Drug Utilization Review Board

Oklahoma Health Care Authority

Wednesday
December 16, 2015
4:30pm

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 December 16, 2015

DATE: December 1, 2015

Note: The DUR Board will meet at 4:30p.m. The meeting will be held at 4345 N Lincoln Blvd.

Enclosed are the following items related to the December 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/Chronic Medication Adherence Program Update – Appendix B

Action Item - Vote to Prior Authorize Ibrance® (Palbociclib) – Appendix C

Action Item - Vote to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract) – Appendix D

Action Item - Vote to Prior Authorize Dyloject™ (Diclofenac Sodium) – Appendix E

Action Item - Vote to Prior Authorize Omidria® (Phenylephrine/Ketorolac Injection) – Appendix F

Action Item - Vote to Update Criteria for Xgeva® (Denosumab) – Appendix G

Action Item - Vote to Prior Authorize Daraprim® (Pyrimethamine) – Appendix H

Action Item - Vote to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin) – Appendix I

Action Item - Vote to Prior Authorize Keveyis™ (Dichlorphenamide) – Appendix J

Action Item - Vote to Prior Authorize Pramosone® (Hydrocortisone/Pramoxine Topical Cream and Lotion) & Enstilar® (Calcipotriene/Betamethasone Dipropionate Foam) – Appendix K

Action Item - Vote to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation) – Appendix L

Action Item - Vote to Prior Authorize Cosentyx® (Secukinumab) – Appendix M

Action Item - Vote to Prior Authorize Tetracycline Capsules, Minocycline Tablets, Ofloxacin Tablets, & Moxifloxacin Tablets – Appendix N

Action Item - Vote to Update Criteria for Xiaflex® (Collagenase Clostridium Histolyticum) – Appendix O

Annual Review of Hepatitis C Medications & 30-Day Notice to Prior Authorize Daklinza™ (Daclatasvir) & Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) – Appendix P

Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) & 30-Day Notice to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-Filgrastim), & Zarxio™ (Filgrastim-Sndz) – Appendix Q

30-Day Notice to Prior Authorize Aggrenox® (Aspirin/Dipyridamole Extended-Release) – Appendix R

Annual Review of HFA Rescue Inhalers and 30-Day Notice to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) – Appendix S

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) – Appendix T

Annual Review of Oral Anti-Fungal Medications and 30-Day Notice to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate) – Appendix U

Action Item - Annual Review of Fibromyalgia Medications – Appendix V

FDA and DEA Updates – Appendix W

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – December 16, 2015 @ 4:30 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

3. **Action Item – Approval of DUR Board Meeting Minutes – See Appendix A**
   A. October 14, 2015 DUR Minutes – Vote
   B. October 14, 2015 DUR Recommendations Memorandum
   D. November 11, 2015 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – See Appendix B**
   A. Medication Coverage Activity for October 2015
   B. Pharmacy Help Desk Activity for October 2015
   C. Medication Coverage Activity for November 2015
   D. Pharmacy Help Desk Activity for November 2015

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

5. **Action Item – Vote to Prior Authorize Ibrance® (Palbociclib) – See Appendix C**
   A. Introduction
   B. Recommendations

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

6. **Action Item – Vote to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract) – See Appendix D**
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Dyloject™ (Diclofenac Sodium) – See Appendix E**
   A. Introduction
   B. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Omidria® (Phenylephrine/Ketorolac Injection) – See Appendix F**
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Update Criteria for Xgeva® (Denosumab) – See Appendix G
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Daraprim® (Pyrimethamine) – See Appendix H
   A. Introduction
   B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin) – See Appendix I
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

12. Action Item – Vote to Prior Authorize Keveyis™ (Dichlorphenamide) – See Appendix J
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

13. Action Item – Vote to Prior Authorize Pramosone® (Hydrocortisone/Pramoxine Topical Cream and Lotion) & Enstilar® (Calcipotriene/Betamethasone Dipropionate Foam) – See Appendix K
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

14. Action Item – Vote to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation) – See Appendix L
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

15. Action Item – Vote to Prior Authorize Cosentyx® (Secukinumab) – See Appendix M
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

16. Action Item – Vote to Prior Authorize Tetracycline Capsules, Minocycline Tablets, Ofloxacin Tablets, & Moxifloxacin Tablets – See Appendix N
   A. Introduction
   B. College of Pharmacy Recommendations

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

17. Action Item – Vote to Update Criteria for Xiaflex® (Collagenase Clostridium Histolyticum) – See Appendix O
   A. Indication(s)
   B. College of Pharmacy Recommendations

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

18. Annual Review of Hepatitis C Medications & 30-Day Notice to Prior Authorize Daklinza™ (Daclatasvir) & Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) – See Appendix P
   A. Introduction
   B. Current Prior Authorization Criteria
   C. Utilization of Hepatitis C Medications
   D. Prior Authorization of Hepatitis C Medications
   E. Market News and Updates

F. Regimen Comparison
G. Other States' Coverage of Direct Acting Antivirals
H. Product Summaries
I. College of Pharmacy Recommendations
J. Utilization Details of Hepatitis C Medications

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

19. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) & 30-Day Notice to Prior Authorize Neulasta® (Pegfilgrastim), Granix® (Tbo-Filgrastim), & Zarxio™ (Filgrastim-Sndz) – See Appendix Q

A. Introduction
B. Utilization of G-CSFs
C. Prior Authorization of G-CSFs
D. Market News and Updates
E. Product Summaries
F. Cost Comparison Ratios: G-CSFs
G. College of Pharmacy Recommendation
H. Utilization Details of G-CSFs

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

20. 30-Day Notice to Prior Authorize Aggrenox® (Aspirin/ Dipyridamole Extended-Release) – See Appendix R

A. Aggrenox® (Aspirin/ Dipyridamole ER) Product Summary
B. Aggrenox® (Aspirin/ Dipyridamole ER) Cost Update
C. Aggrenox® (Aspirin/ Dipyridamole ER) Cost Comparison
D. Utilization Details of Aggrenox® (Aspirin/ Dipyridamole ER)
E. College of Pharmacy Recommendations

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

21. Annual Review of HFA Rescue Inhalers and 30-Day Notice to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) – See Appendix S

A. Current Prior Authorization Criteria
B. Utilization of HFA Rescue Inhalers
C. Prior Authorization of HFA Rescue Inhalers
D. Market News and Updates
E. ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of HFA Rescue Inhalers

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

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) – See Appendix T

A. Current Prior Authorization Criteria
B. Utilization of Maintenance Asthma and COPD Medications
C. Prior Authorization of Maintenance Asthma and COPD Medications
D. Market News and Updates
E. Product Summaries
F. New Indications
G. College of Pharmacy Recommendations
H. Utilization details of Maintenance Asthma and COPD Medications

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

23. Annual Review of Oral Anti-Fungal Medications and 30-Day Notice to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate) – See Appendix U

A. Current Prior Authorization Criteria
B. Utilization of Oral Anti-Fungals
C. Prior Authorization of Oral Anti-Fungals
D. Market News and Updates
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Oral Anti-Fungals

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

24. Action Item – Annual Review of Fibromyalgia Medications – See Appendix V

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

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

25. FDA and DEA Updates – See Appendix W

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

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

A. Anti-Migraine Medications/Migranal® (Dihydroergotamine Nasal Spray)
B. Anti-Emetic Medications/Varubi™ (Rolapitant)
C. Growth Hormone
D. Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) & Duopa™ (Carbidopa/Levodopa Enteral Suspension)
E. Testosterone Products
F. Xuriden™ (Uridine Triacetate)
G. Strensiq™ (Asfotase Alfa)
H. Cortisporin® (Neomycin/Polymyxin B/Hydrocortisone Otic Suspension)

***Future business subject to change.**

27. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF OCTOBER 14, 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	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
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	
Nico Gomez, Chief Executive Officer		x
Sylvia Lopez, M.D.; FAAP; Chief Medical Officer		x
Ed Long, Chief Communications Officer		x
Kelli Brodersen, Marketing Coordinator	x	
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, Deputy State Medicaid Director		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Medicaid Director	x	
Joseph Young, Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Sean Seago, Merck	Fran Kaiser, Merck	Paul McDermott, Celegene
Jana Shardonofsky, Vertex	Quynh Doan, Abbvie	Lon Lowrey, Novartis
Rick Ulasewich, DSL	Phillip Lafferty, Celegene	Roger Grotzinger, BMS
Gay Thomas, BMS	Kaitlin Harrison, Student	Brooke Winegardner
Jim Chapman, AbbVie	Brian Maves, Pfizer	Bob Gustafson, Lundbeck
Michele Puyear, Gilead Science	Mevin Nwamadi, Abbott	Mark DeClerk, Lilly
Jim Fowler, AstraZeneca	Eric Gardner, Vertex	Jason Schwier, Amgen
Kristen Mar, AstraZeneca	Kyle Frohbieter, Zylera	Ron Schnare, Shire

PRESENT FOR PUBLIC COMMENT:	
Fran Kaiser	Merck
Paul McDermott	Celegene
Mai Duong	Novartis
Quynh Doan	AbbVie

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA NO. 9 & 12 SPEAKER: FRAN KAISER

2B: AGENDA NO. 14 SPEAKER: PAUL MCDERMOTT

2C: AGENDA NO. 14 SPEAKER: MAI DUONG

2D: AGENDA NO. 14 SPEAKER: QUYNH DOAN

ACTION: NONE REQUIRED

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

3A: SEPTEMBER 9, 2015 DUR MINUTES – VOTE

3B: SEPTEMBER 9, 2015 DUR RECOMMENDATIONS MEMORANDUM

3C: VERIPRED™ AND MILLIPRED™ PRIOR AUTHORIZATION MEMORANDUM

3D: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **VOTE ON 2016 MEETING DATES**

4A: 2016 DUR BOARD MEETING DATES

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/BOWEL PREPARATION MEDICATION POST- EDUCATIONAL MAILING**

5A: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2015

5B: PHARMACY HELP DESK ACTIVITY FOR SEPTEMBER 2015

5C: BOWEL PREPARATION MEDICATION POST-EDUCATIONAL MAILING

Materials included in agenda packet; presented by Dr. Holderread
Dr. Harrell moved to approve; seconded by Ms. Varalli-Claypool
ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE TYKERB® (LAPATINIB), HALAVEN® (ERIBULIN), IXEMPRA® (IXABEPILONE), KADCYLA® (ADO-TRASTUZUMAB), AFINITOR® (EVEROLIMUS), & PERJETA® (PERTUZUMAB)
6A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented Dr. Schmidt, Dr. Borders, Dr. Medina
Dr. Harrell moved to approve; seconded by Dr. Huddleston
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ORKAMBI™ (LUMACAFTOR/IVACAFTOR)
7A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Teel
Dr. Winegardner moved to approve; seconded by Dr. Rhymer
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE SAVAYSA® (EDOXABAN)
8A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Hsu
Dr. Harrell moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE EPANOVA® (OMEGA-3-CARBOXYLIC ACIDS), PRALUENT® (ALIROCUMAB), & REPATHA™ (EVOLOCUMAB)
9A: COLLEGE OF PHARMACY RECOMMENDATIONS
9B: ATTACHMENT A: DIAGNOSIS OF HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (HeFH)
9C: ATTACHMENT B: FRAMINGHAM HEART STUDY AND FRAMINGHAM RISK SCORE
9D: DRAFT PCSK9 INHIBITOR PRIOR AUTHORIZATION FORM
Materials included in agenda packet; presented by Dr. Adams
Dr. Winegardner moved to approve; seconded by Dr. Rhymer
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MOVANTIK™ (NALOXEGOL), VIBERZI™ (ELUXADOLINE), & XIFAXAN® (RIFAXIMIN)
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
10C: PRIOR AUTHORIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS
10D: MARKET NEWS AND UPDATES
10E: PRODUCT SUMMARIES
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
10G: UTILIZATION DETAILS OF CONSTIPATION AND DIARRHEA MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE DARAPRIM® (PYRIMETHAMINE)**

11A: TOXOPLASMOSIS BACKGROUND INFORMATION
11B: DARAPRIM® (PYRIMETHAMINE) PRODUCT SUMMARY
11C: DARAPRIM® (PYRIMETHAMINE) COST UPDATE
11D: UTILIZATION DETAILS OF DARAPRIM® (PYRIMETHAMINE)
11E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF ALLERGY IMMUNOTHERAPIES AND 30-DAY NOTICE TO PRIOR AUTHORIZE ORALAIR® (SWEET VERNAL, ORCHARD, PERENNIAL RYE, TIMOTHY, & KENTUCKY BLUE GRASS MIXED POLLENS ALLERGEN EXTRACT)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: PRIOR AUTHORIZATION OF ALLERGY IMMUNOTHERAPIES
12C: ORALAIR® (ALLERGEN EXTRACT) PRODUCT SUMMARY
12D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Teel

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DYLOJECT™ (DICLOFENAC SODIUM)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
13C: PRIOR AUTHORIZATION OF NSAIDS
13D: MARKET NEWS AND UPDATES
13E: DYLOJECT™ (DICLOFENAC SODIUM) PRODUCT SUMMARY
13F: NSAID PRICE TRENDS
13G: COLLEGE OF PHARMACY RECOMMENDATIONS
13H: UTILIZATION DETAILS OF NSAIDS

Materials included in agenda packet; presented by Dr. Hsu

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE COSENTYX® (SECUKINUMAB)**

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS
14C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS
14D: MARKET NEWS AND UPDATES
14E: COSENTYX® (SECUKINUMAB) PRODUCT SUMMARY
14F: HIDRADENITIS SUPPURATIVA SUMMARY
14G: COLLEGE OF PHARMACY RECOMMENDATIONS
14H: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **ANNUAL REVIEW OF INHALED TOBRAMYCIN PRODUCTS AND PULMOZYME® (DORNASE ALFA) AND 30-DAY NOTICE TO PRIOR AUTHORIZE CAYSTON® (AZTREONAM INHALATION) & KITABIS™ PAK (TOBRAMYCIN INHALATION)**

15A: INTRODUCTION
15B: CURRENT PRIOR AUTHORIZATION CRITERIA
15C: UTILIZATION OF INHALED TOBRAMYCIN PRODUCTS, DORNASE ALFA, & AZTREONAM INHALATION
15D: PRIOR AUTHORIZATION OF INHALED TOBRAMYCIN PRODUCTS AND DORNASE ALFA
15E: MARKET NEWS AND UPDATES
15F: PRODUCT SUMMARIES
15G: COLLEGE OF PHARMACY RECOMMENDATIONS
15H: UTILIZATION DETAILS OF INHALED TOBRAMYCIN PRODUCTS, DORNASE ALFA, & AZTREONAM INHALATION

Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **ANNUAL REVIEW OF XOLAIR® (OMALIZUMAB)**

16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF XOLAIR® (OMALIZUMAB)
16C: PRIOR AUTHORIZATION OF XOLAIR® (OMALIZUMAB)
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; Questions only
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 18: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

18A: OPHTHALMIC ANTI-INFLAMMATORIES/OMIDRIA™ (PHENYLEPHRINE/KETOROLAC INJECTION)
18B: TOPICAL CORTICOSTEROIDS
18C: XIAFLEX® (COLLAGENASE CLOSTRIDIUM HISTOLYTICUM)
188: XGEVA® (DENOSUMAB)
18E: ERYTHROPOIETIN STIMULATING AGENTS
18F: PRIALT® (ZICONOTIDE)
18G: TETRACYCLINE AND OFLOXACIN 400MG TABLETS
18H: KEVEYIS™ (DICHLOROPHENAMIDE)
18I: IBRANCE® (PALBOCICLIB)

***Future business subject to change.

AGENDA ITEM NO. 19: **ADJOURNMENT**
The meeting was adjourned at 5:24 pm

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

Memorandum

Date: October 15, 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 October 14, 2015

Recommendation 1: Vote on 2016 Meeting Dates

MOTION CARRIED by unanimous approval.

Meetings are held the second Wednesday of every month at 4:00 p.m.

January 13, 2016	May 11, 2016	September 14, 2016
February 10, 2016	June 8, 2016	October 12, 2016
March 9, 2016	July 13, 2016	November 9, 2016
April 13, 2016	August 10, 2016	December 14, 2016

Recommendation 2: Bowel Preparation Medication Post-Educational Mailing: Consideration of Implementation of a Product Based Prior Authorization (PBPA) Category

NO ACTION REQUIRED.

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

1. Conduct a complete drug utilization review of the bowel preparation medication class to evaluate safety, efficacy, and cost of all products.

a. The drug utilization review should also include claims analysis for potential inappropriate use.
2. If appropriate, consider implementation of a PBPA category.
3. Alternatives to a PBPA category include additional targeted educational mailings to encourage appropriate, cost-effective utilization of the bowel preparation medications.

Recommendation 3: Vote to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-Trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab)

MOTION CARRIED by unanimous approval.

Tykerb® (Lapatinib) Approval Criteria:

1. An FDA approved diagnosis of metastatic or recurrent breast cancer; and
2. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
3. Tykerb® must be used in combination with one of the following:
    a. Herceptin® (trastuzumab); or
    b. Xeloda® (capecitabine); or
    c. An aromatase inhibitor [e.g. Aromasin® (exemestane), Femara® (letrozole) or Arimidex® (anastrozole)] if also estrogen receptor positive (ER positive).

Halaven® (Eribulin) Approval Criteria:

1. Diagnosis of metastatic breast cancer; and
2. Previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Ixempra® (Ixabepilone) Approval Criteria:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Usage as either:
    a. In combination with capecitabine after failure of an anthracycline and a taxane; or
        i. May be used in combination in taxane only resistance if anthracyclines not indicated; or
    b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine.

Kadcyla® (Ado-Trastuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Diagnosis of metastatic breast cancer; and
3. Member has previously received trastuzumab and a taxane, separately or in combination; and
4. Members should also have either:
    a. Received prior therapy for metastatic disease; or
    b. Developed disease recurrence during or within six months of completing adjuvant therapy.

Perjeta® (Pertuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Usage for either:
    a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease; or
    b. Neoadjuvant treatment of patients with locally advanced, inflammatory, or early stage breast cancer (either greater than 2cm in diameter or node positive); and
3. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents as well in addition to trastuzumab and docetaxel).

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

1. Diagnosis of advanced breast cancer; and
2. Negative expression of Human Epidermal Receptor Type 2 (HER2); and
3. Hormone receptor-positive (ER positive); and
4. Used in combination with exemestane; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.

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

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

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

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

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

1. Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC); and
2. Not requiring immediate surgery; and
3. Used in pediatric and adult patients with age ≥ 1 year.

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

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

Recommendation 4: Vote to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor)

MOTION CARRIED by unanimous approval.

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

Orkambi™ (Lumacaftor/Ivacaftor) Approval Criteria:

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

Recommendation 5: Vote to Prior Authorize Savaysa® (Edoxaban)

MOTION CARRIED by unanimous approval.

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

Savaysa® (Edoxaban) Approval Criteria:

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

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

Brilinta® (Ticagrelor) Approval Criteria:

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

Recommendation 6: Vote to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), & Repatha™ (Evolocumab)

MOTION CARRIED by unanimous approval.

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

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

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

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

PCSK9 Inhibitors Approval Criteria:

1. An FDA approved diagnosis of heterozygous familial hypercholesterolemia (HeFH) defined by the presence of one of the following criteria:
    a. A documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or
    b. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or
2. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol greater than 500mg/dL and at least one of the following:

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

Recommendation 7: Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin)

NO ACTION REQUIRED.

Recommendation 8: 30-Day Notice to Prior Authorize Daraprim® (Pyrimethamine)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Allergy Immunotherapies and 30-Day Notice to Prior Authorize Oralair® (Sweet Vernal, Orchard, Perennial Rye, Timothy, & Kentucky Blue Grass Mixed Pollens Allergen Extract)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Dyloject™ (Diclofenac Sodium)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Cosentyx® (Secukinumab)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Inhaled Tobramycin Products & Pulmozyme® (Dornase Alfa) and 30-Day Notice to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Xolair® (Omalizumab)

NO ACTION REQUIRED.

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

Memorandum

Date: November 12, 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 DUR packet of November 11, 2015

Recommendation 1: 30-Day Notice to Prior Authorize Ibrance® (Palbociclib)

NO ACTION REQUIRED.

Recommendation 2: 30-Day Notice to Prior Authorize Keveyis™ (Dichlorphenamide)

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Xgeva® (Denosumab)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Pramosone® (Hydrocortisone/Pramoxine Topical Cream and Lotion) and Enstilar® (Calcipotriene/Betamethasone Dipropionate Foam)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Ophthalmic Anti-Inflammatories and 30-Day Notice to Prior Authorize Omidria® (Phenylephrine/Ketorolac) Injection

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Tetracycline and Fluoroquinolone Antibiotics and 30-Day Notice to Prior Authorize Tetracycline Capsules, Minocycline Tablets, Ofloxacin Tablets, & Moxifloxacin Tablets

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Xiaflex® (Collagenase Clostridium Histolyticum)

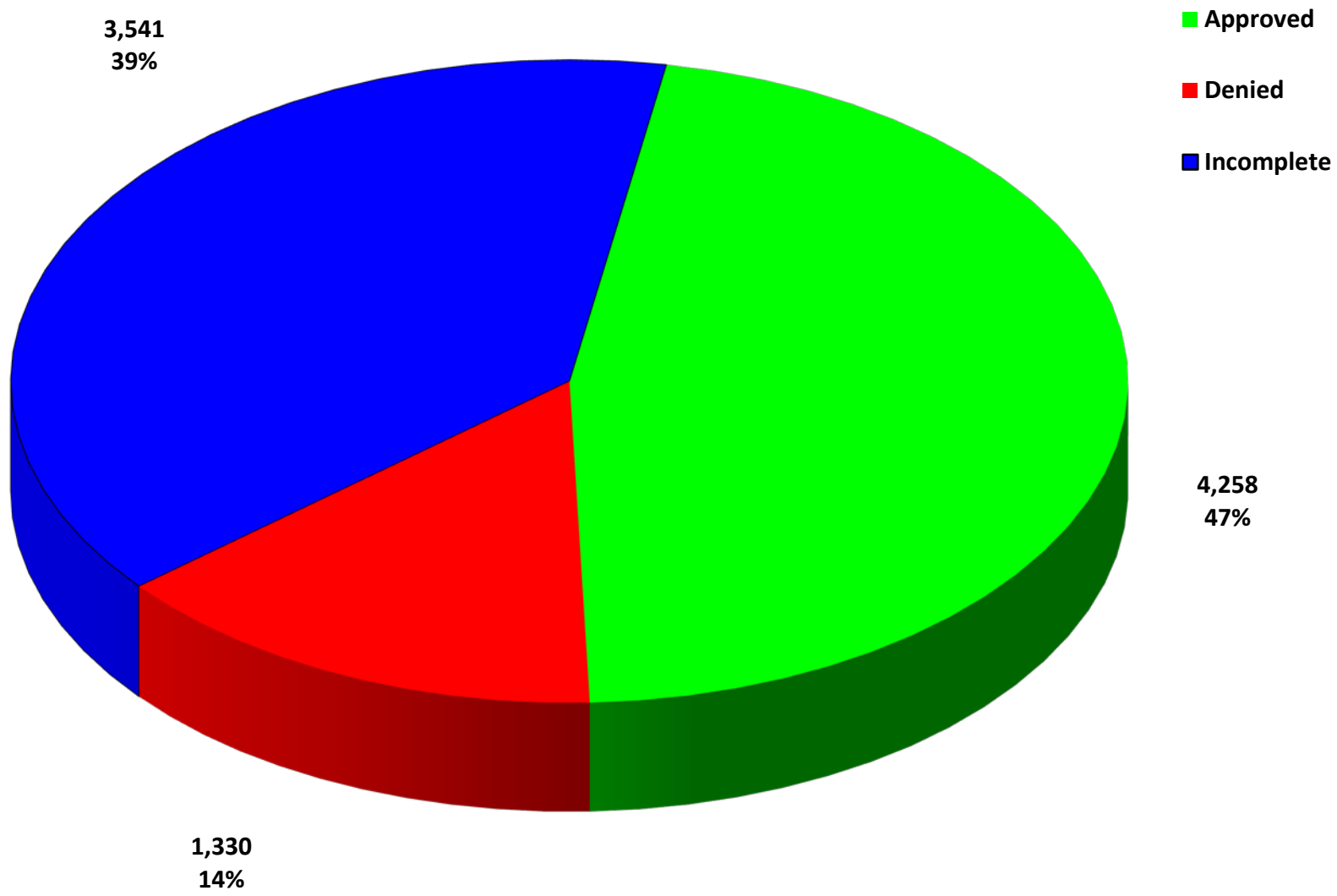
NO ACTION REQUIRED.

Recommendation 8: Annual Review of Erythropoiesis-Stimulating Agents

NO ACTION REQUIRED.

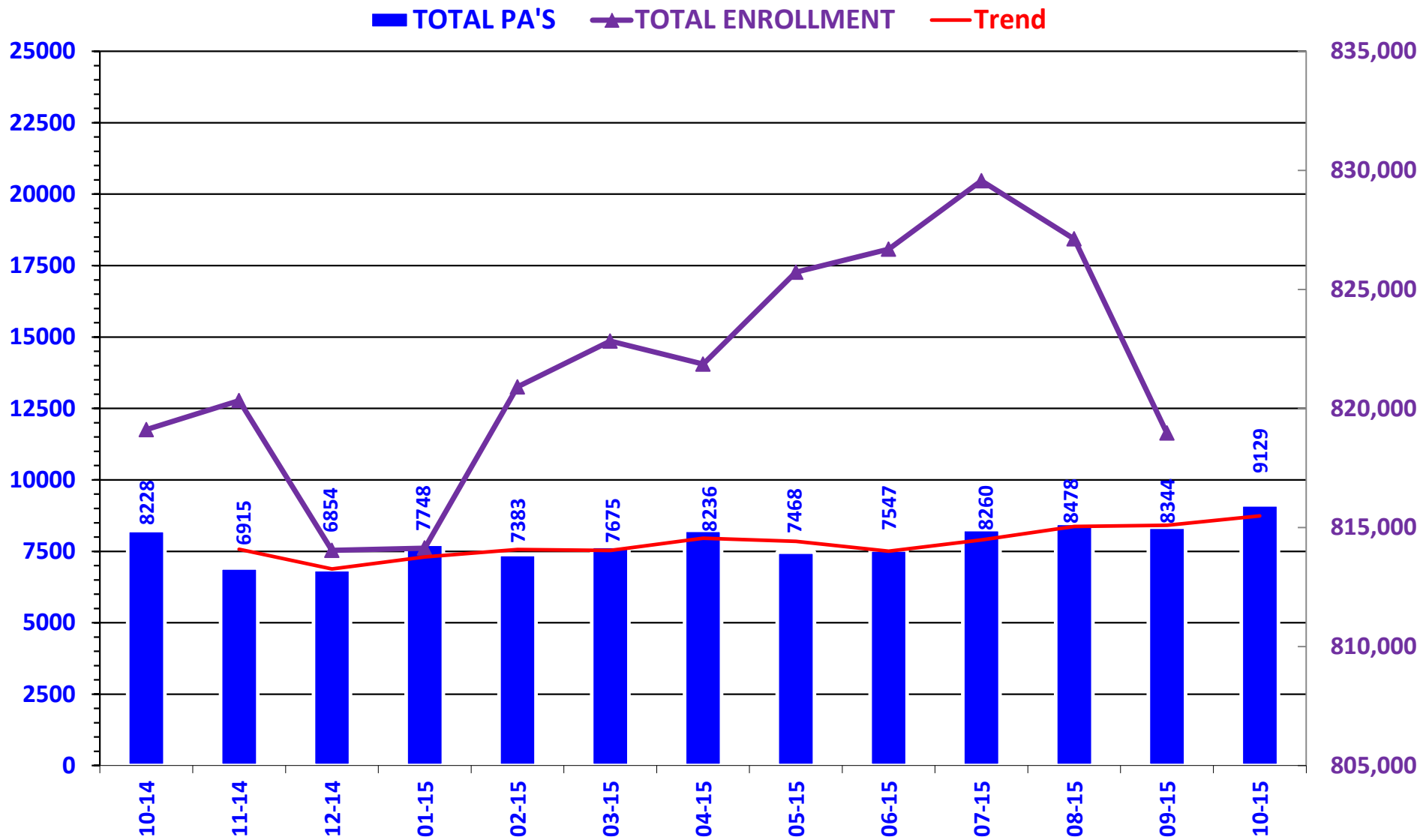
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER 2015



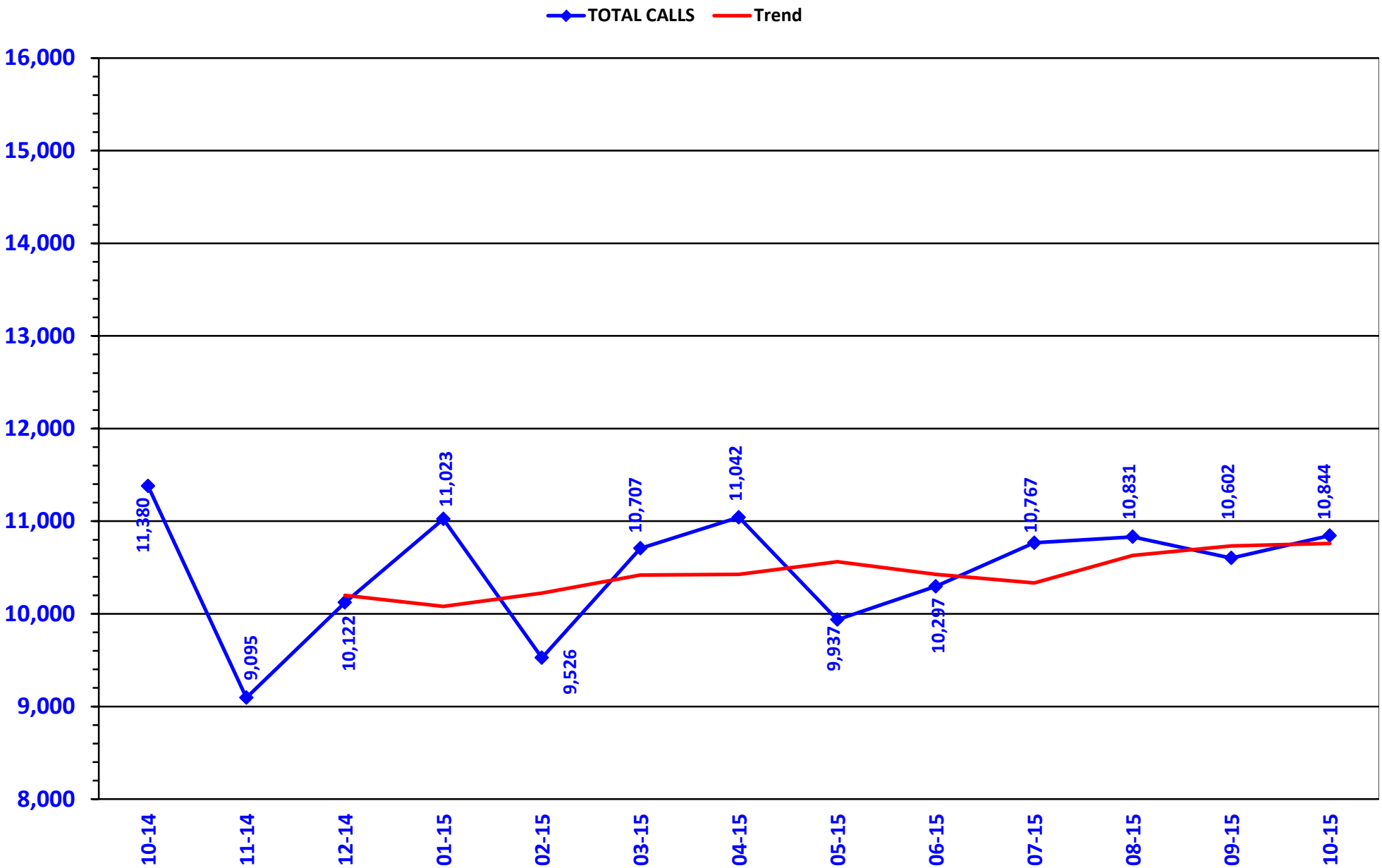
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: OCTOBER 2014 – OCTOBER 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
OCTOBER 2014 – OCTOBER 2015



Prior Authorization Activity

10/1/2015 Through 10/31/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	446	189	58	199	352
Analgesic - NonNarcotic	28	1	4	23	7
Analgesic, Narcotic	456	243	48	165	151
Angiotensin Receptor Antagonist	18	4	1	13	277
Antiasthma	179	74	25	80	338
Antibiotic	48	9	9	30	64
Anticoagulant	13	9	1	3	359
Anticonvulsant	86	37	14	35	349
Antidepressant	101	24	18	59	302
Antidiabetic	162	67	17	78	345
Antifungal	11	2	3	6	24
Antihistamine	234	183	18	33	357
Antimigraine	61	6	14	41	240
Antiulcers	206	54	53	99	134
Anxiolytic	74	52	4	18	247
Atypical Antipsychotics	532	245	56	231	334
Biologics	89	33	18	38	353
Bladder Control	58	17	11	30	324
Blood Thinners	130	84	8	38	323
Botox	26	18	4	4	343
Cardiovascular	86	33	6	47	277
Cephalosporins	11	3	1	7	5
Chronic Obstructive Pulmonary Disease	51	8	11	32	360
Contraceptive	13	7	3	3	263
Corticosteroid	14	1	3	10	28
Dermatological	108	23	49	36	88
Diabetic Supplies	498	255	27	216	230
Endocrine & Metabolic Drugs	63	40	8	15	129
Erythropoietin Stimulating Agents	18	9	5	4	94
Fibromyalgia	146	36	54	56	331
Fish Oils	18	3	4	11	360
Gastrointestinal Agents	108	32	27	49	107
Glaucoma	10	0	2	8	0
Growth Hormones	79	65	4	10	150
Hepatitis C	183	99	50	34	8
HFA Rescue Inhalers	68	19	9	40	353
Insomnia	47	5	11	31	213
Insulin	46	9	9	28	254
Linzess, Amitiza, and Relistor	75	12	23	40	228
Multiple Sclerosis	66	24	16	26	232
Muscle Relaxant	72	14	24	34	72
Nasal Allergy	110	22	28	60	270
Neurological Agents	44	29	4	11	336
NSAIDs	185	31	51	103	314
Ocular Allergy	44	6	8	30	177
Ophthalmic Anti-infectives	10	3	3	4	7
Ophthalmic Corticosteroid	10	3	1	6	9
Ophthalmic NSAIDs	12	2	1	9	23
Osteoporosis	19	9	4	6	318
Other*	242	37	64	141	201
Otic Antibiotic	19	0	3	16	0

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

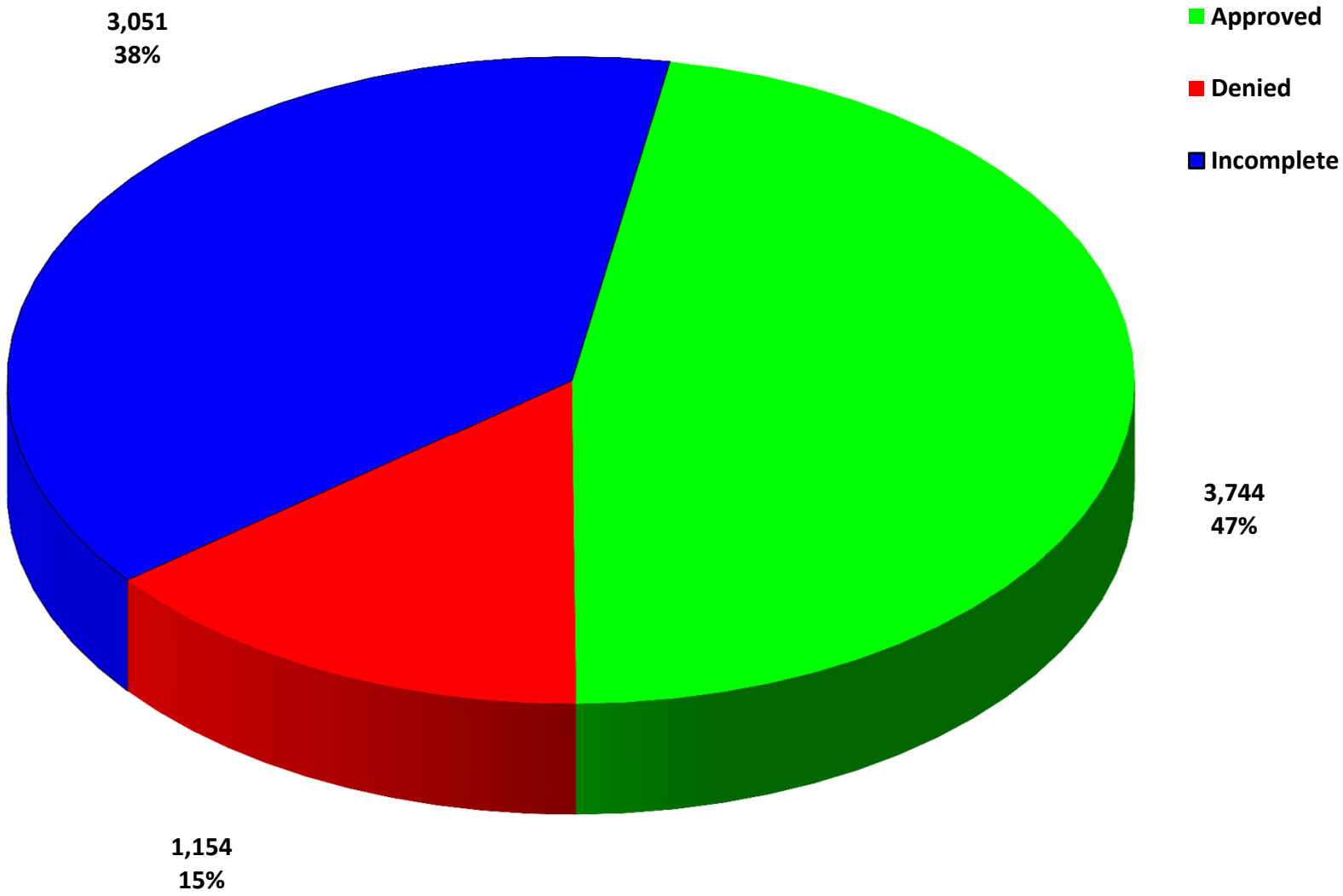
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Pediculicide	235	112	19	104	17
Prenatal Vitamins	17	0	0	17	0
Statins	66	19	11	36	347
Stimulant	1,091	519	127	445	340
Suboxone/Subutex	229	174	6	49	85
Synagis	395	88	133	174	150
Testosterone	57	20	12	25	315
Topical Antibiotic	11	0	0	11	0
Topical Antifungal	37	0	4	33	0
Topical Corticosteroids	71	1	17	53	177
Vitamin	71	22	33	16	283
Pharmacotherapy	80	72	1	7	256
Emergency PAs	0	0	0	0	
Total	**7,793**	**3,217**	**1,260**	**3,316**	
Overrides					
Brand	58	32	6	20	288
Cumulative Early Refill	6	6	0	0	70
Diabetic Supplies	10	8	0	2	142
Dosage Change	352	321	1	30	8
High Dose	2	2	0	0	186
Ingredient Duplication	67	46	2	19	13
Lost/Broken Rx	84	74	6	4	6
NDC vs Age	30	30	0	0	286
Nursing Home Issue	31	27	1	3	5
Opioid Quantity	11	11	0	0	177
Other*	41	39	0	2	11
Prescriber Temp Unlock	1	1	0	0	13
Quantity vs. Days Supply	615	429	46	140	270
STBS/STBSM	15	15	0	0	77
Stolen	13	11	0	2	4
Temporary Unlock	2	1	1	0	27
Third Brand Request	26	14	7	5	22
Overrides Total	**1,336**	**1,041**	**70**	**225**	
Total Regular PAs + Overrides	**9,129**	**4,258**	**1,330**	**3,541**	

Denial Reasons	
Unable to verify required trials.	3,080
Does not meet established criteria.	1,277
Lack required information to process request.	522

Other PA Activity	
Duplicate Requests	601
Letters	6,979
No Process	15
Changes to existing PAs	388
Helpdesk Initiated Prior Authorizations	887
PAs Missing Information	36

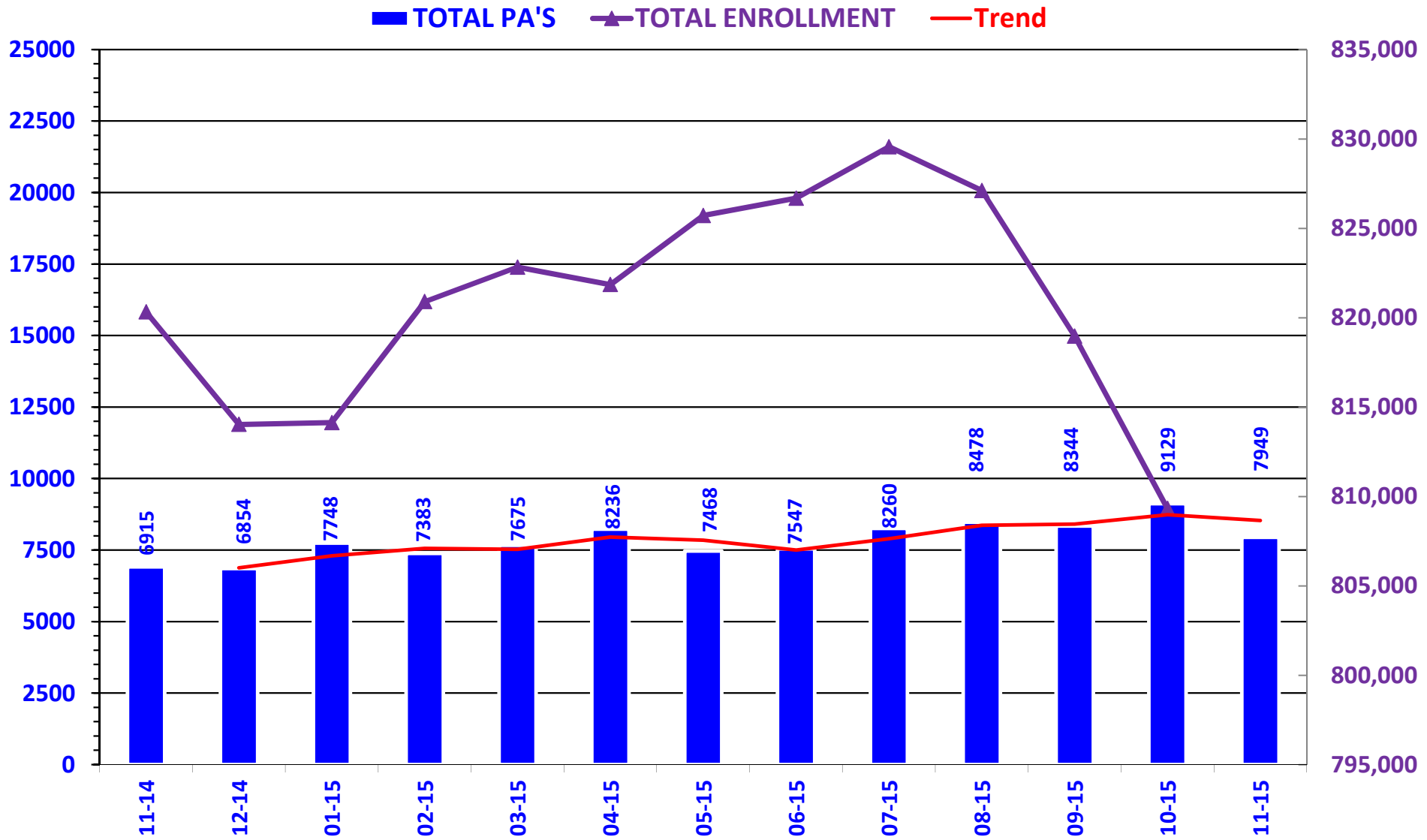
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER 2015



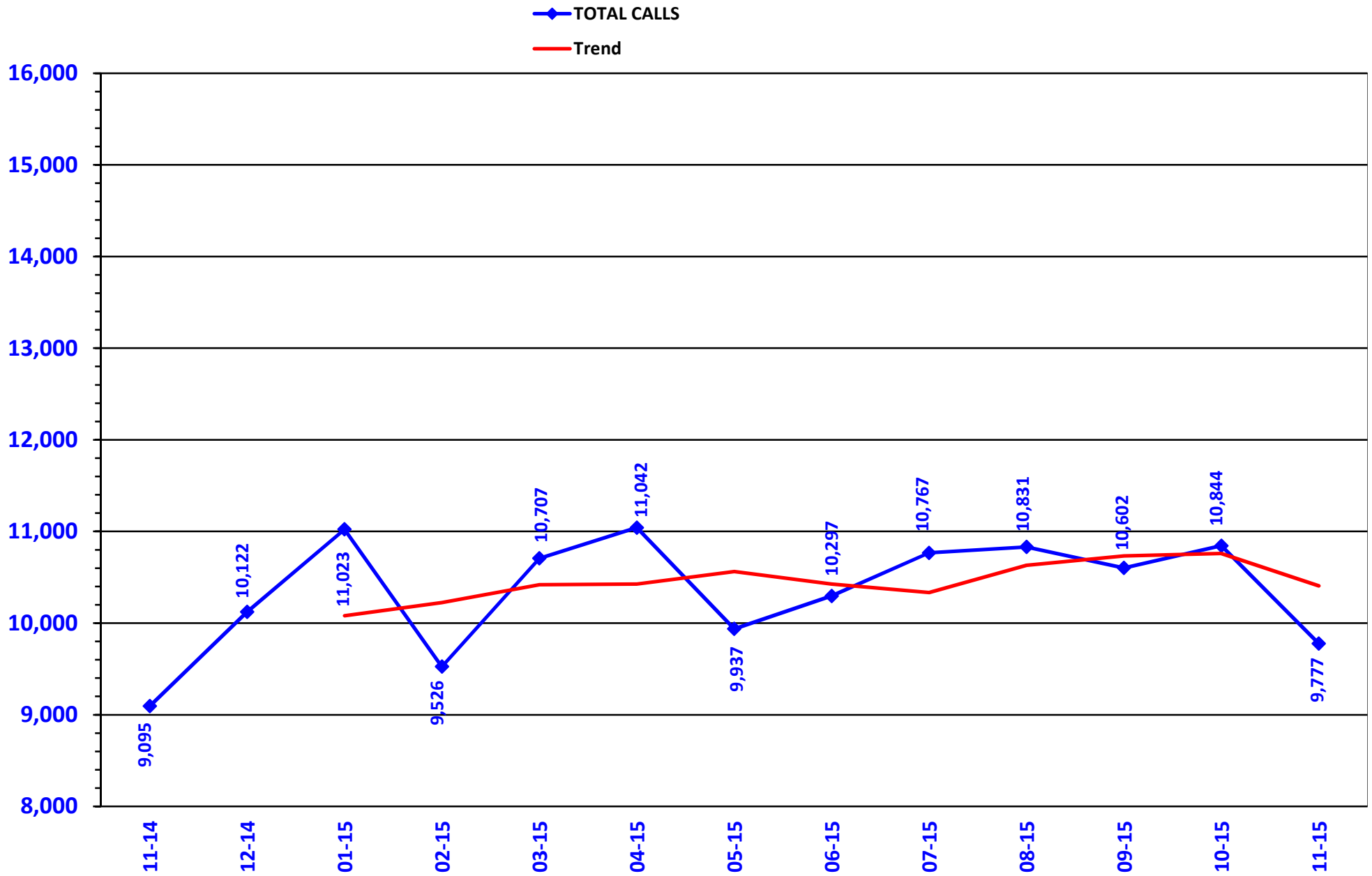
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2014 – NOVEMBER 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
NOVEMBER 2014 – NOVEMBER 2015



Prior Authorization Activity

11/1/2015 Through 11/30/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	375	158	49	168	355
Analgesic - NonNarcotic	29	0	6	23	0
Analgesic, Narcotic	424	235	46	143	159
Angiotensin Receptor Antagonist	27	4	8	15	359
Antiasthma	95	31	20	44	301
Antibiotic	35	9	3	23	182
Anticonvulsant	78	38	8	32	346
Antidepressant	95	21	26	48	359
Antidiabetic	121	49	13	59	354
Antifungal	16	4	4	8	8
Antihistamine	186	149	10	27	360
Antimigraine	42	5	12	25	81
Antiulcers	199	41	59	99	140
Anxiolytic	56	34	4	18	246
Atypical Antipsychotics	466	198	38	230	343
Benign Prostatic Hypertrophy	13	0	7	6	0
Biologics	67	30	11	26	350
Bladder Control	47	14	8	25	359
Blood Thinners	131	79	6	46	328
Botox	25	20	4	1	290
Cardiovascular	49	21	9	19	304
Cephalosporins	14	8	0	6	7
Chronic Obstructive Pulmonary Disease	54	10	12	32	339
Contraceptive	16	16	0	0	257
Dermatological	119	11	71	37	83
Diabetic Supplies	435	213	11	211	233
Endocrine & Metabolic Drugs	73	49	1	23	126
Erythropoietin Stimulating Agents	27	17	2	8	102
Fibromyalgia	114	30	52	32	337
Fish Oils	15	1	5	9	361
Gastrointestinal Agents	107	29	26	52	109
Genitourinary Agents	15	7	1	7	101
Growth Hormones	51	43	1	7	134
Hepatitis C	177	105	27	45	9
HFA Rescue Inhalers	53	15	10	28	337
Insomnia	47	6	14	27	122
Insulin	43	5	14	24	360
Linzess, Amitiza, and Relistor	69	12	22	35	245
Multiple Sclerosis	33	13	7	13	195
Muscle Relaxant	69	11	26	32	56
Nasal Allergy	104	13	27	64	270
Neurological Agents	59	42	8	9	349
NSAIDs	177	17	49	111	299
Ocular Allergy	47	5	8	34	141
Ophthalmic Anti-infectives	20	5	5	10	8
Ophthalmic NSAIDs	10	0	2	8	0
Osteoporosis	13	3	4	6	360
Other*	225	43	46	136	209
Otic Antibiotic	22	1	3	18	10
Pediculicide	170	75	26	69	11
Prenatal Vitamins	14	0	1	13	0
Statins	62	15	17	30	347

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Stimulant	876	422	86	368	332
Suboxone/Subutex	235	175	7	53	76
Synagis	288	109	93	86	141
Testosterone	37	11	11	15	334
Topical Antifungal	36	5	7	24	60
Topical Corticosteroids	58	0	15	43	0
Vaccine	13	3	9	1	15
Vitamin	68	21	27	20	269
Pharmacotherapy	70	60	0	10	290
Emergency PAs	0	0	0	0	
Total	**6,711**	**2,766**	**1,104**	**2,841**	
Overrides					
Quantity vs. Days' Suppl	4	2	0	2	192
Brand	39	26	3	10	299
Cumulative Early Refill	4	3	0	1	70
Diabetic Supplies	6	5	0	1	141
Dosage Change	353	333	1	19	12
High Dose	1	1	0	0	360
Ingredient Duplication	58	49	1	8	13
Lost/Broken Rx	101	95	0	6	8
NDC vs Age	32	32	0	0	229
Nursing Home Issue	28	26	0	2	7
Opioid Quantity	9	5	4	0	112
Other*	30	20	3	7	6
Quantity vs. Days Supply	532	351	37	144	255
STBS/STBSM	11	11	0	0	70
Stolen	18	14	0	4	8
Temporary Unlock	1	1	0	0	27
Third Brand Request	34	19	5	10	21
Overrides Total	**1,238**	**978**	**50**	**210**	
Total Regular PAs + Overrides	**7,949**	**3,744**	**1,154**	**3,051**	

Denial Reasons	
Unable to verify required trials.	2,549
Does not meet established criteria.	1,117
Lack required information to process request.	525

Other PA Activity	
Duplicate Requests	543
Letters	5,935
No Process	3
Changes to existing PAs	739
Helpdesk Initiated Prior Authorizations	753
PAs Missing Information	41

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
December 2015

Prescriber Mailing: Maintenance Diabetes Medications

The College of Pharmacy and the Oklahoma Health Care Authority are engaged in an educational quarterly mailing to prescribers with members on chronic maintenance medications for diabetes, blood pressure, or cholesterol. The purpose of these mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Each mailing includes a prescriber summary report with a "star rating" based on their overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is greater than or equal to 80%. A patient is considered non-adherent if their PDC is less than 80%. Patients must have at least two pharmacy claims for at least one medication in the drug category in the past year to be included in the calculations.

The third mailing was processed in May and addressed adherence to maintenance diabetes medications. Prescribers with three or more patients were eligible for inclusion in the mailing if their percentage of patients considered adherent was greater than or equal to 60% (1 to 5 stars). The review period was for one year and patients were assigned to prescribers based on their designated medical home provider as of April 2015.

A total of 1,559 prescribers were evaluated based on the computed adherence claims. These prescribers had 2,755 flagged patients considered non-adherent based on PDC calculations. A total of 177 prescribers were included in the mailing which accounted for 975 patients intervened for adherence.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	177
Members	**Count**
Total Members Included	975

Example Star Rating[1]

Report date: 04/30/2015 Prescriber: <Prescriber Name>
NPI: <Prescriber NPI> SoonerCare Provider ID: <Provider ID>
Assigned medical home patients on a diabetic medication: <6>
Percentage of patients adherent to metformin-containing medications: <60%>
Percentage of patients adherent to all other diabetic medications: <50%>

Overall percentage of patients adherent to all diabetic medications: <66%>

1 out of 5 stars

Adherence is shown in the Prescriber Summary Report as a percentage for metformin-containing medications, a percentage for all other diabetic medications (excluding insulin and Symlin®), and a final percentage and star rating for all diabetic medications (metformin- and non-metformin-containing medications). Combination products, e.g. Janumet® (metformin/sitagliptin), may be shown in both of the percentages for adherence to metformin-containing products and to all other diabetic medications; however, combination products will only be included one time in the overall percentage and star rating. The star ratings for the overall percentage of patients that are adherent to all diabetic medications (excluding insulin and Symlin®) are based on the 2015 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. A key is shown below to illustrate the star ratings and adherence percentages (based on patients' PDC) for each star rating.

5 Stars: Excellent (≥ 85%)

4 Stars: Above Average (≥ 82% to < 85%)

3 Stars: Average (≥ 79% to < 82%)

2 Stars: Below Average (≥ 74% to < 79%)

1 Star: Poor (≥ 60% to < 74%)

0 Stars: Very Poor (< 60%)

Chronic Medication Adherence PDC by Drug Category

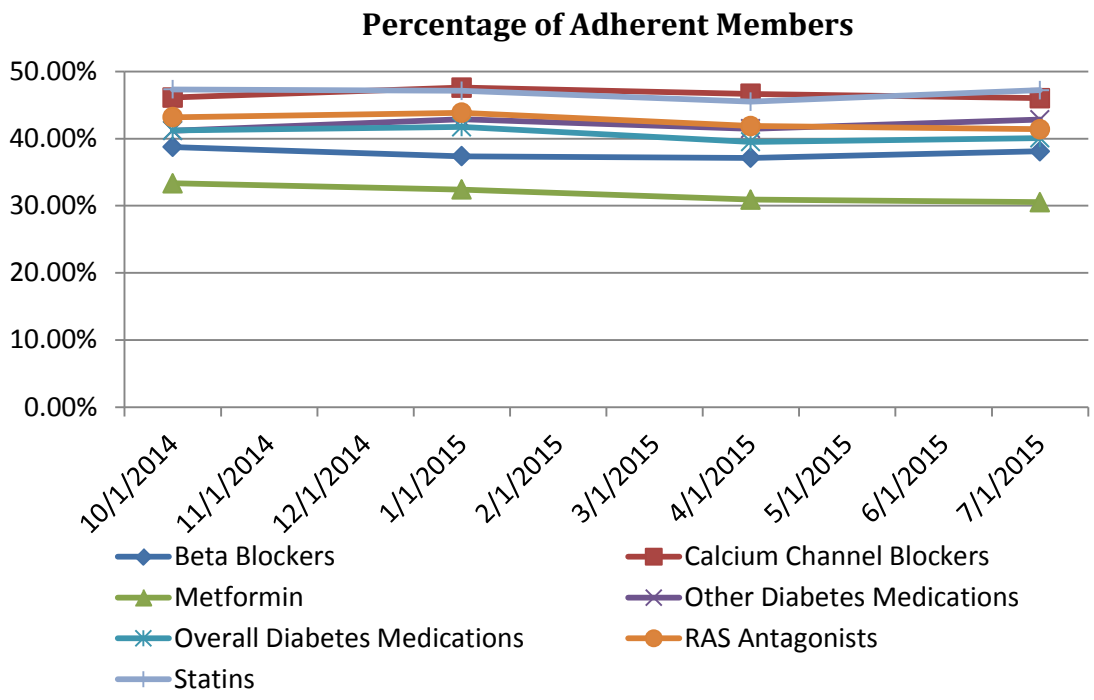
The average member PDC is listed based on drug category below. Also listed is the average prescriber percentage of adherent members (PDC ≥ 80%) for each category and the average star rating for the applicable categories. Star ratings listed as N/A are either subcategories or categories that are not included in Medicare's star ratings thus far.

Drug Category	Member PDC	Prescriber % of Adherent Members	Star Rating
Beta Blockers	65.05%	37.13%	N/A
Calcium Channel Blockers	70.21%	46.66%	N/A
Metformin	60.99%	30.91%	N/A
Other Diabetes Medications	67.64%	41.47%	N/A
Overall Diabetes Medications	66.86%	39.51%	0 stars
RAS Antagonists	68.68%	41.88%	0 stars
Statins	70.71%	45.50%	0 stars

The average member PDC and the percent of adherent members is tracked for all drug categories each time a mailing is processed. The following line graph shows trends in the percentage of adherent members for each drug category since the Chronic Medication Adherence initiative commenced. The line graph depicts the percentage of adherent members for all of SoonerCare and does not differentiate those members who received a mailing. A review of average PDC for prescribers who received a mailing six months after the original diabetes chronic medication adherence mailing did not reveal increases in average PDC for any of the diabetes medication categories.

Of note, the beta blockers and calcium channel blockers are being monitored but have not yet been included in the mailings to prescribers. Topics and dates of previous and current mailings include the following:

- Metformin and other diabetes medications: October 2014
- RAS Antagonists and statins: February 2015
- Metformin and other diabetes medications: May 2015
- RAS Antagonists and statins: August 2015
- Metformin and other diabetes medications: November 2015



Medication Compliance Informational Page [2, 3, 4, 5]

Medication adherence is essential for positive therapeutic outcomes. Non-adherence may lead to false medication failure, resulting in unnecessary dose increases and/or medication changes or additions, complications associated with diabetes, and increased health-care costs. Patients need to understand the importance of taking their diabetic medications as directed to reduce the risk of serious complications associated with diabetes, such as heart disease, stroke, blindness, kidney failure, lower-limb amputations, and pre-mature death. Dosing regimens, possible adverse effects, the importance of medication compliance, and long-term serious complications associated with diabetes should be discussed with the patient to address any concerns and improve medication adherence, resulting in improved glucose control and a decreased risk of serious complications associated with diabetes.

Please refer to the websites below for helpful patient resources!

- *National Consumers League:* Script Your Future (videos, adherence tools for patients, medication guides)
  http://www.scriptyourfuture.org/diabetes/
- *Centers for Disease Control and Prevention (CDC):* Diabetes Basics (information and resources)
  http://www.cdc.gov/diabetes/basics/index.html
- *American Diabetes Association (ADA):* Blood Glucose Log (sample blood glucose log)
  http://professional.diabetes.org/content/PML/Blood_Glucose_Log_5073a4ef-2491-4747-a6e4-fcebcb9589ef/Blood_Glucose_Log.pdf
- *ADA:* Medications for Treating Type 2 Diabetes (how diabetic medications work)
  http://professional.diabetes.org/content/PML/Type_2_-_Medications_480a7300-12ed-447a-8c36-67b6e0a5eb52/Type_2_-_Medications.pdf

- *ADA:* Diabetes Medical Alert Card (basic information and a tear-off medical alert card for patients) http://professional.diabetes.org/content/PML/diabetes-alert-card_d5d4f538-0a4b-4fd6-9b87-7ab349c63b18/diabetes-alert-card.pdf

[1]Centers for Medicare & Medicaid Services: *Medicare 2015 Part C & D Star Rating Technical Notes.* Available online at http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Last updated 12/4/14.
[2]Centers for Disease Control and Prevention: *National Diabetes Statistics Report, 2014.* Available online at: http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf.
[3]Centers for Disease Control and Prevention: *Diabetes Report Card, 2012.* Available online at: http://www.cdc.gov/diabetes/pubs/pdf/diabetesreportcard.pdf.
[4] Cramer, J. A Systematic Review of Adherence with Medications for Diabetes. *Diabetes Care.* 2004. 27: 1218-1224.
[5] Meece, J. Improving Medication Adherence Among Patients with Type 2 Diabetes. *Journal of Pharmacy Practice.* April 2014. 27(2): 187-194.

Appendix C

Vote to Prior Authorize Ibrance® (Palbociclib)

Oklahoma Health Care Authority
December 2015

Introduction[1,2,3]

Palbociclib is a selective inhibitor of CDK 4/6 kinase activity, and was approved under accelerated approval based on progression-free survival (PFS). A phase-2, open-label study assessed the safety and efficacy of palbociclib in combination with letrozole versus letrozole alone as first-line treatment for postmenopausal women with advanced ER-positive, HER2-negative breast cancer. Median PFS reported was 20.2 months for the combination group vs. 10.2 months for the letrozole alone group (HR, 0.488; 95% CI, 0.319-0.748).

Recommendations

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).

[1] NCCN. NCCN Guidelines Version 3.2015 Breast Cancer. Retrieved October 19, 2015, http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
[2] Ibrance® [package insert]. NY, NY: Pfizer; 2015.
[3] Finn RS, Crown JP, Lang I, et al. The cycline-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18: a randomized phase 2 study. *Lancet Oncol* 2015;16:25-35

Appendix D

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

Oklahoma Health Care Authority
December 2015

Indication(s)[1]

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

Recommendations

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, and Kentucky Blue Grass Mixed Pollens Allergen Extract) Approval Criteria:

1. Member must be 10 years of age or older; and
2. Member must have a positive skin test or in vitro testing for pollen specific IgE antibodies to one of the five grass pollens contained in Oralair®; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trials must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 16 weeks prior to the start of the grass pollen season (October 15th) and continue throughout the season; and
7. The first dose must be given in the physician's office, and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 16 weeks prior to the season and continue throughout the season; and

10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as “allergy shots”; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home; and
12. Prescriber must be an allergist, immunologist, or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

[1] Oralair® Product Information. Greer Laboratories, Inc. Available online at: http://oralair.com/docs/ORALAIR%20Prescribing%20Information-Med%20Guide.pdf. Last revised 06/2015. Last accessed 11/2015.

Appendix E

Vote to Prior Authorize Dyloject™ (Diclofenac Sodium)

Oklahoma Health Care Authority
December 2015

Introduction[1]

- Dyloject™ (diclofenac sodium) is a non-steroidal anti-inflammatory drug (NSAID) indicated for the management of mild-to-moderate pain. Dyloject™ is also indicated for the management of moderate-to-severe pain alone or in combination with opioid analgesics.
- Several of the generic Tier-1 NSAIDs have increased in price significantly in recent months. Anaprox® (naproxen sodium) 275mg tablets increased from $0.12 to $1.17, a price increase of more than 875%. Similarly Anaprox® (naproxen sodium) 550mg tablets increased approximately 1,100%.

Recommendations

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

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

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

ER= Extended-Release, EC= Enteric Coated

[1] Dyloject™ Package Insert. Hospira, Inc. Available online at: http://medlibrary.org/lib/rx/meds/dyloject/. Last revised 1/14/2015. Last accessed 11/2015.

Appendix F

Vote to Prior Authorize Omidria® (Phenylephrine/Ketorolac) Injection

Oklahoma Health Care Authority
December 2015

Indication(s)[1]

Omidria® (phenylephrine/ketorolac) is an alpha 1-adrenergic receptor agonist and nonselective cyclooxygenase inhibitor indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative pain. Phenylephrine/ketorolac is added to an irrigation solution used during cataract surgery or intraocular lens replacement.

Recommendations

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.

[1] Omidria® Package Insert. Omeros Corporation. Available online at: http://medlibrary.org/lib/rx/meds/omidria/. Last revised 06/26/2015. Last accessed 11/2015.

Appendix G

Vote to Update Criteria for Xgeva® (Denosumab) for Hypercalcemia of Malignancy

Oklahoma Health Care Authority
December 2015

Indication(s)[1,2,3,4]

The FDA most recently approved Xgeva® (denosumab) for the treatment of hypercalcemia of malignancy (HCM) refractory to bisphosphonate therapy. Xgeva® (denosumab) was first approved in November 2010 for the indication of preventing skeletal-related events in patients with bone metastases from solid tumors. In June 2013, the FDA approved another indication for Xgeva® (denosumab) for the treatment of giant cell tumor of bone.

Recommendations

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.

[1]Amgen Press Release: FDA approves Amgen's Xgeva™ (denosumab) for the prevention of skeletal-related events in patients with bone metastases from solid tumors. Available online at: http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-newsArticle&ID=1498709. Last revised 11/18/2010. Last accessed 11/2015.
[2]Amgen Press Release: FDA approves Amgen's Xgeva® (denosumab) for the treatment of giant cell tumor of bone. Available online at: http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-newsArticle&ID=1829715. Last revised 06/13/2013. Last accessed 11/2015.
[3]Amgen Press Release: FDA approves Amgen's Xgeva® (denosumab) for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. Available online at: http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-newsArticle&ID=1995709. Last revised 12/08/2014. Last accessed 11/2015.
[4]Medscape Medical News: FDA approves new indication for denosumab (Xgeva). Available online at: http://www.medscape.com/viewarticle/836252. Last revised 12/09/2014. Last accessed 11/2015.

Appendix H

Vote to Prior Authorize Daraprim® (Pyrimethamine)

Oklahoma Health Care Authority
December 2015

Introduction[1]

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

Recommendations

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

Daraprim® (Pyrimethamine) Approval Criteria:

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

[1] Daraprim® Prescribing Information, Amedra Pharmaceuticals LLC. Available online at: http://www.daraprimdirect.com/forms/Daraprim-PI.pdf. Last revised 10/2014. Last accessed 11/2015.

Appendix I

Vote to Prior Authorize Movantik™ (Naloxegol), Viberzi™ (Eluxadoline), & Xifaxan® (Rifaximin)

Oklahoma Health Care Authority
December 2015

Indication(s)[1,2,3]

- Movantik™ (naloxegol) is a peripherally-acting mu-opioid receptor antagonist (PAMORA) indicated for the treatment of opioid induced constipation (OIC) in adult patients with chronic non-cancer pain.
- Viberzi™ (eluxadoline) is a locally-acting oral mu-opioid receptor agonist indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adult patients.
- Xifaxan® (rifaximin) is a non-aminoglycoside, semi-synthetic, non-systemic antibiotic indicated for the treatment of traveler's diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older. Rifaximin is also indicated for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults. Lastly, rifaximin is indicated for the treatment of IBS-D in adults.

Recommendations

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).

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[1] Movantik™ Prescribing Information, AstraZeneca Pharmaceuticals LP. Available online at: http://www.azpicentral.com/movantik/movantik.pdf#page=1. Last revised 1/2015. Last accessed 11/2015.
[2] Viberzi™ Prescribing Information, Actavis / Allergan. Available online at: http://www.actavis.com/Actavis/media/PDFDocuments/VIBERZI_PI.pdf. Last revised 5/2015. Last accessed 11/2015.
[3] Xifaxan® Prescribing Information, Salix Pharmaceuticals, Inc. Available online at: https://shared.salix.com/shared/pi/xifaxan550-pi.pdf?id=8251081. Last revised 5/2015. Last accessed 11/2015.

Appendix J

Vote to Prior Authorize Keveyis™ (Dichlorphenamide)

Oklahoma Health Care Authority
December 2015

Indication(s)[1]

Keveyis™ (dichlorphenamide) is an oral carbonic anhydrase inhibitor indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

Recommendations

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.

[1] Keveyis™ Prescribing Information. Taro Pharmaceutical Industries Ltd. Available online at: http://keveyis.com/FINAL%20Approved%20Keveyis%20PI_%208.7.15.pdf. Last revised 08/2015. Last accessed 11/2015.

Appendix K

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

Oklahoma Health Care Authority
December 2015

Indication(s)[1,2,3]

- Pramosone® (hydrocortisone/pramoxine topical cream and lotion) is a topical corticosteroid local anesthetic agent combination indicated for the relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
- Enstilar® foam (calcipotriene/betamethasone dipropionate foam) is a combination of calcipotriene, a vitamin D analog, and betamethasone dipropionate, a corticosteroid, indicated for the topical treatment of plaque psoriasis in patients 18 years of age and older.

Recommendations

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.

Topical Corticosteroids Prior Authorization Criteria

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

Tier-2 Topical Corticosteroid Approval Criteria:

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

The following page contains the recommended Topical Corticosteroid Tier Chart.

Topical Corticosteroids	
Tier-1	**Tier-2**
Ultra-High to High Potency	
augmented betamethasone dipropionate (**Diprolene AF®**) **C, G**	amcinonide **C,O,L**
clobetasol propionate 0.05% (**Temovate®**) **G,So**	augmented betamethasone dipropionate (**Diprolene®**) **O,G,L**
fluocinonide 0.05% **C,O, So**	betamethasone dipropionate (**Diprosone®**) **C**
halobetasol propionate (**Ultravate®**) **C**	clobetasol propionate 0.05% (**Clobex®**) **L,Sh,Spr**; (**Olux®**) **F**, (**Olux-E®**) **F**
betamethasone dipropionate (**Diprosone®**) **O**	desoximetasone 0.25% (**Topicort®**) **C,O** (0.05%) **G**
	fluocinonide 0.05% **G**
	fluocinonide 0.1% (**Vanos®**) **C**
	halcinonide (**Halog®**) **C,O**
	halobetasol propionate/lactic acid (**Ultravate X®**) **C**
	diflorasone diacetate 0.05% (**Apexicon®**) **C,** (**Apexicon E®**) **C,O**
	halobetasol propionate (**Ultravate®**) **O**
	clobetasol propionate 0.05% (**Temovate®**) **C,O**
Medium/High to Medium Potency	
betamethasone dipropionate (**Betanate®**) **L**	betamethasone dipropionate/calcipotriene (**Taclonex®**) **O, Sus, Spr**
betamethasone valerate 0.1% (**Beta-Val®**) **C**	betamethasone valerate 0.1% (**Beta-Val®**) **O,L**
fluocinonide emollient (**Lidex E®**) **C**	betamethasone valerate 0.12% (**Luxiq®**) **F**
fluticasone propionate (**Cutivate®**) **C,O**	desoximetasone 0.05% (**Topicort LP®**) **C**
hydrocortisone butyrate 0.1% **So**	fluocinolone acetonide 0.025% (**Synalar®**) **C,O**
mometasone furoate (**Elocon®**) **C,L**	flurandrenolide tape (**Cordran®**)
triamcinolone acetonide **C,O,L**	fluticasone propionate (**Cutivate®**) **L**
	hydrocortisone butyrate 0.1% **C,O**
	hydrocortisone probutate (**Pandel®**) **C**
	hydrocortisone valerate 0.2% **O, C**
	hydrocortisone valerate (**Westcort®**) **C,O**
	mometasone furoate 0.1% **O**
	prednicarbate (**Dermatop®**) **O,C**
	triamcinolone acetonide (**Kenalog®**) **Spr**
	betamethasone dipropionate/calcipotriene (**Enstilar®**) **F**
Low potency	
alclometasone dipropionate (**Aclovate®**) **C,O**	clocortolone pivalate (**Cloderm®**) **C**
fluocinolone acetonide 0.01% (**Synalar®**) **C**	desonide 0.05% **C,O**
hydrocortisone acetate 2.5% **C,O,L**	desonide 0.05% (**Desonate®**) **G**
hydrocortisone/urea (**U-Cort®**) **C**	desonide 0.05% (**Verdeso®**) **F,L**
	desonide/emollient (**Desowyn®** kit) **C,O**
	fluocinolone acetonide 0.01% (**Capex®**) **Sh**
	hydrocortisone 2.5% (**Texacort®**) **So**
	hydrocortisone/pramoxine (**Pramosone®**) **C, L**
	fluocinolone acetonide 0.01% (**Synalar®**) **So,** (**Derma-Smooth®; Derma-Smooth FS®**) **Oil**

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

[1] Pramosone® Cream Prescribing Information, Sebela Pharmaceuticals Inc. Available online at: http://www.sebelapharma.com/wp-content/uploads/2015/10/6988I-leaflet-1.pdf. Last accessed 11/2015.

[2] Pramosone® Lotion Prescribing Information, Sebela Pharmaceuticals Inc. Available online at: http://www.sebelapharma.com/wp-content/uploads/2015/10/69851-Lotion-2.5percent-samples-leaflet.pdf . Last accessed 11/2015.

[3] Enstilar® Prescribing Information. LEO Pharma Inc. Available online at: http://www.enstilar.com/pdf/enstilar-pi.pdf. Last revised: 10/2015. Last accessed 11/2015.

Appendix L

Vote to Prior Authorize Cayston® (Aztreonam Inhalation) & Kitabis™ Pak (Tobramycin Inhalation)

Oklahoma Health Care Authority
December 2015

Indication(s)[1,2]

- Cayston® (aztreonam inhalation) is a monobactam antibacterial indicated to improve respiratory symptoms in CF patients with *Pseudomonas aeruginosa* in the lungs. The safety and effectiveness of aztreonam inhalation have not been established in pediatric patients below the age of 7 years, patients with forced expiratory volume in 1 second (FEV_1) less than 25% of predicted or greater than 75% of predicted, or patients colonized with *Burkholderia cepacia*.
- Kitabis™ Pak (tobramycin inhalation) is an aminoglycoside antibacterial drug indicated for the management of CF in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*. The safety and efficacy of Kitabis™ Pak have not been demonstrated in patients under the age of 6 years, patients with FEV_1 less than 25% or greater than 75% predicted, or patients colonized with *Burkholderia cepacia*.

Recommendations

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

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

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

[1] Cayston Product Information. Gilead Science Inc. Available online at: http://www.gilead.com/~/media/files/pdfs/medicines/respiratory/cayston/cayston_pi.pdf?la=en. Last revised 05/2014. Last accessed 11/2015.

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

Appendix M

Vote to Prior Authorize Cosentyx® (Secukinumab)

Oklahoma Health Care Authority
December 2015

Indication(s)[1,2]

- Cosentyx® (secukinumab) is a human interleukin-17A antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.
- In September 2015, the FDA approved Humira® (adalimumab) for the treatment of moderate-to-severe hidradenitis suppurativa (HS) making it the first and only FDA-approved treatment for HS.

Recommendations

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

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.

[1] Cosentyx Product Information. Novartis Pharmaceuticals Corporation. Available online at: http://www.pharma.us.novartis.com/product/pi/pdf/cosentyx.pdf. Last revised 01/2015. Last accessed 11/2015.

[2] AbbVie. Abbvie's Humira® (Adalimumab) Receives U.S. First and Only U.S. Food and Drug Administration Approval for Moderate to Severe Hidradenitis Suppurativa. Available online at: http://abbvie.mediaroom.com/2015-09-10-AbbVies-HUMIRA-Adalimumab-Receives-First-and-Only-U-S-Food-and-Drug-Administration-Approval-for-Moderate-to-Severe-Hidradenitis-Suppurativa. Last revised 09/10/2015. Last accessed 11/2015.

Appendix N

Vote to Prior Authorize Tetracycline Capsules, Minocycline Tablets, Ofloxacin Tablets, & Moxifloxacin Tablets

Oklahoma Health Care Authority
December 2015

Introduction

Since fiscal year 2011, the average cost per claim of generic medications has increased by 16.4%. The rising cost of both brand and generic medications have contributed to a total increase in prescription drug expenditures.

- Despite a decrease in overall spending from fiscal year 2014 to fiscal year 2015 in the tetracycline antibiotic class, the cost per unit of tetracycline 250mg and 500mg capsules continued to climb.
    - Tetracycline HCl has increased significantly in price since 2012. The unit price increased 9,100% from $0.11 per unit to $10.12 per unit.
    - Overall costs of minocycline immediate-release have remained similar, however it is important to note the cost of minocycline tablets is significantly greater than the cost of the minocycline capsule formulation despite availability in the same strengths (50mg, 75mg, and 100mg). The average cost per claim of the capsules is around $16.89 compared to the tablet formulation which has an average cost per claim of $99.03.
- Despite a decrease in overall spending and utilization from fiscal year 2014 to fiscal year 2015 in the fluoroquinolone class, the cost per claim varies among the different products and formulations.
    - The average cost per claim for ciprofloxacin during fiscal year 2015 was $8.05/claim. The immediate-release ciprofloxacin products range in cost from $0.31 to $0.43 per tablet. The Ciprofloxacin 100mg tablets and the extended-release formulations (500mg and 1000mg extended-release tablets) are more costly than the standard, immediate-release strengths (100mg: $12.86/tablet, 500mg ER: $8.13/tablet, 1000mg ER: $8.91/tablet).
    - Claims for moxifloxacin and ofloxacin 400mg tablets are 16 times more expensive than the ciprofloxacin and levofloxacin products.

Recommendations

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).

Appendix O

Vote to Update Criteria for Xiaflex®
(Collagenase Clostridium Histolyticum)

Oklahoma Health Care Authority
December 2015

Indication(s)[1]

Xiaflex® was first approved by the FDA in 2010 for the treatment of Dupuytren's contracture, a progressive hand disease that can affect a person's ability to straighten and properly use their fingers. In late 2013, the FDA approved Xiaflex® (collagenase clostridium histolyticum) to treat men with Peyronie's disease (PD). Xiaflex® is the first FDA-approved non-surgical treatment option for men with this condition, who have a plaque (lump) in the penis that results in a curvature deformity of at least 30 degrees upon erection. Xiaflex® is believed to work in PD by breaking down the buildup of collagen that causes the curvature deformity.

Recommendations

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.

[1] US Food and Drug Administration. FDA Approves First Drug Treatment for Peyronie's Disease. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm377849.htm. Last revised 12/06/2013. Last accessed 11/2015.

Appendix P

Fiscal Year 2015 Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Daklinza™ (Daclatasvir) and Technivie™ (Ombitasvir/Paritaprevir/Ritonavir)

Oklahoma Health Care Authority
December 2015

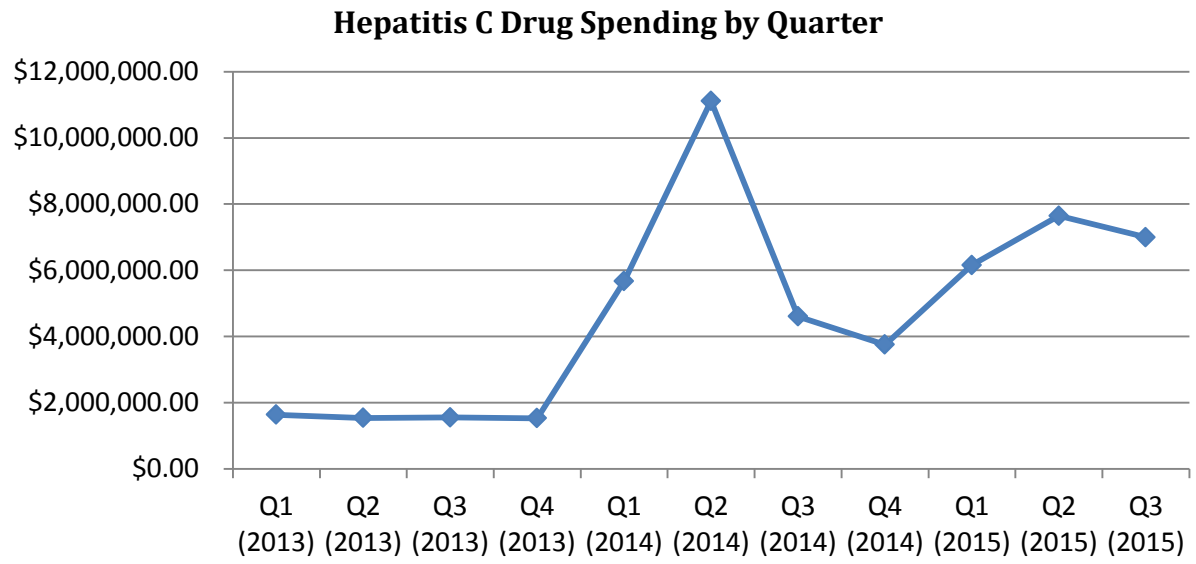
Introduction

Sovaldi® (sofosbuvir) and Olysio® (simeprevir), both FDA approved in the fourth quarter of 2013, were previously restricted under Oklahoma law, preventing prior authorization management by the Oklahoma Health Care Authority. The state law was changed in May of 2014 allowing for prior authorization implementation of the hepatitis C medications effective July 1, 2014.

As new direct-acting antivirals (DAAs) were FDA approved they were subsequently reviewed and recommended to be prior authorized by the DUR board. Harvoni® (ledipasvir/sofosbuvir) was reviewed in November 2014 and Viekira Pak™ (ombitasvir/paritaprevir/ritonavir) was reviewed in January 2015. The newer treatment regimens correlated with an increase in cost ranging in cost from $66,000 to $199,000 per regimen.

	Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015
Total Hepatitis C Drug Spending	$6,931,306.72	$19,873,167.82	$22,159,582.85

Claims analysis of the third and fourth quarter of 2014 revealed a downward trend in hepatitis C spending indicating prior authorization implementation and cost-effective management measures were successful. Despite an increase in spending in the first three quarters of 2015, spending has yet to reach the level seen in Q2 of 2014 when prior authorization management was not yet in place.



Current Prior Authorization Criteria

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

Detailed prior authorization criteria for all hepatitis C products can be found at the end of this report in the recommendations section.

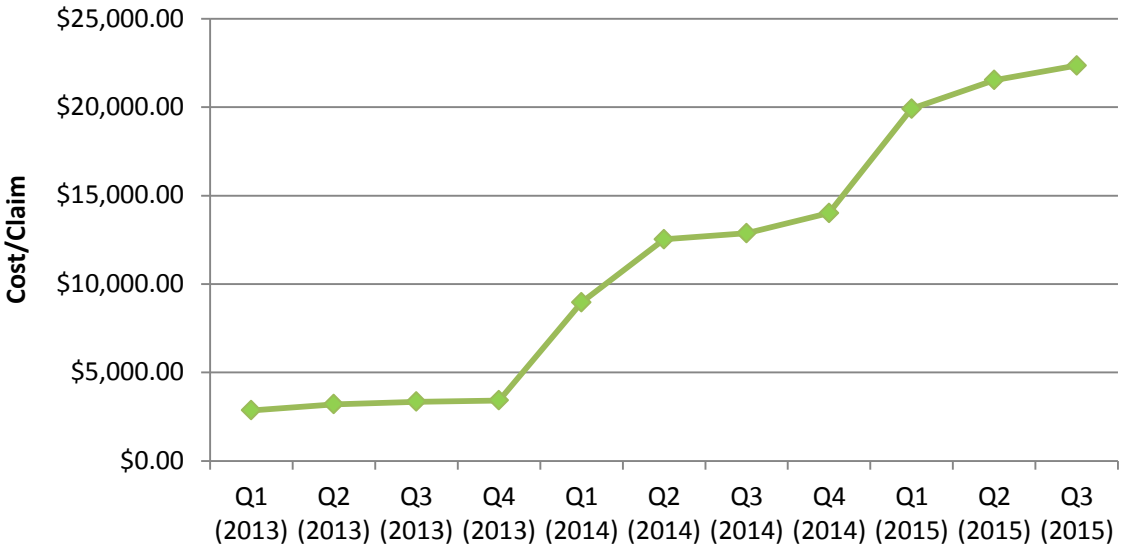
Utilization of Hepatitis C Medications: Fiscal Year 2015

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	311	2,432	$19,873,167.82	$8,171.53	$289.73	201,530	68,593
2015	292	1,290	$22,159,582.85	$17,177.97	$615.19	91,515	36,021
% Change	**-6.10%**	**-47.00%**	**11.50%**	**110.20%**	**112.30%**	**-54.60%**	**-47.50%**
Change	**-19**	**-1,142**	**$2,286,415.03**	**$9,006.44**	**$325.46**	**-110,015**	**-32,572**

*Total number of unduplicated members.
Chart includes utilization of sofosbuvir, simeprevir, sofosbuvir/ledipasvir, ombitasvir/paritaprevir/ritonavir/ dasabuvir, ribavirin, & peginterferon.

Three Year Trend: Cost/Claim of Hepatitis C Medications



Demographics of Members Utilizing Hepatitis C Medications*

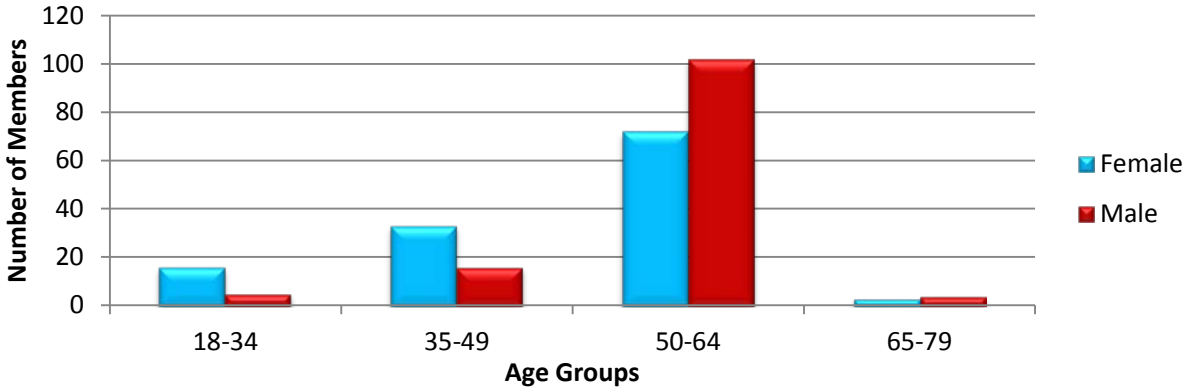


*Chart includes members utilizing sofosbuvir, simeprevir, sofosbuvir/ledipasvir, & ombitasvir/paritaprevir/ritonavir/dasabuvir.

Hepatitis C Summary Statistics for Treated Members

Genotype	Fibrosis Score	Pre-Treatment Viral Load (HCV RNA)	Treatment Length	SVR Cure Rate[+]	Compliance[¥]
1: 71.9% **2:** 13.7% **3:** 13.7% **4:** 0.64%	**Average:** 3.12 **F2:** 31.31% **F3:** 18.85% **F4:** 47.28% **Other:** 2.56%	**Average:** 3,121,693 IU/mL	**Average:** 13.84 **8 weeks**: 20.8% **12 weeks:** 56.5% **16 weeks:** 0.64% **24 weeks:** 22.0%	90% Cure Rate	**Before PA:** 18.8% of members noncompliant **After PA:** 1.9% of members noncompliant

*Table includes data collected from 07/01/2014 to 11/04/2015.
PA = Prior Authorization, SVR = Sustained Virologic Response at least 12 weeks after therapy completion
[+]SVR Cure rate includes data from members who started therapy from 12/01/2013-03/30/2015. The cure rate is based only on members for whom SoonerCare was able to obtain SVR responses (SVR response rate: 61.2%).
[¥]Compliance before prior authorization management was defined as an appropriate regimen length of 12 or 24 weeks.

- Based on the above cure rate and drug spending during the allotted time frame (12/01/2013-03/30/2015), the estimated cost per cure in the SoonerCare population is $91,675.88-$207,079.64. Range varies due to partial SVR response rate.

Top Prescriber Specialties of Hepatitis C Medications by Number of Claims*

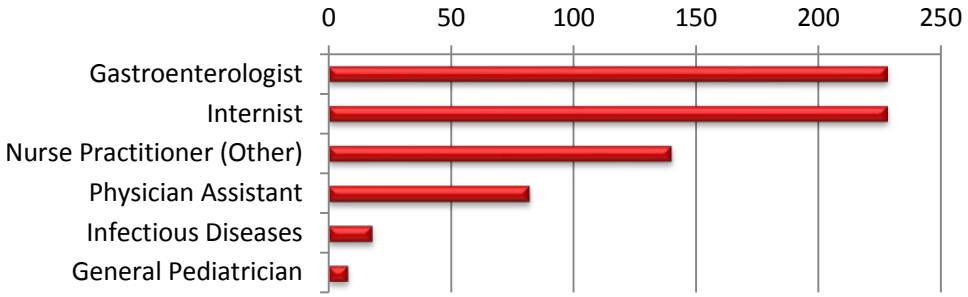
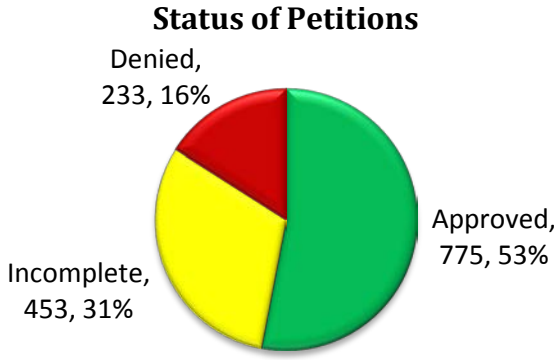


*Chart includes prescribers of sofosbuvir, simeprevir, sofosbuvir/ledipasvir, & ombitasvir/paritaprevir/ritonavir/dasabuvir.

Prior Authorization of Hepatitis C Medications

There were 1,461 prior authorization requests submitted for 431 unique members for hepatitis C medications during fiscal year 2015. Approvals are granted for 28 days of therapy each time, so members will have a prior authorization request for each refill of therapy. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expirations:

- Olysio® (simeprevir): September 2029
- Sovaldi® (sofosbuvir): December 2030
- Harvoni® (ledipasvir/sofosbuvir): December 2030
- Viekira Pak™(ombitasvir/paritaprevir/ritonavir/dasabuvir): September 2032

Removals from Market:

- **August 2014:** Vertex announced it discontinued sales of Incivek® (telaprevir) in the United States effective October 16, 2014. The discontinuation was a business decision by Vertex, and was not based on any safety or efficacy findings.
- **January 2015:** Merck decided to voluntarily discontinue the manufacture and distribution of Victrelis® (boceprevir) in the United States by December 2015. The discontinuation was a business decision by Merck, and was not based on any safety or efficacy findings.

New FDA Approvals:

- **July 2015:** The U.S. Food and Drug Administration (FDA) approved Daklinza™ (daclatasvir) for use with sofosbuvir to treat hepatitis C virus (HCV) genotype-3 infections. Daklinza™ is the first drug that has demonstrated safety and efficacy to treat genotype-3 HCV infections without the need for co-administration of interferon or ribavirin.
- **July 2015:** The FDA approved Technivie™ (ombitasvir/paritaprevir/ritonavir) for use in combination with ribavirin for the treatment of HCV genotype-4 infections in patients without cirrhosis. Technivie™ in combination with ribavirin is the first drug that has demonstrated safety and efficacy to treat genotype-4 HCV infections without the need for co-administration of interferon.

New Indications:

- **November 2015:** Gilead Sciences announced the FDA approval of Harvoni® (ledipasvir/ sofosbuvir) for expanded use in patients with genotypes 4, 5, and 6 chronic HCV infection and in patients co-infected with human immunodeficiency virus (HIV). Additionally, Harvoni® plus ribavirin for 12 weeks was approved as an alternate therapy to 24 weeks of Harvoni for treatment-experienced, genotype-1 patients with cirrhosis. Harvoni® was previously approved in October 2014 for the treatment of chronic HCV genotype-1 infection.

Safety Updates:

- **March 2015:** The FDA warned health care professionals that serious slowing of the heart rate can occur when amiodarone is taken together with either Harvoni® (ledipasvir/ sofosbuvir) or Sovaldi® (sofosbuvir). The FDA required the addition of information about symptomatic bradycardia to the Harvoni® and Sovaldi® labels, and recommended that health care professionals not prescribe either Harvoni® or Sovaldi® with amiodarone.
    - The FDA's review of submitted postmarketing adverse event reports identified the death of one patient due to cardiac arrest and three patients requiring placement of a pacemaker to regulate their heart rhythms. The other patients recovered after discontinuing either the HCV drugs or amiodarone, or both.
- **October 2015:** The FDA warned health care professionals that Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasbuvir) and Technivie™ (ombitasvir/paritaprevir/ ritonavir) can cause serious liver injury in patients with underlying advanced liver disease. The FDA required the manufacturer to add new information about this safety risk to the drug labels.
    - The FDA's review of adverse events identified cases of hepatic decompensation and liver failure in patients with underlying liver cirrhosis who were taking these medicines. Some of these events resulted in liver transplantation or death. These serious outcomes were reported mostly in patients taking Viekira Pak™ who had evidence of advanced cirrhosis even before starting treatment. Since the approvals of Viekira Pak™ and Technivie™, at least 26 worldwide cases were considered to be possibly related to Viekira Pak™ or Technivie™. In most cases, liver injury occurred within 1 to 4 weeks of starting treatment. Some cases occurred in patients for whom these medicines were contraindicated or not recommended.

Pipeline News:

- **July 2015:** Merck announced that the FDA has accepted a New Drug Application (NDA) for grazoprevir/elbasvir, a once-daily, single-tablet therapy for the treatment of adult patients infected with HCV genotypes 1, 4, or 6. Grazoprevir/elbasvir is being evaluated in multiple HCV genotypes and patients with HIV/HCV co-infection, advanced chronic kidney disease, inherited blood disorders, liver cirrhosis and those on opiate substitution therapy. The FDA granted Priority Review for grazoprevir/elbasvir, with a Prescription Drug User Fee Act (PDUFA) action date of January 28, 2016.
- **October 2015:** Bristol-Myers Squibb Company announced that the FDA has accepted three supplemental New Drug Applications (sNDAs) for Daklinza™ (daclatasvir), for use

with sofosbuvir with or without ribavirin. The applications are for the treatment of patients with HIV/HCV co-infection, patients with advanced cirrhosis (including decompensated cirrhosis), and for patients with post-liver transplant recurrence of HCV.

- **October 2015:** Gilead Sciences announced that it has submitted a NDA to the FDA for once-daily sofosbuvir/velpatasvir for the treatment of chronic HCV genotypes 1-6 infection. The NDA is supported by clinical studies exploring the use of 12 weeks of sofosbuvir/velpatasvir in patients with genotypes 1-6 HCV infection, including patients with compensated cirrhosis and 12 weeks of sofosbuvir/velpatasvir with ribavirin for patients with decompensated cirrhosis.

Guideline Updates:

- **October 2015:** The American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) have updated the guidelines on when and in whom to initiate HCV therapy.
    - The updated guidelines recommend treatment for all patients with chronic HCV infection, except those with short life-expectancies that cannot be remediated by treating HCV. The guidelines no longer contain prioritization tables based on fibrosis score.
    - The updated guidelines also state that there is strong evidence that persons who inject drugs have demonstrated adherence to treatment and low rates of reinfection and no longer recommend pretreatment screening for illicit drug or alcohol use to identify a population more likely to successfully complete treatment.

Regimen Comparison[12,13,14,15,16,17,18]

The following table shows the current FDA approved or AASLD/IDSA guideline recommended regimens of DAA products for the treatment of chronic HCV infection in treatment-naïve patients with or without cirrhosis. Specific regimens are used in particular patient populations depending on pre-treatment viral load, prior hepatitis C treatment experience, fibrosis stage, and cirrhosis status. Regimens marked with a star are not currently FDA approved, but are recommended by the AASLD/IDSA treatment guidance. Many non-FDA approved regimens were only studied in very small treatment populations with limited SVR data.

SVR rates found in clinical studies should not be compared across studies, but can be used as a measure of clinical efficacy for each regimen. SVR rates were obtained from studies cited in the AASLD/IDSA treatment guidance or from an individual product's package labeling. SVR rates may vary across studies even when used in similar patient populations. Some SVR percentages in the following table may contain treatment experienced patients if the study did not differentiate.

Genotype	Host/ Viral Factors	Treatment Regimen	Total Cost	SVR in Clinical Studies
Genotype-1a	Treatment naïve, Non-cirrhotic	*DAC + SOF 12 wks	$155,232.00	96%
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	93% or 96%
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	97%
		SIM + SOF 12 wks	$158,780.16	97% (1a & 1b)
	Treatment naïve, Cirrhotic	*DAC + SOF +/- RBV 24 wks	$310,464.00-$311,250.24	Not available
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 24 wks	$176,756.16	95%
		SIM + SOF +/- RBV 24 wks	$317,560.32-$318,346.56	74%-88%¥
Genotype-1b	Treatment naïve, Non-cirrhotic	*DAC + SOF 12 wks	$155,232.00	100%
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	98%
		PAR/RIT/OMB/DAS 12 wks	$87,984.96	100%
		SIM + SOF 12 wks	$158,780.16	97% (1a & 1b)
	Treatment naïve, Cirrhotic	*DAC + SOF +/- RBV 24 wks	$310,464.00-$311,250.24	100%
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	100%
		SIM + SOF +/- RBV 24 wks	$317,560.32-$318,346.56	92%
Genotype-2	Treatment naïve, Non-cirrhotic	*DAC + SOF 12 wks	$155,232.00	100%
		SOF + RBV 12 wks	$89,097.12	96%
	Treatment naïve, Cirrhotic	*DAC + SOF 12 or 24 wks	$155,232.00-$310,464.00	Not available
		*SOF + RBV 16 wks	$118,796.16	78%
Genotype-3	Treatment naïve, Non-cirrhotic	DAC + SOF 12 wks	$155,232.00	97%
		*SOF + RBV + PEG IFN 12 wks	$99,605.04	96%
		SOF + RBV 24 wks	$178,194.24	93%
	Treatment naïve, Cirrhotic	*DAC + SOF +/- RBV 24 wks	$310,464.00-$311,250.24	88%
		*SOF + RBV + PEG IFN 12 wks	$99,605.04	91%
		SOF + RBV 24 wks	$178,194.24	92%
Genotype-4	Treatment naïve, Non-cirrhotic	LED/SOF 12 wks	$99,792.00	93%-100%
		PAR/RIT/OMB + RBV 12 wks	$81,338.88	100%
		*SOF + RBV 24 wks	$178,194.24	84%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	96%
	Treatment naïve, Cirrhotic	LED/SOF 12 wks	$99,792.00	93%-100%
		*SOF + RBV 24 wks	$178,194.24	Not available
		SOF + RBV + PEG IFN 12 wks	$99,605.04	Not available
Genotype-5 or 6	Treatment naïve, Non-cirrhotic & Cirrhotic	LED/SOF 12 wks	$99,792.00	GT5: 93%, GT6: 96%
		*SOF + RBV + PEG IFN 12 wks	$99,605.04	GT5: 100%, GT6: 100%

*Not an FDA approved regimen

¥Lower percentage accounts for those with Q80K polymorphism and some patients with prior treatment experience.

Costs based on estimated acquisition cost (EAC)

Some SVR percentages may contain treatment experienced or cirrhotic patients if the study did not differentiate.

If genotypic subtype not indicated then both GT1a and GT1b were included in the SVR results.

SIM = simeprevir SOF = sofosbuvir LED = ledipasvir PAR = paritaprevir RIT = ritonavir OMB = ombitasvir
DAS = dasabuvir DAC = daclatasvir RBV= Ribavirin PEG IFN= peginterferon alfa GT= Genotype

SVR = sustained virologic response at least 12 weeks after therapy completion

RBV Dosing based >75kg patient (1200mg)

Other States' Coverage of Direct Acting Antivirals[19]

State	Abstain from Alcohol Abuse Before Treatment	Abstain from Injection Drug Use Before Treatment	Minimum METAVIR Fibrosis Score	Specialist Prescriber Requirement
Alabama	Yes	Yes	F2	-
Alaska	Yes	Yes	F3*	-
Arizona	Yes	Yes	F3	Yes
Arkansas	Yes	Yes	F3*	-
California	-	-	F3	-
Colorado	Yes	Yes	F3	Yes
Connecticut[+]	-	-	-	-
Delaware	Yes	Yes	F4	-
District of Colombia	Yes	Yes	F2	Yes
Florida	Yes	Yes	F3	Yes
Georgia	-	-	F3	-
Hawaii	Yes	Yes	F3	Yes
Idaho	Yes	Yes	F3	Yes
Illinois	Yes	Yes	F4	Yes
Indiana	-	-	F4	Yes
Iowa	Yes	Yes	F3*	Yes
Kansas	Yes	Yes	F3	Yes
Kentucky	Yes	Yes	F3	Yes
Louisiana	Yes	Yes	F3*	Yes
Maine	-	-	F1	Yes
Maryland	Yes	Yes	F2	Yes
Massachusetts	-	-	NA	-
Michigan[¥]				
Minnesota	-	-	-	-
Mississippi	Yes	Yes	-	Yes
Missouri	Yes	Yes	F3	-
Montana	Yes	Yes	F3	Yes
Nebraska	Yes	Yes	F3	-
Nevada[+]	-	-	-	-
New Hampshire	Yes	Yes	F3	Yes
New Jersey[¥]				
New Mexico	-	-	F3	-
New York	-	-	F3	Yes
North Carolina	Yes	-	-	-
North Dakota	Yes	Yes	F2	Yes
Ohio	Yes	Yes	F3	Yes
Oklahoma	Yes	Yes	F2	-
Oregon	Yes	Yes	F4	Yes
Pennsylvania	Yes	Yes	F3	Yes
Rhode Island	-	-	F3	-
South Carolina	Yes	Yes	F3	Yes
South Dakota	Yes	Yes	F3	Yes
Tennessee	Yes	Yes	F3	Yes
Texas	Yes	Yes	F3	Yes
Utah	-	-	-	-
Vermont	Yes	Yes	F3	Yes
Virginia	Yes	Yes	F3	Yes
Washington	Yes	Yes	F3	Yes
West Virginia	Yes	Yes	F3	Yes
Wisconsin	Yes	Yes	F3	Yes
Wyoming	Yes	Yes	-	-

Table modified from: Canary LA, Kleevens RM, Holmberg SD. Limited Access to New Hepatitis C Virus Treatment Under State Medicaid Programs. *Ann Intern Med.* 2015 Aug 4; 163(3):226-8.

Dash or (-) represents "No or not required"

*Biopsy required, [+]No prior authorization required, [¥]No published criteria

Daklinza™ (Daclatasvir) Product Summary[17]

FDA Approval: July 2015

Indications: 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.

Dosing:

- Daklinza™ is available as 60mg and 30mg oral tablets.
- The recommended dosing of daclatasvir is 60mg by mouth once daily in combination with sofosbuvir for 12 weeks.
- The optimal duration of daclatasvir and sofosbuvir for patients with cirrhosis has not been established.
- The dose of daclatasvir should be reduced to 30mg once daily when taken with strong CYP3A inhibitors (Examples: atazanavir, ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, voriconazole).
- The dose of daclatasvir should be increased to 90mg once daily when taken with moderate CYP3A inducers (Examples: bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, rifapentine).
- Daclatasvir is contraindicated when taken in combination with strong CYP3A inducers.
- Daclatasvir may be taken with or without food.

Mechanism of Action: Daclatasvir is an inhibitor of NS5A, a nonstructural protein encoded by HCV. Daclatasvir inhibits both viral RNA replication and virion assembly.

Contraindications: Daclatasvir is contraindicated when taken in combination with drugs that strongly induce CYP3A and, thus, may lead to lower exposure and loss of efficacy of daclatasvir *(see drug interactions section)*. Contraindicated drugs include:

- Phenytoin
- Carbamazepine
- Rifampin
- St. John's wort

Warnings and Precautions:

- Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions: The concomitant use of daclatasvir and other drugs may result in known or potentially known significant drug interactions which may lead to loss of therapeutic effect of daclatasvir and possible development of resistance. Other possible drug interaction effects include dosage adjustments of concomitant medications or daclatasvir, or possible adverse reactions from greater exposures of concomitant drugs or daclatasvir *(see drug interactions section)*.
- Serious Symptomatic Bradycardia When Coadministered with Sofosbuvir and Amiodarone: Cases of symptomatic bradycardia and requiring pacemaker intervention have been reported when amiodarone is coadministered with sofosbuvir in combination with another HCV DAA, including daclatasvir. Bradycardia has generally occurred within hours to days, but cases have been observed up to two weeks after initiating HCV

treatment. Patients also taking beta blockers or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone.

- Coadministration of amiodarone with daclatasvir in combination with sofosbuvir is not recommended. Patients taking amiodarone who have no alternative treatment options and who will be coadministered daclatasvir and sofosbuvir should be counseled on the risk of serious symptomatic bradycardia and monitored in an outpatient setting for the first 48 hours of coadminsitration, after which monitoring of the heart rate should occur on a daily basis through at least the first two weeks of treatment.

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

- Headache
- Fatigue
- Nausea
- Diarrhea

Use in Special Populations:

- Pregnancy: No data with daclatasvir in pregnant women are available to inform a drug-associated risk. In animal reproductive studies in rats and rabbits, no evidence of fetal harm was observed with oral administration of daclatasvir at doses up to 22 times the recommended human dose.
- Nursing Mothers: No information regarding the presence of daclatasvir in human milk, the effects on the breastfed infant, or the effects on milk production is available. Daclatasvir is present in the milk of lactating rats.
- Pediatric Use: The safety and effectiveness of daclatasvir in pediatric patients younger than 18 years of age have not been established.
- Geriatric Use: Safety was similar across older and younger subjects in daclatasvir clinical trials. There are no safety findings or dosage adjustments unique to patients 65 years and older.
- Renal Impairment: No dosage adjustment of daclatasvir is required for patients with any degree of renal impairment.
- Hepatic Impairment: No dosage adjustment of daclatasvir is required for patients with mild, moderate, or severe hepatic impairment. Safety and effectiveness of daclatasvir have not been established in patients with decompensated cirrhosis.
- Liver Transplant Patients: The safety and efficacy of daclatasvir combination therapy have not been established in liver transplant patients.

Drug Interactions: Daclatasvir is a substrate of CYP3A. Therefore, moderate or strong inducers of CYP3A may decrease the plasma levels and therapeutic effect of daclatasvir. Strong inhibitors of CYP3A may increase the plasma concentrations of daclatasvir.

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comment(s)**
Strong CYP3A Inhibitors atazanavir/ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, voriconazole	Increased daclatasvir	Dose of daclatasvir should be decreased to 30mg once daily.
Moderate CYP3A Inhibitors atazanavir, ciprofloxacin, darunavir/ ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, verapamil	Increased daclatasvir	Monitor for daclatasvir adverse effects.
Moderate CYP3A Inducers bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, rifapentine	Decreased daclatasvir	Dose of daclatasvir should be increased to 90mg once daily.
Anticoagulants dabigatran etexilate mesylate	Increased daclatasvir	Use of daclatasvir with dabigatran is not recommended in specific renal impairment groups, depending upon the indication.
Antiarrhythimic amiodarone, digoxin	amiodarone: effects unknown digoxin: increased	Coadministration of amiodarone with daclatasvir in combination with sofosbuvir is not recommended because it may result in serious symptomatic bradycardia. Digoxin concentrations should be monitored and the digoxin dosage should be adjusted if necessary.
HMG-CoA Reductase Inhibitors Atorvastatin, fluvastatin, pitvastatin, pravastatin, rosuvastatin, simvastatin	Increased atorvastatin, fluvastatin, pitvastatin, pravastatin, rosuvastatin, simvastatin	Monitor for HMG-CoA reductase inhibitor associated adverse events.

Table modified from: Daklinza™ Product Information. Bristol-Myers Squibb Company.

Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) Product Summary[18]

FDA Approval: July 2015

Indications: 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.

Dosing:

- Technivie™ is available as 12.5mg obmitasvir/75mg paritaprevir/50mg ritonavir oral tablets. It is dispensed in a monthly carton for a total of 28 days of therapy. Each monthly carton contains four weekly cartons, and each weekly carton contains seven daily dose packs. Each seven daily dose pack contains two Technivie™ tablets.
- The recommended dosage of ombitasvir/paritaprevir/ritonavir is two tablets by mouth once daily in the morning in combination with ribavirin for 12 weeks.

- Ombitasvir/paritaprevir/ritonavir is used in combination with ribavirin. The recommended dose of ribavirin when administered with ombitasvir/paritaprevir/ ritonavir is based on weight (1000mg per day for patients less than 75kg and 1200mg per day for those weighing at least 75kg).
- Ombitasvir/paritaprevir/ritonavir without ribavirin for 12 weeks may be considered for treatment-naïve patients who cannot take or tolerate ribavirin.
- Ombitasvir/paritaprevir/ritonavir should be taken with a meal without regard to fat or calorie content.

Mechanism of Action: Technivie™ combines two direct-acting HCV antiviral agents with distinct mechanisms of action and non-overlapping resistance profiles to target HCV at multiple steps in the viral lifecycle.

- Ombitasvir is an inhibitor of HCV NS5A, which is essential for viral RNA replication and virion assembly.
- Paritaprevir is an inhibitor of HCV NS3/4A protease which is necessary for the proteolytic cleavage of the HCV encoded polyprotein and is essential for viral replication.
- Ritonavir is not active against HCV. Ritonavir is a potent CYP3A inhibitor that increases peak and trough plasma concentrations of paritaprevir and overall drug exposure.

Contraindications:

- The contraindications to ribavirin also apply to this combination regimen.
- Ombitasvir/paritaprevir/ritonavir is contraindicated in moderate-to-severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity.
- Ombitasvir/paritaprevir/ritonavir is contraindicated in patients with known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome).
- Ombitasvir/paritaprevir/ritonavir is contraindicated when taken with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events *(see table below)*.
- Ombitasvir/paritaprevir/ritonavir is contraindicated when taken with drugs that are moderate or strong inducers of CYP3A and may lead to reduced efficacy of Ombitasvir/paritaprevir/ritonavir *(see table below)*.

Drugs that are Contraindicated with Ombitasvir/Paritaprevir/Ritonavir		
Concomitant Drug Class	**Drug(s) within Class that are Contraindicated**	**Clinical Comment(s)**
Alpha 1-Adrenoreceptor Antagonist	alfuzosin HCl	Potential for hypotension
Anti-Gout	colchicine	Potential for serious and/or life-threatening reactions in patients with renal and/or hepatic impairment
Anticonvulsants	carbamazepine, phenytoin, phenobarbital	Ombitasvir/paritaprevir/ritonavir exposures may decrease leading to a potential loss of therapeutic activity.
Antimycobacterial	rifampin	Ombitasvir/paritaprevir/ritonavir exposures may decrease leading to a potential loss of therapeutic activity.

Drugs that are Contraindicated with Ombitasvir/Paritaprevir/Ritonavir		
Concomitant Drug Class	**Drug(s) within Class that are Contraindicated**	**Clinical Comment(s)**
Ergot Derivatives	ergotamine, dihydorergotamine, ergonovine, methylergonovine	Acute ergot toxicity characterized by vasospasm and tissue ischemia has been associated with co-administration of ritonavir and ergot derivatives.
Ethinyl Estradiol-Containing Products	ethinyl estradiol containing-medications such as combined oral contraceptives	Potential for ALT elevations
Herbal Products	St. John's Wort	Ombitasvir/paritaprevir/ritonavir exposures may decrease leading to a potential loss of therapeutic activity.
HMG-CoA Reductase Inhibitors	lovastatin, simvastatin	Potential for myopathy including rhabdomyolysis
Neuroleptics	pimozide	Potential for cardiac arrhythmias
Non-Nucleoside Reverse Transcriptase Inhibitors	efavirenz	Co-administration of efavirenz with paritaprevir, ritonavir was poorly tolerated and resulted in liver enzyme elevations.
Phosphodiesterase-5 (PDE5) inhibitor	sildenafil when dosed for the treatment of pulmonary arterial hypertension	There is increased potential for sildenafil-associated adverse events such as visual disturbances, hypotension, priapism, and syncope.
Sedatives/Hypnotics	triazolam, orally administered midazolam	Triazolam and orally administered midazolam are extensively metabolized by CYP3A4. Co-administration of triazolam or orally administered midazolam with ombitasvir/paritaprevir/ritonavir may cause large increases in the concentration of these benzodiazepines. The potential exists for serious and/or life-threatening events such as prolonged or increased sedation or respiratory depression.

Table modified from: Technivie™ Product Information. AbbVie Inc.

Warnings and Precautions:

- Risk of Hepatic Decompensation and Hepatic Failure in Patients with Cirrhosis: Ombitasvir/paritaprevir/ritonavir is not indicated in patients with cirrhosis. Hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, have been reported in patients treated with ombitasvir/paritaprevir/ritonavir with and without dasabuvir or ribavirin. Most patients with these severe outcomes had evidence of advanced cirrhosis prior to initiating therapy. Reported cases typically occurred within one to four weeks of initiating therapy and were characterized by the acute onset of rising direct serum bilirubin levels without ALT elevations in association with clinical signs and symptoms of hepatic decompensation.
- Increased Risk of ALT Elevations: During clinical trials with ombitasvir/paritaprevir/ritonavir with and without dasabuvir or ribavirin, elevations in ALT to greater than five times the upper limit of normal (ULN) occurred in approximately 1% of subjects. ALT elevations were typically asymptomatic, occurred in the first four weeks of treatment, and declined within two to eight weeks of onset with continued dosing.
    - These ALT elevations were significantly more frequent in female subjects who were using ethinyl estradiol-containing medications. Ethinyl estradiol containing

medications should be discontinued prior to starting treatment with ombitasvir/paritaprevir/ritonavir. Alternative methods of contraception are recommended.
    - Hepatic laboratory testing should be performed during the first four weeks of starting treatment and as clinically indicated thereafter.
- Risks Associated with Ribavirin Combination Treatment: The warnings and precautions for ribavirin, in particular the pregnancy avoidance warning, apply to this combination regimen.
- Risks of Adverse Reactions or Reduced Therapeutic Effect Due to Drug Interactions: The concomitant use of ombitasvir/paritaprevir/ritonavir and certain other drugs may result in known or potentially significant drug interactions, some of which may lead to loss of therapeutic effect of ombitasvir/paritaprevir/ritonavir and possible development of resistance, or possible clinically significant adverse reactions from greater exposures of concomitant drugs or components of ombitasvir/paritaprevir/ritonavir *(see drug interactions section)*.
- Risk of HIV-1 Protease Inhibitor Drug Resistance in HCV/HIV-1 Co-Infected Patients: The ritonavir component of ombitasvir/paritaprevir/ritonavir is also an HIV-1 protease inhibitor and can select for HIV-1 protease inhibitor resistance-associated substitutions. Any HCV/HIV-1 co-infected patients treated with ombitasvir/paritaprevir/ritonavir should also be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.

Adverse Reactions: The most common adverse reactions (≥5%) reported during ombitasvir/paritaprevir/ritonavir clinical trials include the following:

- Asthenia
- Fatigue
- Nausea
- Insomnia
- Pruritus
- Skin reactions

Use in Special Populations:

- Pregnancy: Ombitasvir/paritaprevir/ritonavir is pregnancy category B. There are no adequate and well-conducted studies in pregnant women. When ombitasvir/ paritaprevir/ritonavir is administered with ribavirin, the combination is contraindicated in pregnant women and in men whose female partners are pregnant.
- Nursing Mothers: It is not known whether any of the components of ombitasvir/ paritaprevir/ritonavir are present in human milk. Unchanged ombitasvir, paritaprevir, and its hydrolysis product were the predominant components observed in the milk of lactating rats.
- Pediatric Use: The safety and effectiveness of ombitasvir/paritaprevir/ritonavir in pediatric patients younger than 18 years of age have not been established.
- Geriatric Use: No dosage adjustment of ombitasvir/paritaprevir/ritonavir is warrented in geriatric patients. Clinical studies did not include sufficient numbers of patients older than 65 years of age to determine if they responded differently than younger patients.
- Renal Impairment: No dosage adjustment of ombitasvir/paritaprevir/ritonavir is required for patients with mild, moderate, or severe renal impairment. Ombitasvir/paritaprevir/ritonavir has not been studied in patients on dialysis.

- Hepatic Impairment: No dosage adjustment of ombitasvir/paritaprevir/ritonavir is required for patients with mild hepatic impairment (Child-Pugh A). Ombitasvir/ paritaprevir/ritonavir is required in patients with moderate-to-severe hepatic impairment (Child-Pugh B and C).

Drug Interactions: Paritaprevir and ritonavir are primarily metabolized by CYP3A enzymes. Co-administration of ombitasvir/paritaprevir/ritonavir with strong inhibitors of CYP3A may increase paritaprevir and ritonavir concentrations. Ombitasvir is primarily metabolized via amide hydrolysis while CYP enzymes play a minor role in its metabolism.

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	**Effect on Concentration**	**Clinical Comment**
Antiarrhythmics digoxin, amiodarone, bepridil, disopyramide, flecainide, lidocaine (systemic), mexiletine, propafenone, quinidine	Increased digoxin Increased antiarrhythmics	Decrease digoxin dose by 30-50%. Monitor of serum digoxin levels. Caution & concentration monitoring is recommended for antiarrhythmics.
Antifungals ketoconazole, voriconazole	Increased ketoconazole Decreased voriconazole	The maximum daily dose of ketoconazole should be limited to 200mg. Co-administration with voriconazole is not recommended.
Antipsychotics quetiapine	Increased quetiapine	Consider alternative anti-HCV therapy to avoid increases in quetiapine exposures. If co-administration is necessary, reduce quetiapine dose to 1/6th of current dose & monitor.
Calcium Channel Blockers amlodipine	Increased amlodipine	Monitor & consider dose reduction of amlodipine.
Corticosteroids (Inhaled/Nasal) fluticasone	Increased fluticasone	Alternative corticosteroids should be considered.
HIV-Antiviral Agents atazanavir, atazanavir/ritonavir, lopinavir/ritonavir, rilpivirine	Increased paritaprevir Increased rilpivirine	Co-administration owith atazanavir, atazanavir/ritonavir, lopinavir /ritonavir, or rilpivirine is not recommended.
HMG CoA Reductase Inhibitors pravastatin	Increased pravastatin	The dose should not exceed 40mg per day.
Immunosuppressants cyclosporine, tacrolimus	Increased cyclosporine Increased tacrolimus	The dose of cyclosporine should be reduced to 1/5th of the current dose. The dose of tacrolimus should be reduced.
Long-Acting Beta-Adrenoceptor Agonist salmeterol	Increased salmeterol	Co-administration is not recommended.

Table modified from: Technivie™ Product Information. AbbVie Inc.
Not all drug interactions from prescribing information are included in above table. Consult the prescribing information for a detailed list of clinically significant drug interactions.

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 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks
1	Treatment naïve, cirrhotic	Harvoni® for 12 weeks GT1a: Viekira Pak™ + RBV for 24 weeks GT1b: Viekira Pak™ + RBV for 12 weeks
1	Treatment experienced, non-cirrhotic	Harvoni® for 12 weeks 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks
1	Treatment experienced, cirrhotic	Harvoni® + RBV for 12 weeks Harvoni® for 24 weeks GT1a: Viekira Pak™ + RBV for 24 weeks GT1b: Viekira Pak™ + RBV for 12 weeks
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 Sovaldi® + RBV + PEG IFN for 12 weeks
Genotype-3		
3	Treatment naïve, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks
3	Treatment naïve, cirrhotic	Sovaldi® + RBV for 24 weeks Sovaldi® + RBV + PEG IFN for 12 weeks
3	Treatment experienced, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks
3	Treatment experienced, cirrhotic	Sovaldi® + RBV + PEG IFN for 12 weeks
Genotype-4		
4	Treatment naïve, non-cirrhotic	Harvoni® for 12 weeks Technivie™ + RBV for 12 weeks
4	Treatment naïve, cirrhotic	Harvoni® for 12 weeks
4	Treatment experienced, non-cirrhotic	Harvoni® for 12 weeks Technivie™ + RBV for 12 weeks
4	Treatment experienced, cirrhotic	Harvoni® 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 or recommended in AASLD/IDSA treatment guidance.
RBV = Ribavirin PEG IFN = peginterferon alfa GT= Genotype

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Harvoni® (sofosbuvir/ledipasvir) are the preferred regimens for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination or alone for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira Pak™ or Harvoni® 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, 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
    c. **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
    d. 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-2 or 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. 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 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
    b. **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
        ii. **Treatment-naïve, cirrhotic**
            1. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
            2. Sovaldi® with weight-based ribavirin for 24 weeks (if interferon ineligible)
        iii. **Treatment-experienced, non-cirrhotic**
            1. Daklinza™ with Sovaldi® for 12 weeks
        iv. **Treatment-experienced, cirrhotic**
            1. Sovaldi® with weight-based ribavirin and peginterferon alfa for 12 weeks
    c. 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 10^{th} of a month, and for 24 weeks of therapy prior to the 15^{th} of a month in order to prevent prescription limit issues from affecting the member's compliance.

Utilization Details of Hepatitis C Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	% COST	COST/ CLAIM
SOFOSBUVIR PRODUCTS						
SOVALDI 400MG TAB	357	136	$10,529,535.43	2.63	47.52	$29,494.50
Subtotal	**357**	**136**	**$10,529,535.43**	**2.63**	**47.52**	**$29,494.50**
SOFOSBUVIR/LEDIPASVIR PRODUCTS						
HARVONI 400MG/90MG TAB	292	112	$9,713,149.32	2.61	43.83	$33,264.21
Subtotal	**292**	**112**	**$9,713,149.32**	**2.61**	**43.83**	**$33,264.21**
SIMEPREVIR PRODUCTS						
OLYSIO 150MG CAP	40	19	$934,412,.25	2.11	4.22%	$23,360.31
Subtotal	**40**	**19**	**$934,412,.25**	**2.11**	**4.22%**	**$23,360.31**
OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR PRODUCTS						
VIEKIRA PAK	15	6	$439,932.00	2.5	1.99%	$29,328.80
Subtotal	**15**	**6**	**$439,932.00**	**2.5**	**1.99%**	**$29,328.80**
RIBAVIRIN PRODUCTS						
RIBAVIRIN 200MG TAB	212	75	$20,989.35	2.83	0.09%	$99.01
RIBASPHERE 200MG TAB	90	42	$10,033.34	2.14	0.05%	$111.48
RIBASPHERE 200MG CAP	65	23	$6,676.85	2.83	0.03%	$102.72
MODERIBA 200MG TAB	38	12	$3,942.84	3.17	0.02%	$103.76
RIBAVIRIN 200MG CAP	27	14	$2,843.73	1.93	0.01%	$105.32
REBETOL 40MG/ML SOL	13	1	$8,837.19	13	0.04%	$679.78
Subtotal	**445**	**164**	**$53,323.30**	**2.71**	**0.24%**	**$119.83**
PEGINTERFERON PRODUCTS						
PEG-INTRON KIT 120MCG	37	11	$128,084.46	3.36	0.58%	$3,461.74
PEG-INTRON KIT 150MCG	30	9	$108,946.68	3.33	0.49%	$3,631.56
PEGASYS 180MCG	26	11	$91,874.71	2.36	0.41%	$3,533.64
PEGASYS PROCLICK 180MCG	25	12	$87,867.11	2.08	0.40%	$3,514.68
PEG-INTRON KIT 80MCG	7	2	$22,718.50	3.5	0.10%	$3,245.50
PEG-INTRON KIT 120MCG	7	1	$17,367.17	7	0.08%	$2,481.02
PEGINTRON KIT 150MCG	5	1	$18,387.75	5	0.08%	$3,677.55
PEGINTRON KIT 120MCG	2	1	$7,012.64	2	0.08%	$3,506.32
PEGASYS PROCLICK 135MCG	2	1	$6,971.53	2	0.03%	$3,485.77
Subtotal	**141**	**45**	**$489,230.55**	**3.13**	**2.25%**	**$3,469.72**
TOTAL	**1,290**	**292***	**$22,159,582.85**	**4.42**	**100%**	**$17,177.97**

*Total number of unduplicated members.

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Appendix Q

Fiscal Year 2015 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)

Oklahoma Health Care Authority
December 2015

Introduction[1]

Hematopoietic growth factors are a group of glycoproteins that help promote blood cell growth and bone marrow proliferation. There are five classic hematopoietic growth factors, including erythropoietin, granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), macrophage colony-stimulating factor (M-CSF), and interleukin-3 (IL-3). These glycoproteins are produced naturally in lymphocytes and monocytes, and have been demonstrated to stimulate progenitor cells of different hematopoietic cell lineages to form colonies of recognizable mature blood cells. G-CSFs stimulate the bone marrow to produce granulocytes and stem cells and release them into the bloodstream. G-CSFs also stimulate the survival, proliferation, differentiation, and function of neutrophil precursors and mature neutrophils. G-CSFs do not currently require prior authorization.

Utilization of G-CSFs: Fiscal Year 2015

Comparison of Fiscal Years for G-CSFs: Pharmacy Claims
Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Granix® (tbo-filgrastim)

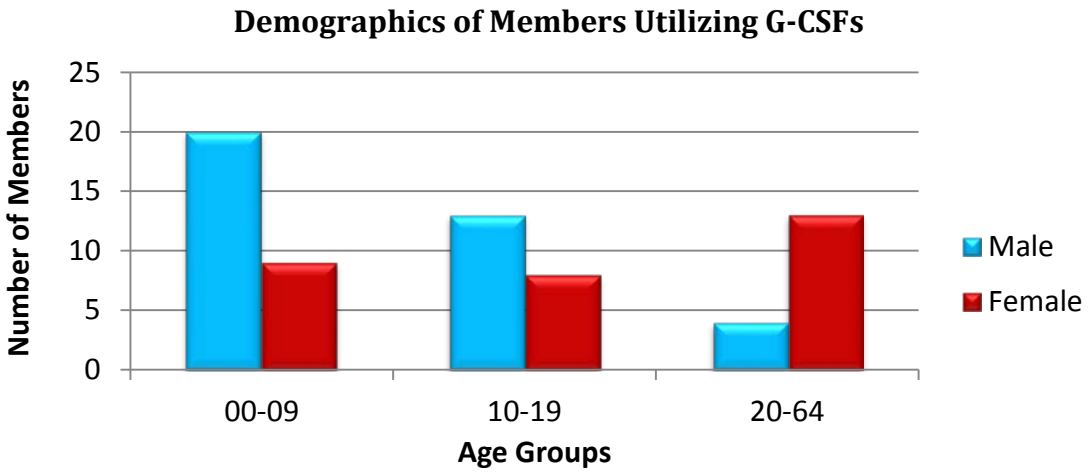
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	67	258	$818,064.17	$3,170.79	$213.04	2,123	3,840
2015	67	267	$1,001,916.87	$3,752.50	$243.07	2,355	4,122
% Change	**0.00%**	**3.50%**	**22.50%**	**18.30%**	**14.10%**	**10.90%**	**7.30%**
Change	**0**	**9**	**$183,852.70**	**$581.71**	**$30.03**	**232**	**282**

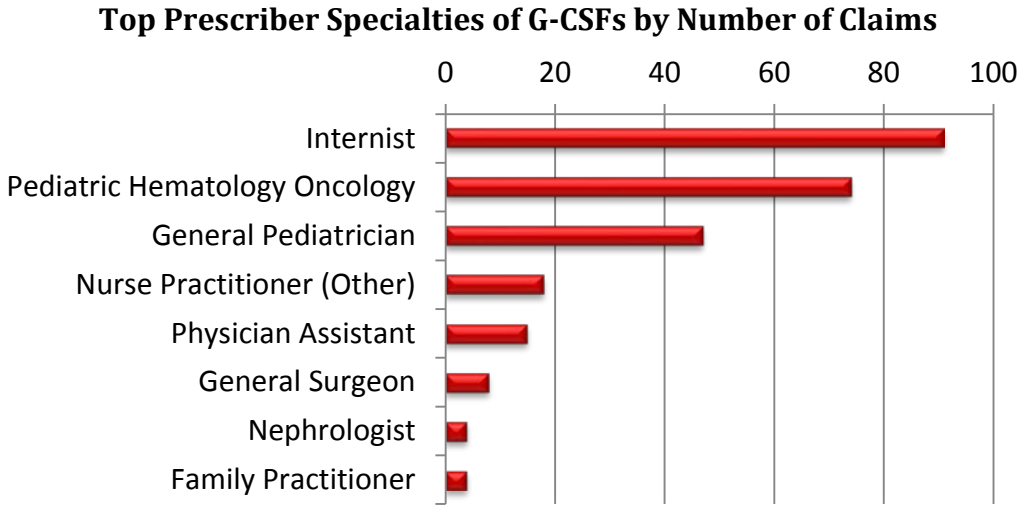
*Total number of unduplicated members.
G-CSFs do not currently require prior authorization. Zarxio™ (filgrastim-sndz) had no utilization in fiscal year 2015.

Fiscal Year 2015 Utilization of G-CSFs: Medical Claims
Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Granix® (tbo-filgrastim)

*Total Members	Total Claims	Total Cost	Cost/Claim
343	1,385	$3,910,285.79	$2,823.31

*Total number of unduplicated members.
G-CSFs do not currently require prior authorization. Zarxio™ (filgrastim-sndz) had no utilization in fiscal year 2015.





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

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

- **August 2015:** The FDA released guidance for the industry regarding nonproprietary naming of biological products. The draft guidance and proposed rule calls for biologics, including reference products and biosimilars, to bear a nonproprietary name with an FDA-designated suffix.

- Information regarding new FDA approved biosimilar products can be found under Product Summaries.

New FDA Approved Indications:

- **November 2015:** The FDA approved Neulasta® (pegfilgrastim) for radiation injury of bone marrow following acute exposure of myelosuppressive radiation doses. This is in addition to the previous FDA approved indication for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy.

Pipeline Updates:

- **December 2014:** Apotex submitted a Biologics License Application (BLA) to the FDA for a proposed biosimilar for Neulasta® (pegfilgrastim).
- **February 2015:** Apotex submitted a BLA to the FDA for Grastofil™, a proposed biosimilar for Neupogen® (filgrastim).
- **November 2015:** Sandoz submitted a BLA to the FDA for a proposed biosimilar for Neulasta® (pegfilgrastim).

Product Summaries[7,8,9,10,11,12,13,14]

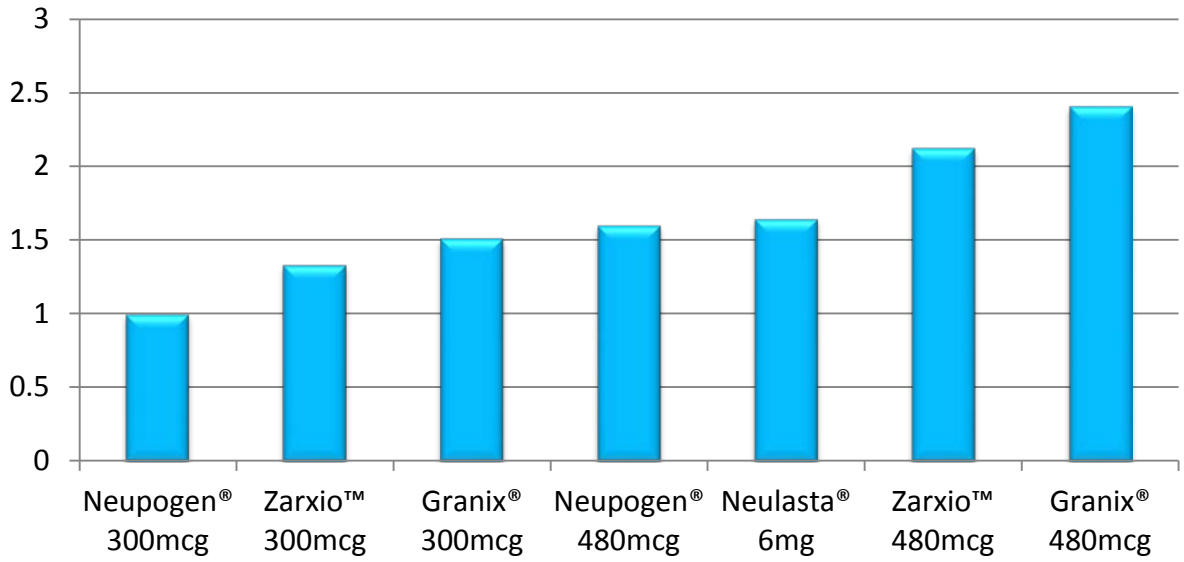
Neulasta® (pegfilgrastim) was FDA approved in 2002 and is a pegylated derivative of Neupogen® (filgrastim). Pegfilgrastim is indicated for prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy and for radiation injury of bone marrow following acute exposure of myelosuppressive radiation doses. Filgrastim has multiple indications (see below in Zarxio™ summary). Pegfilgrastim has a longer elimination half-life compared to filgrastim, and the recommended dosing of pegfilgrastim for prophylaxis of febrile neutropenia is 6mg subcutaneously once per chemotherapy cycle. The recommended dosing of filgrastim for the same indication is 5mcg/kg subcutaneously or intravenously daily until post-nadir absolute neutrophil count (ANC) recovery to normal or near-normal levels by laboratory standards or for a maximum of 2 weeks.

Granix® (tbo-filgrastim) was FDA approved in 2012 under the BLA pathway and although technically a branded product, it is essentially a biosimilar product for filgrastim. However, 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. Filgrastim has multiple indications (see below in Zarxio™ summary). The recommended dosing of tbo-filgrastim is the same as the recommended dosing of filgrastim.

Zarxio™ (filgrastim-sndz) was FDA approved in March 2015 as the first FDA approved biosimilar (approved through the new abbreviated licensure pathway for biosimilar products). Filgrastim-sndz is a biosimilar product for filgrastim, and, by the FDA's definition of a biosimilar, may not be substituted for one another without prescriber intervention. Filgrastim-sndz 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. Filgrastim has all of the listed indications, as well as an additional indication for radiation injury of bone marrow following acute exposure of myelosuppressive radiation doses. Filgrastim also has been designated an orphan product for use in the treatment of neutropenia associated with bone marrow transplant, Acquired Immunodeficiency Syndrome (AIDS) patients with Cytomegalovirus (CMV) retinitis being treated with ganciclovir, severe chronic neutropenia, and acute myeloid leukemia. The recommended dosing of filgrastim-sndz is the same as the recommended dosing of filgrastim.

Cost Comparison Ratios: G-CSFs



The above cost comparison chart differentiates the G-CSFs and strengths available, taking into account federal and supplemental rebate participation. The costs are based on the maximum dose per chemotherapy regimen for the prophylaxis of febrile neutropenia in patients with non-myeloid malignancies who receive myelosuppressive chemotherapy (14 daily doses of Neupogen®, Zarxio™, or Granix® or one dose of Neulasta®). Please note, the majority of Neupogen® use in fiscal year 2015 was for the 300mcg strength.

The estimated cost savings, based on fiscal year 2015 utilization data and average cost per claim for Neupogen®, if members using Neulasta® or Granix® switched to Neupogen® would be approximately $1,426,991.85. This estimated cost savings does not take into account federal or supplemental rebate participation, which could contribute to even more savings. There was no utilization of Zarxio™ in fiscal year 2015.

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).

Utilization Details of G-CSFs: Fiscal Year 2015

G-CSFs: Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
FILGRASTIM PRODUCTS						
NEUPOGEN INJ 300MCG	182	36	$606,518.39	$241.45	$3,332.52	60.54%
NEUPOGEN INJ 480/0.8	21	13	$123,083.82	$292.36	$5,861.13	12.28%
NEUPOGEN INJ 300/0.5	12	6	$34,326.73	$314.92	$2,860.56	3.43%
NEUPOGEN INJ 480MCG	8	4	$34,042.27	$851.06	$4,255.28	3.40%
SUBTOTAL	**223**	**59**	**$797,971.21**	**$258.91**	**$3,578.35**	**79.64%**
PEGFILGRASTIM PRODUCTS						
NEULASTA INJ 6MG/0.6M	40	12	$184,619.40	$194.54	$4,615.49	18.43%
SUBTOTAL	**40**	**12**	**$184,619.40**	**$194.54**	**$4,615.49**	**18.43%**
TBO-FILGRASTIM PRODUCTS						
GRANIX INJ 480/0.8	4	1	$19,326.26	$212.38	$4,831.57	1.93%
SUBTOTAL	**4**	**1**	**$19,326.26**	**$212.38**	**$4,831.57**	**1.93%**
TOTAL	**267**	**67***	**$1,001,916.87**	**$243.07**	**$3,752.50**	**100.00%**

*Total number of unduplicated members.
G-CSFs do not currently require prior authorization.
Zarxio™ had no utilization in fiscal year 2015.

G-CSFs: Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
NEULASTA INJ J2505	1,089	315	$3,713,504.00	$3,410.01
NEUPOGEN INJ J1442	239	43	$176,706.39	$739.36
GRANIX INJ J1446	57	10	$20,075.40	$352.20
TOTAL	**1,385**	**343***	**$3,910,285.79**	**$2,823.31**

*Total number of unduplicated members.
G-CSFs do not currently require prior authorization.
Zarxio™ had no utilization in fiscal year 2015.

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Appendix R

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

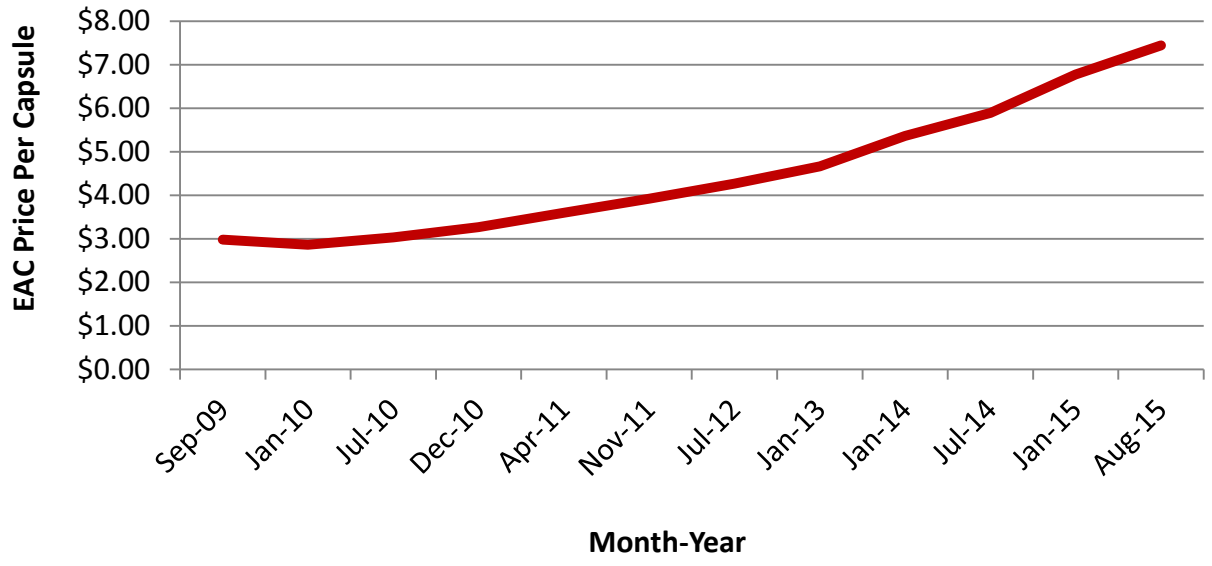
Oklahoma Health Care Authority
December 2015

Aggrenox® (Aspirin/Dipyridamole Extended-Release) Product Summary[1,2,3,4,5,6]

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. The recommended dose of aspirin/ dipyridamole ER is one capsule (25mg aspirin/200mg dipyridamole ER) by mouth twice daily in adult patients. The safety and effectiveness of aspirin/dipyridamole ER in pediatric patients have not been studied, and due to the aspirin component and risk of Reye syndrome, use of aspirin/dipyridamole ER is not recommended in the pediatric population.

Aggrenox® (Aspirin/Dipyridamole ER) Cost Update

The price of Aggrenox® (aspirin/dipyridamole ER) has been steadily increasing over the past few years. The graph below outlines the estimated acquisition cost (EAC) price trend for Aggrenox® since September 2009.



The most recent EAC price updated in August 2015 is $7.44 per capsule, compared to the EAC price approximately one year previously (in July 2014) of $5.89 per capsule. The current EAC of generic aspirin/dipyridamole ER, which recently became available on the market, is $5.85 per capsule.

Aggrenox® (Aspirin/Dipyridamole ER) Cost Comparison

The chart below shows a cost comparison between Aggrenox®, generic aspirin/dipyridamole ER, IR dipyridamole, and over-the-counter (OTC) aspirin.

Medication Name	Strength	Dosing Regimen	Cost/ Unit	Cost/ Month
Aggrenox® (aspirin/dipyridamole ER)	25mg/200mg	1 PO BID	$7.44*	$446.40
aspirin/dipyridamole ER	25mg/200mg	1 PO BID	$5.85*	$351.00
IR dipyridamole	50mg	4 PO BID	$0.22[+]	$52.80
OTC aspirin	81mg	1 PO Qday	$0.02[α]	$0.60

ER = extended-release IR = immediate-release OTC = over-the-counter PO = by mouth BID = Twice daily
*Cost/unit based on estimated acquisition cost (EAC).
[+]Cost/unit based on state maximum allowable cost (SMAC).
[α]Cost/unit based on average cost/tablet of generic aspirin 81mg enteric coated tablets at chain retail pharmacies.
Please note, SoonerCare members have a prescription copay of $4.00, regardless of quantity or day supply.

Utilization Details of Aggrenox® (Aspirin/Dipyridamole ER): Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AGGRENOX CAP 25-200MG	712	95*	$255,875.09	$12.27	$359.38	100.00%

*Total number of unduplicated members.

Recommendations

The College of Pharmacy recommends the prior authorization of Aggrenox® (aspirin/ER dipyridamole) 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 IR dipyridamole and OTC aspirin in place of Aggrenox® must be provided.
4. A quantity limit of 60 capsules for a 30 day supply will apply.

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[4] Teva Pharmaceutical Industries Ltd. Press Release: Teva Launches Generic Aggrenox® Capsules in the United States. Available online at: http://www.tevapharm.com/news/teva_launches_generic_aggrenox_capsules_in_the_united_states_07_15.aspx. Last revised 7/1/15. Last accessed 11/12/15.
[5] *Journal of the Neurological Sciences*: European Stroke Prevention Study 2. Dipyridamole and Acetylsalicylic Acid in the Secondary Prevention of Stroke. Available online at: http://www.sciencedirect.com/science/article/pii/S0022510X96003085. Last revised 11/1996. Last accessed 11/12/15.
[6] *The Lancet*: Aspirin Plus Dipyridamole Versus Aspirin Alone After Cerebral Ischemia of Arterial Origin (ESPRIT): Randomized Controlled Trial. Available online at: http://www.sciencedirect.com/science/article/pii/S0140673606687345. Last revised 5/2006. Last accessed 11/12/15.

Appendix S

Fiscal Year 2015 Annual Review of HFA Rescue Inhalers and 30-Day Notice to Prior Authorize ProAir® RespiClick (Albuterol Sulfate Inhalation Powder)

Oklahoma Health Care Authority
December 2015

Current Prior Authorization Criteria

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

Tier-2 HFA Rescue Inhalers Approval Criteria:

1. 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)

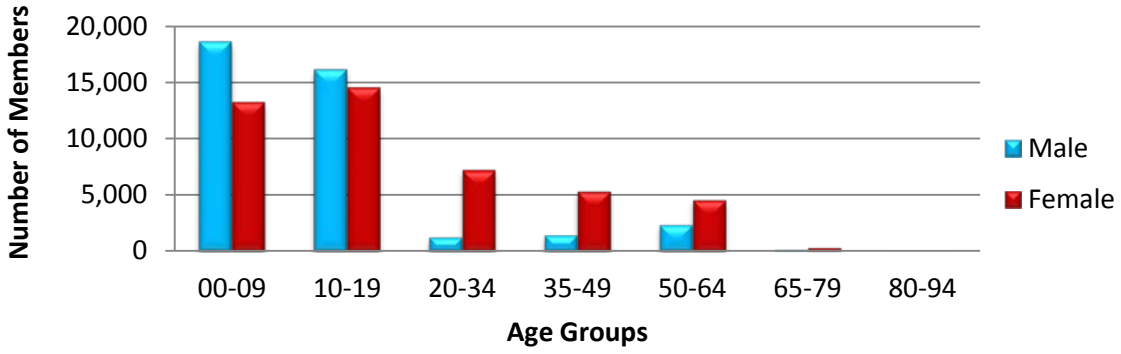
Utilization of HFA Rescue Inhalers: Fiscal Year 2015

Comparison of Fiscal Years

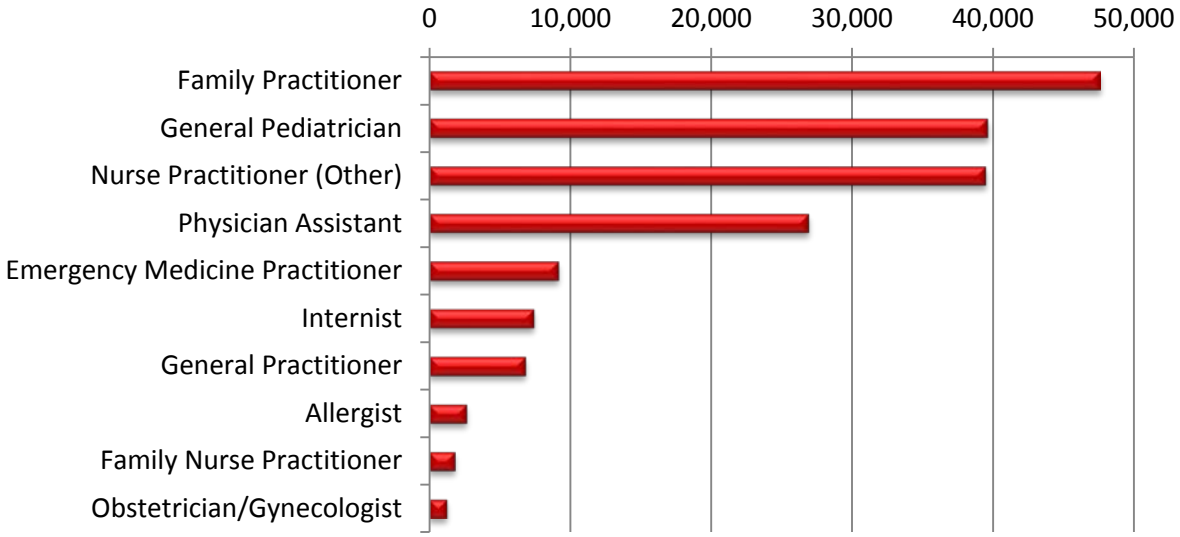
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	84,682	183,313	$11,368,967.61	$62.02	$2.52	1,830,907	4,511,344
2015	85,450	190,328	$12,487,768.92	$65.61	$2.69	1,887,607	4,649,519
% Change	**0.90%**	**3.80%**	**9.80%**	**5.80%**	**6.70%**	**3.10%**	**3.10%**
Change	**768**	**7,015**	**$1,118,801.31**	**$3.59**	**$0.17**	**56,700**	**138,175**

*Total number of unduplicated members.

Demographics of Members Utilizing HFA Rescue Inhalers



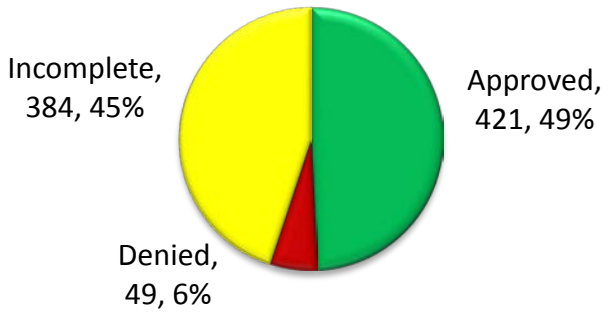
Top Prescriber Specialties of HFA Rescue Inhalers by Number of Claims



Prior Authorization of HFA Rescue Inhalers

There were 854 prior authorization requests submitted for the HFA rescue inhalers medication 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]

Patent Expirations:

- ProAir® (albuterol HFA): September 2028, however; Teva Pharmaceuticals reached a settlement with Perrigo Pharmaceutical Co. and Catalent Pharma Solutions LLC to sell limited units of Perrigo's generic version of the product beginning December 2016.
- Proventil® (albuterol HFA): December 2016
- Xopenex® (levalbuterol HFA): October 2024
- Ventolin® (albuterol HFA): August 2026

New Drug Approvals:

- ProAir® RespiClick (albuterol sulfate inhalation powder): March 31, 2015

ProAir® RespiClick (Albuterol Sulfate Inhalation Powder) Product Summary[4,5]

Indications: 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.

Dosing:

- ProAir® RespiClick is a dry powder inhaler that delivers 108mcg of albuterol sulfate (equivalent to 90mcg of albuterol base) per actuation. The inhaler is supplied for 200 inhalation doses.
- ProAir® RespiClick is for oral inhalation only.
- For the treatment or prevention of bronchospasm in adults and adolescents age 12 and older the recommended dose is two inhalations every 4 to 6 hours. In some patients, one inhalation every 4 hours may be sufficient.
- For the prevention of exercise-induced bronchospasm in adults and adolescents age 12 and over the recommended dos is two inhalations 15 to 30 minutes before exercise.
- ProAir® RespiClick does not require priming.
- ProAir® RespiClick should not be used with a spacer or volume holding chamber.
- The inhaler should be kept clean and dry at all times. Routine maintenance is not required. If the mouthpiece needs cleaning, it should be gently wiped with a dry cloth or tissue as needed. The inhaler should never be washed or put in water.
- ProAir® RespiClick should be discarded when the dose counter displays 0 or after the expiration date on the product, whichever comes first.

Mechanism of Action:

- Albuterol sulfate is a beta$_2$-adrenergic agonist. The pharmacologic effects of albuterol sulfate are attributable to activation of beta$_2$-adrenergic receptors on airway smooth muscle. Activation of beta$_2$-adrenergic receptors leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic-3',5'-adenosine monophosphate (cyclic AMP). This increase of cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Albuterol relaxes the smooth muscle of all airways, from the trachea to the terminal bronchioles. Albuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway.

Contraindications:

- Patients with hypersensitivity to albuterol.
- Patients with severe hypersensitivity to milk proteins.

Safety:

- Life-threatening paradoxical bronchospasm may occur. Discontinue ProAir® RespiClick immediately and treat with an alternative therapy.

- Need for more doses of ProAir® RespiClick than usual may be a sign of deterioration of asthma and requires reevaluation of treatment.
- ProAir® RespiClick is not a substitute for corticosteroids.
- Cardiovascular effects may occur. ProAir® RespiClick should be used with caution in patients sensitive to sympathomimetic drugs and patients with cardiovascular or convulsive disorders.
- Excessive use may be fatal. The recommended dose should not be exceeded.
- Immediate hypersensitivity reactions may occur, and ProAir® RespiClick should be discontinued immediately.
- Hypokalemia and changes in blood glucose may occur.

Adverse Reactions: The most common adverse reactions experienced during clinical trials (≥1% and greater than placebo) are back pain, pain, gastroenteritis (viral), sinus headache, and urinary tract infection.

Efficacy: The safety and efficacy of ProAir® RespiClick were based on placebo controlled trials in 354 patients with asthma or exercise induced bronchospasm (EIB).

- In two 12-week trials in patients with asthma, two inhalations of ProAir® RespiClick produced significantly greater improvement in the mean change of forced expiratory volume in 1 second (FEV_1) over the pre-treatment value compared with placebo.
- In a single trial in patients with EIB, two inhalations of ProAir® RespiClick taken 30 minutes before exercise prevented EIB for the hour following exercise in 97% of patients compared to 42% with placebo.

Cost Comparison:

Drug	Package Size	EACW[+]	Cost per package*
ProAir® RespiClick (albuterol sulfate 90 mcg/actuation)	**1 inhaler (200 metered inhalations)**	**$52.82/inhaler**	**$52.82**
ProAir® HFA (albuterol sulfate 90 mcg/actuation)	8.5 grams (200 metered inhalations)	$6.21/gram	$52.79
Proventil® HFA (albuterol sulfate 90 mcg/actuation)	6.7 grams (200 metered inhalations)	$10.21/gram	$68.41
Ventolin® HFA (albuterol sulfate 90 mcg/actuation)	18 grams (200 metered inhalations	$2.65/gram	$47.70

[+]EACW= estimated wholesaler acquisition cost

*Federal and/or supplemental rebates are not included and prices do not reflect net costs..

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. 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 and older.

Utilization Details of HFA Rescue Inhalers: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 MEDICATIONS						
PROAIR HFA AER	157,000	73,761	$9,961,519.76	$2.61	$63.45	79.77%
PROVENTIL AER HFA	32,189	14,131	$2,453,436.51	$3.06	$76.22	19.65%
TIER-1 SUBTOTAL	**189,189**	**87,892**	**$12,414,956.27**	**$2.84**	**$69.84**	**99.42%**
TIER-2 MEDICATIONS						
XOPENEX HFA AER	637	230	$44,016.66	$2.64	$69.10	0.35%
VENTOLIN HFA AER	502	70	$28,795.99	$2.43	$57.36	0.23%
TIER-2 SUBTOTAL	**1,139**	**300**	**$72,812.65**	**$2.54**	**$63.23**	**0.58%**
TOTAL	**190,328**	**85,450***	**$12,487,768.92**	**$2.69**	**$66.53**	**100%**

*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 10/2015. Last accessed 11/2015.
[2] Teva Reaches Settlement in ProAir® HFA Patent Case: October 2015. Available at: http://www.businesswire.com/news/home/20140620005338/en/Teva-Reaches-Settlement-ProAir%C2%AE-HFA-Patent-Case . Last accessed 11/2015.
[3] Original New Drug Application Approvals March 2015. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.NewOriginalNDA. Last accessed 11/2015.
[4] 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.
[5] ProAir® Respiclick New Formulation Approval. Available online at: https://www.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_ProAir%20RespiClick_2015-0402.pdf . Last accessed 11/2015.

Appendix T

Fiscal Year 2015 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)

Oklahoma Health Care Authority
December 2015

Current Prior Authorization Criteria

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)

*Combination agents that contain a Tier-1 ingredient qualify as Tier-1 agents (Advair®, Symbicort®, and Dulera®).

Long-Acting Beta$_2$ Agonists (LABA) & Long-Acting Anticholinergics (LAMA) Approval Criteria:

1. Tier-1 medications do not require prior authorization with a COPD diagnosis.
2. Tier-2 Approval Criteria:
    a. Member must be 18 years of age or older; and
    b. An FDA approved diagnosis of COPD, chronic bronchitis, or emphysema; and
    c. A four week trial of at least one LABA and a four week trial of one LAMA within the past 90 days; or
    d. A documented adverse effect, drug interaction, or contraindication to all available Tier-1 products.
    e. A clinical exception may apply for members who are unable to effectively use hand-actuated devices, such as Spiriva® Handihaler®, or who are stable on nebulized therapy.

Advair®, Symbicort®, and Dulera® Approval Criteria:

1. An FDA approved diagnosis of Chronic Obstructive Pulmonary Disease (COPD); or
2. An FDA approved diagnosis of Asthma:
    a. Medication must be indicated for member's age; and
    b. Member must have used an inhaled corticosteroid (ICS) product for at least one month immediately prior to request for authorization; and
    c. 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
    d. Clinical situation warranting initiation with combination therapy due to severity of asthma.

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

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

Anoro™ Ellipta™ (Umeclidinium/Vilanterol) 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.

Daliresp® (Roflumilast) Approval Criteria:

1. An FDA approved diagnosis of COPD with history of chronic bronchitis; and
2. Forced expiratory volume (FEV) less than or equal to 50% of predicted; and
3. Inadequately controlled symptoms on long-acting beta$_2$ agonist (LABA) therapy (must have three or more claims for a long-acting beta$_2$ agonist in the previous six months.)

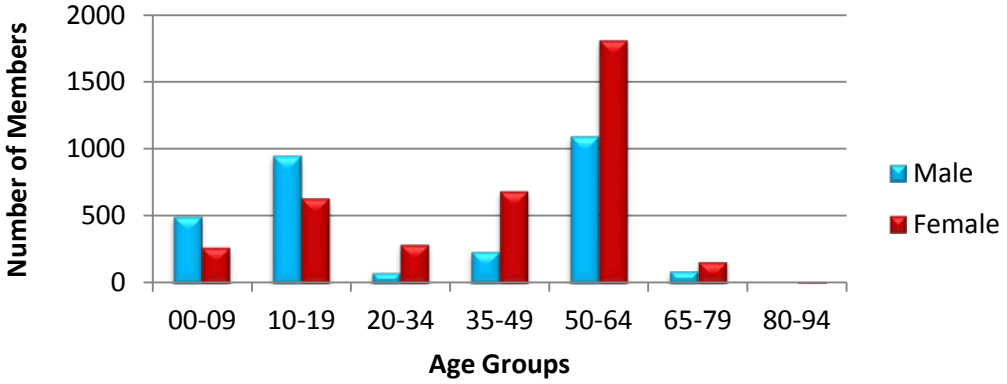
Utilization of Maintenance Asthma and COPD Medications: Fiscal Year 2015

Comparison of Fiscal Years

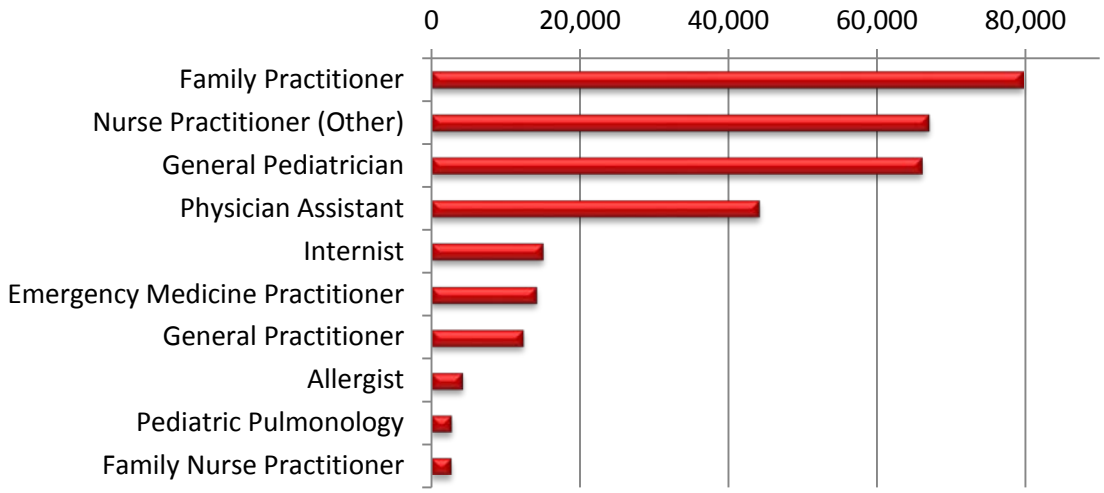
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	7,073	33,875	$9,606,676.78	$283.59	$9.30	1,269,804	1,033,325
2015	6,830	33,983	$10,215,311.94	$300.60	$9.84	1,182,997	1,038,601
% Change	**-3.40%**	**0.30%**	**6.30%**	**6.00%**	**5.80%**	**-6.80%**	**0.50%**
Change	**-243**	**108**	**$608,635.16**	**$17.01**	**$0.54**	**-86,807**	**5,276**

*Total number of unduplicated members.

Demographics of Members Utilizing Maintenance Asthma and COPD Medications



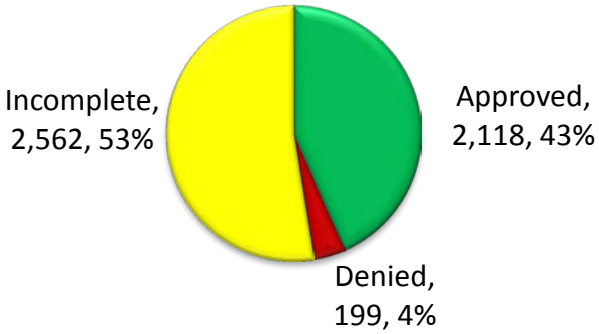
Top Prescriber Specialties of Maintenance Asthma and COPD Medications by Number of Claims



Prior Authorization of Maintenance Asthma and COPD Medications

There were 4,879 prior authorization requests submitted for the maintenance asthma and COPD medications category during fiscal year 2015. Computer edits are in place to detect Tier-1 medications in members' recent claims history and generate automated prior authorizations where possible. Computer edits are also in place to detect a COPD diagnosis in a member's recent diagnosis history and generate automated prior authorizations for Tier-1 combination long-acting beta$_2$-adrenergic agonist (LABA)/inhaled corticosteroid (ICS) products. 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:

- Advair® Diskus® (fluticasone propionate/salmeterol): August 2016
- Serevent® (salmeterol): August 2016
- Dulera® (mometasone/formoterol): May 2020
- Foradil® (formoterol aerosolized powder): November 2020
- Perforomist® (formoterol nebulizer solution): June 2021
- Brovana® (arformoterol nebulizer solution): November 2021
- Daliresp® (roflumilast oral tablet): March 2024
- Spiriva® HandiHaler® (tiotropium): March 2027
- Tudorza® (aclidinium inhalation powder): April 2027
- Arcapta® (indacaterol inhalation powder): October 2028
- Symbicort® (budesonide/formoterol): April 2029
- Spiriva® Respimat® (tiotropium soft mist inhaler): December 2029
- Striverdi® Respimat® (olodaterol inhalation spray): December 2029
- Breo® Ellipta™ (fluticasone furoate/vilanterol inhalation powder): October2030
- Anoro™ Ellipta® (umeclidinium/vilanterol inhalation powder): October 2030
- Incruse™ Ellipta® (umeclidinium inhalation powder): October 2030

New FDA Approvals:

- Arnuity™ Ellipta® (fluticasone furoate inhalation powder): August 2014
- Stiolto™ Respimat® (tiotropium bromide/olodaterol inhalation spray): May 2015
- Utibron™ Neohaler® (indacaterol/glycopyrrolate inhalation powder): October 2015
- Seebri™ Neohaler® (glycopyrrolate inhalation powder): October 2015
- Nucala® (mepolizumab injection): November 2015

New FDA Approved Indications:

- Breo® Ellipta™ (fluticasone furoate/vilanterol inhalation powder) was FDA approved for the once-daily treatment of asthma in patients aged 18 years and older on April 30, 2015.
- Spiriva® Respimat® (tiotropium soft mist inhaler) was FDA approved for long-term, once-daily, maintenance treatment of asthma in patients 12 years of age and older on September 16, 2015.

Discontinued Drugs:

- Foradil® (formoterol aerosolized powder) is being voluntarily discontinued for distribution in the United States and Puerto Rico due to a joint decision by Merk and Novartis. The joint decision was made for business reasons and was not due to the efficacy and safety profile of Foradil®. Based on current inventory levels and expected demand, it is anticipated that inventory will be exhausted and no longer distributed in or around January 2016, although inventory may be exhausted earlier.

Chronic Obstructive Pulmonary Disease (COPD) Product Summaries

Stiolto™ Respimat® (Tiotropium Bromide/Olodaterol) Product Summary[8,9]

Indications: Stiolto™ Respimat® (tiotropium bromide/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).

Important Limitations:

- Stiolto™ Respimat® is not indicated to treat acute deterioration of COPD.
- Stiolto™ Respimat® is not indicated to treat asthma.

Dosing:

- Stiolto™ Respimat® is an inhalation spray available as 4 grams (60 metered inhalations).
- Each actuation from the mouthpiece contains 3.124mcg tiotropium bromide (equivalent to 2.5mcg tiotropium), and 2.736mcg olodaterol hydrochloride (equivalent to 2.5mcg olodaterol).
- Two inhalations of Stiolto™ Respimat® once-daily at the same time of the day.
- Stiolto™ Respimat® is for oral inhalation only.
- Two actuations are equivalent to one dose.

Mechanism of Action:

- Tiotropium is a long-acting, muscarinic antagonist which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors, M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3-receptors at the smooth muscle leading to bronchodilation. The competitive and reversible nature of antagonism was shown with human and animal origin receptors and isolated organ preparations. In preclinical *in vitro* as well as *in vivo* studies, prevention of methacholine-induced bronchoconstriction effects was dose-dependent and lasted longer than 24 hours. The bronchodilation following inhalation of tiotropium is predominantly a site-specific effect.
- Olodaterol is a long-acting beta$_2$-adrenergic agonist (LABA). The compound exerts its pharmacological effects by binding and activation of beta$_2$-adrenoceptors after topical administration by inhalation. Activation of these receptors in the airways results in a stimulation of intracellular adenyl cyclase, an enzyme that mediates the synthesis of

cyclic-3', 5' adenosine monophosphate (cAMP). Elevated levels of cAMP induce bronchodilation by relaxation of airway smooth muscle cells.

Contraindications:

- All LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication. Stiolto™ Respimat® is not indicated for the treatment of asthma.
- Hypersensitivity to tiotropium, ipratropium, olodaterol, or any component of this product.

Adverse Reactions: The most common adverse reactions experienced during clinical trials with Stiolto™ Respimat® (>3% incidence and more than an active control) were nasopharyngitis, cough, and back pain.

Efficacy:

- The efficacy of Stiolto™ Respimat® was evaluated in two confirmatory active-controlled trials in 5,162 COPD patients.
- The confirmatory Trials 1 and 2 were 52-week, replicate, randomized, double-blind, active controlled, parallel group trials that compared Stiolto™ Respimat® to tiotropium 5mcg and olodaterol 5mcg monotherapies, all delivered via the Respimat® inhaler.
- In both Trials 1 and 2, Stiolto™ Respimat® demonstrated significant improvements in FEV_1 $AUC_{0\text{-}3hr}$ and trough FEV_1 after 24 weeks compared to tiotropium 5mcg or olodaterol 5mcg ($p \leq 0.0001$ for all comparisons between Stiolto™ Respimat® and the monotherapies). The increased bronchodilator effects of Stiolto™ Respimat® compared to tiotropium 5mcg or olodaterol 5mcg were maintained throughout the 52-week treatment period. Stiolto™ Respimat® displayed a mean increase in FEV_1 from baseline of 0.137 L (range: 0.133-0.140 L) within 5 minutes after the first dose. Patients treated with Stiolto™ Respimat® used less rescue medication compared to patients treated with tiotropium 5mcg or olodaterol 5mcg.

New Data:

- In August 2015, new data was published in *Respiratory Medicine* from Phase IIIb OTEMTO® 1 and 2 trials. These studies measured health-related quality of life as reported by the St. George's Respiratory Questionnaire (SGRQ). In COPD, health-related quality of life is commonly measured using SGRQ, a disease-specific patient-reported instrument that evaluates symptoms, activity limitation, and the social and emotional impact of the disease. A reduction in SGRQ score represents an improvement, while a reduction of 4 points or more compared to placebo is considered clinically meaningful. In the OTEMTO® trials, patients taking Stiolto™ Respimat® reported a reduction in SGRQ total score of 4.67 points (total score after 12 weeks of treatment in the combined data set) compared to placebo. The FDA recently accepted for review a Supplemental New Drug Application (sNDA) to include these SGRQ data in the Stiolto™ Respimat® label.

Cost:

Drug	Package Size	EAC+	Cost per Month*
Stiolto™ Respimat® (tiotropium bromide and olodaterol)	**4 grams (60 metered actuations)**	**$83.34/gram**	**$333.36**
Serevent® (salmeterol inhalation powder)	60 blisters	$4.94/blister	$296.40
Spiriva® HandiHaler® (tiotropium inhalation powder)	30 capsules	$11.11/capsule	$333.30
Anoro™ Ellipta™ (Umeclidinium/Vilanterol)	60 blisters	$5.24/blister	$314.40
Advair® Diskus 250-50 mcg (fluticasone propionate/salmeterol)	60 blisters	$5.45/blister	$327.00

+EAC= estimated acquisition cost
*Federal and/or supplemental rebates are not included and prices do not reflect net costs.

Utibron™ Neohaler® (Indacaterol/Glycopyrrolate) Product Summary[10,11]

Indications: Utibron™ Neohaler® (indacaterol/glycopyrrolate) is a combination of indacaterol, a long-acting beta$_2$-adrenergic agonist (LABA), and glycopyrrolate, an anticholinergic, indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).

Important Limitations: Utibron™ Neohaler® is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Dosing:

- Utibron™ Neohaler® is available as an inhalation powder. Each Utibron™ capsule contains 27.5mcg of indacaterol and 15.6mcg glycopyrrolate inhalation powder for use with the Neohaler® device.
- Utibron™ is for oral inhalation only. The Utibron™ capsules should not be swallowed, and should only be used with the Neohaler® device.
- The recommended dose for maintenance treatment of COPD is inhaling the powder contents of one Utibron™ capsule twice daily.

Mechanism of Action:

- Indacaterol is a long-acting beta$_2$-adrenergic agonist (LABA). Glycopyrrolate is a long-acting muscarinic antagonist, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5.

Contraindications:

- All LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication. Utibron™ Neohaler® is not indicated for the treatment of asthma.

- History of known hypersensitivity to indacaterol, glycopyrrolate, or to any of the ingredients.

Adverse Reactions: The most common adverse reactions experienced during clinical trials with Utibron™ Neohaler® (incidence ≥2% and higher than placebo) were nasopharyngitis and hypertension.

Efficacy:

- The efficacy of Utibron™ Neohaler® was evaluated in two placebo- and active-controlled confirmatory trials in 2,043 subjects with additional support from one active-controlled 12-month trial in 615 subjects with COPD.
- The confirmatory trials included two (Trial 1 and Trial 2) 12-week, randomized, double-blinded, placebo- and active-controlled, parallel-group trials in subjects with COPD designed to evaluate the efficacy and safety of Utibron™ Neohaler®; and one 12-month, randomized, double-blind, active-controlled trial (Trial 3) that evaluated bronchodilation and effects on long-term safety.
- In both Trials 1 and 2, Utibron™ Neohaler® demonstrated a larger increase in mean change from baseline in FEV_1 $AUC_{0\text{-}12h}$ compared to placebo, indacaterol 27.5mcg twice daily, and glycopyrrolate 15.6mcg twice daily.
- The St. George's Respiratory Questionnaire (SGRQ) was assessed in Trials 1 and 2. In Trial 2, the SGRQ responder rate (defined as an improvement in score of 4 or more as threshold) was 57%, 46%, 48%, and 39%, for Utibron™ Neohaler®, glycopyrrolate, indacaterol, and placebo, respectively, with odds ratios of 1.6 (95% CI 1.1, 2.3), 1.5 (95% CI 1.1, 2.2), and 2.2 (95% CI 1.5, 3.2), for Utibron™ Neohaler® vs. glycopyrrolate, Utibron™ Neohaler® vs. indacaterol, and Utibron™ Neohaler® vs. placebo, respectively. Trial 1 trends were similar to Trial 2.
- At week 52 (Trial 3), Utibron™ Neohaler® demonstrated a significant treatment effect with an increase of 0.080 L in pre-dose trough FEV_1 compared to indacaterol 75mcg once-daily.

Launch Date: Utibron™ Neohaler® is anticipated to be available in the first quarter of 2016.

Cost Comparison:

Drug	Package Size	EAC+	Cost per Month *
Utibron™ Neohaler® 27.5-15.6 mcg (indacterol/glycopyrrolate)	**60 blisters**	**$5.24/blister**	**$314.40**
Anoro™ Ellipta™ 62.5-25mcg (umeclidinium/vilanterol)	60 blisters	$5.24/blister	$314.40
Spiriva® Handihaler® 18 mcg (tiotropium)	30 blisters	$11.11/blister	$333.30
Foradil® Aerolizer® 12 mcg (formoterol)	60 blisters	$4.28/blister	$256.80
Advair® Diskus 250-50 mcg (fluticasone propionate/salmeterol)	60 blisters	$5.45/blister	$327.00

+EAC= estimated acquisition cost

*Federal and/or supplemental rebates are not included and prices do not reflect net costs.

Seebri™ Neohaler® (Glycopyrrolate) Product Summary[12,13]

Indications: Seebri™ Neohaler® (glycopyrrolate) is an anticholinergic indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).

Dosing:

- Seebri™ Neohaler® is available as an inhalation powder. Each Seebri™ capsule contains 15.6mcg glycopyrrolate inhalation powder for use with the Neohaler® device.
- Seebri™ Neohaler® is for oral inhalation only.
- Seebri™ capsules should not be swallowed, and should only be used with the Neohaler® device.
- The recommended dose for maintenance treatment of COPD is inhaling the powder contents of one Seebri™ capsule (15.6mcg) twice-daily.

Mechanism of Action:

- See glycopyrrolate mechanism of action under Utibron™ Neohaler®.

Contraindications:

- History of known hypersensitivity to glycopyrrolate, or to any of the ingredients.

Adverse Reactions: Most common adverse reactions experienced during clinical trials with Seebri™ Neohaler® (incidence greater than or equal to 2% and higher than placebo) were upper respiratory tract infection and nasopharyngitis.

Efficacy:

- The efficacy of Seebri™ Neohaler® was evaluated in two placebo-controlled confirmatory trials in 867 subjects with COPD.
- The confirmatory trials included two (Trial 1 and Trial 2) similar 12-week, randomized, double-blinded, placebo-controlled, parallel-group trials in subjects with COPD designed to evaluate the efficacy of Seebri™ Neohaler® on lung function.
- Trial 1 and Trial 2 evaluated Seebri™ Neohaler® 15.6mcg twice-daily and placebo twice-daily. The primary endpoint was the change from baseline in FEV_1 $AUC_{0\text{-}12h}$ following the morning dose at Day 85 (defined as the mean FEV_1 change from baseline over 0 to 12 hours divided by 12 hours) compared with placebo. In both trials, Seebri™ Neohaler® twice-daily demonstrated a larger increase in mean change from baseline in FEV1 $AUC_{0\text{-}12h}$ compared to placebo.
- The St. George's Respiratory Questionnaire (SGRQ) was assessed in Trials 1 and 2. In Trial 1, the SGRQ responder rate (defined as an improvement in score of 4 or more as threshold) for the Seebri™ Neohaler® treatment arm was 49% compared to 41% for placebo [Odds Ratio: 1.43, 95% CI: 0.95, 2.15]. In Trial 2, the SGRQ responder rate for the Seebri™ Neohaler® treatment arm was 55% compared to 42% for placebo [Odds Ratio: 1.78; 95% CI: 1.17, 2.71].

Launch Date: Seebri™ Neohaler® is anticipated to be available in the first quarter of 2016.

Cost Comparison:

Drug	Package Size	EAC+	Cost per Month *
Seebri™ Neohaler® 15.6 mcg (glycopyrrolate)	**60 blisters**	**$5.24/blister**	**$314.40**
Spiriva® Handihaler® 18 mcg (tiotropium)	30 blisters	$11.11/blister	$333.30

+EAC= estimated acquisition cost

*Federal and/or supplemental rebates are not included and prices do not reflect net costs.

Asthma Product Summaries

Arnuity™ Ellipta® (Fluticasone Furoate Inhalation Powder) Product Summary[14,15]

Indications: Arnuity® Ellipta® (fluticasone furoate inhalation powder) is a corticosteroid indicated for once-daily maintenance treatment of asthma as prophylactic therapy in patients aged 12 years and older.

Important Limitations: Arnuity™ Ellipta® is not indicated for relief of acute bronchospasm.

Dosing:

- Arnuity™ Ellipta® (fluticasone furoate inhalation powder) is available as an inhalation powder containing 100 or 200mcg of fluticasone furoate per actuation.
- Arnuity™ Ellipta® is for oral inhalation only.
- The recommended dose for the treatment of asthma in patients aged 12 years and older is one inhalation once daily at the same time every day.
- The starting dose is based on prior asthma therapy and disease severity.
- The usual recommended starting dose for patients not on an inhaled corticosteroid is 100mcg.
- Arnuity™ Ellipta® should not be used more than one time every 24 hours.
- The maximum recommended dose is 200mcg per day.
- The maximum benefit may not be achieved for up to 2 weeks or longer after starting treatment.

Mechanism of Action:

- Fluticasone furoate is a synthetic tri-fluorinated corticosteroid with anti-inflammatory activity. The precise mechanism of corticosteroid action on asthma is not known. Inflammation is an important component in the pathogenesis of asthma. Corticosteroids have been shown to have a wide range of actions on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) involved in inflammation. These anti-inflammatory actions of corticosteroids contribute to their efficacy in asthma.

Contraindications:

- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures**.**
- Severe hypersensitivity to milk proteins or any ingredients of Arnuity™ Ellipta®.

Safety:

- Localized Infections: *Candida albicans* infection of the mouth and throat may occur. Patients should be monitored periodically. Patients should rinse his/her mouth with water without swallowing after inhalation.
- Deterioration of Asthma and Acute Episodes: Arnuity™ Ellipta® should not be used for relief of acute symptoms. Patients require immediate re-evaluation during rapidly deteriorating asthma.
- Immunosuppression: Potential worsening of existing tuberculosis, fungal, bacterial, viral, parasitic infections or ocular herpes simplex may occur. Arnuity™ Ellipta® should be used with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.
- Transferring Patients from Systemic Corticosteroids: There is risk of impaired adrenal function when transferring from systemic corticosteroids. Patients should be weaned slowly from systemic corticosteroids if transferring to Arnuity™ Ellipta®.
- Hypercorticism and Adrenal Suppression: Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, Arnuity™ Ellipta® should be discontinued slowly.
- Paradoxical Bronchospasm: If paradoxical bronchospasm occurs Arnuity™ Ellipta® should be discontinued and alternative therapy instituted.
- Decreases in Bone Mineral Density: Patients with major risk factors for decreased bone mineral content should be monitored
- Effect on Growth: The growth of adolescent patients should be monitored.
- Glaucoma and Cataracts: Close monitoring for glaucoma and cataracts is warranted.

Adverse Reactions: The most common adverse reactions experienced during clinical trials with Arnuity™ Ellipta® (reported in greater than or equal to 5% of subjects) were upper respiratory tract infection, nasopharyngitis, headache, and bronchitis.

Efficacy:

- The safety and efficacy of Arnuity™ Ellipta® were demonstrated in clinical trials involving 3,611 asthma patients.
- The mean change in trough FEV_1 from baseline was greater with Arnuity™ Ellipta® than placebo, and Arnuity™ Ellipta® 200mcg showed trends toward greater mean changes in FEV_1 from baseline than Arnuity™ Ellipta® 100mcg.
- In a trial comparing Arnuity™ Ellipta® 200mcg once daily against fluticasone propionate 500mcg twice daily, the change from baseline in weighted mean FEV_1 was 328mL for Arnuity™ Ellipta® and 258mL for fluticasone propionate (difference of 70mL; 95% CI: -67, 208).

Cost Comparison:

Drug	Package Size	EAC+	Cost per Month *
Arnuity™ Ellipta® 100 mcg (fluticasone furoate)	**30 blisters**	**$4.86/blister**	**$145.80**
Arnuity™ Ellipta® 200 mcg (fluticasone furoate)	**30 blisters**	**$6.51/blister**	**$195.30**
Flovent® Diskus® 100 mcg (fluticasone propionate)	60 blisters	$2.64/blister	$158.40
Flovent® Diskus® 250 mcg (fluticasone propionate)	60 blisters	$3.53/blister	$211.80

+EAC= estimated acquisition cost

*Federal and/or supplemental rebates are not included and prices do not reflect net costs.

Nucala® (Mepolizumab Injection) Product Summary[16, 17]

Indications: 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.

Important Limitations:

- Nucala® is not for treatment of other eosinophilic conditions.
- Nucala® is not for relief of acute bronchospasm or status asthmaticus.

Dosing:

- Nucala® (mepolizumab injection) is available as a 100mg single-dose vial of lyophilized powder for reconstitution.
- The recommended dose of Nucala® is 100mg administered subcutaneously once every four weeks into the upper arm, thigh, or abdomen.
- Nucala® is for subcutaneous use only.
- Nucala® should be reconstituted and administered by a healthcare professional.

Mechanism of Action:

- Mepolizumab is an interleukin-5 antagonist (IgG1 kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Mepolizumab binds to IL-5 with a dissociation constant of 100 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation. Mepolizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma has not been definitively established.

Contraindications:

- History of hypersensitivity to mepolizumab or excipients in the formulation.

Safety:

- Hypersensitivity reactions (e.g., angioedema, bronchospasm, hypotension, urticaria, and rash) have occurred after administration of Nucala®. Nucala® should be discontinued in the event of a hypersensitivity reaction.
- Nucala® should not be used to treat acute bronchospasm or status asthmaticus.
- Herpes zoster infections have occurred in patients receiving Nucala®. Consideration should be given to varicella vaccination if medically appropriate prior to starting therapy with Nucala®.
- Systemic or inhaled corticosteroids should not be discontinued abruptly upon initiation of therapy with Nucala®. Corticosteroids should be decreased gradually, if appropriate.
- Patients with pre-existing helminth infections should be treated before therapy with Nucala®. If patients become infected while receiving treatment with Nucala® and do not respond to anti-helminth treatment, Nucala® should be discontinued until the parasitic infection resolves.

Adverse Reactions: The most common adverse reactions experienced during clinical trials with Nucala® (incidence greater than or equal to 5%) include headache, injection site reaction, back pain, and fatigue.

Efficacy: The efficacy of Nucala® was based on three double-blind, randomized, placebo-controlled studies involving 1,327 patients with severe asthma using currently available therapies. Nucala® was administered every four weeks in all three trials as add-on to background treatment. All subjects continued their background asthma therapy throughout the duration of the trials.

- Patients receiving Nucala® had fewer exacerbations requiring hospitalization and/or emergency department visits, and a longer time to the first exacerbation compared to patients receiving placebo.
- Compared to patients receiving placebo, patients on Nucala® experienced greater reductions in their daily maintenance oral corticosteroid dose, while maintaining asthma control.
- Of note, patients enrolled with a historical blood eosinophil count of 300 cell/mcL or greater in the past 12 months, but who had a baseline blood eosinophil count less than 150 cell/mcL, had virtually no exacerbation benefit following treatment with Nucala® compared to placebo.
- Treatment with Nucala® did not result in a significant improvement in lung function, as measured by the volume of air exhaled by patients in one second.

Cost Comparison:

Drug	Package Size	EACW+	Cost per month*
Nucala® 100mg vial (mepolizumab)	**1 single-dose vial**	**$2,640.00/vial**	**$2,640.00**
Flovent® HFA 220 mcg (fluticasone)	12 grams (120 inhalations)	$27.40/gram	$328.80
Advair® Diskus® 500-50 mcg (fluticasone/salmeterol)	60 blisters	$7.17/blister	$430.20

+EACW= estimated wholesaler acquisition cost

*Federal and/or supplemental rebates are not included and prices do not reflect net costs.

Breo® Ellipta® (Fluticasone Furoate and Vilanterol) New Indication[4,18]

Breo® Ellipta® (fluticasone furoate and vilanterol) was approved by the FDA in May 2013 for the long-term, once-daily, maintenance treatment of airflow obstruction and for reducing exacerbations in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. A sNDA for use of Breo® Ellipta® in the treatment of asthma was submitted to the FDA in June 2014 and was approved in April 2015 for the once-daily treatment of asthma in patients aged 18 years and older. The safety and efficacy of Breo® Ellipta® was evaluated in 9,969 patients with asthma, and efficacy is based primarily on the dose-ranging trial and four confirmatory trials. Patients treated with Breo® Ellipta® showed improved and/or similar lung function versus placebo and comparators and reduced exacerbations versus comparators.

Spiriva® Respimat® (Tiotropium Bromide Soft Mist Inhaler) New Indication[19, 20,21]

On September 16, 2015, the FDA approved Spiriva® Respimat® (tiotropium soft mist inhaler), an anticholinergic, for the long-term, once-daily, maintenance treatment of asthma in patients 12 years of age and older. Spiriva® Respimat® is also indicated for the long-term, once-daily, maintenance treatment of bronchospasm associated with COPD, and for reducing COPD exacerbations. The new indication for Spiriva® Respimat® is based on efficacy and safety data from a comprehensive clinical trial program involving over 3,800 patients with symptomatic asthma on at least an inhaled corticosteroid (ICS). Data from these trials showed the addition of Spiriva® Respimat® to ICS therapy significantly improved lung function and reduced exacerbations for asthma patients, compared to placebo.

Spiriva® Handihaler® (tiotropium bromide inhalation powder) is FDA approved for the long-term, once daily, maintenance treatment of bronchospasm associated with COPD and for reducing COPD exacerbations. Asthma studies using tiotropium 18mcg in the Handihaler® device in addition to an ICS have shown improved symptoms and lung function in patients with inadequately controlled asthma.

The Global Initiative for Asthma (GINA) 2015 update recommends tiotropium for patients 18 years and older with a history of exacerbations in the stepwise approach to treat asthma as another secondary option to the preferred controller choices. Tiotropium was previously described in GINA as an add-on option on the basis of clinical trial evidence but is now included in recommendations and the stepwise figure following regulatory approval.

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 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 ($\geq$ 880 mcg/day fluticasone propionate or equivalent daily dose or $\geq$ 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 3 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 for the diagnosis of asthma.

Utilization Details of Maintenance Asthma and COPD Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
COMBINATION LABA/ICS PRODUCTS						
ADVAIR DISKU AER 250/50	6,841	1,637	$2,058,125.95	$9.98	$300.85	20.15%
SYMBICORT AER 160-4.5	4,499	1,120	$1,220,495.02	$8.52	$271.28	11.95%
ADVAIR HFA AER 115/21	2,649	747	$777,576.65	$9.46	$293.54	7.61%
ADVAIR DISKU AER 500/50	2,492	553	$985,922.17	$13.14	$395.63	9.65%
ADVAIR DISKU AER 100/50	2,112	579	$513,105.65	$8.05	$242.95	5.02%
DULERA AER 200-5MCG	1,068	301	$270,287.75	$8.13	$253.08	2.65%
DULERA AER 100-5MCG	891	258	$231,150.12	$8.44	$259.43	2.26%
SYMBICORT AER 80-4.5	865	241	$201,437.84	$7.24	$232.88	1.97%
ADVAIR HFA AER 230/21	780	245	$311,587.40	$12.93	$399.47	3.05%
ADVAIR HFA AER 45/21	268	104	$63,934.92	$7.72	$238.56	0.63%
BREO ELLIPTA INH 100-25	14	5	$4,101.35	$9.11	$292.95	0.04%
SUBTOTAL	**22,479**	**5,790**	**$6,637,724.82**	**$9.34**	**$289.15**	**64.98%**
INDIVIDUAL COMPONENT LABA PRODUCTS						
TIER-1						
SEREVENT DIS AER 50MCG	409	155	$98,992.72	$7.77	$242.04	0.97%
FORADIL CAP AEROLIZE	207	61	$46,330.59	$7.56	$223.82	0.45%
SUBTOTAL	**616**	**216**	**$145,323.31**	**$7.67**	**$232.93**	**1.42%**
TIER-2						
BROVANA NEB 15MCG	97	26	$60,883.16	$19.53	$627.66	0.60%
PERFOROMIST NEB 20MCG	53	10	$30,950.28	$20.05	$583.97	0.30%
SUBTOTAL	**150**	**36**	**$91,833.44**	**$19.79**	**$605.82**	**0.90%**
INDIVIDUAL COMPONENT LAMA PRODUCTS						
TIER-1						
SPIRIVA CAP HANDIHLR	10,233	2,339	$3,199,976.22	$10.38	$312.71	31.33%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SUBTOTAL	**10,233**	**2,339**	**$3,199,976.22**	**$10.38**	**$312.71**	**31.33%**
TIER-2						
SPIRIVA SPR RESPIMAT	154	98	$49,298.67	$10.53	$320.12	0.48%
TUDORZA PRES AER	68	18	$18,989.77	$9.31	$279.26	0.19%
SUBTOTAL	**222**	**116**	**$68,288.44**	**$9.92**	**$299.69**	**0.67%**
COMBINATION LABA/LAMA PRODUCTS						
ANORO ELLIPT AER 62.5-25	14	8	$4,327.56	$6.87	$309.11	0.04%
SUBTOTAL	**14**	**8**	**$4,327.56**	**$6.87**	**$309.11**	**0.04%**
PHOSPHODIESTERASE-4 ENZYME INHIBITOR PRODUCTS						
DALIRESP TAB 500MCG	267	38	$67,093.35	$8.58	$251.29	0.66%
SUBTOTAL	**267**	**38**	**$67,093.35**	**$8.58**	**$251.29**	**0.66%**
SPECIAL PRIOR AUTHORIZATON INHALED CORTICOSTEROID PRODUCTS						
ARNUITY ELPT INH	2	1	$744.80	$12.41	$372.40	0.01%
SUBTOTAL	**2**	**1**	**$744.80**	**$12.41**	**$372.40**	**0.01%**
TOTAL	**33,983**	**6,830***	**$10,215,311.94**	**$10.27**	**$319.19**	**100%**

*Total number of unduplicated members.

Utilization Details of Tier-1 Inhaled Corticosteroids: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
INHALED CORTICOSTEROID PRODUCTS						
BUDESONIDE SUS	7,053	4,209	$2,013,121.80	$11.46	$285.43	27.35%
QVAR AER 40MCG	6,422	3,159	$894,664.01	$4.07	$139.31	12.15%
BUDESONIDE SUS	5,177	2,791	$2,025,915.82	$14.46	$391.33	27.52%
ASMANEX 30 AER 220MCG	1,716	531	$274,350.20	$5.32	$159.88	3.73%
PULMICORT INH 90MCG	1,619	809	$230,960.71	$5.07	$142.66	3.14%
ASMANEX 30 AER 110MCG	1,572	497	$237,420.74	$5.02	$151.03	3.23%
PULMICORT INH 180MCG	1,532	854	$286,269.91	$5.11	$186.86	3.89%
ASMANEX 60 AER 220MCG	1,416	479	$269,775.25	$6.10	$190.52	3.66%
PULMICORT SUS	949	543	$278,176.48	$11.63	$293.13	3.78%
ALVESCO AER 80MCG	518	209	$104,928.98	$6.18	$202.57	1.43%
PULMICORT SUS	478	198	$415,471.87	$30.66	$869.19	5.64%
AEROSPAN AER 80MCG	343	209	$54,662.18	$4.76	$159.36	0.74%
PULMICORT SUS 0.5MG/2	331	179	$131,763.18	$17.83	$398.08	1.79%
ASMANEX 120 AER	320	147	$79,514.38	$6.05	$248.48	1.08%
ALVESCO AER 160MCG	291	113	$58,690.64	$6.65	$201.69	0.80%
ASMANEX HFA AER 200	16	16	$3,242.88	$3.99	$202.68	0.04%
ASMANEX HFA AER 100	15	14	$2,379.91	$4.66	$158.66	0.03%
TOTAL	**29,768**	**13,986***	**$7,361,308.94**	**$8.40**	**$257.70**	**100.00%**

*Total number of unduplicated members.

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Appendix U

Fiscal Year 2015 Annual Review of Oral Anti-Fungals and 30-Day Notice to Prior Authorize Noxafil® (Posaconazole) and Cresemba® (Isavuconazonium Sulfate)

Oklahoma Health Care Authority
December 2015

Current Prior Authorization Criteria

Ketoconazole Oral Tablets Approval Criteria:

1. An FDA approved indication of systemic fungal infections with one of the following:
    a. Blastomycosis
    b. Coccidioidomycosis
    c. Histoplasmosis
    d. Chromomycosis
    e. Paracoccidioidomycosis; and
2. Member must be three years old or older; and
3. Member must not have underlying hepatic disease; and
4. Trials with other effective oral antifungal therapies, including fluconazole, itraconazole, and voriconazole, have failed to resolve infection; or
5. Other effective oral antifungal therapies are not tolerated or potential benefits outweigh the potential risks; and
6. Hepatic function tests must be done at baseline and weekly during treatment.
7. A clinical exception may apply for members with a diagnosis of Cushing's disease when other modalities are not available.

Lamisil® (Terbinafine Oral Granules) Approval Criteria:

1. An FDA approved indication of tinea capitis or onychomychosis; and
2. No improvement after at least three weeks of therapy with griseofulvin; and
3. Intolerance or hypersensitivity to griseofulvin or penicillin; and
4. Member is unable to swallow tablets.

Onmel® (Itraconazole Oral Tablets) Approval Criteria:

1. An FDA approved diagnosis of onychomychosis of the toenail caused by *Trichophyton rubrum* or *T. mentagrophytes*; and
2. A patient-specific, clinically significant reason why itraconazole 100mg oral capsules cannot be used in place of Onmel® 200mg tablets.

Oravig® (Miconazole Buccal Tablets) Approval Criteria:

1. An FDA approved diagnosis of oropharyngeal candidiasis in adults age 18 and older.
2. Recent trials (within the last month) of the following medications at recommended dosing and duration of therapy:
    a. Clotrimazole troches; and
    b. Nystatin suspension; and
    c. Fluconazole tablets; or
3. Contraindication(s) to all available alternative medications.

Utilization of Oral Anti-Fungals: Fiscal Year 2015

Comparison of Fiscal Years

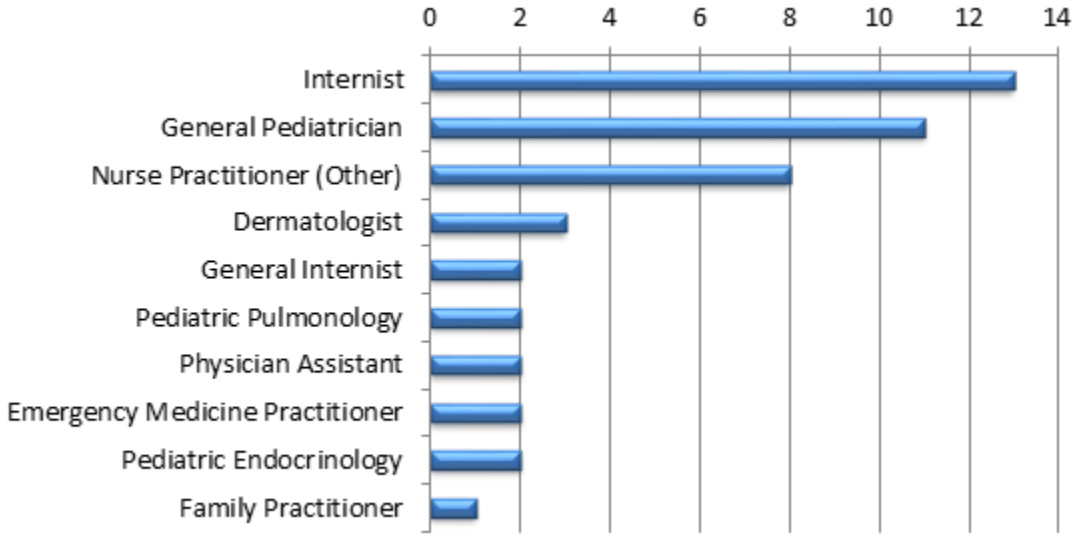
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	248	311	$68,321.09	$219.68	$10.58	9,812	6,457
2015	20	46	$117,403.24	$2,552.24	$89.83	4,105	1,307
% Change	**-91.9%**	**-85.2%**	**71.8%**	**1,061.8%**	**749.10%**	**-58.20%**	**-79.80%**
Change	**-228**	**-265**	**$49,082.15**	**$2,332.56**	**$79.25**	**-5,707**	**-5,150**

*Total number of unduplicated members.
Chart includes ketoconazole tablets, terbinafine oral granules, and posaconazole tablets and oral suspension

Demographics of Members Utilizing Oral Anti-Fungals

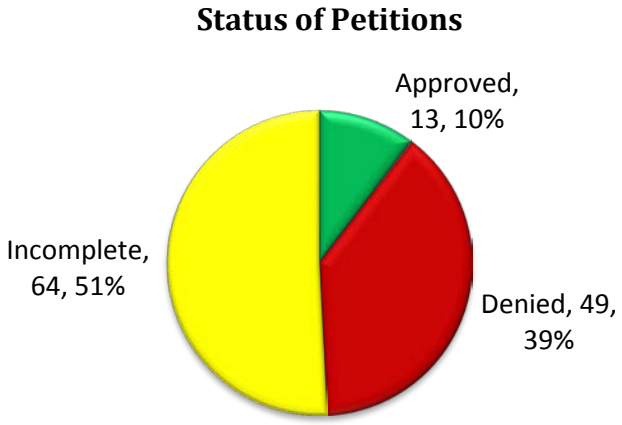
- Demographics could not be provided due to the small number of members utilizing oral anti-fungals.

Top Prescriber Specialties of Oral Anti-Fungals by Number of Claims



Prior Authorization of Oral Anti-Fungals

There were 126 prior authorization requests submitted for oral anti-fungals during fiscal year 2015. The following chart shows the status of the submitted petitions.



Market News and Updates[1, 2, 3]

Anticipated Patent Expirations:

- Noxafil® (posaconazole) delayed-release tablets: July 2019
- Cresemba® (isavuconazonium sulfate) capsules: October 2020
- Noxafil® (posaconazole) oral suspension: April 2022
- Oravig® (miconazole) buccal tablets: September 2022
- Onmel® (itraconazole) tablets: October 2028

FDA Approvals and New Indications:

- In March 2015, the FDA approved Cresemba® (isavuconazonium sulfate), an azole anti-fungal used to treat patients with invasive mucormycosis and invasive aspergillosis.

Noxafil® (Posaconazole) Product Summary[4]

FDA Approved: September 2006

Indications:

- 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.

Dosing:

- Posaconazole is available as an 18mg/mL (300mg/16.7mL) injection, 100mg delayed-release tablets, and 40mg/mL oral suspension.

Indication	Dose and Duration of Therapy
Prophylaxis of invasive *Aspergillus* and *Candida* infections in high risk patients	Injection: 300mg injection intravenously twice a day on the first day and 300mg injection intravenously once a day thereafter. Delayed-Release Tablets: 300mg (three 100mg delayed-release tablets) twice a day on the first day and 300mg once a day thereafter. Oral Suspension: 200mg (5mL) three times a day. Duration of therapy with the injection, delayed-release tablets, and oral suspension is based on recovery from neutropenia or immunosuppression.
Oropharyngeal Candidiasis (OPC)	100mg (2.5mL) twice a day on the first day and then 100mg once a day for 13 days.
OPC Refractory (rOPC) to Itraconazole and/or Fluconazole	400mg (10mL) twice a day. Duration of therapy is based on the severity of the patient's underlying disease and clinical response.

Mechanism of Action: Posaconazole is an azole anti-fungal that blocks the synthesis of ergosterol, a key component of the fungal cell membrane. Posaconazole inhibits lanosterol 14-alpha-demethylase, which converts lanosterol to ergosterol. This leads to a decrease of ergosterol and weakens the function and structure of the fungal cell membrane.

Contraindications:

- Known hypersensitivity to posaconazole or other azole anti-fungal agents
- Coadministration with the following drugs which posaconazole increases concentrations of:
  - Sirolimus
  - CYP 3A4 substrates, such as pimozide or quinidine
  - HMG-CoA reductase inhibitors (e.g. simvastatin)
  - Ergot alkaloids (e.g. ergotamine)

Warnings and Precautions:

- Calcineurin inhibitor toxicity
- Arrhythmias and QTc prolongation
- Hepatic toxicity
- Moderate or severe renal impairment (creatinine clearance <50 mL/min) with the posaconazole injection
- Prolongation of midazolam hypnotic/sedative effects

Adverse Reactions: The most common adverse reactions during clinical trials were nausea, vomiting, diarrhea, hypokalemia, fever, headache, and coughing.

Special Populations:

- Pregnancy: Posaconazole is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women and should only be used in pregnancy if the potential benefit outweighs the potential risk to the fetus.
- Nursing Mothers: It is not known if posaconazole is excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- Pediatric Use: The safety and effectiveness of posaconazole injection in pediatric patients below the age of 18 years have not been established. The safety and effectiveness of posaconazole oral suspension and delayed-release tablets have been established in pediatric patients in the age group 13 to 17 years.
- Geriatric Use: No overall differences in the pharmacokinetics and safety were observed between elderly and young subjects during clinical trials, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: Due to the variability in exposure, patients with severe renal impairment taking posaconazole oral suspension should be monitored closely for breakthrough fungal infections. Similar recommendations apply to posaconazole delayed-release tablets, but a specific study has not been conducted. Posaconazole injection should be avoided in patients with moderate or severe renal impairment (eGFR <50mL/min), unless an assessment of the benefits outweighs the risk.
- Hepatic Impairment: No dose adjustments of posaconazole oral suspension are needed in patients with mild to severe hepatic impairment. Similar recommendations apply to posaconazole delayed-release tablets and injection, but a specific study has not been conducted with either.
- Body Weight: Patients weighing greater than 120kg may have lower posaconazole plasma drug exposure. It is recommended to closely monitor for breakthrough fungal infections.

Efficacy:

- The efficacy of posaconazole in the prophylaxis of *Aspergillus* and *Candida* infections in high risk patients due to severely compromised immune systems was evaluated in two randomized, controlled studies. The first study (Oral Suspension Study 1) was a randomized, double-blind trial that compared posaconazole oral suspension (200mg three times a day) with fluconazole capsules (400mg once daily) as prophylaxis against invasive fungal infections (IFIs) in allogeneic hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD). Efficacy was evaluated using a composite endpoint of proven/probable IFIs, death, or treatment with systemic antifungal therapy. The mean duration of therapy was comparable between the two groups (80 days, posaconazole; 77 days, fluconazole). The clinical failure rate of posaconazole (33%) was similar to fluconazole (37%), (95% CI for the difference posaconazole-comparator -11.5% to 3.7%). All-cause mortality was similar at 16 weeks for both groups (19%, posaconazole; 20%, fluconazole). The second study (Oral

Suspension Study 2) was a randomized, open-label study that compared posaconazole oral suspension (200mg three times a day) with fluconazole suspension (400mg once daily) or itraconazole oral solution (200mg twice a day) as prophylaxis against IFIs in neutropenic patients who were receiving cytotoxic chemotherapy for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). Efficacy of prophylaxis was evaluated using a composite endpoint of proven/probable IFIs, death, or treatment with systemic antifungal therapy. The mean duration of therapy was comparable between the treatment groups (29 days, posaconazole; 25 days, fluconazole or itraconazole). The clinical failure was lower for patients in the posaconazole group (27%) compared to the fluconazole/itraconazole group (42%), (95% CI for the difference posaconazole-comparator -22.9% to 7.8%). All-cause mortality was lower at 100 days for patients treated with posaconazole (14% versus 21%, fluconazole/itraconazole).

- Posaconazole Oral Suspension Study 3 was a randomized, controlled, evaluator-blinded study in HIV-infected patients with oropharyngeal candidiasis (OPC). Patients were treated with posaconazole or fluconazole oral suspension (100mg twice a day for 1 day, then 100mg once a day for 13 days). The majority of participants had *C. albicans* as the baseline pathogen. Clinical success at Day 14 (complete or partial resolution of all ulcers and/or plaques and symptoms) was similar between the two groups (91.7%, posaconazole; 92.5% fluconazole). The clinical relapse rates (recurrence of signs or symptoms after initial cure or improvement) 4 weeks after the end of treatment were also similar between the groups (29.0%, posaconazole; 35.1%, fluconazole). Mycologic eradication rates (absence of colony forming units in quantitative culture at the end of therapy, Day 14) were 52.1% in the posaconazole group and 50.0% in the fluconazole group. Mycologic relapse rates (4 weeks after the end of treatment) were similar as well (55.6%, posaconazole; 63.7% fluconazole).
- Posaconazole Oral Suspension Study 4 was a noncomparative study of posaconazole in HIV-infected patients with OPC that was refractory to treatment with fluconazole or itraconazole. Refractory OPC was considered as failure to improve or worsening of OPC after treatment with fluconazole greater than or equal to 100mg/day for at least 10 consecutive days or itraconazole 200mg/day for at least 10 consecutive days and treatment with either fluconazole or itraconazole had not been discontinued for more than 14 days prior to treatment with posaconazole. Out of the 199 subjects that enrolled in the study, 89 met the criteria for refractory infection. The efficacy of posaconazole was assessed by the clinical success (cure or improvement) rate after 4 weeks of treatment. The clinical success rate was 74.2%.

Utilization: In Fiscal Year 2015, there were 29 claims for posaconazole.

Cost Comparison:

Medication Name	Cost Per Unit	Cost Per Package	Cost Per 30 Days
Noxafil® (posaconazole) oral suspension 40mg/mL	**$12.25[+]**	**$1,286.25**	**$6,431.25**
Diflucan® (fluconazole) oral suspension 40mg/mL	$0.76*	$26.60	$266.60
Noxafil® (posaconazole) 100mg tablet	**$61.26[+]**	**-------**	**$5,697.18**
Diflucan® (fluconazole) 200mg tablet	$2.14*	-------	$128.40
Noxafil® (posaconazole) injection 300mg/16.7mL	**$33.54[+]**	**$560.12**	**$17,363.72**

[+]EAC= estimated acquisition cost
*State Maximum Allowable Cost (SMAC)
Dosing regimen based on prophylaxis of invasive *Aspergillus* and *Candida* infections

Cresemba® (Isavuconazonium Sulfate) Product Summary[5]

FDA Approved: March 2015

Indications:

- Invasive aspergillosis
- Invasive mucormycosis

Dosing:

- Cresemba® (isavuconazonium) is available as capsules containing 186mg of isavuconazonium sulfate (equivalent to 100mg of isavuconazole) and as a single-dose vial for injection containing 372mg of isavuconazonium sulfate (equivalent to 200mg of isavuconazole). The injection must be administered through an in-line filter over a minimum of one hour.

Dosage Formulation	Loading Dose	Maintenance Dose
Capsules	2 capsules (372mg) q 8 hours for 6 doses (48 hours)	2 capsules (372mg) once daily
Injection	1 reconstituted vial (372mg) intravenously q 8 hours for 6 doses (48 hours)	1 reconstituted vial (372mg) intravenously once daily

Mechanism of Action: Isavuconazonium sulfate is the prodrug of isavuconazole. Isavuconazole is an azole anti-fungal that blocks the synthesis of ergosterol, a key component of the fungal cell membrane. Isavuconazole inhibits lanosterol 14-alpha-demethylase, which converts lanosterol to ergosterol. This leads to a decrease of ergosterol and weakens the function and structure of the fungal cell membrane.

Contraindications:

- Known hypersensitivity to isavuconazonium or other azole anti-fungal agents
- Use in patients with familial short QT syndrome
- Coadministration with strong CYP 3A4 inducers, such as:
  - Rifampin
  - St. John's wort

- Carbamazepine
- Long acting barbiturates (e.g. phenobarbital, mephobarbital)

Warnings and Precautions:

- Hepatic adverse drug reactions
- Infusion-related reactions
- Hypersensitivity reactions
- Embryo-fetal toxicity
- Drug interactions
- Drug particulates

Adverse Reactions: The most common adverse reactions during clinical trials were nausea, vomiting, diarrhea, constipation, elevated liver chemistry tests, cough, peripheral edema, hypokalemia, back pain, and dyspnea.

Special Populations:

- Pregnancy: Isavuconazonium sulfate is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women and should only be used in pregnancy if the potential benefit outweighs the potential risk to the fetus.
- Nursing Mothers: Mothers should not breast feed while taking isavuconazonium sulfate.
- Pediatric Use: The safety and effectiveness of isavuconazonium sulfate in pediatric patients below the age of 18 years have not been established.
- Geriatric Use: The pharmacokinetics of isavuconazole are comparable in young and elderly subjects (65 years of age and older). No dose adjustment is needed in elderly patients.
- Renal Impairment: No dose adjustment is needed in patients with mild, moderate, or severe renal impairment, including those patients with End Stage Renal Disease (ESRD).
- Hepatic Impairment: No dose adjustment is needed in patients with mild or moderate hepatic impairment. Isavuconazonium sulfate has not been studied in patients with severe hepatic impairment and should only be used in these patients if the benefits outweigh the risks.

Efficacy: The safety and efficacy of isavuconazonium sulfate was evaluated in the treatment of invasive aspergillosis and mucormycosis was evaluated in two trials.

- Trial 1 was a randomized, double-blind, non-inferiority active controlled trial that compared isavuconazonium sulfate versus voriconazole in the treatment of invasive fungal disease caused by *Aspergillus* species or other filamentous fungi. Patients were eligible if they had probable, possible, or proven IFIs according to the criteria of the European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG). The majority of patients were Caucasians (78%), male (60%), with fungal disease involving the lungs (95%). The mean age of patients was 51 years and the range was 17 years to 87 years. The protocol-defined maximum treatment duration was 84 days. The mean treatment duration was 47 days for both treatment groups, of which 8 to 9 days was by an intravenous route of administration. All-cause mortality through Day 42 in the overall population was 18.6% in the isavuconazonium sulfate treatment

group and 20.2% in the voriconazole treatment group for an adjusted difference of -1.0% with 95% confidence interval of -8.0% to 5.9%. Similar results were seen in patients with proven or probable invasive aspergillosis confirmed by histology, culture, or serology (18.6% all-cause mortality in isavuconazonium sulfate group versus 22.2% in the voriconazole group; adjusted difference of -2.7% with 95% confidence interval -13.6% to 8.2%). In the patients with proven or probable invasive aspergillosis confirmed by histology, culture, or serology, overall success at End-of-Treatment (EOT) was seen in 35% of patients treated with isavuconazonium sulfate versus 38.9% of patients treated with voriconazole. The adjusted treatment difference was -4.0% with 95% confidence interval of -16.3% to 8.4%.

- Trial 2 was an open-label non-comparative trial that evaluated the treatment of isavuconazonium sulfate in patients with invasive mucormycosis. According to criteria from the EORTC/MSG, 37 patients had proven or probable mucormycosis. The mean age was 49 years with a range from 22 years to 79 years. The patients were mainly white (68%), male (81%), and 59% of patients had pulmonary disease involvement, half of whom also had other organ involvement. The most common non-pulmonary disease locations were bone (14%), CNS (16%), eye (19%), and sinus (43%). The median treatment duration was 85 days for patients classified as intolerant, 33 days for refractory, and 102 days for primary. The total all-cause mortality through Day 42 was 38% and the total overall response success rate at End-of-Treatment was 31%.

Utilization: There has been no utilization of isavuconazonium sulfate since it was approved by the FDA in March 2015.

Cost Comparison:

Medication Name	Cost Per Unit	Cost Per 30 Days
Cresemba® (isavuconazonium sulfate) 186mg capsule	**$73.92[+]**	**$4,730.88**
Vfend® (voriconazole) 200mg tablet	$20.93*	$1,255.80
Cresemba® (isavuconazonium sulfate) injection 372mg/mL	**$251.86[+]**	**$8,815.10**

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

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

b. Treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole

2. 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.

Utilization Details of Oral Anti-Fungals: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
KETOCONAZOLE ORAL TABLETS						
KETOCONAZOLE TAB 200MG	6	3	$82.40	$0.56	2.00	$13.73
SUBTOTAL	**6**	**3**	**$82.40**	**$0.56**	**2.00**	**$13.73**
LAMISIL GRANULES						
LAMISIL GRA 125MG	8	7	$4,288.70	$16.31	1.14	$536.09
LAMISIL GRA 187.5MG	3	2	$1,881.42	$19.20	1.50	$627.14
SUBTOTAL	**11**	**9**	**$6,170.12**	**$17.09**	**1.22**	**$560.92**
POSACONAZOLE PRODUCTS						
NOXAFIL TAB 100MG	17	6	$96,267.20	$197.27	2.83	$5,662.78
NOXAFIL SUS 40MG/ML	12	3	$14,883.52	$48.01	4.00	$1,240.29
SUBTOTAL	**29**	**9**	**$111,150.72**	**$139.29**	**3.63**	**$3,832.78**
TOTAL	**46**	**20***	**$117,403.24**	**$89.83**	**2.30**	**$2,552.24**

*Total number of unduplicated members.

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[1]FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 11/5/15. Last accessed 11/9/15.

[2]FDA News Release: FDA approves new antifungal drug Cresemba. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm437106.htm. Last revised 3/9/15. Last accessed 11/9/15.

[3]Medscape Medical News: FDA approves new antifungal Cresemba. Available online at: http://www.medscape.com/viewarticle/841050. Last revised 3/6/15. Last accessed 11/9/15.

[4]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.

[5]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 V

Fiscal Year 2015 Annual Review of Fibromyalgia Medications

Oklahoma Health Care Authority
December 2015

Current Prior Authorization Criteria

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

*Tier-2 includes 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.
4. Clinical exceptions include:
    a. Diagnosis of seizures, diabetic neuropathy, or postherpetic neuralgia for Lyrica® (pregabalin)

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.

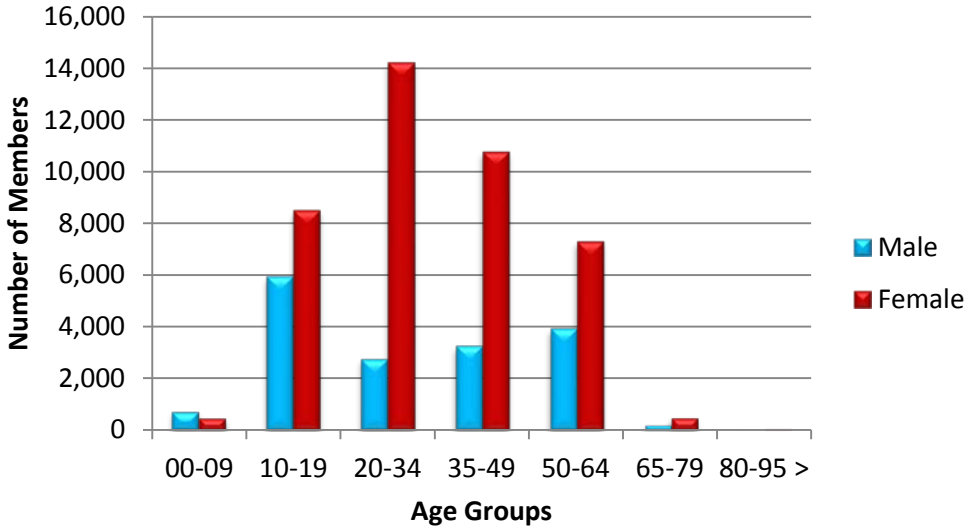
Utilization of Fibromyalgia Medications: Fiscal Year 2015

Comparison of Fiscal Years

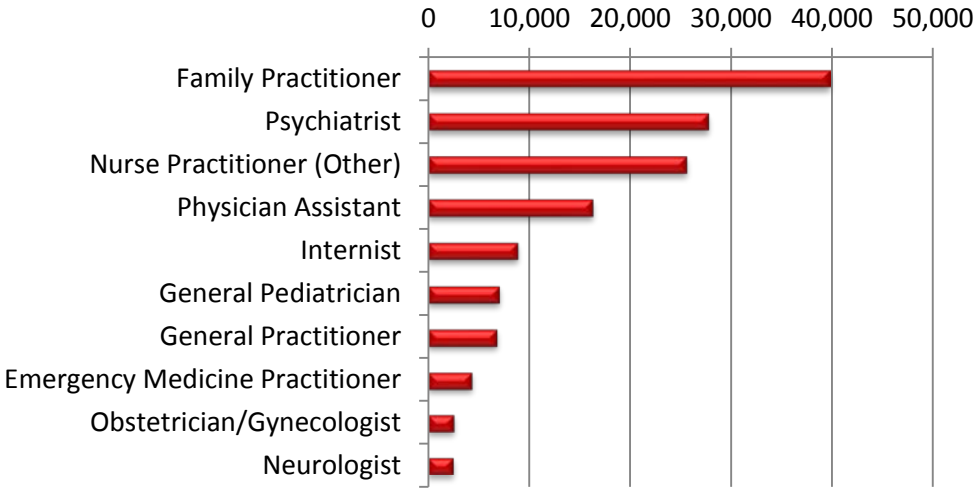
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	60,934	222,821	$9,298,559.02	$41.73	$1.58	12,030,470	5,875,379
2015	58,725	223,848	$7,244,111.07	$32.36	$1.20	12,058,249	6,012,959
% Change	**-3.60%**	**0.50%**	**-22.10%**	**-22.50%**	**-24.10%**	**0.20%**	**2.30%**
Change	**-2,209**	**1,027**	**-$2,054,447.95**	**-$9.37**	**-$0.38**	**27,779**	**137,580**

*Total number of unduplicated members.

Demographics of Members Utilizing Fibromyalgia Medications



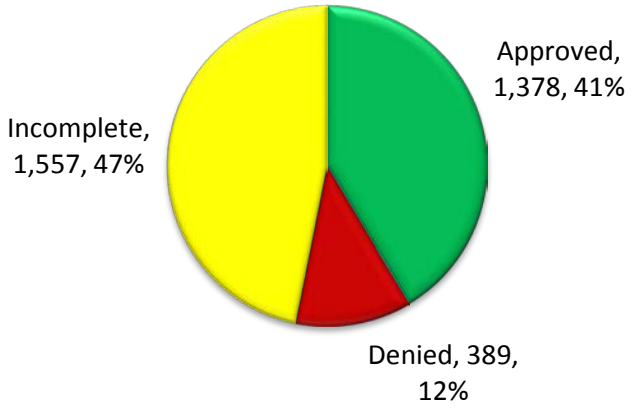
Top Prescriber Specialties of Fibromyalgia Medications by Number of Claims



Prior Authorization of Fibromyalgia Medications

There were 3,324 prior authorization requests submitted for fibromyalgia medications during fiscal year 2015. Computer edits are in place to detect Tier-1 medications in members' 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]

Anticipated Patent Expirations:

- Lyrica® (pregabalin): December 2018
- Savella® (milnacipran): September 2029

Medications in the Pipeline:

- **Mirogabalin:** In February 2015, Daiichi Sankyo Company announced enrollment of patients in three large-scale, multi-national Phase 3 programs. The programs are evaluating the safety and efficacy of an investigational drug, mirogabalin, in the treatment of diabetic peripheral neuropathic pain, pain associated with postherpetic neuralgia, and pain associated with fibromyalgia. Mirogabalin selectively binds to alpha-2 delta ligand, which is a protein that may help regulate how pain signals are processed by the brain. It has a long duration of action and is the first preferentially selective alpha-2 delta ligand.
- **TNX-102 SL:** In May 2015, Tonix Pharmaceuticals announced the start of a Phase 3 clinical study of cyclobenzaprine HCl sublingual tablets, 2.8mg (TNX-102 SL). The study is evaluating the safety and efficacy of TNX-102 SL, when taken daily at bedtime, in improving pain and sleep quality in patients with fibromyalgia.

Recommendations

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 or a patient-specific, clinically significant reason why duloxetine 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.

Utilization Details of Fibromyalgia Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
TIER-1 UTILIZATION						
AMITRIPTYLINE PRODUCTS						
AMITRIPTYLIN TAB 10MG	3,927	1,497	$31,140.98	$0.25	2.62	$7.93
AMITRIPTYLIN TAB 25MG	7,832	2,818	$98,548.08	$0.38	2.78	$12.58
AMITRIPTYLIN TAB 50MG	5,259	1,710	$101,672.76	$0.56	3.08	$19.33
AMITRIPTYLIN TAB 75MG	1,238	344	$31,125.68	$0.70	3.60	$25.14
AMITRIPTYLIN TAB 100MG	2,977	750	$107,862.53	$1.02	3.97	$36.23
AMITRIPTYLIN TAB 150MG	1,145	271	$64,631.44	$1.57	4.23	$56.45
SUBTOTAL	**22,378**	**7,390**	**$434,981.47**	**$0.58**	**3.03**	**$19.44**
CYCLOBENZAPRINE PRODUCTS						
CYCLOBENZAPR TAB 5MG	7,073	4,677	$40,599.24	$0.31	1.51	$5.74
CYCLOBENZAPR TAB 10MG	42,770	18,905	$225,503.74	$0.23	2.26	$5.27
SUBTOTAL	**49,843**	**23,582**	**$266,102.98**	**$0.24**	**3.00**	**$5.34**
DULOXETINE PRODUCTS						
CYMBALTA CAP 20MG	3	2	$125.91	$1.40	1.50	$41.97
CYMBALTA CAP 30MG	62	30	$9,240.65	$4.37	2.07	$149.04
CYMBALTA CAP 60MG	159	45	$26,059.82	$5.29	3.53	$163.90
DULOXETINE CAP 20MG	623	243	$40,961.50	$2.15	2.56	$65.75
DULOXETINE CAP 30MG	5,140	1,890	$365,048.68	$2.20	2.72	$71.02
DULOXETINE CAP 60MG	12,982	3,064	$920,152.50	$2.00	4.24	$70.88
SUBTOTAL	**18,969**	**5,274**	**$1,361,589.06**	**$2.09**	**3.60**	**$71.78**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 10MG	11,533	3,948	$65,112.54	$0.18	2.92	$5.65
FLUOXETINE CAP 20MG	30,529	9,218	$158,927.88	$0.16	3.31	$5.21
FLUOXETINE CAP 40MG	13,893	3,675	$134,150.52	$0.28	3.78	$9.66
FLUOXETINE SOL 20MG/5ML	1,150	272	$9,161.55	$0.27	4.23	$7.97
FLUOXETINE TAB 10MG	3,333	1,194	$50,672.84	$0.50	2.79	$15.20
FLUOXETINE TAB 20MG	1,459	598	$62,568.16	$1.39	2.44	$42.88
FLUOXETINE TAB 60MG	34	4	$4,769.93	$4.68	8.50	$140.29
PROZAC CAP 20MG	38	13	$15,687.24	$13.88	2.92	$412.82
PROZAC CAP 40MG	6	1	$7,412.66	$17.65	6.00	$1,235.44
SUBTOTAL	**61,975**	**18,923**	**$508,463.32**	**$0.25**	**3.28**	**$8.20**
TRAMADOL PRODUCTS						
TRAMADOL HCL TAB 50MG	57,259	22,355	$318,430.63	$0.29	2.56	$5.56
ULTRAM TAB 50MG	6	1	$245.85	$5.34	6.00	$40.98
SUBTOTAL	**57,265**	**22,356**	**$318,676.48**	**$0.29**	**2.56**	**$5.56**
TIER-1 SUBTOTAL	**210,430**	**57,835***	**$2,889,813.31**	**$0.51**	**3.64**	**$13.73**
TIER-2 UTILIZATION						
PREGABALIN PRODUCTS						
LYRICA CAP 25MG	122	51	$34,336.92	$9.36	2.39	$281.45
LYRICA CAP 50MG	1,393	409	$471,920.12	$11.75	3.41	$338.78
LYRICA CAP 75MG	2,868	751	$892,437.60	$10.57	3.82	$311.17
LYRICA CAP 100MG	2,414	544	$862,942.94	$12.12	4.44	$357.47
LYRICA CAP 150MG	3,882	701	$1,288,587.80	$11.26	5.54	$331.94
LYRICA CAP 200MG	852	153	$248,158.83	$9.94	5.57	$291.27
LYRICA CAP 225MG	380	68	$121,673.15	$10.73	5.59	$320.19
LYRICA CAP 300MG	1,206	179	$370,864.24	$10.28	6.74	$307.52

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
LYRICA SOL 20MG/ML	1	1	$584.24	$38.95	1.00	$584.24
SUBTOTAL	**13,118**	**2,857**	**$4,291,505.84**	**$11.11**	**4.59**	**$327.15**
TIER-2 SUBTOTAL	**13,118**	**2,857**	**$4,291,505.84**	**$11.11**	**4.59**	**$327.15**
TIER-3 UTILIZATION						
MILNACIPRAN PRODUCTS						
SAVELLA MIS TITR PAK	8	7	$1,662.51	$7.29	1.14	$207.81
SAVELLA TAB 12.5MG	2	1	$237.94	$7.93	2.00	$118.97
SAVELLA TAB 25MG	2	2	$417.95	$6.97	1.00	$208.98
SAVELLA TAB 50MG	143	27	$29,778.02	$7.04	5.30	$208.24
SAVELLA TAB 100MG	145	20	$30,695.50	$7.06	7.25	$211.69
SUBTOTAL	**300**	**57**	**$62,791.92**	**$7.06**	**5.26**	**$209.31**
TIER-3 SUBTOTAL	**300**	**57**	**$62,791.92**	**$7.06**	**5.26**	**$209.31**
TOTAL	**223,848**	**58,725***	**$7,244,111.07**	**$1.20**	**3.81**	**$32.36**

*Total number of unduplicated members.

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[1]FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 11/5/15. Last accessed 11/6/15.

[2]Daiichi Sankyo Press Release: Daiichi Sankyo announces first patients in large-scale, multi-national phase 3 clinical programs for mirogabalin. Available online at: http://www.daiichisankyo.com/media_investors/media_relations/press_releases/detail/006245.html Last revised 2/4/2015. Last accessed 11/9/15.

[3]Tonix Pharmaceuticals Press Release: Tonix Pharmaceuticals launches phase 3 clinical study of TNX-102 SL in fibromyalgia. Available online at: http://www.tonixpharma.com/news-events/press-releases/detail/976/tonix-pharmaceuticals-launches-phase-3-clinical-study-of. Last revised 5/13/2015. Last accessed 11/9/15.

Appendix W

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

FDA NEWS RELEASE

For Immediate Release: November 10th, 2015

FDA approves Cotellic as part of combination treatment for advanced melanoma

The U.S. Food and Drug Administration approved Cotellic (cobimetinib) to be used in combination with vemurafenib to treat advanced melanoma that has spread to other parts of the body or can't be removed by surgery, and that has a certain type of abnormal gene (BRAF V600E or V600K mutation).

Melanoma is the most aggressive and dangerous form of skin cancer in the United States. It forms in the skin cells that develop the skin's pigment and if not diagnosed early, the cancer is likely to spread to other parts of the body. The National Cancer Institute estimates that 73,870 Americans will be diagnosed with melanoma and 9,940 will die from the disease this year.

Cotellic works by blocking the activity of an enzyme known as MEK, which is part of a larger signaling pathway. Abnormal activity of signaling pathways can lead to cancer. Cotellic prevents or slows cancer cell growth. Vemurafenib, marketed in the U.S. as Zelboraf, is a BRAF inhibitor that affects a different part of the same pathway and was approved in 2011 to treat patients with melanoma that has spread to other parts of the body or cannot be removed by surgery, whose tumors express a gene mutation called BRAF V600E, as detected by an FDA approved test. Health care providers should confirm the presence of BRAF V600 E or V600K mutation in their patients' tumor specimens using one of the available FDA approved tests prior to starting treatment with Cotellic in combination with vemurafenib.

The safety and efficacy of Cotellic taken in combination with vemurafenib were demonstrated in a randomized clinical study of 495 patients with previously untreated, BRAF V600 mutation-positive melanoma that is advanced or cannot be removed by surgery. All study participants received vemurafenib and were then randomly selected to also take either Cotellic or a placebo. On average, patients taking Cotellic plus vemurafenib experienced a delay in the amount of time it took for their disease to worsen (approximately 12.3 months after starting treatment) compared to approximately 7.2 months after starting treatment for those taking vemurafenib only. In addition, patients taking Cotellic plus vemurafenib lived longer, with approximately 65 percent of patients alive 17 months after starting treatment as compared to half of those taking vemurafenib only. Additionally, 70 percent of those taking Cotellic plus vemurafenib experienced complete or partial shrinkage of their tumors, compared to 50 percent among those taking vemurafenib plus placebo.

The most common side effects of treatment with Cotellic in combination with vemurafenib are diarrhea, sensitivity to ultraviolet (UV) light (photosensitivity reaction), nausea, fever (pyrexia) and vomiting.

Cotellic may cause severe side effects including damage to the heart muscle (cardiomyopathy) or to other muscles (rhabdomyolysis), new skin tumors (primary cutaneous malignancies), eye disease (retinal detachment), severe skin rash, liver damage (hepatotoxicity), hemorrhage and severe skin rash due to increased sensitivity to sunlight (photosensitivity). People taking Cotellic should avoid sun exposure, wear protective clothing, and a broad spectrum ultraviolet A/ultraviolet B sunscreen to protect against sunburn. Women taking Cotellic should use effective contraception, as the medication can cause harm to a developing fetus.

Cotellic was reviewed under the FDA's priority review program that provides for an expedited six-month review of drugs that, at the time the application was submitted, have the potential to be a significant improvement in safety or effectiveness in the treatment of a serious condition. Cotellic also received orphan drug designation, which provides incentives such as tax credits, user fee waivers and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.

Cotellic and Zelboraf are both marketed by Genentech of San Francisco, California.

FDA NEWS RELEASE

For Immediate Release: November 13th, 2015

FDA approves new pill to treat certain patients with non-small cell lung cancer

The U.S. Food and Drug Administration granted accelerated approval for an oral medication to treat patients with advanced non-small cell lung cancer (NSCLC). Tagrisso (osimertinib) is now approved for patients whose tumors have a specific epidermal growth factor receptor (EGFR) mutation (T790M) and whose disease has gotten worse after treatment with other EGFR-blocking therapy.

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. The most common type of lung cancer, NSCLC occurs when cancer cells form in the tissues of the lung. EGFR is a protein involved in the growth and spread of cancer cells.

Today, the FDA also approved the first companion diagnostic test (cobas EGFR Mutation Test v2) to detect the type of EGFR resistance mutation that Tagrisso is known to target. The newly approved version (v2) of the test adds the T790M mutation to the clinically relevant mutations detected by the original cobas EGFR Mutation Test (v1).

The safety and efficacy of Tagrisso were demonstrated in two multicenter, single-arm studies involving a total of 411 patients with advanced EGFR T790M mutation-positive NSCLC whose disease worsened after treatment with an EGFR-blocking medication. In these two studies, 57 percent of patients in the first study and 61 percent of patients in the second study experienced a complete or partial reduction in their tumor size (known as objective response rate).

Continued approval for this indication may be contingent upon further confirmatory studies.

The most common side effects of Tagrisso are diarrhea, skin and nail conditions such as dry skin, rash and infection or redness around the fingernails. Tagrisso may cause serious side effects, including inflammation of the lungs and injury to the heart. It also may cause harm to a developing fetus.

The FDA granted Astra Zeneca breakthrough therapy designation, priority review and orphan drug designation for Tagrisso. Breakthrough therapy designation is granted for a drug that is intended to treat a serious condition when, at the time an application is submitted, preliminary clinical evidence indicates that a drug may demonstrate substantial improvement over available therapies. Priority review designation is granted to drug applications that show a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan drug designation provides incentives such as tax credits, user fee waivers, and eligibility for market exclusivity to assist and encourage the development of drugs for rare diseases.

Tagrisso was approved under the agency's accelerated approval program, which allows the approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials.

Tagrisso is marketed by Astra Zeneca Pharmaceuticals based in Wilmington, Delaware. The cobas EGFR Mutation Test v2 is marketed by Roche Molecular Systems of Pleasanton, California.

FDA NEWS RELEASE

For Immediate Release: November 16th, 2015

FDA approves Darzalex for patients with previously treated multiple myeloma

The U.S. Food and Drug Administration granted accelerated approval for Darzalex (daratumumab) to treat patients with multiple myeloma who have received at least three prior treatments. Darzalex is the first monoclonal antibody approved for treating multiple myeloma.

Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells (a type of white blood cell) found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems. The National Cancer Institute estimates there will be 26,850 new cases of multiple myeloma and 11,240 related deaths in the United States this year.

Darzalex injection, given as an infusion, is a monoclonal antibody that works by helping certain cells in the immune system attack cancer cells.

The safety and efficacy of Darzalex were demonstrated in two open-label studies. In one study of 106 participants receiving Darzalex, 29 percent of patients experienced a complete or partial reduction in their tumor burden, which lasted for an average of 7.4 months. In the second study of 42 participants receiving Darzalex, 36 percent had a complete or partial reduction in their tumor burden.

The most common side effects of Darzalex were infusion-related reactions, fatigue, nausea, back pain, fever and cough. Darzalex may also result in low counts of infection-fighting white blood cells (lymphopenia, neutropenia, and leukopenia) or red blood cells (anemia) and low levels of blood platelets (thrombocytopenia).

Blood banks should be informed that patients are receiving Darzalex because the drug may interfere with certain tests that are done by blood banks (such as antibody screening) for patients who need a blood transfusion. Women who are pregnant should not use Darzalex, and women planning to become pregnant should use effective contraceptives during and for at least three months after treatment.

The FDA granted breakthrough designation for this application based on preliminary clinical evidence suggesting that if approved, Darzalex may offer a substantial improvement over available therapies. Darzalex also received priority review and orphan drug designations. Priority review status is granted to applications for drugs that, if approved, would be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan drug designation provides incentives such as tax credits, user fee waivers and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.

Darzalex was approved under the agency's accelerated approval program, which allows the approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials.

Darzalex is marketed by Janssen Biotech of Horsham, Pennsylvania.

FDA NEWS RELEASE

For Immediate Release: November 18th, 2015

FDA moves quickly to approve easy-to-use nasal spray to treat opioid overdose

Naloxone in nasal spray form provides important new alternative for family members, first responders

The U.S. Food and Drug Administration approved Narcan nasal spray, the first FDA-approved nasal spray version of naloxone hydrochloride, a life-saving medication that can stop or reverse the effects of an opioid overdose. Opioids are a class of drugs that include prescription medications such as oxycodone, hydrocodone, and morphine, as well as the illegal drug heroin.

Drug overdose deaths, driven largely by prescription drug overdoses, are now the leading cause of injury death in the United States – surpassing motor vehicle crashes. In 2013, the Centers for Disease Control and Prevention reported the number of drug overdose deaths had steadily increased for more than a decade. When someone overdoses on an opioid, it can be difficult to awaken the person, and breathing may become shallow or stop – leading to death if there is no medical intervention. If naloxone is administered quickly, it can counter the overdose effects, usually within two minutes.

Until this approval, naloxone was only approved in injectable forms, most commonly delivered by syringe or auto-injector. Many first responders and primary caregivers, however, feel a nasal spray formulation of naloxone is easier to deliver, and eliminates the risk of a contaminated needle stick. As a result, there has been widespread use of unapproved naloxone kits that combine an injectable formulation of naloxone with an atomizer that can deliver naloxone nasally. Now, people have access to an FDA-approved product for which the drug and its delivery device have met the FDA's high standards for safety, efficacy and quality. Narcan nasal spray does not require assembly and delivers a consistent, measured dose when used as directed. This prescription product can be used on adults or children and is easily administered by anyone, even those without medical training. The drug is sprayed into one nostril while the patient is lying on his or her back, and can be repeated if necessary. However, it is important to note that it is not a substitute for immediate medical care, and the person administering Narcan nasal spray should seek further immediate medical attention on the patient's behalf.

The FDA granted fast-track designation and priority review for Narcan nasal spray. Fast track is a process designed to facilitate development and expedite review of drugs intended to treat serious conditions and that demonstrate the potential to address an unmet medical need. The agency's priority review program provides for an expedited review of drugs that offer a significant improvement in the safety or effectiveness of the treatment, prevention, or diagnosis of a serious condition. Narcan nasal spray is being approved in less than four months, significantly ahead of the product's prescription drug user fee goal date of January 20, 2016.

In clinical trials conducted to support the approval of Narcan nasal spray, administering the drug in one nostril delivered approximately the same levels or higher of naloxone as a single dose of an FDA-approved naloxone intramuscular injection, and achieved these levels in approximately the same time frame.

The National Institute on Drug Abuse played a critical role in the development of Narcan nasal spray as well, forming a public-private partnership by designing and conducting the clinical trials required to determine that the intranasal formulation delivered naloxone as quickly and as effectively as an injection. NIDA then worked with its private sector partners to obtain FDA approval.

Increasing access to and the use of naloxone is part of the targeted strategy that Health and Human Services Secretary Sylvia M. Burwell put forward in March to address the opioid epidemic and save lives. In

July, addiction and advocacy groups called for expanded availability of naloxone during an FDA-sponsored public workshop exploring the uptake and use of the drug.
The use of Narcan nasal spray in patients who are opioid dependent may result in severe opioid withdrawal characterized by body aches, diarrhea, increased heart rate (tachycardia), fever, runny nose, sneezing, goose bumps (piloerection), sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness, and increased blood pressure.
Narcan nasal spray is distributed by Adapt Pharma, Inc., of Radnor, Pennsylvania.

FDA NEWS RELEASE

For Immediate Release: November 20th, 2015

FDA approves Ninlaro, new oral medication to treat multiple myeloma

The U.S. Food and Drug Administration granted approval for Ninlaro (ixazomib) in combination with two other therapies to treat people with multiple myeloma who have received at least one prior therapy.
Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells (a type of white blood cell) found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems. The National Cancer Institute estimates there will be 26,850 new cases of multiple myeloma and 11,240 related deaths in the United States this year.
Ninlaro is a type of cancer drug called a proteasome inhibitor and works by blocking enzymes from multiple myeloma cells, hindering their ability to grow and survive. Ninlaro is the first oral proteasome inhibitor and is approved in combination with another FDA-approved treatment for multiple myeloma called Revlimid (lenalidomide) and dexamethasone.
The safety and efficacy of Ninlaro were demonstrated in an international, randomized, double-blind clinical trial of 722 patients whose multiple myeloma came back after, or did not respond to, previous treatment. Study participants received either Ninlaro in combination with lenalidomide and dexamethasone or placebo plus lenalidomide and dexamethasone. Those taking Ninlaro lived longer without their disease worsening (average 20.6 months) compared to participants taking the other regimen (14.7 months).
The most common side effects of Ninlaro are diarrhea, constipation, low blood platelet count (thrombocytopenia), peripheral neuropathy (numbness and pain from nerve damage, usually in the hands and feet), nausea, peripheral edema, vomiting and back pain.
The FDA granted priority review and orphan drug designations for Ninlaro. Priority review status is granted to applications for drugs that, if approved, would be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan drug designation provides incentives such as tax credits, user fee waivers, and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.
Ninlaro is marketed by Takeda Pharmaceuticals based in Osaka, Japan. Farydak is marketed by East Hanover, New Jersey-based Novartis Pharmaceuticals. Darzalex is marketed by Janssen Biotech of Horsham, Pennsylvania. Revlimid is marketed by Celgene Corporation, based in Summit, New Jersey.

FDA NEWS RELEASE

For Immediate Release: November 24th, 2015

FDA approves Portrazza to treat advanced squamous non-small cell lung cancer

The U.S. Food and Drug Administration approved Portrazza (necitumumab) in combination with two forms of chemotherapy to treat patients with advanced (metastatic) squamous non-small cell lung cancer (NSCLC) who have not previously received medication specifically for treating their advanced lung cancer.
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. The most common type of lung cancer, non-small cell lung cancer, is further divided into two main types named for the kinds of cells found in the cancer – squamous cell and non-squamous cell (which includes adenocarcinoma).
Portrazza is a monoclonal antibody that blocks activity of EGFR, a protein commonly found on squamous NSCLC tumors.
The safety and efficacy of Portrazza were evaluated in a multicenter, randomized, open-label clinical study of 1,093 participants with advanced squamous NSCLC who received the chemotherapies gemcitabine and cisplatin with or without Portrazza. Those taking Portrazza plus gemcitabine and cisplatin lived longer on average (11.5 months) compared to those only taking gemcitabine and cisplatin (9.9 months). Portrazza was not found to be an effective treatment in patients with non-squamous NSCLC.

The most common side effects of Portrazza are skin rash and magnesium deficiency (hypomagnesemia), which can cause muscular weakness, seizure, irregular heartbeats and can be fatal. Portrazza includes a boxed warning to alert health care providers of serious risks of treatment with Portrazza, including cardiac arrest and sudden death, as well as hypomagnesemia.
Portrazza is marketed by Eli Lilly and Company, based in Indianapolis, Indiana.

FDA NEWS RELEASE

For Immediate Release: November 23rd, 2015

FDA approves Opdivo to treat advanced form of kidney cancer

The U.S. Food and Drug Administration approved Opdivo (nivolumab) to treat patients with advanced (metastatic) renal cell carcinoma, a form of kidney cancer, who have received a certain type of prior therapy.
Torisel (temsirolimus), approved in 2007, is the only other FDA-approved therapy that has demonstrated overall survival in renal cell cancer.
Renal cell carcinoma is the most common form of kidney cancer in adults and forms in the tissues of the kidney that make urine. The National Cancer Institute estimates 61,560 new cases and 14,080 deaths from kidney and renal pelvis cancer in the United States this year.
Opdivo works by targeting the cellular pathway known as PD-1/PD-L1 (proteins found on the body's immune cells and some cancer cells). By blocking this pathway, Opdivo may help the body's immune system fight cancer cells. Opdivo is intended for use in renal cell carcinoma in patients who have received prior anti-angiogenic therapy (treatments that interfere with the blood vessels that contribute to the growth of cancerous cells).
The safety and efficacy of Opdivo for this use were demonstrated in an open-label, randomized study of 821 patients with advanced renal cell carcinoma whose disease worsened during or after treatment with an anti-angiogenic agent. Patients were treated with Opdivo or another type of kidney cancer treatment called everolimus (marketed as Afinitor). Those treated with Opdivo lived an average of 25 months after starting treatment compared to 19.6 months in those treated with Afinitor. This effect was observed regardless of the PD-L1 expression level of patients' renal cell tumors. Additionally, 21.5 percent of those treated with Opdivo experienced a complete or partial shrinkage of their tumors, which lasted an average of 23 months, compared to 3.9 percent of those taking Afinitor, lasting an average of 13.7 months.
The most common side effects of Opdivo for this use are conditions relating to abnormal weakness or lack of energy, cough, nausea, rash, difficulty breathing (dyspnea), diarrhea, constipation, decreased appetite, back pain and joint pain (arthralgia).
Opdivo also has the potential to cause serious side effects that result from the immune system effect of Opdivo (known as "immune-mediated side effects"). These severe immune-mediated side effects involve healthy organs, including the lung, colon, liver, kidneys, hormone-producing glands and the brain.
The FDA granted the Opdivo application a breakthrough therapy designation, fast track 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.
Opdivo is marketed by Bristol-Myers Squibb based in Princeton, New Jersey. Torisel is marketed by Pfizer, based in New York, New York. Afinitor is marketed by Novartis Pharmaceuticals of East Hanover, New Jersey.

FDA NEWS RELEASE

For Immediate Release: November 30th, 2015

FDA approves Empliciti, a new immune-stimulating therapy to treat multiple myeloma

The U.S. Food and Drug Administration granted approval for Empliciti (elotuzumab) in combination with two other therapies to treat people with multiple myeloma who have received one to three prior medications.
Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. This disease may result in a weakened immune system, and cause other bone and kidney problems. The National Cancer Institute estimates there will be 26,850 new cases of multiple myeloma and 11,240 related deaths in the United States this year.
Darzalex (daratumumab), approved earlier this month, is the only other FDA-approved monoclonal antibody for the treatment of patients with multiple myeloma.

Empliciti activates the body's immune system to attack and kill multiple myeloma cells. It is approved in combination with another FDA-approved treatment for multiple myeloma called Revlimid (lenalidomide) and dexamethasone.
The safety and efficacy of Empliciti were tested in a randomized, open-label clinical study of 646 participants whose multiple myeloma came back after, or did not respond to previous treatment. Those taking Empliciti plus Revlimid and dexamethasone experienced a delay in the amount of time before their disease worsened (19.4 months) compared to participants taking only Revlimid and dexamethasone (14.9 months). Additionally, 78.5 percent of those taking Empliciti with Revlimid and dexamethasone saw a complete or partial shrinkage of their tumors compared to 65.5 percent in those only taking Revlimid and dexamethasone.
The most common side effects of Empliciti are fatigue, diarrhea, fever, constipation, cough, nerve damage resulting in weakness or numbness in the hands and feet (peripheral neuropathy), infection of the nose and throat (nasopharyngitis), upper respiratory tract infection, decreased appetite and pneumonia.
The FDA granted breakthrough therapy designation for this application, which is granted when a drug is intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints. Empliciti also received priority review and orphan drug designations. Priority review status is granted to applications for drugs that, if approved, would be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan drug designation provides incentives such as tax credits, user fee waivers and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.
Empliciti is marketed by Bristol-Myers Squibb of New York, New York. Darzalex is marketed by Janssen Biotech of Horsham, Pennsylvania. Revlimid is marketed by Celgene Corporation, based in Summit, New Jersey.

SAFETY ANNOUNCEMENTS

FDA Drug Safety Communication: FDA review finds long-term treatment with blood-thinning medicine Plavix (clopidogrel) does not change risk of death

[11-6-2015] A U.S. Food and Drug Administration (FDA) review has determined that long-term use of the blood-thinning drug Plavix (clopidogrel) does not increase or decrease overall risk of death in patients with, or at risk for, heart © clopidogrel. Health care professionals should consider the benefits and risks of available antiplatelet medicines before starting treatment.
Clopidogrel is an antiplatelet medicine used to prevent blood clots in patients who have had a heart attack, stroke, or problems with the circulation in the arms and legs. It works by helping to keep the platelets in the blood from sticking together and forming clots that can occur with certain medical conditions.
Results from the DAPT trial were published in the New England Journal of Medicine in November 2014. The DAPT trial compared treatment with dual antiplatelet therapy (either clopidogrel [Plavix] or prasugrel [Effient] plus aspirin) for 12 months versus 30 months in patients who had undergone placement of a drug-eluting coronary stent. Compared to patients taking clopidogrel for 12 months, patients who were treated with clopidogrel for 30 months had lower rates of heart attacks and stent thrombosis but higher rates of death, primarily from cancer or trauma.
In order to investigate the increased risk of death and cancer-related death reported with clopidogrel in the DAPT trial, we examined the results of the DAPT trial and other large, long-term clinical trials of clopidogrel with data available on rates of death, death from cancer, or cancer reported as an adverse event.
We performed meta-analyses of other long-term clinical trials to assess the effects of clopidogrel on death rates from all causes. The results indicate that long-term (12 months or longer) dual antiplatelet therapy with clopidogrel and aspirin do not appear to change the overall risk of death when compared to short-term (6 months or less) clopidogrel and aspirin, or aspirin alone. Also, there was no apparent increase in the risks of cancer-related deaths or cancer-related adverse events with long-term treatment.
The following table shows the results from the meta-analyses:

	Number of patients included	Long-term clopidogrel plus aspirin	Short term clopidogrel plus aspirin or aspirin alone
Overall incidence of death	56,799	6.7%	6.6%
Incidence of cancer adverse events	37,835	4.2%	4.0%
Incidence of cancer death	40,855	0.9%	1.1%

We urge health care professionals and patients to report side effects involving clopidogrel or other antiplatelet medicines to the FDA MedWatch program

Current Drug Shortages Index (as of November 30th, 2015):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Aprepitant (Emend) Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
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***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam (Keppra) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
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***
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***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sumatriptan (Imitrex) Nasal Spray	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***