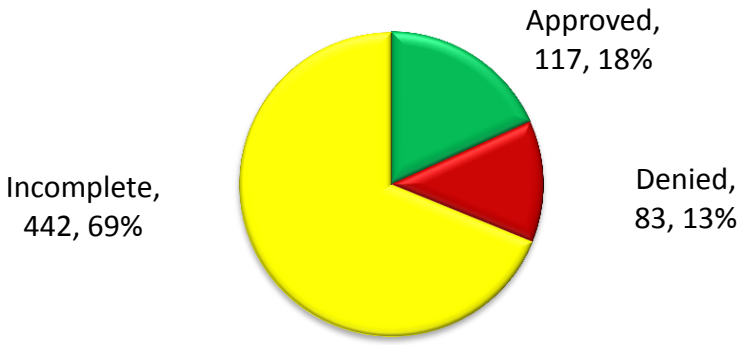

### Top Prescriber Specialties of Anti-Migraine Medications by Number of Claims



## Prior Authorization of Anti-Migraine Medications

There were 642 prior authorization requests submitted for the anti-migraine medication category during fiscal year 2015. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

**Status of Petitions**




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

**Patent Expirations:**

- Frova® (frovatriptan tablets): November 2015, patent expired however no generic is currently available.
- Relpax® (eletriptan tablets): August 2017
- Zomig® (zolmitriptan nasal spray): May 2021
- Treximet® (sumatriptan/naproxen tablets): October 2025
- Sumavel® DosePro® (sumatriptan needle-free injection): November 2026
- Zecuity® (sumatriptan): November 2030

**Updates**:

- **June 2014:** Semprana™ (dihydroergotamine oral inhalation), formally Levadex®, which is being developed as an acute treatment of migraine was rejected for approval by the FDA for the third time in June 2014. The FDA's Complete Response Letter (CRL) cited issues regarding content uniformity on the improved canister filling process and on standards for the device actuation. There were no issues cited related to clinical safety and efficacy and Allergan is continuing to work towards FDA approval.
- **May 2015:** Treximet® (sumatriptan/naproxen tablets) was FDA approved May 2015 for the acute treatment of migraine with or without aura in pediatric patients 12 years and older. Treximet® was previously only indicated in adult patients for the acute treatment of migraine with or without aura.
- **June 2015:** Zomig® (zolmitriptan nasal spray) was FDA approved June 2015 for use in pediatric members aged 12 years and older for acute treatment of migraine with or

without aura. Zomig® was originally FDA approved for acute treatment of migraine with or without aura in adult patients.

- **November 2015:** The patent for Axert® (almotriptan tablets) expired November 2015 and generic products are being produced by multiple manufacturers.
- **November 2015:** Rizaport™ (rizatriptan oral dissolving thin film) was granted its first national approval in Germany in November 2015 for the treatment of migraine. Rizaport™ submitted a New Drug Application (NDA) to the FDA in 2013. In March 2014, the FDA responded with a CRL citing issues related to third party CMC (chemistry, manufacturing, and controls) and to the packaging and labeling of the product. RedHill and IntelGenx submitted a response to the FDA and the FDA's review of the Rizaport™ NDA continues.

## Migranal® (Dihydroergotamine Mesylate Nasal Spray) Product Summary[7,8]

**Indications:**

- Migranal® (dihydroergotamine mesylate nasal spray) is indicated for the acute treatment of migraine headaches with or without aura.
- Migranal® nasal spray is not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

**Dosing:**

- Migranal® nasal spray is available (as a clear, colorless to faintly yellow solution) in 3.5mL amber single-use glass vials containing 4mg of dihydroergotamine mesylate.
- Migranal® nasal spray is provided as a package of eight single-use units, each unit consists of one vial and one sprayer. Each vial contains a total of four sprays.
- The recommended dose is one spray (0.5mg) in each nostril; if needed, the patient can repeat after 15 minutes, up to a total of four sprays (2mg).
- Patients should not exceed six sprays (3mg) in a 24-hour period.
- The safety of doses greater than 4mg in a 7-day period has not been established.
- Dihydroergotamine nasal spray should not be used for chronic daily administration.
- Prior to administration, dihydroergotamine nasal spray pump must be primed.
- Once the nasal spray applicator has been prepared, it should be discarded (with any remaining drug in open vial) after eight hours.
- Dihydroergotamine nasal spray is for intranasal use only and should not be injected.
- Dihydroergotamine nasal spray solution contains 10mg caffeine per vial.

**Mechanism of Action:**

- Dihydroergotamine binds with high affinity to 5-$HT_{1D\alpha}$ and 5-$HT_{1D\beta}$ receptors. It also binds with high affinity to serotonin 5-$HT_{1A}$, 5-$HT_{2A}$, and 5-$HT_{2C}$ receptors, noradrenaline $\alpha_{2A}$, $\alpha_{2B}$ and $\alpha_1$ receptors, and dopamine $D_{2L}$ and $D_3$ receptors.
- The therapeutic activity of dihydroergotamine in migraine is generally attributed to the agonist effect at 5- $HT_{1D}$ receptors. Two current theories have been proposed to explain the efficacy of 5-$HT_{1D}$ receptor agonists in migraine. One theory suggests that activation of 5-$HT_{1D}$ receptors located on intracranial blood vessels, including those on arterio-

venous anastomoses, leads to vasoconstriction, which correlates with the relief of migraine headache. The alternative hypothesis suggests that activation of 5-$HT_{1D}$ receptors on sensory nerve endings of the trigeminal system results in the inhibition of pro-inflammatory neuropeptide release.

**Contraindications:**

- Concomitant use with Cytochrome P450 3A4 Inhibitors: The use of potent CYP3A4 inhibitors (ritonavir, nelfinavir, indinavir, erythromycin, clarithromycin, troleandomycin, ketoconazole, and itraconazole) with dihydroergotamine is contraindicated. There have been a few reports of serious adverse events associated with the coadministration of dihydroergotamine and potent CYP3A4 inhibitors resulting in vasospasm that led to cerebral ischemia and/or ischemia of the extremities.
- Ischemic Heart Disease: Dihydroergotamine nasal spray should not be given to patients with ischemic heart disease (angina pectoris, history of myocardial infarction, or documented silent ischemia) or to patients who have clinical symptoms or findings consistent with coronary artery vasospasm including Prinzmetal's variant angina.
- Uncontrolled Hypertension: Because dihydroergotamine nasal spray may increase blood pressure, it should not be given to patients with uncontrolled hypertension.
- Hemiplegic or Basilar Migraine: Dihydroergotamine nasal spray should not be administered to patients with hemiplegic or basilar migraine.
- Drug Interactions: Dihydroergotamine nasal spray is contraindicated to use within 24 hours of use of 5-$HT_1$ agonists (e.g. sumatriptan), ergotamine-containing, or ergot-type medications.
- Other Conditions: Dihydroergotamine nasal spray is contraindicated in patients with known peripheral arterial disease, sepsis, severely impaired hepatic or renal function, and following vascular surgery.
- Pregnancy: Dihydroergotamine nasal spray may cause fetal harm when administered to a pregnant woman. Dihydroergotamine possesses oxytocic properties, and therefore, should not be administered during pregnancy. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.
- Nursing: Dihydroergotamine mesylate should not be used by nursing mothers.
- Hypersensitivity to Ergot Alkaloids: Dihydroergotamine nasal spray is contraindicated in patients who have previously shown hypersensitivity to ergot alkaloids.
- Concomitant use with Peripheral and Central Vasoconstrictors: Dihydroergotamine mesylate should not be used with peripheral and central vasoconstrictors (stimulants, decongestants, etc.) because the combination may result in additive or synergistic elevation of blood pressure.

**Safety:**

- Dihydroergotamine nasal spray should only be used where a clear diagnosis of migraine headache has been established.
- Fibrotic Complications: There have been reports of pleural and retroperitoneal fibrosis in patients following prolonged daily use of injectable dihydroergotamine mesylate.

Rarely, prolonged daily use of other ergot alkaloid drugs has been associated with cardiac valvular fibrosis. Rare cases have also been reported in association with the use of injectable dihydroergotamine mesylate; however, in those cases, patients also received drugs known to be associated with cardiac valvular fibrosis. Administration of dihydroergotamine nasal spray should not exceed the dosing guidelines and should not be used for chronic daily administration.

- Patients at Risk for Coronary Heart Disease: Dihydroergotamine nasal spray should not be used by patients with documented ischemic or vasospastic coronary artery disease. It is strongly recommended that dihydroergotamine nasal spray not be given to patients in whom unrecognized coronary artery disease (CAD) is predicted by the presence of risk factors (e.g. hypertension, hypercholesterolemia, smoker, obesity, diabetes, strong family history of CAD, females who are surgically or physiologically postmenopausal, or males who are over 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease. For patients with risk factors predictive of CAD who are determined to have a satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose of dihydroergotamine nasal spray take place in the setting of a physician's office or similar medically staffed and equipped facility unless the patient has previously received dihydroergotamine mesylate.
- Cardiac Events and Fatalities: No deaths have been reported in patients using dihydroergotamine nasal spray. However, the potential for adverse cardiac events exists. Serious adverse cardiac events, including acute myocardial infarction, life-threatening disturbances of cardiac rhythm, and death have been reported to have occurred following the administration of dihydroergotamine mesylate injection (e.g. D.H.E. 45® Injection).
- Drug-Associated Cerebrovascular Events and Fatalities: Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported in patients treated with D.H.E. 45® Injection; and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the D.H.E. 45® Injection having been administered with the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. It should be noted that patients with migraine may be at increased risk of certain cerebrovascular events (e.g. stroke, hemorrhage, and transient ischemic attack).
- Other Vasospasm Related Events: Dihydroergotamine nasal spray, like other ergot alkaloids, may cause vasospastic reactions other than coronary artery vasospasm. Myocardial and peripheral vascular ischemia has been reported with dihydroergotamine nasal spray. Dihydroergotamine nasal spray associated vasospastic phenomena may also cause muscle pains, numbness, coldness, pallor, and cyanosis of the digits. In patients with compromised circulation, persistent vasospasm may result in gangrene or death; dihydroergotamine nasal spray should be discontinued immediately if signs or symptoms of vasoconstriction develop.
- Increase in Blood Pressure: Significant elevation in blood pressure has been reported on rare occasions in patients with and without a history of hypertension treated with

dihydroergotamine nasal spray and injection. Dihydroergotamine nasal spray is contraindicated in patients with uncontrolled hypertension.

- Local Irritation: Approximately 30% of patients using dihydroergotamine nasal spray (compared to 9% of placebo patients) have reported irritation in the nose, throat, and/or disturbances in taste. Irritative symptoms include congestion, burning sensation, dryness, paraesthesia, discharge, epistaxis, pain, or soreness. The symptoms were predominantly mild-to-moderate in severity and transient.

**Adverse Reactions:** The most common adverse reactions experienced during clinical trials (not reported at an equal incidence by placebo-treated patients) were rhinitis, altered sense of taste, application site reactions, dizziness, nausea, and vomiting.

**Efficacy:** The efficacy of dihydroergotamine nasal spray for the acute treatment of migraine headaches was evaluated in four randomized, double-blind, placebo-controlled trials in the U.S. Patients treated a single moderate-to-severe migraine headache with a single dose of study medication (dihydroergotamine or placebo) and assessed pain severity over 24 hours. Headache response was determined 0.5, 1, 2, 3, and 4 hours following treatment and was defined as a reduction in headache severity to mild or no pain based on pain intensity as interpreted by the patient. Studies 1 and 2 used a four-point pain intensity scale and Studies 3 and 4 used a five-point scale. Rescue medication was allowed in all four studies but patients were instructed not to take them during the four hour observation period. The percentage of patients who achieved headache response four hours after treatment with dihydroergotamine nasal spray was significantly greater compared to those receiving placebo in 3 of the 4 studies.

| Study | Drug | Number of Patients | 2 Hours | 4 hours |
|---|---|---|---|---|
| **Study 1** | Migranal® | 105 | 61% | 70% |
| | Placebo | 98 | 23% | 28% |
| **Study 2** | Migranal® | 103 | 47% | 56% |
| | Placebo | 102 | 33% | 35% |
| **Study 3** | Migranal® | 50 | 32% | 48% |
| | Placebo | 50 | 20% | 22% |
| **Study 4** | Migranal® | 47 | 30% | 47% |
| | Placebo | 50 | 20% | 30% |

**Cost Comparison:**

| Drug | Package Size | EACW | SMAC | Cost per Month |
|---|---|---|---|---|
| Migranal® (dihydroergotamine nasal spray) | 8 single-use vials (4 sprays per vial) | $444.98/vial | N/A | $3,559.84* |
| Dihydroergotamine nasal spray | 8 single-use vials (4 sprays per vial) | $398.88/vial | N/A | $3,191.04* |
| Dihydroergotamine Injection | 5 ampules (1mg/mL ampule) | N/A | $107.98/ampule | $2,699.50* |
| Sumatriptan 100mg tablet | Varies | N/A | $0.99/tablet | $17.82[+] |

EACW= estimated wholesaler acquisition cost
SMAC= state maximum allowed cost
*Based on maximum recommended dosing
[+]Based on maximum quantity limit of 18 tablets per 30 days

## Recommendations

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

1. The addition of a special prior authorization (PA) category:
    a. Placement of sumatriptan (Sumavel® DosePro®), sumatriptan patch (Zecuity®), sumatriptan injection (Imitrex®), and sumatriptan nasal spray (Imitrex®) into the special PA category.
    b. Placement of sumatriptan/naproxen (Treximet®) into the special PA category and require a patient-specific, clinically significant reason why the member cannot use the individual components separately.
    c. Placement of dihydroergotamine nasal spray (Migranal®) and dihydroergotamine injection (D.H.E. 45®) in the special PA category with the following criteria in red.

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

**Anti-Migraine Medications Tier-2 Approval Criteria:**

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

**Anti-Migraine Medications Tier-3 Approval Criteria:**

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

**Anti-Migraine Medications Special Prior Authorization Approval Criteria:**

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

| Anti-Migraine Medications | | | |
|---|---|---|---|
| **Tier-1** | **Tier-2** | **Tier-3** | **Special PA** |
| sumatriptan (Imitrex®)<br>rizatriptan (Maxalt®, Maxalt MLT®) | naratriptan (Amerge®)<br>zolmitriptan (Zomig®, Zomig-ZMT®) | almotriptan (Axert®)<br>eletriptan (Relpax®)<br>frovatriptan (Frova®)<br>zolmitriptan nasal spray (Zomig®) | dihydroergotamine injection (D.H.E. 45®)<br>dihydroergotamine nasal spray (Migranal®)<br>sumatriptan injection (Imitrex®)<br>sumatriptan nasal spray (Imitrex®)<br>sumatriptan (Sumavel® DosePro®)<br>sumatriptan (Zecuity®)*<br>sumatriptan/Naproxen (Treximet®) |

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

## Utilization Details of Anti-Migraine Medications: Fiscal Year 2015

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| **TIER-1 MEDICATIONS** | | | | | | |
| SUMATRIPTAN TAB 50MG | 3,839 | 2,054 | $50,852.33 | $0.83 | $13.25 | 18.25% |
| SUMATRIPTAN TAB 100MG | 3,779 | 1,628 | $48,080.24 | $0.84 | $12.72 | 17.25% |
| SUMATRIPTAN TAB 25MG | 2,400 | 1,299 | $29,277.00 | $0.80 | $12.20 | 10.51% |
| RIZATRIPTAN TAB 10MG | 606 | 300 | $12,147.46 | $0.85 | $20.05 | 4.36% |
| RIZATRIPTAN TAB 10MG ODT | 564 | 279 | $11,293.62 | $0.88 | $20.02 | 4.05% |
| RIZATRIPTAN TAB 5MG | 204 | 144 | $4,149.26 | $0.85 | $20.34 | 1.49% |
| RIZATRIPTAN TAB 5MG ODT | 192 | 113 | $3,821.35 | $0.87 | $19.90 | 1.37% |
| MAXALT-MLT TAB 10MG | 60 | 25 | $832.39 | $0.49 | $13.87 | 0.30% |
| MAXALT-MLT TAB 5MG | 29 | 13 | $410.10 | $0.49 | $14.14 | 0.15% |
| MAXALT TAB 10MG | 2 | 1 | $47.78 | $0.80 | $23.89 | 0.02% |
| IMITREX TAB 100MG | 1 | 1 | $13.13 | $0.44 | $13.13 | 0.00% |
| **TIER-1 SUBTOTAL** | **11,676** | **5,857** | **$160,924.66** | **$0.74** | **$16.68** | **57.75%** |
| **TIER-2 MEDICATIONS** | | | | | | |
| NARATRIPTAN TAB 2.5MG | 188 | 57 | $8,774.16 | $2.60 | $46.67 | 3.15% |
| ZOLMITRIPTAN TAB 5MG | 32 | 9 | $1,682.20 | $1.85 | $52.57 | 0.60% |
| NARATRIPTAN TAB 1MG | 31 | 15 | $1,611.31 | $2.50 | $51.98 | 0.58% |
| ZOLMITRIPTAN TAB 2.5MG | 7 | 3 | $351.25 | $1.67 | $50.18 | 0.13% |
| ZOLMITRIPTAN TAB 5MG | 5 | 3 | $280.62 | $2.08 | $56.12 | 0.10% |
| ZOLMITRIPTAN TAB 2.5 MG | 3 | 3 | $159.92 | $1.78 | $53.31 | 0.06% |
| **TIER-2 SUBTOTAL** | **266** | **90** | **$12,859.46** | **$2.08** | **$51.81** | **4.62%** |
| **TIER-3 MEDICATIONS** | | | | | | |
| RELPAX TAB 40MG | 62 | 10 | $22,802.04 | $27.47 | $367.77 | 8.18% |
| SUMATRIPTAN SPR 20MG/ACT | 60 | 23 | $16,681.05 | $10.28 | $278.02 | 5.99% |
| SUMATRIPTAN INJ 6MG/0.5 | 56 | 20 | $22,708.45 | $21.48 | $405.51 | 8.15% |
| SUMATRIPTAN SPR 5MG/ACT | 49 | 26 | $12,371.82 | $12.78 | $252.49 | 4.44% |
| ZOMIG NASAL SPR 5MG | 17 | 2 | $5,342.66 | $10.48 | $314.27 | 1.92% |
| FROVA TAB 2.5MG | 13 | 1 | $6,107.03 | $18.01 | $469.77 | 2.19% |
| SUMATRIPTAN INJ 6MG/0.5 | 12 | 6 | $1,321.42 | $5.98 | $110.12 | 0.47% |
| AXERT TAB 12.5MG | 10 | 4 | $2,055.05 | $26.01 | $205.51 | 0.74% |
| RELPAX TAB 20MG | 7 | 1 | $3,066.47 | $22.22 | $438.07 | 1.10% |
| TREXIMET TAB 85-500MG | 6 | 1 | $3,569.45 | $19.83 | $594.91 | 1.28% |
| SUMATRIPTAN INJ 6MG/0.5 | 5 | 2 | $1,315.66 | $9.75 | $263.13 | 0.47% |
| SUMAVEL DOSE INJ 6MG/0.5 | 5 | 1 | $4,632.32 | $30.88 | $926.46 | 1.66% |
| AXERT TAB 6.25MG | 4 | 2 | $1,611.12 | $17.51 | $402.78 | 0.58% |
| ZOMIG SPR 2.5MG | 2 | 2 | $637.92 | $10.63 | $318.96 | 0.23% |
| SUMATRIPTAN INJ 4MG/0.5 | 1 | 1 | $655.23 | $21.84 | $655.23 | 0.24% |
| **TIER-3 SUBTOTAL** | **309** | **102** | **$104,877.69** | **$17.68** | **$400.20** | **37.64%** |
| **TOTAL** | **12,251** | **5,495*** | **$278,661.81** | **$1.35** | **$203.04** | **100.00%** |

*Total number of unduplicated members.

## Utilization Details of Dihydroergotamine Products: Fiscal Year 2015

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | % COST |
|---|---|---|---|---|---|---|
| **TIER-1 MEDICATIONS** | | | | | | |
| DIHYDROERGOT SPRAY | 17 | 9 | $40,397.76 | $99.01 | $2,376.34 | 74.82% |
| MIGRANAL SPRAY | 4 | 4 | $12,703.95 | $141.16 | $3,175.99 | 23.53% |
| DIHYDROERGOT | 4 | 2 | $893.25 | $22.90 | $223.31 | 1.65% |
| **TOTAL** | **25** | **15*** | **$53,994.96** | **$100.55** | **$1,925.21** | **100.00%** |

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 11/2015. Last accessed 12/2015.
[2] First-Time Generic Drug Approvals-July 2015. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/ANDAGenericDrugApprovals/ucm455936.htm . Last accessed 12/2015.
[3] FDA Okays Sumatriptan/Naproxen (Treximet®) for Migraine in Teens. Available at: http://www.medscape.com/viewarticle/844752 . Last accessed 12/2015.
[4] FDA Approves Zomig® (zolmitriptan) Nasal Spray for Migraine in Pediatric Patients (12-17). Available at: http://www.prnewswire.com/news-releases/fda-approves-zomig-zolmitriptan-nasal-spray-for-migraine-in-pediatric-patients-ages-12-17-300099548.html . Last accessed 12/2015.
[5] Rizaport™ (Migraine). Available at: http://www.redhillbio.com/rizaport. Last accessed 12/2015.
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[7] Migranal® Prescribing Information, Valeant™ Pharmaceuticals North America. Available online at: http://valeant.com/Portals/25/Pdf/PI/Migranal-PI.pdf. Last revised: 06/2007. Last accessed 12/2015.
[8] Label: Migranal-dihydroergotamine mesylate spray. Available at: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a24befa8-b952-48ac-942a-379585250782. Last accessed: 12/2015.

# Appendix J

# 30-Day Notice to Prior Authorize Strensiq™ (Asfotase Alfa)

**Oklahoma Health Care Authority**
**January 2016**

## Hypophosphatasia Overview[1,2,3,4,5]

Hypophosphatasia (HPP) is a rare, genetic, progressive metabolic disease which is characterized by low alkaline phosphatase (ALP) activity and defective bone mineralization that can lead to deformity of bones and other skeletal abnormalities. Low ALP levels can also contribute to systemic complications such as muscle weakness with loss of mobility, seizures, pain, and respiratory failure leading to premature infant death. Severe forms of HPP are estimated to affect one in 100,000 newborns, but milder cases that appear in childhood or adulthood may occur more frequently.

HPP results from an inherited molecular defect in the ALP gene encoding tissue non-specific alkaline phosphatase (TNSALP). TNSALP is an enzyme responsible for dephosphorlation of inorganic pyrophosphate (PPi) and pyridoxal 5'-phosphate (PLP), a major form of vitamin $B_6$. TNSALP dephosphorlation of PPi results in two phosphate molecules available to bind with calcium which aid osteoblasts in bone mineralization. TNSALP deficiency impairs bone mineralization, leading to rickets in infants and children and osteomalacia in adults. Some patients develop pseudogout, osteoarthritis, and/or nephrocalcinosis due to accumulation of calcium and increased endogenous PPi levels. TNSALP deficiency results in vitamin $B_6$ deficiency in the brain causing impaired synthesis of neurotransmitters which can result in seizures.

HPP symptoms vary depending on severity and age at initial presentation; the earlier the presentation, the more severe the disease. Perinatal HPP is the most pernicious form, resulting in a high percent of stillborn births. Newborns that survive birth have an estimated mortality of about 50% in the first year of life with many complications including respiratory failure due to rachitic chest disease and hypoplastic lungs. HPP in childhood has variable symptoms; however, premature loss of primary teeth before the age of five is classical feature of HPP. Children may present with delayed mobility, waddling gait, delayed growth, frequent fractures, and osteopenia. Adult HPP can be associated with rickets, premature loss of primary teeth, or early loss of adult teeth. Adults may also suffer from pain due to osteomalacia, fracture, pseudogout, and calcific periarthritis.

HPP diagnosis is made by laboratory testing confirming low ALP activity after the hallmark symptoms are present. There are no formal treatment guidelines to manage HPP. Disease management has focused on supportive therapy to alleviate symptoms and use of dental, orthopedic, and other interventions as necessary. High-dose vitamin D, calcium supplements, and bisphosphonates should not be used due to exacerbation of HPP symptoms. Vitamin $B_6$ supplementation may be considered in HPP patients affected by seizures. Nonsteroidal anti-

inflammatory drugs (NSAIDs) have been used to improve pain-associated with physical impairment and have been shown to help improve walking distance.

Strensiq™ (asfotase alfa) was FDA approved October 23, 2015 and is the first FDA approved treatment for perinatal, infantile, and juvenile-onset HPP. Strensiq™ was granted breakthrough therapy designation, orphan drug designation, and a rare pediatric disease priority review voucher by the FDA. Strensiq™ is a TNSALP produced by recombinant DNA technology and works by replacing the TNSALP enzyme in patients with HPP.

## Strensiq™ (Asfotase Alfa) Product Summary[6,7]

**FDA Approved:** October 2015

**Indications:** Strensiq™ (asfotase alfa) is a tissue nonspecific alkaline phosphatase indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

**Dosing:**

- Strensiq™ (asfotase alfa) is available as a solution for injection in single use vials in the following strengths: 18mg/0.45mL, 28mg/0.7mL, 40mg/mL, and 80mg/0.8mL.
- The recommended dosage regimen is 2mg/kg administered subcutaneously three times per week, or 1mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.
- The dose may be increased to 3mg/kg three times per week for insufficient efficacy for the diagnosis of perinatal/infantile-onset HPP.
- The 80mg/0.8mL vial should not be used in pediatric patients weighing less than 40kg because the systemic asfotase alfa exposure achieved with the 80mg/0.8mL vial (higher concentration) is lower than that achieved with the other strength vials (lower concentrations). A lower exposure may not be adequate for this subgroup of patients.
- For more detailed information regarding weight-based dosing by treatment regimen, consult the full prescribing information.
- Asfotase alfa is for subcutaneous injection only.
- Injection sites should be rotated, and asfotase alfa should not be administered to areas that are reddened, inflamed, or swollen.

**Mechanism of Action:** HPP is caused by a deficiency in TNSALP enzyme activity, which leads to elevations in several TNSALP substrates, including PPi. Elevated extracellular levels of PPi block hydroxyapatite crystal growth which inhibits bone mineralization and causes an accumulation of unmineralized bone matrix which manifests as rickets and bone deformation in infants and children and as osteomalacia (softening of bones) once growth plates close. Replacement of the TNSALP enzyme with asfotase alfa treatment reduces the enzyme substrate levels.

**Contraindications:** None.

**Warnings and Precautions:**

- Hypersensitivity Reactions: Patients should be monitored for hypersensitivity reactions and if a severe reaction occurs, treatment should be discontinued and appropriate medical treatment initiated.
- Lipodystrophy: Localized reactions were reported after several months of treatment; proper injection technique should be followed and injection sites should be rotated.
- Ectopic Calcifications (Eye and Kidneys): Patients should be monitored for ectopic calcifications using ophthalmologic examinations and renal ultrasounds at baseline and periodically during treatment.

**Adverse Reactions:** The most common adverse reactions (≥10%) experienced during clinical trials include the following:

- Injection site reactions
- Lipodystrophy
- Ectopic calcifications
- Hypersensitivity reactions

**Use in Special Populations:**

- Pregnancy: There are no available human data on asfotase alfa use in pregnant women to inform a drug-associated risk. In animal reproduction studies, asfotase alfa administered intravenously to pregnant rats and rabbits during the period of organogenesis showed no evidence of fetotoxicity, embryolethality, or teratogenicity at doses causing plasma exposures up to 21 and 24 times, respectively, the exposure at the recommended human dose.
- Nursing Mothers: There are no data on the presence of asfotase alfa in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for asfotase alfa and any potential adverse effects on the breastfed infant from asfotase alfa or from the underlying maternal condition.
- Pediatric Use: The safety and effectiveness of asfotase alfa have been established in pediatric patients. Use of asfotase alfa is based on four prospective, open-label clinical trials conducted in 99 adult and pediatric patients with perinatal/infantile-onset or juvenile-onset HPP. The majority of patients were pediatric patients 1 day to 16 years of age (89/99 [90%]).
- Geriatric Use: No patients with perinatal/infantile- or juvenile-onset HPP aged 65 years or older were enrolled in clinical trials of asfotase alfa. Therefore, there is no information available to determine whether patients aged 65 years or older respond differently from younger patients.

**Efficacy:** The approval of Strensiq™ was based on data from four open-label trials involving 99 patients with perinatal/infantile-onset or juvenile-onset HPP who received treatment with asfotase alfa for up to 6.5 years.

- In patients with perinatal/infantile-onset HPP, 97% of patients treated with asfotase alfa were alive at one year of age versus 42% of control patients from a natural history study group. The invasive ventilation-free survival rate at one year of age was 85% for asfotase alfa-treated patients versus 25% for the control group.

- In patients with juvenile-onset HPP, all asfotase alfa-treated patients had improvement in low weight or short stature or maintained normal height and weight versus approximately 20% of control patients that had growth delays. Also, all asfotase alfa-treated patients demonstrated substantial healing of rickets on x-rays while 6% (2/32) of control patients showed increasing signs of rickets over time.

**Cost Comparison:**

| Medication | EAC Per Vial | Cost per Month* |
|---|---|---|
| Strensiq™ (asfotase alfa) 18mg/0.45 mL | $2,956.80 | $354,816.00 |
| Strensiq™ (asfotase alfa) 28mg/0.7 mL | $2,956.80 | $212,889.60 |
| Strensiq™ (asfotase alfa) 40mg/mL | $2,956.80 | $141,926.40 |
| Strensiq™ (asfotase alfa) 80mg/0.8 mL | $7,392.00 | $177,408.00 |

EAC = estimated acquisition cost
*Based on 80kg patient injecting six times a week

Asfotase alfa dosing is weight-based and regimen can vary from three injections to six injections per week. Each vial is single-use only and any unused product must be discarded. The full prescribing information provides detailed tables of weight-based dosing by treatment regimen. The minimum regimen listed is one 18mg vial three times per week which would be **$35,481.60 per month**. The maximum regimen listed is two 80mg vials six times per week which would be **$354,816.00 per month**.

## Recommendations

The College of Pharmacy recommends the prior authorization of Strensiq™ (asfotase alfa) with the following criteria:

**Strensiq™ (Asfotase Alfa) Approval Criteria:**

1. An FDA approved indication for the treatment of patients with perinatal/infantile-onset and juvenile-onset hypophosphatasia (HPP); and
2. Confirmed diagnosis by laboratory testing of:
    a. Low age-adjusted ALP activity; and
    b. Elevated pyridoxal 5'-phophate (PLP) levels; and
3. Member's weight (kg) must be provided and have been taken within the last four weeks to ensure accurate weight based dosing; and
4. The 80mg/0.8mL vial should not be used in pediatric patients weighing less than 40kg; and
5. For use of the 80mg/0.8mL vial, provider must document a patient-specific, clinically significant reason the member cannot use lower strength vials to achieve the same dose. (The higher concentration formulation, 80mg/mL vial, achieved an approximately 25% lower systemic exposure compared to lower concentration formulations at the same dose.)

[1] UpToDate: Periodontal disease in children: Associated systemic conditions. Available online at: http://www.uptodate.com/contents/periodontal-disease-in-children-associated-systemic-conditions?source=machineLearning&search=hypophosphatasia&selectedTitle=2%7E18&sectionRank=1&anchor=H11#H11 . Last revised 11/2015. Last accessed 12/2015.

[2] Hypophosphatasia Health Care Provider Site. Available online at: http://hypophosphatasia.com/hcp/ . Last accessed 12/2015.

[3] Girschick, H.J, H.W. Seyberth, and H.I. Huppertz. "Treatment of Childhood Hypophosphatasia with Nonsteroidal Antiinflammatory Drugs." Available online at: http://ac.els-cdn.com/S8756328299002033/1-s2.0-S8756328299002033-main.pdf?_tid=940598f8-a5a7-11e5-9c78-00000aacb35e&acdnat=1450457666_fe040f1200d7bca9191ed0e78294bde1. Last accessed 12/2015.

[4] Hypophosphatasia. Available online at: https://en.wikipedia.org/wiki/Hypophosphatasia . Last revised 11/2015. Last accessed 12/2015.

[5] Food and Drug Administration News Release: FDA approves new treatment for rare metabolic disorder. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468836.htm. Last accessed 12/2015.

[6] Strensiq™ Prescribing Information. Alexion Pharmaceutical, Inc. Available online at: http://www.strensiq.com/images/pi.pdf. Last accessed 12/2015.

[7] Strensiq ™ (asfotase alfa) New Orphan Drug Approval. Optum RX. https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Strensiq_2015-1027.pdf . Last accessed 12/2015.

# Appendix K

# Fiscal Year 2015 Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Varubi™ (Rolapitant)

**Oklahoma Health Care Authority**
**January 2016**

## Current Prior Authorization Criteria

**Kytril® and Sancuso® (Granisetron), Anzemet® (Dolasetron), and Emend® (Aprepitant) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length will be based on duration of need.

**Akynzeo® (Netupitant/Palonosetron) Approval Criteria:**

1. An FDA approved diagnosis for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length based on duration of need.
4. A quantity limit of one capsule per chemotherapy cycle will apply.

**Marinol® (Dronabinol) and Cesamet® (Nabilone) Approval Criteria:**

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

**Zuplenz® (Ondansetron) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot take all other available formulations of generic ondansetron.

**Diclegis® (Doxylamine/Pyridoxine) Approval Criteria:**

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. Trials with at least two prescription medications that have failed to relieve nausea and vomiting; and
4. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin $B_6$ (pyridoxine).

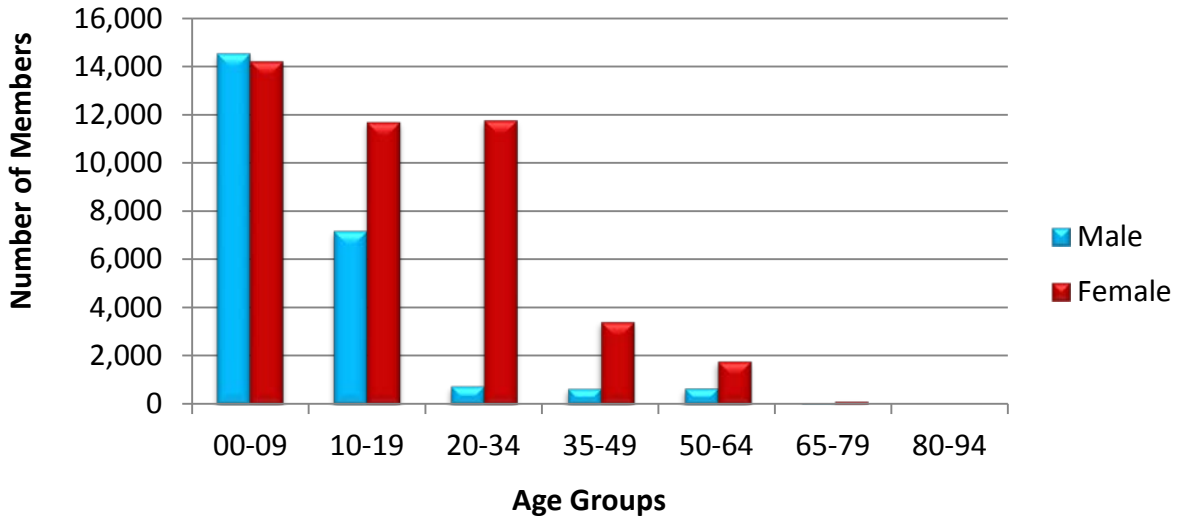
## Utilization of Anti-Emetic Medications: Fiscal Year 2015

### Comparison of Fiscal Years

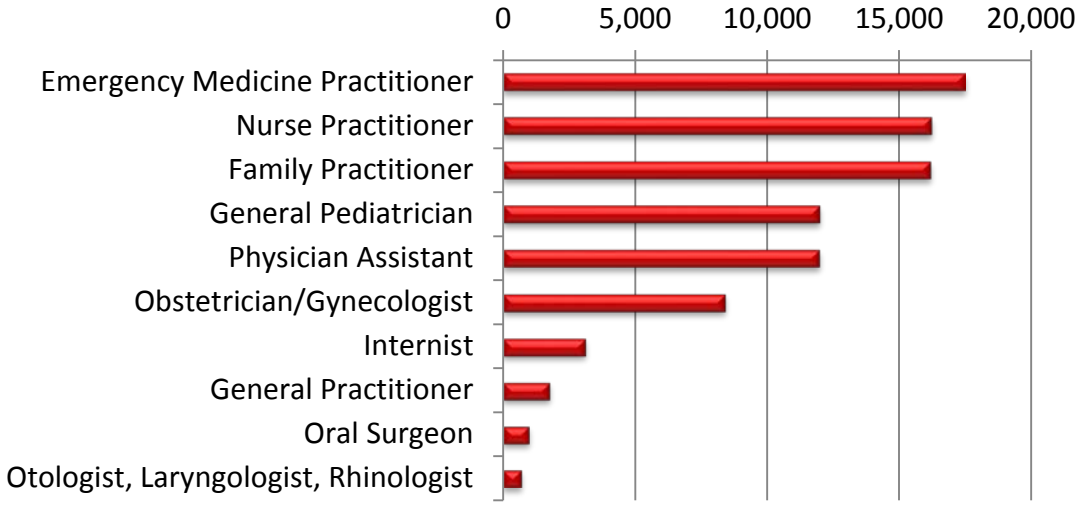
| Fiscal Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2014** | 62,022 | 86,805 | $1,213,172.73 | $13.98 | $1.11 | 1,245,122 | 1,088,807 |
| **2015** | 67,071 | 95,026 | $1,253,815.24 | $13.19 | $1.60 | 1,474,041 | 785,183 |
| **% Change** | **8.10%** | **9.50%** | **3.40%** | **-5.70%** | **44.10%** | **18.40%** | **-27.90%** |
| **Change** | **5,049** | **8,221** | **$40,642.51** | **-$0.79** | **$0.49** | **228,919** | **-303,624** |

*Total number of unduplicated members.

### Demographics of Members Utilizing Anti-Emetic Medications

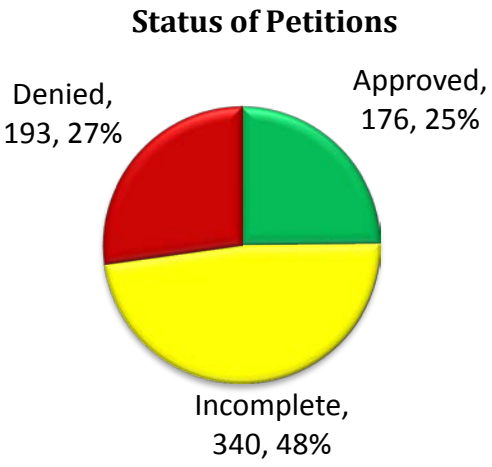



### Top Prescriber Specialties of Anti-Emetic Medications by Number of Claims



## Prior Authorization of Anti-Emetic Medications

There were 709 prior authorization requests submitted for the anti-emetic medications category during fiscal year 2015. The following chart shows the status of the submitted petitions.




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

**Anticipated Patent Expirations:**

- Diclegis® (doxylamine/pyridoxine): June 2021
- Sancuso® (granisetron transdermal patch): October 2024
- Emend® (aprepitant): September 2027
- Zuplenz® (ondansetron oral soluble film): July 2030
- Akynzeo® (netupitant/palonosetron): November 2030

**New FDA Approvals and Indications:**

- **September 2015:** The FDA approved a supplemental new drug application (sNDA) for Emend® (aprepitant) capsules, a substance P/neurokinin 1 (NK1) receptor antagonist, in combination with other anti-emetic agents for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC) in patients 12 years of age and older and patients less than 12 years of age who weigh at least 30 kg. With this approval, Emend® is the first and only NK1 receptor antagonist to be approved for the prevention of acute and delayed phases of chemotherapy-induced nausea and vomiting (CINV) in pediatric patients 12 to 17 years of age and pediatric patients less than 12 years of age who weigh at least 30kg receiving HEC or MEC. Emend® was first FDA approved in 2003 for the prevention of acute and delayed CINV in adults patients.
- **September 2015:** The FDA approved Varubi™ (rolapitant), a selective and competitive substance P/NK1 receptor antagonist, for the prevention of CINV in adult patients receiving highly emetogenic cisplatin-based chemotherapy, MEC, or regimens containing the combination of an anthracycline and cyclophosphamide.

- **December 2015:** The FDA approved a 125mg/5mL oral suspension formulation of Emend® (aprepitant) for use in pediatric patients 6 months to less than 12 years of age and in pediatric and adult patients unable to swallow capsules. This is in addition to the currently available Emend® (aprepitant) oral capsules and Emend® (fosaprepitant) intravenous (IV) powder for solution.

**Updated Treatment Guidelines:**

- **August 2015:** The American College of Obstetricians and Gynecologists (ACOG) published an updated practice bulletin regarding the treatment of nausea and vomiting of pregnancy. Significant recommendations and conclusions include:
  - The standard recommendation to take prenatal vitamins for three months before conception may reduce the incidence and severity of nausea and vomiting of pregnancy.
  - Treatment of nausea and vomiting of pregnancy with vitamin $B_6$ (pyridoxine) or vitamin $B_6$ (pyridoxine) plus doxylamine is safe and effective and should be considered first-line pharmacotherapy.
  - Treatment of nausea and vomiting of pregnancy with ginger has shown beneficial effects in reducing nausea symptoms and can be considered as a non-pharmacological option.
  - Early treatment of nausea and vomiting of pregnancy is recommended to prevent progression to hyperemesis gravidarum.

**Medications in the Pipeline:**

- **Substance P/NK1 Receptor Antagonist and Substance P/NK1 Receptor Antagonist Combination Product with 5-$HT_3$ Receptor Antagonist:** Helsinn's netupitant (oral and IV) and netupitant/palonosetron (IV) are currently in clinical trials for the prevention of CINV. Helsinn's Akynzeo® (netupitant/palonosetron) oral capsules were FDA approved in October 2014 for the prevention of acute and delayed CINV.
- **5-$HT_3$ Receptor Antagonist:** Heron Therapeutics has filed a new drug application (NDA) for Sustol® (granisetron extended-release subcutaneous injection) for the prevention of acute and delayed CINV, with a Prescription Drug User Fee Act (PDUFA) date of January 2016. Granisetron is currently available as oral tablets, oral solution, IV solution, and transdermal patches.

## Varubi™ (Rolapitant) Product Summary[10,11,12,13]

**Indications:** Varubi™ (rolapitant) is indicated in combination with other anti-emetic medications for the prevention of delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cisplatin-based chemotherapy, moderately emetogenic chemotherapy, or regimens containing the combination of an anthracycline and cyclophosphamide in adult patients.

**Dosing:**

- Rolapitant is available as 90mg oral tablets and can be taken without regard to meals.

- Rolapitant should be taken prior to the initiation of each chemotherapy cycle, but at no less than two week intervals.
- The recommended dosing of rolapitant is 180mg approximately one to two hours prior to chemotherapy in combination with dexamethasone and a 5-$HT_3$ receptor antagonist (*see following table for the recommended dosing regimens*).

| | **Day 1** | **Day 2** | **Day 3** | **Day 4** |
|---|---|---|---|---|
| **Prevention of Nausea and Vomiting Associated with Cisplatin-Based Highly Emetogenic Chemotherapy** | | | | |
| rolapitant | 180mg* | none | | |
| dexamethasone | 20mg[+] | 8mg twice daily | 8mg twice daily | 8mg twice daily |
| 5-$HT_3$ receptor antagonist | Per prescribing information[¥] | none | | |
| **Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Chemotherapy and Combinations of Anthracycline and Cyclophosphamide** | | | | |
| rolapitant | 180mg* | none | | |
| dexamethasone | 20mg[+] | none | | |
| 5-$HT_3$ receptor antagonist | Per prescribing information[¥] | Per prescribing information[¥] | | |

* Rolapitant should be taken approximately one to two hours prior to chemotherapy.
[+] Dexamethasone should be taken 30 minutes prior to chemotherapy.
[¥] Appropriate dose based on the prescribing information for the co-administered 5-$HT_3$ receptor antagonist.

**Mechanism of Action:** Rolapitant is a selective and competitive antagonist of human substance P/neurokinin 1 (NK1) receptors with anti-emetic activity.

**Contraindications:** Rolapitant is contraindicated in patients receiving thioridazine, a CYP2D6 substrate, due to a significant increase in plasma concentrations of thioridazine, which may result in QT prolongation and Torsades de Pointes.

**Safety:**

- Interaction with CYP2D6 Substrates with a Narrow Therapeutic Index: The inhibitory effect of rolapitant on CYP2D6 lasts at least seven days and may last longer after a single dose administration of rolapitant. Rolapitant use should be avoided in patients who are receiving pimozide, a CYP2D6 substrate. An increase in plasma concentrations of pimozide may result in QT prolongation. Patients should be monitored for adverse reactions if concomitant use of rolapitant and other CYP2D6 substrates with a narrow therapeutic index cannot be avoided.
- Renal Impairment: In population pharmacokinetic analyses, creatinine clearance (CrCl) at baseline did not show a significant effect on rolapitant pharmacokinetics in cancer patients with mild (CrCl 60-90mL/min) or moderate (CrCl 30-60mL/min) renal impairment compared to cancer patients with normal kidney function. Information is insufficient for the effect of severe renal impairment, and the pharmacokinetics of rolapitant was not studied in patients with end-stage renal disease requiring hemodialysis.

- Hepatic Impairment: No dosage adjustment is needed in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. There are no clinical or pharmacokinetic data in patients with severe hepatic impairment (Child-Pugh Class C). Rolapitant use should be avoided in patients with severe hepatic impairment. If use cannot be avoided, patients should be monitored for adverse reactions related to rolapitant.
- Pediatric Use: The safety and efficacy of rolapitant in pediatric patients have not been established.

**Adverse Reactions:**

- The safety of rolapitant was evaluated in approximately 2,800 patients in four controlled clinical trials in patients receiving emetogenic chemotherapy. Rolapitant was given in combination with dexamethasone and a 5-$HT_3$ receptor antagonist. The control group received placebo, dexamethasone, and a 5-$HT_3$ receptor antagonist.
- On day one of chemotherapy cycle one, 1,567 patients were treated with rolapitant, and 1,198 of these patients continued into the optional multiple cycle extension for up to six cycles of chemotherapy. The median number of chemotherapy cycles where rolapitant was administered was four.
- Adverse reactions in the multiple-cycle extensions of highly and moderately emetogenic chemotherapy studies for up to six cycles of chemotherapy were generally similar to that observed in chemotherapy cycle one.
- The most common adverse reactions to rolapitant reported in clinical trials following chemotherapy cycle one, occurring at an incidence of at least 3% and with a higher incidence than control, include:
    - In patients receiving highly emetogenic cisplatin-based chemotherapy: neutropenia, hiccups, and abdominal pain.
    - In patients receiving moderately emetogenic chemotherapy and combinations of anthracycline and cyclophosphamide: decreased appetite, neutropenia, dizziness, dyspepsia, urinary tract infection, stomatitis, and anemia.

**Efficacy:**

- The safety and efficacy of rolapitant was evaluated in three studies which included:
    - Two multicenter, double-blind, parallel group, controlled clinical studies in patients receiving a chemotherapy regimen that included cisplatin [cisplatin-based highly emetogenic chemotherapy (HEC); HEC Study 1 and HEC Study 2]
    - One multicenter, randomized, double-blind, parallel group, controlled clinical study in patients receiving moderately emetogenic chemotherapy, that included at least 50% of patients receiving a combination of anthracycline and cyclophosphamide [moderately emetogenic chemotherapy (MEC) and combinations of anthracycline and cyclophosphamide chemotherapy; MEC Study 3].
    - The rolapitant group (rolapitant, granisetron, and dexamethasone) was compared with a control group (placebo, granisetron, and dexamethasone) in all three studies.

- The primary endpoint in all three studies was complete response (defined as no emetic episodes and no rescue medication) in the delayed phase (25 to 120 hours) of chemotherapy-induced nausea and vomiting.
- There was a statistically significant difference for the rolapitant treatment group versus the control group for the primary endpoint in HEC Study 1 and MEC Study 3; however, there was no statistically significant difference in HEC Study 2 (*see following tables*).

| HEC Study 1 | | | |
|---|---|---|---|
| **Endpoint** | **Rolapitant (N=264) Rate (%)** | **Control (N=262) Rate (%)** | **P-value Treatment Difference (95% C.I.)** |
| Primary endpoint: complete response in the delayed phase | 72.7% | 58.4% | <0.001<br>14.3%<br>(6.3, 22.4) |

| HEC Study 2 | | | |
|---|---|---|---|
| **Endpoint** | **Rolapitant (N=271) Rate (%)** | **Control (N=273) Rate (%)** | **P-value Treatment Difference (95% C.I.)** |
| Primary endpoint: complete response in the delayed phase | 70.1% | 61.9% | 0.043<br>8.2%<br>(0.3, 16.1) |

| MEC Study 3 | | | |
|---|---|---|---|
| **Endpoint** | **Rolapitant (N=666) Rate (%)** | **Control (N=666) Rate (%)** | **P-value Treatment Difference (95% C.I.)** |
| Primary endpoint: complete response in the delayed phase | 71.3% | 61.6% | <0.001<br>9.8%<br>(4.7, 14.8) |

## Cost Comparison: Substance P/NK1 Receptor Antagonists

| Medication | Cost/Unit* | Quantity/Cycle+ | Cost/Cycle |
|---|---|---|---|
| Varubi™ (rolapitant) 90mg tablets | $279.84 | 2 tablets | $559.68 |
| Emend® (aprepitant) 125mg & 80mg capsules dosing pack | $189.94 | 3 capsules | $569.82 |
| Akynzeo® (netupitant/palonosetron) 300mg/0.5mg capsules | $502.66 | 1 capsule | $502.66 |

*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.
+Quantity/cycle based on FDA approved dosing regimen per chemotherapy cycle.

## Recommendations

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Emend® (aprepitant) to include specific criteria for the oral suspension formulation
2. Revising the existing criteria for Diclegis® (doxylamine/pyridoxine) in response to the updated 2015 ACOG practice guidelines for the treatment of nausea and vomiting of pregnancy
3. Revising the existing criteria for Akynzeo® (netupitant/palonosetron) to require a failed trial of aprepitant (Emend®) based on estimated net cost per chemotherapy cycle
4. The prior authorization of Varubi™ (rolapitant) with the criteria listed below

New proposed criteria specific to each medication is as follows:

**Kytril® and Sancuso® (Granisetron), Anzemet® (Dolasetron), and Emend® (Aprepitant) Approval Criteria:**

1. An FDA approved diagnosis; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length will be based on duration of need.
4. For Emend® (aprepitant) oral suspension, an age restriction of six years and younger will apply. Members older than six years of age will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used.

**Diclegis® (Doxylamine/Pyridoxine) Approval Criteria:**

1. An FDA approved diagnosis of nausea and vomiting of pregnancy that is not responsive to conservative management; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. ~~Trials with at least two prescription medications that have failed to relieve nausea and vomiting; and~~
4. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin $B_6$ (pyridoxine).

**Akynzeo® (Netupitant/Palonosetron) Approval Criteria:**

1. An FDA approved diagnosis for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. A previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. Approval length based on duration of need.
4. A quantity limit of one capsule per chemotherapy cycle will apply.

**Varubi™ (Rolapitant) Approval Criteria:**

1. An FDA approved indication for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy; and
2. A previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. Approval length based on duration of need.
4. A quantity limit of two tablets per chemotherapy cycle will apply.

## Utilization Details of Anti-Emetic Medications: Fiscal Year 2015

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | PERCENT COST |
|---|---|---|---|---|---|---|
| **ONDANSETRON PRODUCTS** | | | | | | |
| ONDANSETRON TAB 4MG ODT | 54,349 | 43,409 | $587,197.97 | $1.46 | $10.80 | 46.83% |
| ONDANSETRON TAB 4MG | 15,545 | 11,275 | $143,465.14 | $0.96 | $9.23 | 11.44% |
| ONDANSETRON TAB 8MG ODT | 12,469 | 8,623 | $170,886.54 | $1.63 | $13.70 | 13.63% |
| ONDANSETRON TAB 8MG | 6,412 | 4,053 | $81,518.66 | $1.27 | $12.71 | 6.50% |
| ONDANSETRON SOL 4MG/5ML | 5,966 | 5,260 | $204,129.63 | $3.47 | $34.22 | 16.28% |
| ONDANSETRON INJ 4MG/2ML | 63 | 45 | $699.27 | $3.22 | $11.10 | 0.06% |
| ONDANSETRON INJ 40/20ML | 32 | 8 | $1,080.07 | $3.23 | $33.75 | 0.09% |
| **SUBTOTAL** | **94,836** | **72,673** | **$1,188,977.28** | **$1.52** | **$12.54** | **94.83%** |
| **DRONABINOL PRODUCTS** | | | | | | |
| DRONABINOL CAP 5MG | 71 | 22 | $22,078.45 | $10.75 | $310.96 | 1.76% |
| DRONABINOL CAP 2.5MG | 34 | 14 | $6,447.02 | $7.00 | $189.62 | 0.51% |
| DRONABINOL CAP 10MG | 19 | 6 | $11,732.89 | $21.33 | $617.52 | 0.94% |
| **SUBTOTAL** | **124** | **42** | **$40,258.36** | **$11.42** | **$324.66** | **3.21%** |
| **APREPITANT PRODUCTS** | | | | | | |
| EMEND PAK 80 & 125 | 20 | 12 | $11,694.95 | $28.81 | $584.75 | 0.93% |
| EMEND CAP 80MG | 6 | 3 | $1,582.92 | $143.90 | $263.82 | 0.13% |
| **SUBTOTAL** | **26** | **15** | **$13,277.87** | **$31.84** | **$510.69** | **1.06%** |
| **GRANISETRON PRODUCTS** | | | | | | |
| GRANISETRON TAB 1MG | 16 | 8 | $810.46 | $3.17 | $50.65 | 0.06% |
| GRANISETRON INJ 4MG/4ML | 11 | 5 | $293.45 | $26.68 | $26.68 | 0.02% |
| SANCUSO DIS 3.1MG | 6 | 3 | $8,276.24 | $58.70 | $1,379.37 | 0.66% |
| GRANISETRON INJ 1MG/ML | 2 | 1 | $19.94 | $9.97 | $9.97 | 0.00% |
| **SUBTOTAL** | **35** | **17** | **$9,400.09** | **$22.93** | **$268.57** | **0.75%** |
| **DOXYLAMINE/PYRIDOXINE PRODUCTS** | | | | | | |
| DICLEGIS TAB 10-10MG | 5 | 4 | $1,901.64 | $12.76 | $380.33 | 0.15% |
| **SUBTOTAL** | **5** | **4** | **$1,901.64** | **$12.76** | **$380.33** | **0.15%** |
| **TOTAL** | **95,026** | **67,071*** | **$1,253,815.24** | **$1.60** | **$13.19** | **100.00%** |

*Total number of unduplicated members.

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[12] Micromedex 2.0: Varubi™ Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 10/29/15. Last accessed 12/9/15.
[13] UpToDate: Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting. Available online at: http://www.uptodate.com/contents/prevention-and-treatment-of-chemotherapy-induced-nausea-and-vomiting. Last revised 11/6/15. Last accessed 12/9/15.

# Appendix L

# 30-Day Notice to Prior Authorize Cortisporin® and Pediotic® (Neomycin/Polymyxin B/Hydrocortisone Otic)

**Oklahoma Health Care Authority**
**January 2016**

## Current Prior Authorization Criteria

| Otic Anti-Infectives | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Special PA** |
| acetic acid (VoSol®, Acetasol®) | chloroxylenol/benzocaine/HC (Trioxin®) | acetic acid/HC (Acetasol® HC, VoSol® HC) |
| ciprofloxacin/dexamethasone (Ciprodex®) | chloroxylenol/pramoxine/zinc/ glycerin (Zinotic®, Zinotic® ES) | antipyrine/benzocaine/ glycerin/zinc (Neotic®) |
| neomycin/polymyxin B/HC (Cortisporin®, Pediotic®) | ciprofloxacin (Cetraxal®) | |
| | ciprofloxacin/HC (Cipro® HC) | |
| | finafloxacin (Xtoro™) | |
| | neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S) | |
| | ofloxacin (Floxin® Otic) | |

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

**Otic Anti-Infectives Tier-2 Approval Criteria:**

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

**Otic Anti-Infectives Special Prior Authorization (PA) Approval Criteria:**

1. Diagnosis of acute otitis externa; and
2. Recent (within 6 months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

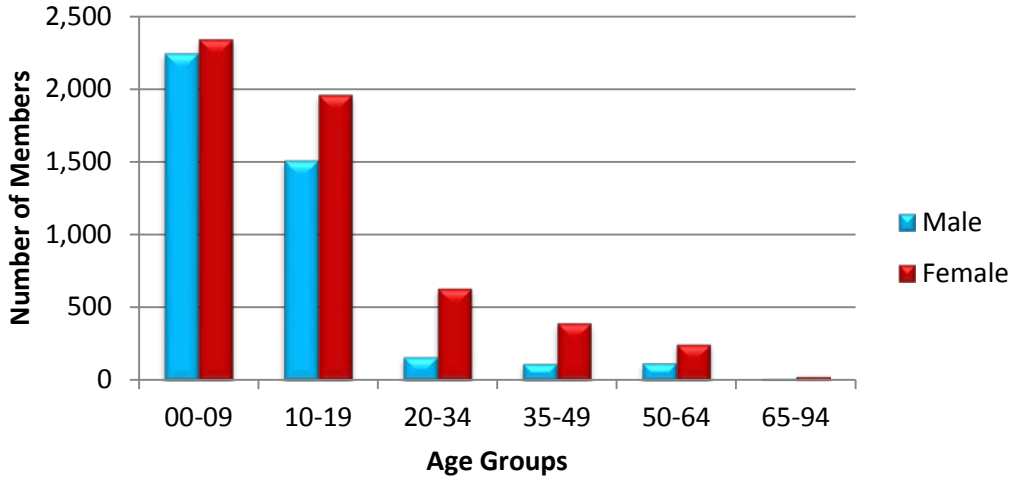
## Utilization of Cortisporin® and Pediotic® Otic

### Comparison of Fiscal Years

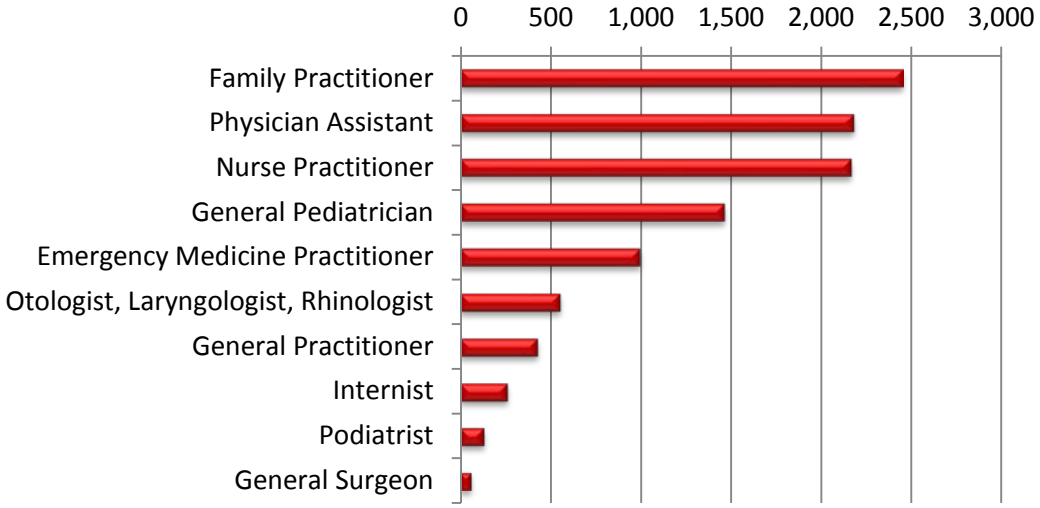
| Fiscal Year | Total Members* | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2014** | 10,815 | 11,855 | $289,100.40 | $24.39 | $2.36 | 119,059 | 122,626 |
| **2015** | 9,781 | 10,931 | $265,281.39 | $24.27 | $2.31 | 109,489 | 114,694 |
| % Change | -9.60% | -7.80% | -8.20% | -0.50% | -2.10% | -8.00% | -6.50% |
| Change | -1,034 | -924 | -$23,819.01 | -$0.12 | -$0.05 | -9,570 | -7,932 |

*Total number of unduplicated members.

### Demographics of Members Utilizing Cortisporin® and Pediotic® Otic

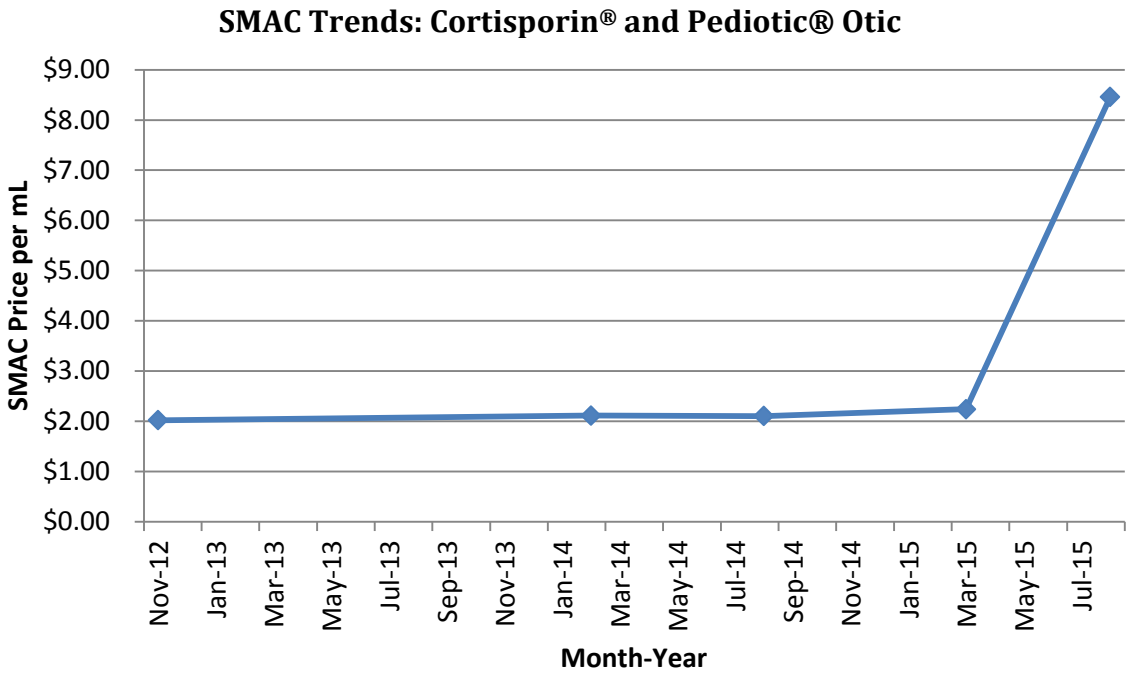



### Top Prescriber Specialties of Cortisporin and Pediotic® Otic by Number of Claims



## Market News and Updates[1,2]

Cortisporin® and Pediotic® otic have increased in price by more than 450% since November of 2012. No information is readily available to account for the increase in price, however the increase does not appear to be transient. The graph below outlines the state maximum allowable cost (SMAC) price increase trend for Cortisporin® otic since November of 2012.




The most recent SMAC price updated in August 2015 is $8.46 per mL, resulting in a 10mL bottle costing around $84.60. This price is significantly greater than the $20.20 cost per bottle in November of 2012. In quarter one of fiscal year 2015, a total of 3,917 members utilized Cortisporin® otic for a total of 4,042 claims. Based on these utilization estimates, the Cortisporin® otic price increase could result in an annual total increase in spending of approximately $1,041,220.00.

It is important to note that all Tier-1 otic anti-infectives have similar spectrum coverage including *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and that all pathogens covered by Cortisporin® otic are covered by at least one Tier-1 alternative. Tier-1 alternatives that could be used in place of Cortisporin® otic include the following treatment options:

- Cortisporin® TC, Coly-Mycin® S (neomycin/colistin/hydrocortisone/thonzonium) otic for those who need a similar otic antibiotic.
  - In comparison to Cortisporin® otic, Cortisporin® TC and Coly-Mycin® S contain similar active ingredients with the addition of thonzonium.
  - A benefit of thonzonium is it is a surface-active agent that promotes tissue contact of the medication by dispersion and penetration of the cellular debris and exudate.
- Other Tier-1 options available without prior authorization include: acetic acid (Vosol®, Acetasol®) and ciprofloxacin/dexamethasone (Ciprodex®).

## Recommendations

The College of Pharmacy recommends the following changes to the Otic Anti-Infectives Product Based Prior Authorization (PBPA) category:

1. Place neomycin/polymyxin B/HC (Cortisporin®, Pediotic®) into Tier-2.
    a. The existing criteria for this category will apply.
2. Place neomycin/colistin/HC/thonzonium (Cortisporin® TC, Coly-Mycin® S) into Tier-1.
    a. The existing criteria for this category will apply.
3. Initiate an educational mailing regarding these tier changes, which will include the option of utilizing neomycin/colistin/HC/thonzonium (Cortisporin® TC, Coly-Mycin® S) for otic conditions as well other Tier-1 otic anti-infectives.

| Otic Anti-Infectives | | |
|---|---|---|
| **Tier-1** | **Tier-2** | **Special PA** |
| acetic acid (VoSol®, Acetasol®) | chloroxylenol/benzocaine/HC (Trioxin®) | acetic acid/HC (Acetasol® HC, VoSol® HC) |
| ciprofloxacin/dexamethasone (Ciprodex®) | chloroxylenol/pramoxine/zinc/ glycerin (Zinotic®, Zinotic® ES) | antipyrine/benzocaine/ glycerin/zinc (Neotic®) |
| **neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S)** | ciprofloxacin (Cetraxal®) | |
| | ciprofloxacin/HC (Cipro® HC) | |
| | finafloxacin (Xtoro™) | |
| | ofloxacin (Floxin® Otic) | |
| | **neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)** | |

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

**Otic Anti-Infectives Tier-2 Approval Criteria:**

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

**Otic Anti-Infectives Special Prior Authorization (PA) Approval Criteria:**

1. Diagnosis of acute otitis externa; and
2. Recent (within 6 months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

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[1] Cortisporin. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; August 2015. Accessed December 18, 2015.
[2] Cortisporin-TC. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; November 2015. Accessed December 18, 2015.

# Appendix M

# Fiscal Year 2015 Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Duopa™ (Carbidopa/Levodopa Enteral Suspension) and Rytary™ (Carbidopa/Levodopa Extended-Release Capsules)

**Oklahoma Health Care Authority**
**January 2016**

## Current Prior Authorization Criteria

**Requip XL® (Ropinirole) & Mirapex ER® (Pramipexole) Approval Criteria:**

1. An FDA approved diagnosis of Parkinson's Disease; and
2. A patient-specific, clinically significant reason why the immediate-release products cannot be used.

**Neupro® (Rotigotine Transdermal System) Approval Criteria:**

1. For the diagnosis of Parkinson's Disease the following criteria apply:
   a. An FDA approved indication for the treatment of signs and symptoms of Parkinson's Disease; and
   b. Member must be 18 years of age or older; and
   c. Failed treatment, intolerance, or a patient-specific, clinically significant reason why the member cannot use oral dopamine agonists.
2. For the diagnosis of Restless Leg Syndrome the following criteria apply:
   a. An FDA approved indication of Restless Leg Syndrome; and
   b. Member must be 18 years of age or older; and
   c. Documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
      i. carbidopa/levodopa; or
      ii. pramipexole; or
      iii. ropinirole

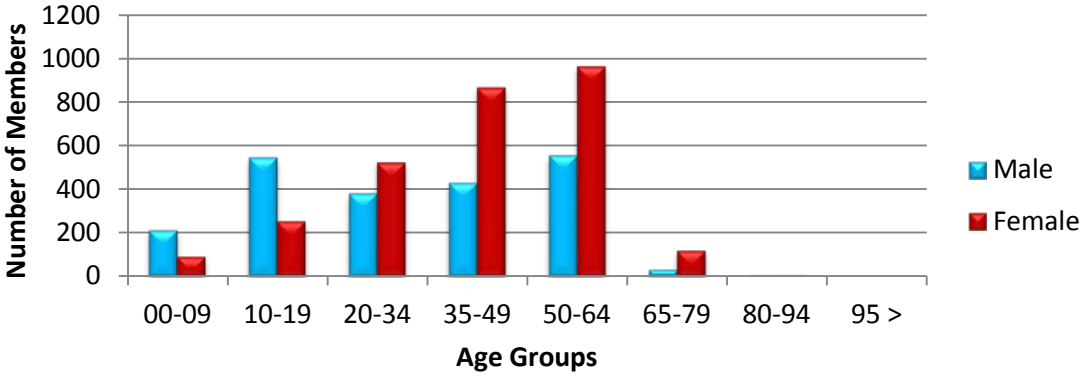
## Utilization of Parkinson's Disease Medications: Fiscal Year 2015

**Comparison of Fiscal Years**

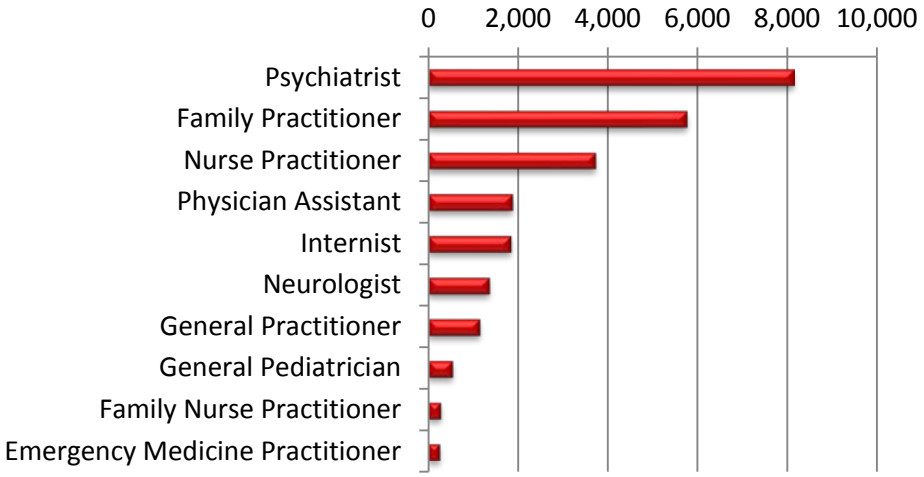
| Fiscal Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2014** | 4,897 | 25,861 | $691,128.09 | $26.72 | $0.83 | 1,578,636 | 831,345 |
| **2015** | 4,993 | 26,216 | $763,233.42 | $29.11 | $0.91 | 1,634,665 | 836,144 |
| **% Change** | **2.00%** | **1.40%** | **10.40%** | **8.90%** | **9.60%** | **3.50%** | **0.60%** |
| **Change** | **96** | **355** | **$72,105.33** | **$2.39** | **$0.08** | **56,029** | **4,799** |

*Total number of unduplicated members.

**Demographics of Members Utilizing Parkinson's Disease Medications**



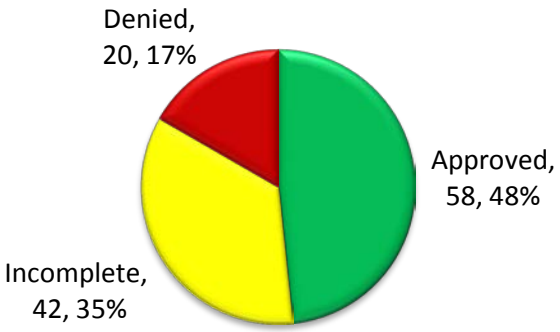

**Top Prescriber Specialties of Parkinson's Disease Medications by Number of Claims**




## Prior Authorization of Parkinson's Disease Medications

There were 120 prior authorization requests submitted for Parkinson's disease medications during fiscal year 2015. The following chart shows the status of the submitted petitions.

**Status of Petitions**



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

**Anticipated Patent Expirations:**

- Azilect® (rasagiline): August 2027
- Neupro® (rotigotine): September 2027

**New FDA Approvals:**

- **January 2015:** The U.S. Food and Drug Administration (FDA) approved Rytary™ an extended-release capsule formulation of carbidopa/levodopa for the treatment of Parkinson's disease (PD), postencephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication. Rytary™ contains immediate-release and extended-release beads, with a specific amount of carbidopa and levodopa in a 1:4 ratio, and provides both initial and extended levodopa plasma concentrations after a single dose.
- **January 2015:** The FDA approved Duopa™ (carbidopa/levodopa) enteral suspension for the treatment of motor fluctuations for people with advanced Parkinson's disease. Duopa™ is administered using a small, portable infusion pump that delivers carbidopa and levodopa directly into the small intestine for 16 continuous hours via a procedurally-placed tube. Duopa™ was approved by the FDA as an orphan drug, a designation granted to products intended for the treatment of rare diseases or conditions affecting fewer than 200,000 patients in the United States.

## Duopa™ (Carbidopa/Levodopa Enteral Suspension) Product Summary[4]

**Indications:** Duopa™ (carbidopa/levodopa enteral suspension) is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid) indicated for the treatment of motor fluctuations in patients with advanced Parkinson's disease.

**Dosing:**

- Duopa™ is available as an enteral suspension containing 4.63mg carbidopa and 20mg levodopa per mL in a single-use cassette. Each cassette contains approximately 100mL of suspension. Cassette reservoirs are specifically designed to be connected to the CADD®-Legacy 1400 pump. An opened cassette should not be reused.
- Duopa™ is administered over a 16-hour infusion period via either a naso-jejunal tube for short-term administration or into the jejunum through a percutaneous endoscopic gastrostomy with jejunal tube (PEG-J) for long-term administration.
- Establishment of the transabdominal port should be performed by a gastroenterologist or other healthcare provider experienced in this procedure.
- The daily dose is determined by individualized patient titration and composed of:
    - A morning dose
    - A continuous dose
    - Extra doses
- The maximum recommended daily dose of Duopa™ is 2000mg of the levodopa component (i.e. one cassette per day) administered over 16 hours.

- At the end of the daily 16-hour infusion, patients will disconnect the pump from the PEG-J and take their night-time dose of oral immediate-release carbidopa/levodopa tablets.
- Duopa™ has an extra dose function that can be used to manage acute "Off" symptoms that are not controlled by the Morning Dose and the Continuous Dose administered over 16 hours. The extra dose function should be set at 1mL (20mg of levodopa) when starting Duopa™.
- The dose of Duopa™ should be titrated as needed based on individual clinical response and tolerability.
- Sudden discontinuation or rapid dose reduction in patients taking Duopa™ should be avoided.
- Details regarding conversion from other forms of carbidopa/levodopa to Duopa™ can be found in the Duopa™ prescribing information.

**Mechanism of Action:** Duopa™ is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid).

- Carbidopa: When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the central nervous system. Carbidopa inhibits the decarboxylation of peripheral levodopa, making more levodopa available for delivery to the brain.
- Levodopa: Levodopa is the metabolic precursor of dopamine; it crosses the blood-brain barrier, and presumably is converted to dopamine in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson's disease.

**Contraindications:** Duopa™ is contraindicated in patients who are currently taking a nonselective monoamine oxidase (MAO) inhibitor (e.g. phenelzine and tranylcypromine) or have recently (within two weeks) taken a nonselective MAO inhibitor. Hypertension can occur if these drugs are used concurrently.

**Warnings and Precautions:**

- Gastrointestinal and Gastrointestinal Procedure-Related Risks: Because Duopa™ is administered using a PEG-J or naso-jejunal tube, gastrointestinal complications can occur. These complications include bezoar, ileus, implant site erosion/ulcer, intestinal hemorrhage, intestinal ischemia, intestinal obstruction, intestinal perforation, pancreatitis, peritonitis, pneumoperitoneum, and post-operative wound infection.
- Falling Asleep During Activities of Daily Living and Somnolence: Patients treated with levodopa have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles. Although many of these patients reported somnolence while on levodopa, some perceived that they had no warning signs and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1 year after initiation of treatment. Before initiating treatment with Duopa™, patients should be advised of the potential to develop drowsiness and factors that may increase the risk for somnolence.

- Orthostatic Hypotension: Duopa™-treated patients were more likely to experience a decline in orthostatic blood pressure than patients treated with oral immediate-release carbidopa/levodopa in the controlled clinical study. Patients should be monitored for orthostatic hypotension, especially after starting Duopa™ or increasing the dose.
- Hallucinations/Psychosis/Confusion: There is an increased risk for hallucinations and psychosis in patients taking Duopa™. Hallucinations present shortly after the initiation of therapy and may be responsive to dose reduction in levodopa. Confusion, insomnia, and excessive dreaming may accompany hallucinations. Because of the risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Duopa™. In addition, medications that antagonize the effects of dopamine used to treat psychosis may exacerbate the symptoms of Parkinson's disease and may decrease the effectiveness of Duopa™.
- Impulse Control/Compulsive Behaviors: Patients may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges while taking Duopa™.
- Depression and Suicidality: In the controlled clinical trial, 11% of Duopa™-treated patients developed depression compared to 3% of oral immediate-release carbidopa/levodopa-treated patients. Patients should be monitored for the development of depression and concomitant suicidal tendencies.
- Withdrawal-Emergent Hyperpyrexia and Confusion: A symptom complex resembling neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability) has been reported in association with rapid dose reduction, withdrawal of, or changes in dopaminergic therapy. Sudden discontinuation or rapid dose reduction should be avoided in patients taking Duopa™. If Duopa™ is discontinued, the dose should be tapered to reduce the risk of hyperpyrexia and confusion.
- Dyskinesia: Duopa™ may cause or exacerbate dyskinesias. The occurrence of dyskinesias may require a dosage reduction of Duopa™ or other medications used to treat Parkinson's disease.
- Neuropathy: In clinical studies, 5% patients treated with Duopa™ developed a generalized polyneuropathy. Most cases were classified as subacute or chronic in onset. The neuropathy was most often characterized as sensory or sensorimotor.
- Cardiovascular Ischemic Events: In clinical studies, myocardial infarction and arrhythmia were reported in patients taking carbidopa/levodopa.
- Melanoma: Epidemiological studies have shown that patients with Parkinson's disease have a higher risk (2 to approximately 6-fold higher) of developing melanoma than the general population. Whether the increased risk observed was due to Parkinson's disease or other factors, such as drugs used to treat Parkinson's disease, is unclear. Qualified health care providers should perform periodic skin examinations to monitor for melanoma in patients receiving Duopa™.
- Laboratory Test Abnormalities: Duopa™ may increase the risk for elevated (above the upper limit of normal for the reference range) blood urea nitrogen (BUN) and creatine phosphokinase (CPK). Patients taking levodopa or carbidopa/levodopa may have

increased levels of catecholamines and their metabolites in plasma and urine giving false positive results suggesting the diagnosis of pheochromocytoma.

- Glaucoma: Carbidopa/levodopa may cause increased intraocular pressure in patients with glaucoma. Intraocular pressure should be monitored in patients with glaucoma after starting Duopa™.

**Adverse Reactions:** The most common adverse reactions for Duopa™ (incidence at least 7% greater than oral immediate-release carbidopa/levodopa) during clinical trials were:

- Complication of device insertion
- Nausea
- Depression
- Peripheral edema
- Hypertension
- Upper respiratory tract infection
- Oropharyngeal pain
- Atelectasis
- Incision site erythema

**Use in Special Populations:**

- Pregnancy: Duopa™ is pregnancy category C. There are no adequate or well-controlled studies in pregnant women. It has been reported from individual cases that levodopa crosses the human placental barrier, enters the fetus, and is metabolized. In animal studies, carbidopa/levodopa has been shown to be developmentally toxic at clinically relevant doses. Duopa™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: Carbidopa is excreted in rat milk. In a study of one nursing mother with Parkinson's disease, excretion of levodopa in human milk was reported. Caution should be exercised when Duopa™ is administered to a nursing woman.
- Pediatric Use: The safety and effectiveness of Duopa™ in pediatric patients have not been established.
- Geriatric Use: In the controlled clinical trial, 49% of patients were 65 years and older, and 8% were 75 years and older. In patients 65 years and older, there was an increased risk for elevation of BUN and CPK (above the upper limit of the normal reference range) during treatment with Duopa™ compared to the risk for patients less than 65 years.

**Drug Interactions:**

- Monoamine Oxidase (MAO) Inhibitors: The use of nonselective MAO inhibitors with Duopa™ is contraindicated. The use of selective MAO-B inhibitors (e.g. rasagiline and selegiline) with Duopa™ may be associated with orthostatic hypotension.
- Antihypertensive Drugs: The concurrent use of Duopa™ with antihypertensive medications can cause symptomatic postural hypotension. A dose reduction of the antihypertensive medication may be needed after starting or increasing the dose of Duopa™.
- Dopamine D2 Receptor Antagonists and Isoniazid: Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone, metoclopramide, papaverine) and isoniazid may reduce the effectiveness of levodopa.
- Iron Salts: Iron salts or multi-vitamins containing iron salts can form chelates with levodopa/carbidopa and can cause a reduction in the bioavailability of Duopa™.

- High-Protein Diet: Because levodopa competes with certain amino acids for transport across the gut wall, the absorption of levodopa may be decreased in patients on a high-protein diet.

**Efficacy:** The efficacy of Duopa™ was established in a randomized, double-blind, double-dummy, active-controlled, parallel group, 12-week study in patients with advanced Parkinson's disease who were levodopa-responsive and had persistent motor fluctuations while on treatment with oral immediate-release carbidopa/levodopa. Patients were eligible for participation in the studies if they were experiencing 3 hours or more of "Off" time on their current Parkinson's disease drug treatment and they demonstrated a clear responsiveness to treatment with levodopa. Patients were randomized to either Duopa™ and placebo capsules or placebo suspension and oral immediate-release carbidopa/levodopa 25/100 mg capsules. The clinical outcome measure was the mean change from baseline in the total daily mean "Off" time, based on a Parkinson's disease diary. The mean score decrease (i.e. improvement) in "Off" time from baseline to Week 12 for Duopa™ was significantly greater (p=0.0015) than for oral immediate-release carbidopa/levodopa. Additionally, the mean score increase (i.e. improvement) in "On" time without troublesome dyskinesia from baseline to Week 12 was significantly greater (p=0.0059) for Duopa™ than for oral immediate-release carbidopa/ levodopa. The treatment difference for decrease in "Off" time was approximately 1.9 hours and the treatment difference for the increase in "On" time without troublesome dyskinesia was approximately 1.9 hours.

**Cost Comparison:**

| Medication | Cost Per mL or Capsule | Cost for 30 Days of Therapy |
|---|---|---|
| **Duopa™ (carbidopa/levodopa enteral suspension) single-use cassette** | **$2.13*** | **$6,390.00** |
| Sinemet® CR (carbidopa/levodopa sustained-release tablets) | $0.30-$0.53[+] | $31.80-$190.80 |

Dosing based on maintenance and maximum recommended dosing according to package labeling,
Costs do not reflect supplemental rebated prices or net costs.
*EAC = Estimated Acquisition Cost
[+]SMAC = State Maximum Allowable Cost

## Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) Product Summary[5]

**Indications:** Rytary™ (carbidopa/levodopa extended-release capsules) is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid) indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.

**Dosing:**

- Rytary ™ is available as combination carbidopa/levodopa extended-release capsules in the following strengths: 23.75mg/95mg, 36.25mg/145mg, 48.75mg/195mg, and 61.25mg/245mg.
- The recommended starting dosage of Rytary ™ in levodopa-naïve patients is 23.75mg/ 9mg by mouth three times daily for the first three days.

- The dosing frequency may be changed from three times a day to a maximum of five times a day if more frequent dosing is needed and if tolerated. The maximum recommended daily dose of Rytary ™ is 612.5mg/2450mg.
- Patients should be maintained on the lowest dosage required to achieve symptomatic control and to minimize adverse reactions such as dyskinesia and nausea.
- The dosages of other carbidopa and levodopa products are not interchangeable with the dosages of Rytary ™.
- Use of Rytary ™ in combination with other levodopa products has not been studied.
- Rytary ™ should be swallowed whole with or without food. A high-fat, high-calorie meal may delay the absorption of levodopa by approximately two hours.
- Capsules should not be chewed, divided or crushed. For patients who have difficulty swallowing intact capsules, Rytary ™ can be administered by opening the capsule, sprinkling the contents on a small amount of applesauce (1 to 2 tablespoons), and consuming immediately.

**Mechanism of Action:** Rytary™ is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid).

- Carbidopa: When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the central nervous system. Carbidopa inhibits the decarboxylation of peripheral levodopa, making more levodopa available for delivery to the brain.
- Levodopa: Levodopa is the metabolic precursor of dopamine; it crosses the blood-brain barrier, and presumably is converted to dopamine in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson's disease.

**Contraindications:**

- Rytary™ is contraindicated in patients who are currently taking a nonselective monoamine oxidase (MAO) inhibitor (e.g. phenelzine and tranylcypromine) or have recently (within two weeks) taken a nonselective MAO inhibitor. Hypertension can occur if these drugs are used concurrently.

**Warnings and Precautions:**

- Falling Asleep During Activities of Daily Living and Somnolence: Patients treated with levodopa have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles. Although many of these patients reported somnolence while on levodopa, some perceived that they had no warning signs and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1 year after initiation of treatment. Before initiating treatment with Rytary™, patients should be advised of the potential to develop drowsiness and factors that may increase the risk for somnolence.
- Withdrawal-Emergent Hyperpyrexia and Confusion: A symptom complex that resembles neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), has been reported in association with rapid dose reduction, withdrawal of, or changes in dopaminergic

therapy. Sudden discontinuation or rapid dose reduction should be avoided in patients taking Rytary™.

- Cardiovascular Ischemic Events: Cardiovascular ischemic events have occurred in patients taking Rytary™. In a clinical study in patients with early Parkinson's disease, 2.4% of Rytary™-treated patients experienced cardiovascular ischemic adverse reactions compared to 1.1% of placebo-treated patients. In patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmias, cardiac function should be monitored in an intensive cardiac care facility during the period of initial dosage adjustment.
- Hallucinations/Psychosis: There is an increased risk for hallucinations and psychosis in patients taking Rytary™. Hallucinations present shortly after the initiation of therapy and may be responsive to dose reduction in levodopa. Because of the risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Rytary™. In addition, medications that antagonize the effects of dopamine used to treat psychosis may exacerbate the symptoms of Parkinson's disease and may decrease the effectiveness of Rytary™.
- Impulse Control/Compulsive Behaviors: Case reports suggest that patients taking Rytary™ can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges.
- Dyskinesia: Rytary™ can cause dyskinesias that may require a dosage reduction of Rytary™ or other medications used for the treatment of Parkinson's disease.
- Peptic Ulcer Disease: Treatment with Rytary™ may increase the possibility of upper gastrointestinal hemorrhage in patients with a history of peptic ulcer.
- Glaucoma: Rytary™ may cause increased intraocular pressure in patients with glaucoma.
- Melanoma: Epidemiological studies have shown that patients with Parkinson's disease have a higher risk of developing melanoma than the general population. Whether the increased risk observed was due to Parkinson's disease or other factors, such as drugs used to treat Parkinson's disease, is unclear.

**Adverse Reactions:** The most common adverse reactions (≥5% and more frequently than placebo) reported during Rytary™ clinical trials include the following:

- Nausea
- Dizziness
- Headache
- Insomnia
- Abnormal Dreams
- Dry Mouth
- Dyskinesia
- Anxiety
- Constipation
- Vomiting
- Orthostatic Hypotension

**Use in Special Populations:**

- Pregnancy: Rytary™ is pregnancy category C. There are no adequate and well-conducted studies in pregnant women. It has been reported from individual cases that levodopa crosses the human placental barrier, enters the fetus, and is metabolized. In animal studies, carbidopa-levodopa has been shown to be developmentally toxic (including teratogenic effects) at clinically relevant doses. Rytary™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

- Nursing Mothers: Carbidopa is excreted in rat milk. In a study of one nursing mother with Parkinson's disease, excretion of levodopa in human milk was reported. Caution should be exercised when Rytary™ is administered to a nursing woman.
- Pediatric Use: The safety and effectiveness of Rytary™ in pediatric patients have not been established.
- Geriatric Use: In controlled clinical trials of Rytary™, 418 patients were 65 years or older and no overall differences in safety and efficacy were observed between these patients and those under 65 years of age.

**Drug Interactions:**

- Monoamine Oxidase (MAO) Inhibitors: The use of nonselective MAO inhibitors with Rytary™ is contraindicated. Nonselective MAO inhibitors should be discontinued at least two weeks prior to initiating Rytary™. The use of selective MAO-B inhibitors (e.g. rasagiline and selegiline) with Rytary™ may be associated with orthostatic hypotension.
- Dopamine D2 Receptor Antagonists and Isoniazid: Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone, metoclopramide) and isoniazid may reduce the effectiveness of levodopa.
- Iron Salts: Iron salts or multi-vitamins containing iron salts can form chelates with levodopa/carbidopa and can cause a reduction in the bioavailability of Rytary™.

**Efficacy:**

- Early Parkinson's Disease: The effectiveness of Rytary™ in patients with early Parkinson's disease was established in a randomized, double-blind, placebo-controlled 30-week clinical trial (Study 1). Eligible patients were randomized to placebo or one of three fixed doses of Rytary™ (carbidopa/levodopa doses of 36.25mg/145mg, 61.25mg/245mg, or 97.5mg/390mg, three times a day). Patients continued taking concomitant selective MAO-B inhibitors, amantadine, and anticholinergics provided the doses were stable for at least four weeks before screening. The clinical outcome measure was the mean change from baseline in the sum of the Unified Parkinson's Disease Rating Scale (UPDRS) Part II (activities of daily living) score, and UPDRS Part III (motor score) at Week 30. The mean score decrease (i.e. improvement) from baseline to Week 30 for each of the three Rytary™ dosage groups (-11.7, -12.9, -14.9, $p<0.05$) was significantly greater than for placebo (-0.6).
- Advanced Parkinson's Disease: Study 2 was a 22-week trial consisting of a 3-week dose adjustment of current levodopa treatment prior to a 6-week conversion to Rytary™, which was followed by a 13-week, randomized, multicenter, double-blind, levodopa-containing active control, double-dummy trial. The study enrolled patients who had been maintained on a stable regimen of at least 400mg per day of levodopa prior to entry into the trial. Patients were continued on concomitant dopamine agonists, selective MAO-B inhibitors, amantadine, and anticholinergics provided the doses were stable for at least four weeks prior to screening. Patients were randomized to receive either Rytary™ or immediate-release carbidopa/levodopa. The clinical outcome measure was the percentage of "off" time during waking hours at Week 22, as assessed by the patient's Parkinson's disease diary. The "off" time was significantly improved in

Rytary™-treated patients compared to immediate-release carbidopa/levodopa-treated patients (Rytary™: 6.1 hours decreased to 3.9 hours, IR carbidopa/levodopa: 5.9 hours decreased to 4.9 hours, $p<0.05$). The decrease in "off" time observed with Rytary™ occurred with a concomitant increase in "on time" without troublesome dyskinesia.

**Cost Comparison:**

| Medication | Cost Per Capsule or Tablet | Cost for 30 Days of Therapy |
|---|---|---|
| **Rytary™ (carbidopa/levodopa extended-release capsules)** | **$2.43-$3.05*** | **$218.70-$915.00** |
| Sinemet® CR (carbidopa/levodopa sustained-release tablets) | $0.30-$0.53[+] | $31.80-$190.80 |

Dosing based on maintenance and maximum recommended dosing according to package labeling,
Costs do not reflect supplemental rebated prices or net costs.
*EAC = Estimated Acquisition Cost
[+]SMAC = State Maximum Allowable Cost

## Recommendations

The College of Pharmacy recommends the prior authorization of Duopa™ (carbidopa/levodopa enteral suspension) and Rytary™ (carbidopa/levodopa extended-release capsules) with the following criteria:

**Duopa™ (Carbidopa/Levodopa Enteral Suspension) Approval Criteria:**

1. An FDA approved diagnosis of advanced Parkinson's disease; and
2. For long-term administration, member or caregivers must be willing and able to administer Duopa® through a percutaneous endoscopic gastrostomy; and
3. Patients must be experiencing three hours or more of "Off" time on their current Parkinson's disease drug treatment and they must have demonstrated a clear responsiveness to treatment with levodopa; and
4. Approvals will be for a quantity of one cassette per day.

**Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) Approval Criteria**

1. An FDA approved diagnosis of Parkinson's disease, post-encephalitic parkinsonism, or parkinsonism that may follow carbon monoxide intoxication or manganese intoxication; and
2. A patient-specific, clinically significant reason why the member cannot use other generic carbidopa/levodopa combinations including Sinemet® CR (carbidopa/levodopa extended-release tablets).

## Utilization Details of Parkinson's Disease Medications: Fiscal Year 2015

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| **AMANTADINE PRODUCTS** | | | | | |
| AMANTADINE CAP 100MG | 3,408 | 717 | $311,694.33 | 4.75 | $91.46 |
| AMANTADINE TAB 100MG | 759 | 320 | $88,026.35 | 2.37 | $115.98 |
| AMANTADINE SYP 50MG/5ML | 247 | 100 | $2,208.87 | 2.47 | $8.94 |
| **Subtotal** | **4,414** | **1,004** | **$401,929.55** | **4.4** | **$91.06** |
| **BENZTROPINE PRODUCTS** | | | | | |
| BENZTROPINE TAB 1MG | 5,431 | 1,090 | $54,948.48 | 4.98 | $10.12 |
| BENZTROPINE TAB 2MG | 3,118 | 567 | $34,579.24 | 5.5 | $11.09 |
| BENZTROPINE TAB 0.5MG | 1,511 | 313 | $15,597.65 | 4.83 | $10.32 |
| BENZTROPINE INJ 1MG/ML | 1 | 1 | $208.61 | 1 | $208.61 |
| **Subtotal** | **10,061** | **1,780** | **$105,333.98** | **5.65** | **$10.47** |
| **ROPINIROLE PRODUCTS** | | | | | |
| ROPINIROLE TAB 1MG | 1,851 | 507 | $17,996.42 | 3.65 | $9.72 |
| ROPINIROLE TAB 0.5MG | 1,070 | 355 | $11,252.54 | 3.01 | $10.52 |
| ROPINIROLE TAB 2MG | 884 | 217 | $8,898.00 | 4.07 | $10.07 |
| ROPINIROLE TAB 0.25MG | 604 | 214 | $5,884.68 | 2.82 | $9.74 |
| ROPINIROLE TAB 3MG | 231 | 57 | $2,347.52 | 4.05 | $10.16 |
| ROPINIROLE TAB 4MG | 193 | 50 | $1,816.76 | 3.86 | $9.41 |
| ROPINIROLE TAB 5MG | 105 | 16 | $1,382.27 | 6.56 | $13.16 |
| **Subtotal** | **4,938** | **1,219** | **$49,578.19** | **4.05** | **$10.04** |
| **TRIHEXPHENIDYL PRODUCTS** | | | | | |
| TRIHEXYPHEN TAB 5MG | 1,451 | 271 | $15,663.21 | 5.35 | $10.79 |
| TRIHEXYPHEN TAB 2MG | 1,171 | 257 | $10,492.46 | 4.56 | $8.96 |
| TRIHEXYPHEN ELX 0.4MG/ML | 54 | 11 | $1,281.80 | 4.91 | $23.74 |
| **Subtotal** | **2,676** | **508** | **$27,437.47** | **5.27** | **$10.25** |
| **CARBIDOPA/LEVODOPA PRODUCTS** | | | | | |
| CARB/LEVO TAB 25-100MG | 947 | 195 | $15,976.65 | 4.86 | $16.87 |
| CARB/LEVO TAB 10-100MG | 313 | 61 | $4,642.45 | 5.13 | $14.83 |
| CARB/LEVO TAB 25-250MG | 304 | 45 | $8,422.84 | 6.76 | $27.71 |
| CARB/LEVO CR TAB 50-200MG | 174 | 28 | $6,106.47 | 6.21 | $35.09 |
| CARB/LEVO CR TAB 25-100MG | 96 | 21 | $2,439.74 | 4.57 | $25.41 |
| CARB/LEVO/ENTACAPONE 25-100-200MG | 16 | 3 | $3,699.52 | 5.33 | $231.22 |
| CARB/LEVO ODT 25-100MG | 15 | 4 | $726.78 | 3.75 | $48.45 |
| CARB/LEVO ODT 10-100MG | 12 | 2 | $362.94 | 6 | $30.25 |
| CARB/LEVO/ENTACAPONE 37.5-150-200MG | 12 | 1 | $3,055.72 | 12 | $254.64 |
| CARB/LEVO/ ENTACAPONE 12.5-50-200MG | 3 | 1 | $363.24 | 3 | $121.08 |
| CARB/LEVO/ENTACAPONE 50-200-200MG | 2 | 1 | $516.00 | 2 | $258.00 |
| CARB/LEVO ODT 25-250MG | 1 | 1 | $133.07 | 1 | $133.07 |
| **Subtotal** | **1,895** | **331** | **$46,445.42** | **5.73** | **$24.51** |
| **PRAMIPEXOLE PRODUCTS** | | | | | |
| PRAMIPEXOLE TAB 0.125MG | 520 | 157 | $3,375.67 | 3.31 | $6.49 |

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | CLAIMS/ MEMBER | COST/ CLAIM |
|---|---|---|---|---|---|
| PRAMIPEXOLE TAB 0.5MG | 478 | 127 | $3,283.89 | 3.76 | $6.87 |
| PRAMIPEXOLE TAB 0.25MG | 406 | 123 | $2,650.66 | 3.3 | $6.53 |
| PRAMIPEXOLE TAB 1MG | 266 | 61 | $2,056.90 | 4.36 | $7.73 |
| PRAMIPEXOLE TAB 1.5MG | 69 | 19 | $554.92 | 3.63 | $8.04 |
| PRAMIPEXOLE TAB 0.75MG | 22 | 5 | $183.57 | 4.4 | $8.34 |
| **Subtotal** | **1,761** | **421** | **$12,105.61** | **4.18** | **$6.87** |
| **BROMOCRIPTINE PRODUCTS** | | | | | |
| BROMOCRIPTIN TAB 2.5MG | 340 | 73 | $52,721.06 | 4.66 | $155.06 |
| BROMOCRIPTIN CAP 5MG | 23 | 3 | $10,944.39 | 7.67 | $475.84 |
| **Subtotal** | **363** | **74** | **$63,665.45** | **4.91** | **$175.39** |
| **ENTACAPONE PRODUCTS** | | | | | |
| ENTACAPONE TAB 200MG | 49 | 7 | $18,903.00 | 4.31 | $385.78 |
| **Subtotal** | **49** | **7** | **$18,903.00** | **4.31** | **$385.78** |
| **RASAGILINE PRODUCTS** | | | | | |
| AZILECT TAB 1MG | 36 | 12 | $25,287.16 | 3 | $702.42 |
| AZILECT TAB 0.5MG | 8 | 4 | $6,799.12 | 2 | $849.89 |
| **Subtotal** | **44** | **15** | **$32,086.28** | **2.93** | **$729.23** |
| **ROTIGOTINE PRODUCTS** | | | | | |
| NEUPRO DIS 4MG/24HR | 9 | 3 | $4,803.27 | 3 | $533.70 |
| NEUPRO DIS 2MG/24HR | 1 | 1 | $521.52 | 1 | $521.52 |
| **Subtotal** | **10** | **4** | **$5,324.79** | **2.5** | **$532.48** |
| **SELEGILINE PRODUCTS** | | | | | |
| SELEGILINE CAP 5MG | 4 | 2 | $329.48 | 2 | $82.37 |
| SELEGILINE TAB 5MG | 1 | 1 | $94.20 | 1 | $94.20 |
| **Subtotal** | **5** | **3** | **$423.68** | **1.67** | **$84.74** |
| **TOTAL** | **26,216** | **4,993*** | **$763,233.42** | **5.25** | **$29.11** |

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

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[2] Brooks, Megan. Medscape. "FDA Okays Carbidopa/Levodopa ER (Rytary) in Parkinson's." Available online at: http://www.medscape.com/viewarticle/837773. Last revised 01/08/2015. Last accessed 12/29/2015.
[3] AbbVie Inc. "Abbvie Announces U.S. Fda Approval of Duopa™ (Carbidopa and Levodopa) Enteral Suspension for the Treatment of Motor Fluctuations in Patients with Advanced Parkinson's Disease." Available online at: http://abbvie.mediaroom.com/2015-01-12-AbbVie-Announces-U-S-FDA-Approval-of-DUOPA-carbidopa-and-levodopa-Enteral-Suspension-for-the-Treatment-of-Motor-Fluctuations-in-Patients-with-Advanced-Parkinsons-Disease. Last revised 01/12/2015. Last accessed 12/29/2015.
[4] Duopa™ Product Information. AbbVie Inc. Available online at: http://www.rxabbvie.com/pdf/duopa_pi.pdf. Last revised: 05/2015. Last accessed 12/29/2015.
[5] Rytary™ Product Information. Impax Pharmaceuticals. Available online at: http://documents.impaxlabs.com/rytary/pi.pdf. Last revised: 01/2015. Last accessed 12/29/2015.

# Appendix N

# 30-Day Notice to Prior Authorize Xuriden™ (Uridine Triacetate)

**Oklahoma Health Care Authority**
**January 2016**

## Hereditary Orotic Aciduria Overview[1,2,3,4,5]

Hereditary Orotic Aciduria (HOA) or Type I Hereditary Orotic Aciduria is a rare autosomal recessive disorder characterized by anemia and developmental delays. The prevalence of this disorder is less than one in one million with approximately twenty known cases worldwide.

HOA is caused by a defect or a deficiency in uridine 5'-monophosphate (UMP) synthase, an enzyme in the pyrimidine pathway. It is coded by a single gene localized to chromosome 3q13. Lack of UMP synthase affects two enzyme activities, orotic phosphoribosyltransferase and orotidine monophosphate decarboxylase which reside in a single protein. This results in the body being unable to synthesize the enzyme uridine. This enzyme is necessary for the production of RNA and DNA. The interruption in this pathway leads to excessive production of orotic acid as there is no feedback inhibition from the products normally produced. The overproduction of orotic acid leads to accumulation which is excreted in the urine in large quantities. Additionally, the inability to form nucleic acids leads to decreased erythrocyte formation, which leads to anemia.

The symptoms of HOA include blood abnormalities (megaloblastic anemia), developmental delays (physical and intellectual), urinary tract obstruction due to the formation of orotic acid crystals in the urinary tract, and failure to thrive. Additionally, marked susceptibility to infection is seen in individuals with HOA. There are two known cases in which the patients exhibited orotic aciduria, but did not have megaloblastic anemia. It is thought that these individuals had sufficient UMP synthase to prevent anemia. Additionally there is one reported individual with only orotidylic decarboxylase deficiency with normal expression of phosphoribosyltransferase. This condition is referred to as Type II Hereditary Orotic aciduria.

Treatment of HOA includes taking supplements of uridine, and ingesting high dietary levels of uridine (broccoli, yeast, tomatoes, organ meat). In September 2015, the U.S. Food and Drug Administration (FDA) approved Xuriden™ (uridine triacetate), the first FDA-approved treatment for patients with HOA. Xuriden™ (uridine triacetate) delivers 4- to 6-fold more uridine into the systemic circulation compared to equivalent doses of uridine itself. In clinical trials, patients switched from oral uridine to Xuriden™ had hematological parameters that continued to be stable and growth parameters showed an increase in weight and continued stability in height. Additionally, continued normal levels of urine orotic acid and orotidine were noted.

## Xuriden™ (Uridine Triacetate) Product Summary[1,6]

**FDA Approved:** September 2015

**Indications:** Xuriden™ (uridine triacetate) is a pyrimidine analog indicated for uridine replacement therapy in individuals with hereditary orotic aciduria. Uridine triacetate is the first FDA-approved treatment for patients with hereditary orotic aciduria.

**Dosing:**

- Xuriden ™ (uridine triacetate) is available in 2g single-use packets containing orange-flavored oral granules.
- The prescribed dose is measured and mixed with applesauce, yogurt, pudding or infant formula/milk just prior to administration.
- The recommended starting dose is 60mg/kg once daily.
- Dosing should be adjusted based on weight and/or efficacy.
- Dosing may be increased to 120mg/kg daily (not to exceed 8g daily).

**Mechanism of Action:** Uridine triacetate is an acetylated form of uridine. Nonspecific esterases in the body deacetylate uridine triacetate and produce uridine in systemic circulation. Uridine can then be used by all cells to make uridine nucleotides. When uridine nucleotides are restored into the normal range, orotic acid is reduced by feedback inhibition. This in turn reduces urinary excretion of orotic acid. Additionally, uridine nucleotides restore the biochemical pathway for nucleic acid production, and resolve anemia.

**Contraindications:** None

**Warnings and Precautions:** None

**Adverse Reactions:** The safety of uridine triacetate was assessed in four patients with HOA. They ranged in age from 3 to 19 years and received 60mg/kg of uridine triacetate once daily for six weeks. These patients continued to receive the medication at dosages of up to 120mg/kg daily for at least nine months. No adverse reactions were reported.

**Use in Special Populations:**

- Pregnancy: Data is not available for the use of uridine triacetate in pregnant women. When administered orally to pregnant rats at doses similar to that of humans, it was not teratogenic and did not produce adverse effects on embryo-fetal development.
- Lactation: There is no data available on the presence of uridine triacetate in human milk, the effect on the breastfed infant or the effect on milk production. The benefits of breastfeeding should be considered along with the mother's clinical need for uridine triacetate. Additionally, the possible adverse effects of uridine triacetate on a breastfed infant should be considered.
- Pediatric Use: The safety and effectiveness of uridine triacetate have been established for pediatric patients. The use of uridine triacetate is supported by a single open-label trial in four patients and a retrospective review of clinical course in 18 patients with HOA. These patients were treated with uridine triacetate beginning at ages 2 months to 12 years with no differences in clinical response between adult and pediatric patients.

**Efficacy:** The efficacy of uridine triacetate was assessed in an open-label study of four patients with HOA (three male, one female; ages 3 to 19 years). The patients were administered an oral dose of uridine triacetate at 60mg/kg once daily for six weeks. Three of the patients were treated with uridine prior to the study and then switched to uridine triacetate upon entry to the study. The study evaluated the patients' pre-specified hematologic parameters including: neutrophil count and percent neutrophils, white blood cell count, and mean corpuscular volume. For patients who switched from oral uridine to uridine triacetate, the primary endpoint was stability of the hematologic parameter. For the treatment-naïve patient, the primary endpoint was improvement of the hematologic parameter. For all patients the secondary endpoints were urine orotic acid and orotidine levels and growth (height and weight).
The hematologic parameters remained stable for the patients previously on uridine, but the treatment-naïve patient did not meet the endpoint for improvement. For the secondary endpoints of urine orotic acid and urine orotidine levels all previously stable patients remained stable. Three of the four patients were assessed for growth. Two patients showed weight growth while one remained stable. All three patients remained stable for height growth.

**Utilization/Cost:** There has been no utilization of Xuriden™ since its approval in September 2015. The cost of Xuriden™ is not yet available. Uridine supplements are available over-the-counter, but are not FDA approved and do not have a National Drug Code (NDC).

## Recommendations

The College of Pharmacy recommends the prior authorization of Xuriden™ (uridine triacetate) with the following criteria:

**Xuriden™ (Uridine Triacetate) Approval Criteria:**

1. An FDA approved diagnosis of Hereditary Orotic Aciduria defined by at least one of the following:
    a. Assay of the orotate phosphoribosyltransferase and orotidylic acid decarboxylase enzymes in the patients erythrocytes showing deficiency in both enzymes or deficiency in orotidylic acid decarboxylase alone; or
    b. Evidence of megaloblastic anemia; or
        i. Shown not to improve with iron supplements
        ii. Normal serum folate and vitamin B12 levels and no evidence of Transcobalamine II deficiency
    c. Orotic acid crystals visualized in the urine via microscopy; and
2. Current weight of member must be provided on the prior authorization request; and
    a. Weights should be reassessed every six months to ensure proper dosing and effectiveness; or
    b. Prescriber can indicate urine orotic acid levels are within normal ranges and dosing remains appropriate; and
3. The prescriber must verify that the patient/caregiver is able to properly measure and administer medication; and
4. A quantity limit of four packets per day will apply.

[1] Xuriden™ Prescribing Information. Wellstat Therapeutics Corporation. Available online at: http://www.xuriden.com/FPI.pdf. Last revised 09/2015. Last accessed 12/2015.
[2] OMIM®Online Mendelian Inheritance in Man ®: #258900 Orotic Aciduria. Available online at: http://www.omim.org/entry/258900?search=hereditary%20orotic%20aciduria&highlight=orotic%20aciduria%20hereditary. Last revised 9/2011. Last accessed 12/2015.
[3] Biochemistry for Medics©. Available online at: http://www.namrata.co/orotic-aciduria-causes-clinical-manifestations-diagnosis-and-treatment/. Last revised 02/2013 Last Last accessed 12/2015.
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[6] Food and Drug Administration. FDA approves new orphan drug to treat rare autosomal recessive disorder. http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm457867.htm. Last revised 09/2015. Last accessed 12/2015.

# Appendix O

# Fiscal Year 2015 Annual Review of Testosterone Products

**Oklahoma Health Care Authority**
**January 2016**

## Current Prior Authorization Criteria

| Testosterone Products | | |
|---|---|---|
| **Tier-1*** | **Tier-2** | **Special PA** |
| methyltestosterone powder | testosterone nasal gel (Natesto™) | fluoxymesterone oral tablet (Androxy®) |
| testosterone cypionate injection (Depo-Testosterone®) | testosterone patch (Androderm®) | methyltestosterone oral tablet/capsule (Android®, Methitest®, Testred®) |
| testosterone enanthate injection | testosterone topical gel (Fortesta®, Testim®, Vogelxo™) | testosterone buccal tablet (Striant®) |
| testosterone topical gel (Androgel®)[+] | testosterone topical solution (Axiron®) | testosterone pellets (Testopel®) |
| | testosterone undecanoate injection (Aveed®) | |

* Tier-1 products include generic injectable products and supplemental rebated topical products.
[+] Brand name preferred

**Initial Approval Criteria for All Testosterone Products:**

1. An FDA approved diagnosis:
    a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome, or orchidectomy; or
    b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation; or
    c. Delayed puberty; or
    d. Advanced inoperable metastatic mammary cancer in females one to five years postmenopausal, or premenopausal females with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and
2. Must include two labs showing pre-medication, morning testosterone (total testosterone) levels below 300ng/dL; and
3. Must include one lab showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis; or
4. Testosterone and gonadotropin labs are not required for authorization of testosterone therapy if documentation is provided for established hypothalamic pituitary or gonadal disease, if the pituitary gland or testes has/have been removed, or for postmenopausal females with advanced inoperable metastatic mammary cancer or premenopausal females with breast cancer benefitting from oophorectomy and that have been determined to have a hormone-responsive tumor.

**Testosterone Products Tier-2 Authorization Criteria:**

1. All diagnoses and laboratory requirements listed in the initial approval criteria for all testosterone products must be met; and
2. A trial of at least two Tier-1 products (must include at least one injectable and one topical formulation) at least 12 weeks in duration; or
3. A patient-specific, clinically significant reason why member cannot use all available Tier-1 medications; or
4. Prior stabilization on a Tier-2 medication (within the past 180 days).
5. Approvals will be for the duration of one year.

**Testosterone Products Special Prior Authorization Criteria:**

1. All diagnoses and laboratory requirements listed in the initial approval criteria for all testosterone products must be met; and
2. A patient-specific, clinically significant reason why member cannot use all other available formulations of testosterone.
3. Approvals will be for the duration of one year.

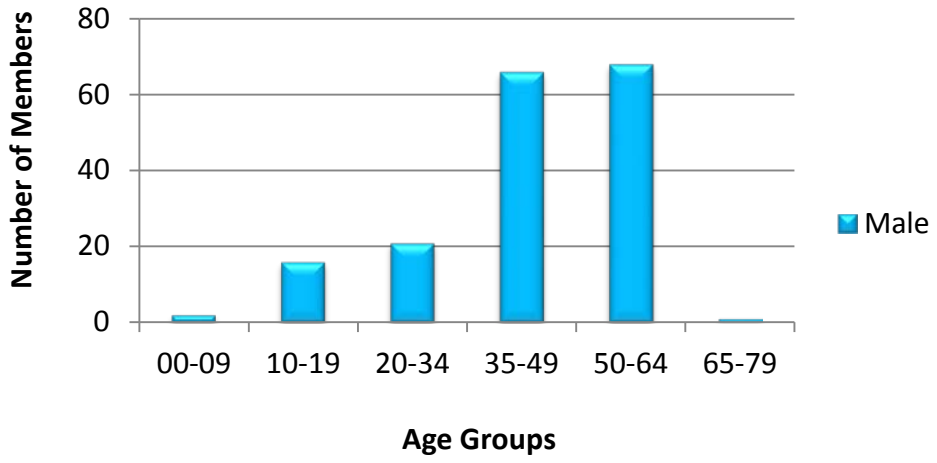
## Utilization of Testosterone Products: Fiscal Year 2015

### Comparison of Fiscal Years

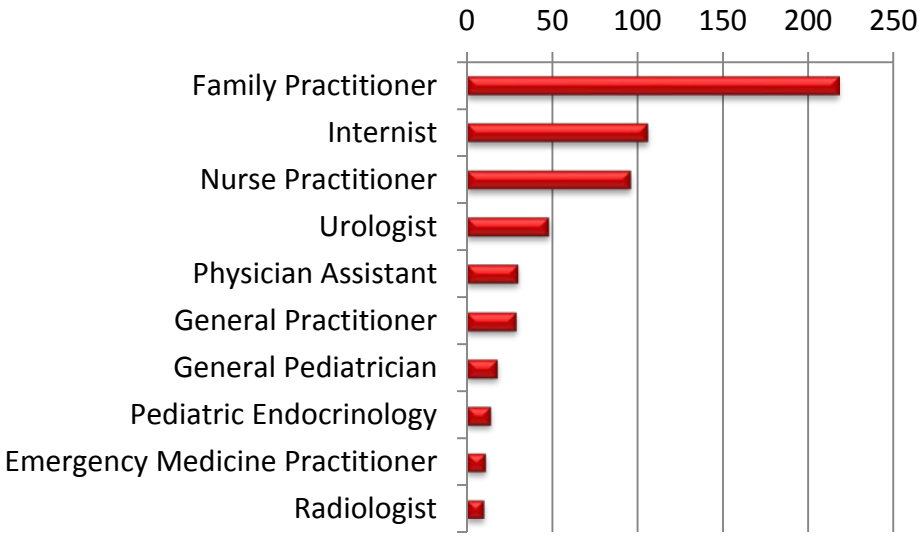
| Fiscal Year | *Total Members | Total Claims | Total Cost | Cost/ Claim | Cost/ Day | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2014** | 273 | 864 | $245,505.07 | $284.15 | $5.86 | 63,698 | 41,874 |
| **2015** | 175 | 622 | $154,357.26 | $248.16 | $5.18 | 32,799 | 29,813 |
| % Change | -35.90% | -28.00% | -37.10% | -12.70% | -11.60% | -48.50% | -28.80% |
| Change | -98 | -242 | -$91,147.81 | -$35.99 | -$0.68 | -30,899 | -12,061 |

*Total number of unduplicated members.

### Demographics of Members Utilizing Testosterone Products



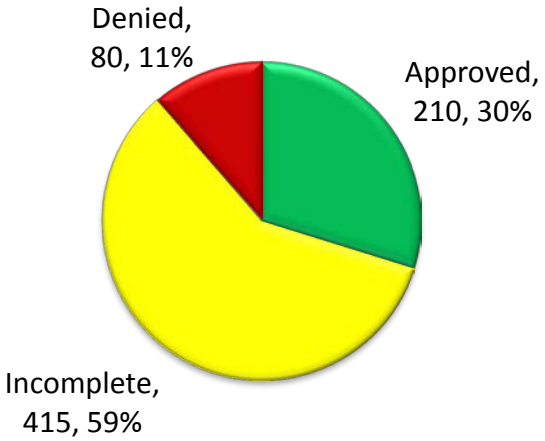
**Top Prescriber Specialties of Testosterone Products by Number of Claims**




## Prior Authorization of Testosterone Products

There were 705 prior authorization requests submitted for the testosterone products category during fiscal year 2015. The following chart shows the status of the submitted petitions.

**Status of Petitions**




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

**Anticipated Patent Expirations:**

- Striant® (testosterone buccal tablets): August 2019
- Natesto™ (testosterone nasal gel): February 2024
- Androgel® 1.62% (testosterone topical gel): October 2026
- Aveed™ (testosterone undecanoate injection): March 2027
- Axiron® (testosterone topical solution): September 2027
- Volgelxo™ (testosterone topical gel): February 2034

**FDA Safety Alert:**

- **March 2015:** In January 2014, the FDA announced that they were investigating the risk of stroke, heart attack, and death in men taking FDA-approved testosterone products. Based on available evidence from published studies and expert input from an Advisory Committee meeting, the FDA has concluded that there is a possible increased cardiovascular risk associated with testosterone use. The FDA cautions the use of testosterone products for low testosterone due to aging and is requiring labeling changes for all prescription testosterone products to reflect the possible increased risk of heart attacks and strokes associated with testosterone use. The FDA is also requiring manufacturers of approved testosterone products to conduct a well-designed clinical trial to more clearly address the question of whether an increased risk of heart attack or stroke exists among users of these products.

**Updated Treatment Guidelines:**

- **October 2015:** The Canadian Men's Health Foundation published clinical practice guidelines regarding the diagnosis and management of testosterone deficiency syndrome in men. Significant recommendations and conclusions include:
  - The initial biochemical test should be total testosterone level measured in serum samples taken in the morning between 7:00am and 11:00am, or within 3 hours after waking in the case of shift workers.
  - Measurement of sex hormone-binding globulin with calculated free or bioavailable testosterone should be restricted to men with symptoms of testosterone deficiency and equivocally low testosterone levels.
  - Investigation for secondary or reversible causes of hypogonadism is recommended in all men with testosterone deficiency syndrome.
  - Men with documented testosterone deficiency syndrome and no contraindications should receive treatment with testosterone.
  - Men with testosterone deficiency syndrome and stable cardiovascular disease are candidates for testosterone treatment.
  - Testosterone replacement therapy is not recommended in men more interested in maintaining fertility over symptomatic improvement.
  - Response and adverse effects should be assessed at three and six months after onset of therapy, and testosterone levels should be assessed at three and six months after onset of therapy and annually thereafter if stable.

**Pipeline Updates:**

- **September 2014:** The FDA Bone, Reproductive, and Urologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee rejected an NDA submitted by Clarus Therapeutics for Rextoro™, testosterone undecanoate oral capsules, saying the overall benefit-risk profile wasn't sufficient to support the approval of Rextoro™ for testosterone replacement therapy. The FDA is not required to follow the committee's decision, but will consider its findings during the NDA review of Rextoro™. The NDA for Rextoro™ is pending a final decision from the FDA.

- **October 2015:** Lipocine submitted an NDA to the FDA for LPCN 1021, a testosterone undecanoate oral product. The FDA has assigned a Prescription Drug User Fee Act (PDUFA) goal date of June 2016 for completion of the review of the NDA for LPCN 1021. Lipocine has another oral testosterone product (LPCN 1111) currently in development.
- **November 2015:** Clarus Therapeutics filed a lawsuit against Lipocine for infringing a Clarus patent ("the '428 patent" entitled "Pharmaceutical Delivery Systems for Hydrophobic Drugs and Compositions Comprising Same"), asserting that the patent covers Lipocine's LPCN 1021 product. Clarus seeks an injunction to prevent the commercial manufacture, use, and sale of Lipocine's LPCN 1021 product.

## Recommendations

The College of Pharmacy does not recommend any changes to the Testosterone Product Based Prior Authorization (PBPA) category at this time.

## Utilization Details of Testosterone Products: Fiscal Year 2015

| PRODUCT UTILIZED | TOTAL CLAIMS | TOTAL MEMBERS | TOTAL COST | COST/ DAY | COST/ CLAIM | PERCENT COST |
|---|---|---|---|---|---|---|
| **TESTOSTERONE INJECTABLE PRODUCTS** | | | | | | |
| TESTOST CYP INJ 200MG/ML | 244 | 95 | $16,469.62 | $1.06 | $67.50 | 10.67% |
| DEPO-TESTOST INJ 200MG/ML | 67 | 22 | $3,862.77 | $1.50 | $57.65 | 2.50% |
| TESTOST ENAN INJ 200MG/ML | 20 | 7 | $1,566.26 | $0.83 | $78.31 | 1.01% |
| DEPO-TESTOST INJ 100MG/ML | 7 | 5 | $554.24 | $0.58 | $79.18 | 0.36% |
| TESTOST CYP INJ 100MG/ML | 3 | 3 | $114.05 | $0.31 | $38.02 | 0.07% |
| **SUBTOTAL** | **341** | **132** | **$22,566.94** | **$1.06** | **$66.18** | **14.62%** |
| **TESTOSTERONE TOPICAL PRODUCTS** | | | | | | |
| ANDROGEL GEL 1.62% | 145 | 34 | $77,128.72 | $17.73 | $531.92 | 49.97% |
| ANDROGEL GEL 1%(50MG) | 45 | 10 | $18,740.86 | $14.04 | $416.46 | 12.14% |
| TESTOSTERONE GEL 1%(50MG) | 30 | 7 | $12,188.88 | $13.39 | $406.30 | 7.90% |
| ANDRODERM DIS 2MG/24HR | 16 | 2 | $6,063.07 | $12.08 | $378.94 | 3.93% |
| TESTOSTERONE GEL PUMP 1% | 11 | 5 | $3,335.93 | $9.53 | $303.27 | 2.16% |
| ANDROGEL GEL PUMP 1% | 11 | 9 | $4,471.66 | $11.92 | $406.51 | 2.90% |
| TESTIM GEL 1%(50MG) | 9 | 2 | $4,517.92 | $16.73 | $501.99 | 2.93% |
| AXIRON SOL 30MG/ACT | 5 | 1 | $2,250.44 | $15.00 | $450.09 | 1.46% |
| ANDRODERM DIS 4MG/24HR | 3 | 1 | $1,184.59 | $13.16 | $394.86 | 0.77% |
| FORTESTA GEL 10MG/ACT | 3 | 1 | $1,184.34 | $13.16 | $394.78 | 0.77% |
| ANDROGEL GEL 1.62% | 3 | 2 | $723.91 | $8.04 | $241.30 | 0.47% |
| **SUBTOTAL** | **281** | **74** | **$131,790.32** | **$15.48** | **$469.00** | **85.38%** |
| **TOTAL** | **622** | **175*** | **$154,357.26** | **$5.18** | **$248.16** | **100.00%** |

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/22/15. Last accessed 12/23/15.
[2] FDA Drug Safety Communication: FDA Cautions About Using Testosterone Products for Low Testosterone Due to Aging; Requires Labeling Change to Inform of Possible Increased Risk of Heart Attack and Stroke with Use. Available online at: http://www.fda.gov/drugs/drugsafety/ucm436259.htm. Last revised 3/3/15. Last accessed 12/23/15.
[3] Canadian Men's Health Foundation: Multidisciplinary Canadian Clinical Practice Guidelines on the Diagnosis and Management of Testosterone Deficiency Syndrome in Adult Males. Available online at: http://www.cmaj.ca/content/suppl/2015/10/26/cmaj.150033.DC1/15-0033-1-at.pdf. Last revised 10/26/15. Last accessed 12/23/15.
[4] Clarus Therapeutics Press Release: Clarus Therapeutics Reports FDA Advisory Committees Vote on Rextoro™ for Low Testosterone in Men. Available online at: http://clarustherapeutics.com/content/investors-and-media/releases/091814.htm. Last revised 9/18/14. Last accessed 12/23/15.
[5] Lipocine: Pipeline Overview. Available online at: http://www.lipocine.com/pipeline/index.htm. Last revised 10/2015. Last accessed 12/23/15.
[6] Lipocine Press Release: Lipocine Announces PDUFA Goal Date for LPCN 1021 NDA. Available online at: http://ir.lipocine.com/releasedetail.cfm?ReleaseID=942504. Last revised 11/12/15. Last accessed 12/23/15.
[7] Clarus Therapeutics Press Release: Clarus Therapeutics, Inc. Seeks Injunction Against the Marketing of Lipocine, Inc.'s Oral Product for Testosterone Replacement Therapy (LPCN 1021). Available online at: http://clarustherapeutics.com/content/investors-and-media/releases/110215.htm. Last revised 11/2/15. Last accessed 12/23/15.

# Appendix P

# Election of the Drug Utilization Review Board 2016-2017 Officers

# Appendix Q

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

## FDA NEWS RELEASE

**For Immediate Release: December 8th, 2015**

**FDA approves first drug to treat a rare enzyme disorder in pediatric and adult patients**

The U.S. Food and Drug Administration approved Kanuma (sebelipase alfa) as the first treatment for patients with a rare disease known as lysosomal acid lipase (LAL) deficiency.

Patients with LAL deficiency (also known as Wolman disease and cholesteryl ester storage disease [CESD]) have no or little LAL enzyme activity. This results in a build-up of fats within the cells of various tissues that can lead to liver and cardiovascular disease and other complications. Wolman disease often presents during infancy (around 2 to 4 months of age) and is a rapidly progressive disease. Patients with Wolman disease rarely survive beyond the first year of life. CESD is a milder, later-onset form of LAL deficiency and presents in early childhood or later. Life expectancy of patients with CESD depends on the severity of the disease and associated complications. Wolman disease affects one to two infants per million births, and CESD affects 25 individuals per million births.

The FDA's action involved approvals from two FDA centers. The Center for Veterinary Medicine (CVM) approved an application for a recombinant DNA (rDNA) construct in chickens that are genetically engineered (GE) to produce a recombinant form of human lysosomal acid lipase (rhLAL) protein in their egg whites. The FDA regulates GE animals under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act, because an rDNA construct introduced into an animal to change its structure or function meets the definition of a drug. The Center for Drug Evaluation and Research (CDER) approved the human therapeutic biologic (Kanuma), which is purified from those egg whites, based on its safety and efficacy in humans with LAL deficiency.

The new therapy, Kanuma, provides an rhLAL protein that functions in place of the missing, partially active or inactive LAL protein in the patient. Kanuma is produced by GE chickens containing an rDNA construct responsible for producing rhLAL protein in their egg whites. These egg whites are refined to extract the rhLAL protein that is eventually used to produce Kanuma and treat patients with LAL deficiency. The GE chickens are used only for producing the drug substance, and neither the chicken nor the eggs are allowed in the food supply.

Kanuma is approved for use in patients with LAL deficiency. Treatment is provided via intravenous infusion once weekly in patients with rapidly progressive LAL deficiency presenting in the first six months of life, and once every other week in all other patients.

CDER evaluated the safety and efficacy of Kanuma in an open-label, historically controlled trial in nine infants with rapidly progressive Wolman disease and in a double-blind, placebo-controlled trial in 66 pediatric and adult patients with CESD. In the trial in infants with Wolman disease, six of nine infants (67 percent) treated with Kanuma were alive at 12 months of age, whereas none of the 21 infants in the historical control group survived. In the trial in CESD patients, there was a statistically significant improvement in LDL-cholesterol levels and other disease-related parameters in those treated with Kanuma versus placebo after 20 weeks of treatment.

The most common side effects observed in patients treated with Kanuma are diarrhea, vomiting, fever, rhinitis, anemia, cough, headache, constipation, and nausea.

In its review of the GE chicken application, CVM assessed the safety of the rDNA construct, including the safety of the rDNA construct to the animals, as well as a full review of the construct and its stability in the genome of the chicken over several generations. No adverse outcomes were noted in the chickens. As required by the National Environmental Policy Act and its implementing regulations, CVM evaluated the potential environmental impacts of approval of the sponsor's GE chickens and determined that the approval does not cause any significant impact on the environment, because the chickens are raised in highly secure indoor facilities.

The FDA granted Kanuma orphan drug designation because it treats a rare disease affecting fewer than 200,000 patients in the United States. Orphan drug designation provides financial incentives for rare disease drug development such as clinical trial tax credits, user fee waivers, and eligibility for market exclusivity to promote rare disease drug development. Kanuma was also granted breakthrough therapy designation as it is the first and only treatment available for Wolman disease, the very severe infant form of the disease. The breakthrough therapy designation program encourages the FDA to work collaboratively with sponsors, by

providing timely advice and interactive communications, to help expedite the development and review of important new drugs for serious or life-threatening conditions. The Kanuma application was also granted a priority review, which is granted to drug applications that show a significant improvement in safety or effectiveness in the treatment of a serious condition. The manufacturer of Kanuma was granted a rare pediatric disease priority review voucher — a provision intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases.
Kanuma is produced by Alexion Pharmaceuticals Inc., based in Cheshire, Connecticut.

## FDA NEWS RELEASE

**For Immediate Release: December 11th, 2015**

**FDA approves new oral therapy to treat ALK-positive lung cancer**

The U.S. Food and Drug Administration approved Alecensa (alectinib) to treat people with advanced (metastatic) ALK-positive non-small cell lung cancer (NSCLC) whose disease has worsened after, or who could not tolerate treatment with, another therapy called Xalkori (crizotinib).
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. An ALK (anaplastic lymphoma kinase) gene mutation can occur in several different types of cancer cells, including lung cancer cells. ALK gene mutations are present in about 5 percent of patients with NSCLC. In metastatic cancer, the disease spreads to new parts of the body. In ALK-positive NSCLC metastatic patients, the brain is a common place for the disease to spread.
Alecensa is an oral medication that blocks the activity of the ALK protein, which may prevent NSCLC cells from growing and spreading.
The safety and efficacy of Alecensa were studied in two single-arm clinical trials of patients with metastatic ALK-positive NSCLC whose disease was no longer controlled by treatment with Xalkori. Study participants received Alecensa twice daily to measure the drug's effect on their lung cancer tumors. In the first study, 38 percent of participants experienced a partial shrinkage of their NSCLC tumors, an effect that lasted for an average of 7.5 months. In the second study, 44 percent of participants experienced a partial shrinkage of their NSCLC tumors, lasting for an average of 11.2 months. The trials also examined Alecensa's effect on individuals' brain metastases, a common occurrence in this population. Sixty-one percent of participants in the two trials who had measurable brain metastases experienced a complete or partial reduction in their brain tumors, lasting an average of 9.1 months.
The most common side effects of Alecensa are fatigue, constipation, edema and myalgia. Alecensa may cause serious side effects, including liver problems, severe or life-threatening inflammation of the lungs, very slow heartbeats and severe muscle problems. Treatment with Alecensa may cause sunburn when patients are exposed to sunlight.
Alecensa was approved using the accelerated approval regulatory pathway, which allows the FDA to approve products for serious or life-threatening diseases based on evidence that the product has an effect on an outcome that is reasonably likely to predict clinical benefit. In the case of Alecensa, the tumor response to treatment, along with the duration of response, provided this evidence. Under the accelerated approval requirements, a confirmatory study is required to verify and describe the clinical benefit of Alecensa.
The FDA granted the Alecensa application breakthrough therapy designation and priority review status. These are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions. Alecensa also received orphan drug designation, which provides incentives such as tax credits, user fee waivers and eligibility for exclusivity to assist and encourage the development of drugs for rare diseases.
Alecensa is marketed by Genentech, based in San Francisco, California. Xalkori is marketed by Pfizer, based in New York, New York.

## FDA NEWS RELEASE

**For Immediate Release: December 11th, 2015**

**FDA approves first emergency treatment for overdose of certain types of chemotherapy**

The U.S. Food and Drug Administration approved Vistogard (uridine triacetate) for the emergency treatment of adults and children who receive an overdose of the cancer treatment fluorouracil or capecitabine, or who develop certain severe or life-threatening toxicities within four days of receiving these cancer treatments.

Fluorouracil (taken by infusion) and capecitabine (taken orally) are similar types of chemotherapy that have been used for decades to treat several types of cancer, including breast and gastrointestinal cancers. An overdose of fluorouracil or capecitabine is rare, but when it occurs, the effects are serious and can be fatal. Vistogard, taken orally, blocks cell damage and cell death caused by fluorouracil chemotherapy. Patients should take Vistogard as soon as possible after the overdose (whether or not they have symptoms) or early-onset (within four days) of severe or life-threatening toxicity. The patient's health care provider will determine when he or she should return to the prescribed chemotherapy after treatment with Vistogard.
The efficacy and safety of Vistogard were studied in 135 adult and pediatric cancer patients who were treated in two separate trials and had either received an overdose of flourouracil or capecitabine, or had early-onset, unusually severe or life-threatening toxicities within 96 hours after receiving flourouracil (not due to an overdose). The studies' primary measure was survival at 30 days or until chemotherapy could resume if prior to 30 days. Of those who were treated with Vistogard for overdose, 97 percent were still alive at 30 days. Of those treated with Vistogard for early-onset severe or life-threatening toxicity, 89 percent were alive at 30 days. In both studies, 33 percent of patients resumed chemotherapy in less than 30 days.
Vistogard is not recommended for treating non-emergency adverse reactions associated with flourouracil or capecitabine because Vistogard may lessen the efficacy of these drugs. The safety and efficacy of Vistogard initiated more than 96 hours following the end of treatment with flourouracil or capecitabine have not been established.
The most common side effects of treatment with Vistogard were diarrhea, vomiting and nausea.
The FDA granted Vistogard orphan drug designation, which provides financial incentives, like clinical trial tax credits, user fee waivers, and eligibility for market exclusivity to promote rare disease drug development. Vistogard was also granted priority review and fast track designations, which are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions.
Vistogard is marketed by Wellstat Therapeutics Corporation based in Gaithersburg, Maryland.

## FDA NEWS RELEASE

**For Immediate Release: December 22nd, 2015**

**FDA approves new orphan drug to treat pulmonary arterial hypertension**

On December 21, the U.S. Food and Drug Administration approved Uptravi (selexipag) tablets to treat adults with pulmonary arterial hypertension (PAH), a chronic, progressive, and debilitating rare lung disease that can lead to death or the need for transplantation.
PAH is high blood pressure that occurs in the arteries that connect the heart to the lungs. It causes the right side of the heart to work harder than normal, which can lead to limitations on exercise ability and shortness of breath, among other more serious complications.
Uptravi belongs to a class of drugs called oral IP prostacyclin receptor agonists. The drug acts by relaxing muscles in the walls of blood vessels to dilate (open) blood vessels and decrease the elevated pressure in the vessels supplying blood to the lungs.
Uptravi's safety and efficacy were established in a long-term clinical trial of 1,156 participants with PAH. Uptravi was shown to be effective in reducing hospitalization for PAH and reducing the risks of disease progression compared to placebo. Participants were exposed to Uptravi in this trial for a median duration of 1.4 years.
Common side effects observed in those treated with Uptravi in the trial include headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in an extremity, and flushing.
Uptravi was granted orphan drug designation. Orphan drug designation provides incentives such as tax credits, user fee waivers, and eligibility for exclusivity to assist and encourage the development of drugs for rare diseases.
Uptravi is marketed by San Francisco-based Actelion Pharmaceuticals US, Inc.

## FDA NEWS RELEASE

**For Immediate Release: December 22nd, 2015**

**FDA approves Zurampic to treat high blood uric acid levels associated with gout**

The U.S. Food and Drug Administration approved Zurampic (lesinurad) to treat high levels of uric acid in the blood (hyperuricemia) associated with gout, when used in combination with a xanthine oxidase inhibitor (XOI), a type of drug approved to reduce the production of uric acid in the body.

Gout is a painful form of arthritis caused by the buildup of too much uric acid in the body, and usually appears first as redness, soreness, and swelling in the big toe. Uric acid in the blood is produced by the breakdown of substances called purines, which are found in all the body's tissues. Uric acid usually dissolves in the blood then passes through the kidneys and out of the body in urine. Uric acid can build up in the blood, a condition called hyperuricemia. This occurs when the body increases the amount of uric acid it makes, the kidneys do not get rid of enough uric acid, or a person eats too many foods high in purines. Most people with hyperuricemia do not develop gout, but if uric acid forms crystals in the body, gout can develop.
Zurampic works by helping the kidney excrete uric acid. It does this by inhibiting the function of transporter proteins involved in uric acid reabsorption in the kidney.
The safety and efficacy for Zurampic were evaluated in three randomized, placebo-controlled studies in combination with a XOI involving 1,537 participants for up to 12 months. Participants treated with Zurampic in combination with a XOI experienced reduced serum uric acid levels compared to placebo.
The most common adverse reactions in clinical trials were headache, influenza, increased blood creatinine, and gastroesophageal reflux disease.
Zurampic has a boxed warning that provides important safety information for health care professionals, including the risk for acute renal failure, which is more common when used without an XOI and with higher than approved doses of Zurampic.
The FDA is also requiring a postmarketing study to further evaluate the renal and cardiovascular safety of Zurampic.
Zurampic is manufactured by AstraZeneca Pharmaceuticals LP, based in Wilmington, Delaware.

## Safety Announcements

### FDA Drug Safety Communication: FDA eliminates the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone-containing diabetes medicines

**[12-16-2015]** The U.S. Food and Drug Administration (FDA) is eliminating the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone-containing type 2 diabetes medicines, which are approved as Avandia, Avandamet, Avandaryl, and generics. The REMS is no longer necessary to ensure that the benefits of rosiglitazone medicines outweigh their risks.
In 2013, we required removal of the prescribing and dispensing restrictions for rosiglitazone medicines after determining that data did not demonstrate an increased risk of heart attack with rosiglitazone medicines compared to the standard type 2 diabetes medicines metformin and sulfonylurea. We also required the drug manufacturers to provide educational training to health care professionals about the current state of knowledge regarding the heart risks of rosiglitazone medicines. Manufacturers have since fulfilled these requirements.
We have continued monitoring these medicines and identified no new pertinent safety information. As a result, we have determined the REMS is no longer necessary to ensure that the benefits of rosiglitazone medicines outweigh their risks. We will update the public if any new information becomes available.

## Safety Announcements

### FDA Drug Safety Communication: FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections

**[12-4-2015]** A U.S. Food and Drug Administration (FDA) safety review has resulted in adding warnings to the labels of sodium-glucose cotransporter-2 (SGLT2) inhibitors about the risks of too much acid in the blood and of serious urinary tract infections. Both conditions can result in hospitalization.
Patients should **stop taking their SGLT2 inhibitor and seek medical attention immediately** if they have any symptoms of ketoacidosis, a serious condition in which the body produces high levels of ketones. Symptoms of ketoacidosis include nausea, vomiting, abdominal pain, tiredness, and trouble breathing. Patients should also be alert for signs and symptoms of a urinary tract infection, such as a feeling of burning when urinating or the need to urinate often or right away; pain in the lower part of the stomach area or pelvis; fever; or blood in the urine. Contact a health care professional if you experience any of these symptoms.
Health care professionals should assess for ketoacidosis and urinary tract infections in patients taking SGLT2 inhibitors who present with suggestive symptoms. Ketoacidosis associated with the use of SGLT2 inhibitors can occur even if the blood sugar level is not very high. If ketoacidosis is suspected, the SGLT2 inhibitor should be discontinued and treatment instituted promptly.

SGLT2 inhibitors are a class of prescription medicines that are FDA-approved for use with diet and exercise to lower blood sugar in adults with type 2 diabetes. When untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. Medicines in the SGLT2 inhibitor class include canagliflozin, dapagliflozin, and empagliflozin. SGLT2 inhibitors are not FDA-approved for use in patients with type 1 diabetes.

We issued a Drug Safety Communication in May 2015 warning about the risk of ketoacidosis with SGLT2 inhibitors and alerting that we would continue to evaluate this safety issue. Our review of the FDA Adverse Event Reporting System (FAERS) database from March 2013 to May 2015 identified 73 cases of ketoacidosis in patients with type 1 or type 2 diabetes treated with SGLT2 inhibitors. FAERS includes only reports submitted to FDA, so there are likely additional cases about which we are unaware. All patients required hospitalization or treatment in an emergency department. In many cases, ketoacidosis was not immediately recognized because the blood glucose levels were below those typically expected for diabetic ketoacidosis. As a result, treatment of the ketoacidosis was delayed in some cases.

We also identified 19 cases of life-threatening blood infections (urosepsis) and kidney infections (pyelonephritis) that started as urinary tract infections with the SGLT2 inhibitors reported to FAERS from March 2013 through October 2014. All 19 patients were hospitalized, and a few required admission to an intensive care unit or dialysis in order to treat kidney failure.

As a result, we have added new *Warnings and Precautions* to the labels of all SGLT2 inhibitors to describe these two safety issues, and to provide prescribing and monitoring recommendations. We are also requiring manufacturers of SGLT2 inhibitors to conduct a required postmarketing study. This required enhanced pharmacovigilance study requests that manufacturers perform analyses of spontaneous postmarketing reports of ketoacidosis in patients treated with SGLT2 inhibitors, including specialized follow-up to collect additional information, for a period of 5 years.

## Safety Announcements

### FDA Drug Safety Communication: FDA cautions about dosing errors when switching between different oral formulations of antifungal Noxafil (posaconazole); label changes approved

**[1-4-2016]** The U.S. Food and Drug Administration (FDA) is cautioning that differences in dosing regimens between the two oral formulations of the antifungal Noxafil (posaconazole) have resulted in dosing errors. To help prevent additional medication errors, the drug labels were revised to indicate that the two oral formulations cannot be directly substituted for each other but require a change in dose. Direct mg for mg substitution of the two formulations can result in drug levels that are lower or higher than needed to effectively treat certain fungal infections.

Prescribers should specify the dosage form, strength, and frequency on all prescriptions they write for Noxafil. Pharmacists should request clarification from prescribers when the dosage form, strength, or frequency is not specified. Patients should talk to their health care professional before they switch from one oral formulation to the other.

Noxafil is approved in two oral formulations: an oral suspension and a delayed-release tablet. It is also approved as an intravenous solution for injection. Noxafil is used to help prevent certain invasive fungal infections caused by fungi called Aspergillus and Candida. Noxafil is used in patients who have an increased chance of getting these infections due to weakened immune systems. Noxafil oral suspension is also used to treat a fungal infection called thrush caused by Candida in the mouth or throat area.

Our review of the FDA Adverse Event Reporting System (FAERS) database identified cases of dosing errors with Noxafil. Noxafil was approved in 2006 as an oral suspension formulation. Since the approval of Noxafil delayed-release tablets in November 2013, FDA received eleven reports of the wrong oral formulations being prescribed and/or dispensed to patients. One case resulted in death, and an additional case resulted in hospitalization. According to the reports, these outcomes were a result of health care professionals not knowing that the two oral formulations cannot be substituted for each other without adjusting the dose due to differences in how the medicine is absorbed and handled by the body.

In addition to changes to the outer carton of Noxafil, its manufacturer Merck revised the prescribing information and the patient information in the drug label to alert patients and their health care professionals that the two oral formulations of Noxafil cannot be substituted for each other.

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

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

| | |
|---|---|
| Acetohydroxamic Acid (Lithostat) Tablets | ***Currently in Shortage*** |
| Ammonium Chloride Injection | ***Currently in Shortage*** |
| 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*** |
| Eptifibatide (Integrilin) Injection | ***Currently in Shortage*** |
| Ethiodized Oil (Lipiodol) Injection | ***Currently in Shortage*** |
| Fentanyl Citrate (Sublimaze) Injection | ***Currently in Shortage*** |
| Fomepizole Injection | ***Currently in Shortage*** |
| Gemifloxacin Mesylate (Factive) Tablets | ***Currently in Shortage*** |
| Haloperidol Lactate Injection | ***Currently in Shortage*** |
| Imipenem and Cilastatin for Injection, USP | ***Currently in Shortage*** |
| Indigotindisulfonate Sodium (Indigo Carmine) Injection | ***Currently in Shortage*** |
| L-Cysteine Hydrochloride Injection | ***Currently in Shortage*** |
| Leucovorin Calcium Lyophilized Powder for Injection | ***Currently in Shortage*** |
| Leuprolide Acetate Injection | ***Currently in Shortage*** |
| Levetiracetam (Keppra) Injection | ***Currently in Shortage*** |
| Lidocaine Hydrochloride (Xylocaine) Injection | ***Currently in Shortage*** |
| LifeCare PCA™ Sterile Empty Vial and Injector | ***Currently in Shortage*** |
| Liotrix (Thyrolar) Tablets | ***Currently in Shortage*** |
| Mecasermin [rDNA origin] (Increlex) Injection | ***Currently in Shortage*** |
| 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*** |
| Morphine Sulfate Injection, USP, CII, (Preservative-Free)(For PCA Use Only) | ***Currently in Shortage*** |
| Multi-Vitamin Infusion (Adult and Pediatric) | ***Currently in Shortage*** |
| Mupirocin Calcium Nasal Ointment | ***Currently in Shortage*** |
| Nebivolol (BYSTOLIC) Tablets | ***Currently in Shortage*** |
| Nimodipine (Nymalize) Oral Solution | ***Currently in Shortage*** |
| Peritoneal Dialysis Solutions | ***Currently in Shortage*** |
| Phentolamine Mesylate Injection | ***Currently in Shortage*** |

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|---|---|
| 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*** |
| Sodium Chloride 0.9% Injection Bags | ***Currently in Shortage*** |
| Sodium Chloride 23.4% Injection | ***Currently in Shortage*** |
| Sufentanil Citrate (Sufenta) Injection | ***Currently in Shortage*** |
| Sumatriptan (Imitrex) Nasal Spray | ***Currently in Shortage*** |
| Technetium Tc99m Succimer Injection (DMSA) | ***Currently in Shortage*** |
| Tigecycline (Tygacil) Injection | ***Currently in Shortage*** |
| Tiopronin (Thiola) | ***Currently in Shortage*** |
| Tobramycin Injection | ***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*** |