Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
March 11, 2015
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – March 11, 2015

DATE: March 2, 2015

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

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

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a) – Appendix C

Action Item – Vote to Prior Authorize Brisdelle® (Paroxetine Mesylate) – Appendix D

Action Item – Vote to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Suspension) – Appendix E

Action Item – Vote to Prior Authorize Myalept™ (Metreleptin) – Appendix F

Action Item – Annual Review of Ilaris® (Canakinumab) – Appendix G

30-Day Notice to Prior Authorize Sylvant™ (Siltuximab) – Appendix H

Annual Review of Topical Antifungal Medications and 30-Day Notice to Prior Authorize Ecoza™ (Econazole Nitrate), Jublia® (Efinaconazole), and Kerydin™ (Tavaborole) – Appendix I

Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Izba® (Travoprost) – Appendix J

Annual Review of Soliris® (Eculizumab) – Appendix K

Annual Review of Botulinum Toxins – Appendix L

Annual Review of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release) – Appendix M

FDA and DEA Updates – Appendix N

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – March 11, 2015 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

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

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

4. **Update on Medication Coverage Authorization Unit/FDA Safety Alerts – See Appendix B**
   A. Medication Coverage Activity for February 2015
   B. Pharmacy Help Desk Activity for February 2015
   C. FDA Safety Alerts

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

5. **Action Item – Vote to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a) – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Brisdelle® (Paroxetine Mesylate) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Suspension) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Myalept™ (Metreleptin) – See Appendix F**
   A. College of Pharmacy Recommendations

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

9. Action Item – Annual Review of Ilaris® (Canakinumab) – See Appendix G

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Ilaris® (Canakinumab)
D. Prior Authorization of Ilaris® (Canakinumab)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Ilaris® (Canakinumab)

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

10. 30-Day Notice to Prior Authorize Sylvant™ (Siltuximab) – See Appendix H

A. Introduction
B. Sylvant™ (Siltuximab) Product Summary
C. College of Pharmacy Recommendations

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

11. Annual Review of Topical Antifungal Medications and 30-Day Notice to Prior Authorize Ecoza™ (Econazole Nitrate), Jublia® (Efinaconazole), and Kerydin™ (Tavaborole) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Topical Antifungal Medications
C. Prior Authorization of Topical Antifungal Medications
D. Market News and Updates
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Topical Antifungal Medications

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

12. Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Izba® (Travoprost Ophthalmic Solution) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Glaucoma Medications
C. Prior Authorization of Glaucoma Medications
D. Market News and Updates
E. Izba® (Travoprost Ophthalmic Solution) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Glaucoma Medications

Non-Presentation, Questions Only:

13. Annual Review of Soliris® (Eculizumab) – See Appendix K

A. Indication
B. Current Prior Authorization Criteria
C. Utilization of Soliris® (Eculizumab)
D. Prior Authorization of Soliris® (Eculizumab)
E. College of Pharmacy Recommendations
F. Utilization Details of Soliris® (Eculizumab)

Non-Presentation, Questions Only:

14. Annual Review of Botulinum Toxins – See Appendix L

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

Non-Presentation, Questions Only:

15. Annual Review of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release) – See Appendix M

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)
D. Prior Authorization of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)

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

16. FDA and DEA Updates – See Appendix N

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

17. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

18. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF FEBRUARY 11, 2015

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Anetta Harrell, 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
Melissa Anderson, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist	x	
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Graduate Students: David George, Pharm.D.		x
Tammy Lambert, Pharm.D.	x	
Timothy Pham, Pharm.D.	x	
Visiting Pharmacy Student(s): Kyle Clark, Selma Alami, Michael Willner	x	

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

OTHERS PRESENT:		
Clint Degner, Novartis	Jeff Knappen, Allergan	Rick Ulasewich, DSI
Brent Hildebrand, Gilead	Chris Desimone, Aegerion	Roger Grotzinger, BMS
Melvin Nwamadi, Abbott	Karen Ward, Aegerion	Mai Duong, Novartis
Patrick Harvey, Walgreens	Bob Gustafson, Lundbeck	Larry Goolsby, J & J
Jim Dunlap, PhRMA	Aaron Zimmerman, Teva	Doug Wood, ViiV
Jim Chapman, AbbVie	Mark DeClerk, Lilly	Jim Fowler, Astra Zeneca
Brian Maves, Pfizer	Holly Weatherford, BMS	Joe Summers, UCB
Michelle Settle, Lundbeck	John Omick, Lundbeck	Ruthel Goss, Genzyme
Ronald Cain, Pfizer	Toby Thompson, Pfizer	Bob Atkins, Biogen
Roberto Pedroza, Salix		

PRESENT FOR PUBLIC COMMENT:	
Michelle Settle	Lundbeck
Quynh Chau Doan	AbbVie
Ben Skoog	Biogen

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: QUYNH CHAU DOAN AGENDA NO. 5
2B: MICHELLE SETTLE AGENDA NO. 6
2C: BEN SKOOG AGENDA NO. 10

ACTION: NONE REQUIRED

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

3A: JANUARY 14, 2015 DUR MINUTES – VOTE
3B: JANUARY 14, 2015 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore
Dr. Preslar moved to approve; seconded by Dr. Winegardner

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/LONG-ACTING BETA AGONIST UTILIZATION: PEDIATRIC MEMBERS**

4A: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2015
4B: PHARMACY HELP DESK ACTIVITY FOR JANUARY 2015
4C: LONG-ACTING BETA AGONIST UTILIZATION: PEDIATRIC MEMBERS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE VIEKIRA PAK™ (OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR)**

5A: COLLEGE OF PHARMACY RECOMMENDATIONS
5B: HEPATITIS C THERAPY PHARMACY AGREEMENT
5C: HEPATITIS C THERAPY INTENT TO TREAT CONTRACT

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE NORTHERA™ (DROXIDOPA)**

6A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE AKYNZEO® (NETUPITANT/PALONOSETRON)**

7A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Anderson

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **30-DAY NOTICE TO PRIOR AUTHORIZE MYALEPT™ (METRELEPTIN)**

8A: INTRODUCTION

8B: MYALEPT™ (METRELEPTIN) PRODUCT SUMMARY

8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Anderson

Dr. Winegardner recommended and the board agreed to change to every 3 months to evaluate compliance and ensure the prescriber is assessing continued efficacy.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ORENITRAM™ (TREPROSTINIL) AND REVATIO® (SILDENAFIL ORAL SUSPENSION)**

9A: INTRODUCTION

9B: TREATMENT

9C: CURRENT PRIOR AUTHORIZATION CRITERIA

9D: UTILIZATION OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS

9E: PRIOR AUTHORIZATION OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS

9F: MARKET NEWS AND UPDATES

9G: PRODUCT SUMMARIES

9H: COLLEGE OF PHARMACY RECOMMENDATIONS

9I: UTILIZATION DETAILS OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF MULTIPLE SCLEROSIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE LEMTRADA™ (ALEMTUZUMAB) AND PLEGRIDY™ (PEGINTERFERON B-1A)**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF MULTIPLE SCLEROSIS MEDICATIONS

10C: PRIOR AUTHORIZATION OF MULTIPLE SCLEROSIS MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: PRODUCT SUMMARIES

10F: COLLEGE OF PHARMACY RECOMMENDATIONS

10G: UTILIZATION DETAILS OF MULTIPLE SCLEROSIS MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE BRISDELLE® (PAROXETINE MESYLATE)**

11A: INTRODUCTION

11B: BRISDELLE® (PAROXETINE MESYLATE) PRODUCT SUMMARY

11C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Teel

Dr. Garton recommends that authorization requires a patient –specific clinically significant reason why paroxetine 10mg is not appropriate for the member; and two trials of either an SSRI or SNRI or both.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF RAVICTI® (GLYCEROL PHENYLBUTYRATE)
12A: INDICATION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF RAVICTI® (GLYCEROL PHENYLBUTYRATE)
12D: PRIOR AUTHORIZATION OF RAVICTI® (GLYCEROL PHENYLBUTYRATE)
12E: MARKET NEWS AND UPDATES
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Anderson
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF PROCYSBI® (CYSTEAMINE BITARTRATE DELAYED-RELEASE)
13A: INDICATION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA
13C: UTILIZATION OF PROCYSBI® (CYSTEAMINE BITARTRATE DELAYED-RELEASE)
13D: PRIOR AUTHORIZATION OF PROCYSBI® (CYSTEAMINE BITARTRATE DELAYED-RELEASE)
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF PROCYSBI® (CYSTEAMINE BITARTRATE DELAYED-RELEASE)
Materials included in agenda packet; presented by Dr. Anderson
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF FULYZAQ® (CROFELEMER)
14A: INDICATION
14B: CURRENT PRIOR AUTHORIZATION CRITERIA
14C: UTILIZATION OF FULYZAQ® (CROFELEMER)
14D: PRIOR AUTHORIZATION OF FULYZAQ® (CROFELEMER)
14E: MARKET NEWS AND UPDATES
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 16: FUTURE BUSINESS
16A: ANNUAL REVIEWS
16B: NEW PRODUCT REVIEWS
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT
The meeting was adjourned at 4:57 pm

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

Memorandum

Date: February 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 Meeting of February 11, 2015

Recommendation 1: Long-Acting Beta Agonist Utilization: Pediatric Members

NO ACTION REQUIRED.

SoonerCare claims analysis of pediatric utilization of single-component Long-Acting $Beta_2$ Agonist (LABA) medications did not reveal a pressing need for intervention. Most pediatric members utilizing single-component LABA medications required a unique dosage formulation or were being followed by a pulmonary specialist. Based on these findings the College of Pharmacy does not recommend any changes to the current LABA criteria at this time.

Recommendation 2: Vote to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) with the following criteria:

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** with a METAVIR fibrosis score of **F2** or greater; and

3. 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
4. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
5. 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
6. 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
7. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
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. Female partners of male patients should also be checked for pregnancy for informational purposes. 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. 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
16. 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

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; and
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, 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.

Additionally, the College of Pharmacy recommends Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Harvoni® (sofosbuvir/ledipasvir) be 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 will require patient-specific, clinically significant reasoning why Viekira Pak™ or Harvoni® is not appropriate for the member.

Recommendation 3: Vote to Prior Authorize Northera™ (Droxidopa)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Northera™ (droxidopa) with the following criteria:

Northera™ (Droxidopa) Approval Criteria:

1. An FDA approved diagnosis of symptomatic neurogenic orthostatic hypotension caused by primary autonomic failure (Parkinson's disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, or non-diabetic autonomic neuropathy; and
2. Member must be 18 years of age or older; and
3. Member must have tried and failed two of the following medications at recommended dosing within the last 90 days:
    a. Midodrine; or
    b. Fludrocortisone; or
    c. Pyridostigmine; or
    d. Have a contraindication to all preferred medications.
4. Initial approval will be for the duration of two weeks of treatment only.
5. Continued approval will require the prescriber to provide information regarding improved member response/effectiveness of this medication to determine whether Northera™ is continuing to provide a benefit.
6. Continued approval will be for the duration of three months. Each approval will require prescriber documentation of member response/effectiveness to Northera™.

Recommendation 4: Vote to Prior Authorize Akynzeo® (Netupitant/Palonosetron)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Akynzeo® (netupitant/palonosetron) with the following criteria:

Akynzeo® (Netupitant/Palonosetron) Approval Criteria:

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

Recommendation 5: 30-Day Notice to Prior Authorize Myalept™ (Metreleptin)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Oral Suspension)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a)

NO ACTION REQUIRED.

Recommendation 8: 30-Day Notice to Prior Authorize Brisdelle® (Paroxetine Mesylate)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Ravicti® (Glycerol Phenylbutyrate)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Procysbi® (Cysteamine Bitartrate Delayed-Release)

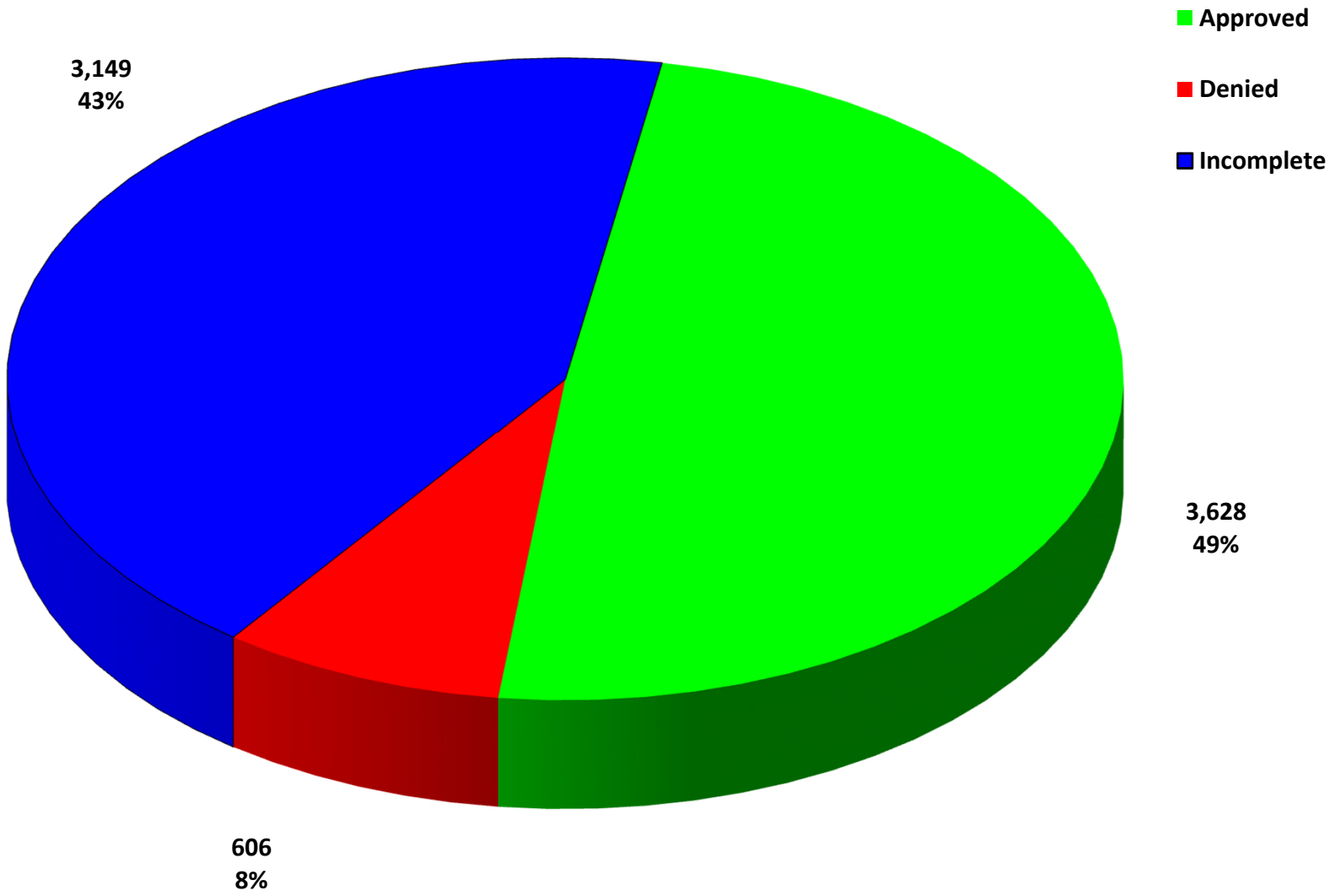
NO ACTION REQUIRED.

Recommendation 11: Annual Review of Fulyzaq® (Crofelemer)

NO ACTION REQUIRED.

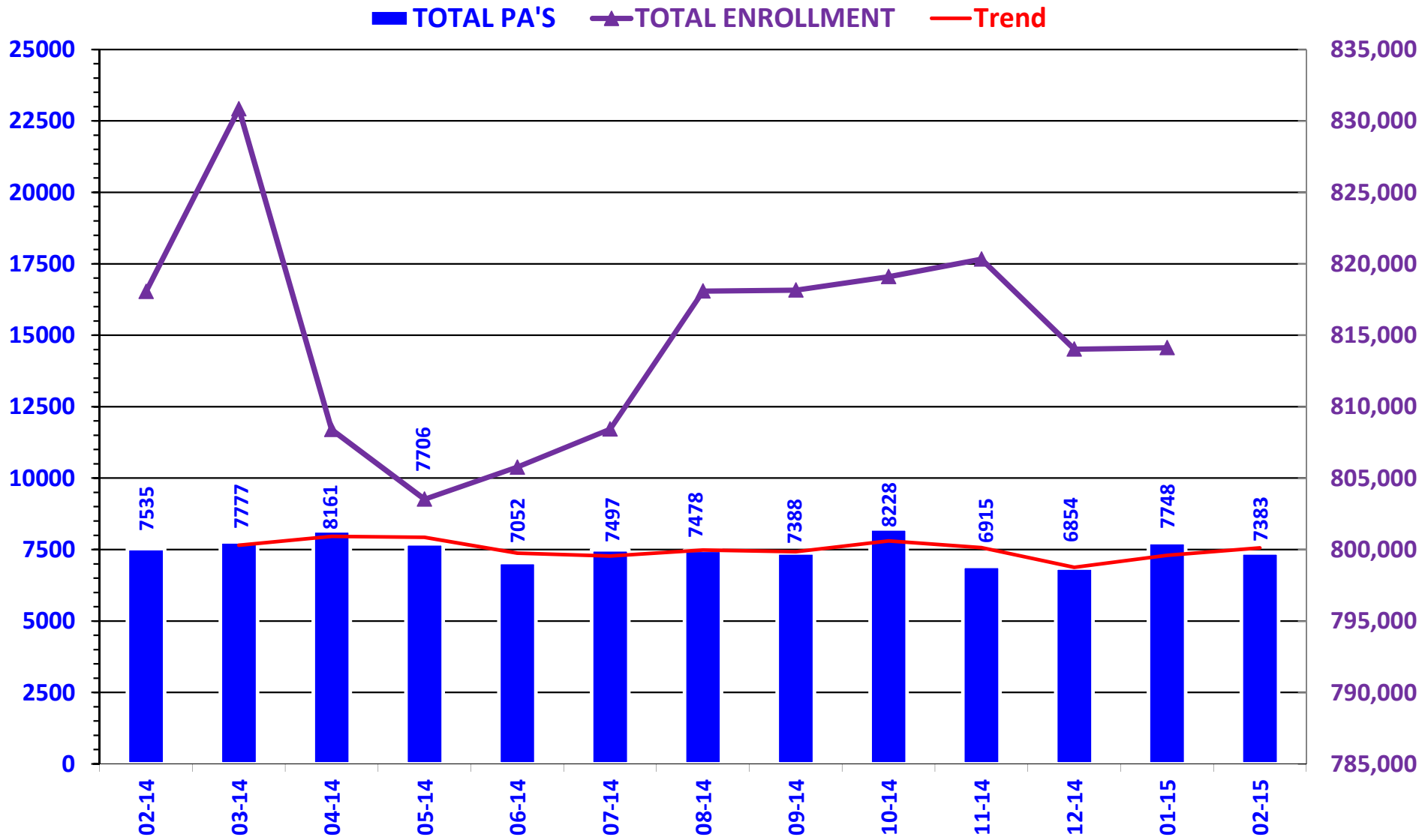
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY



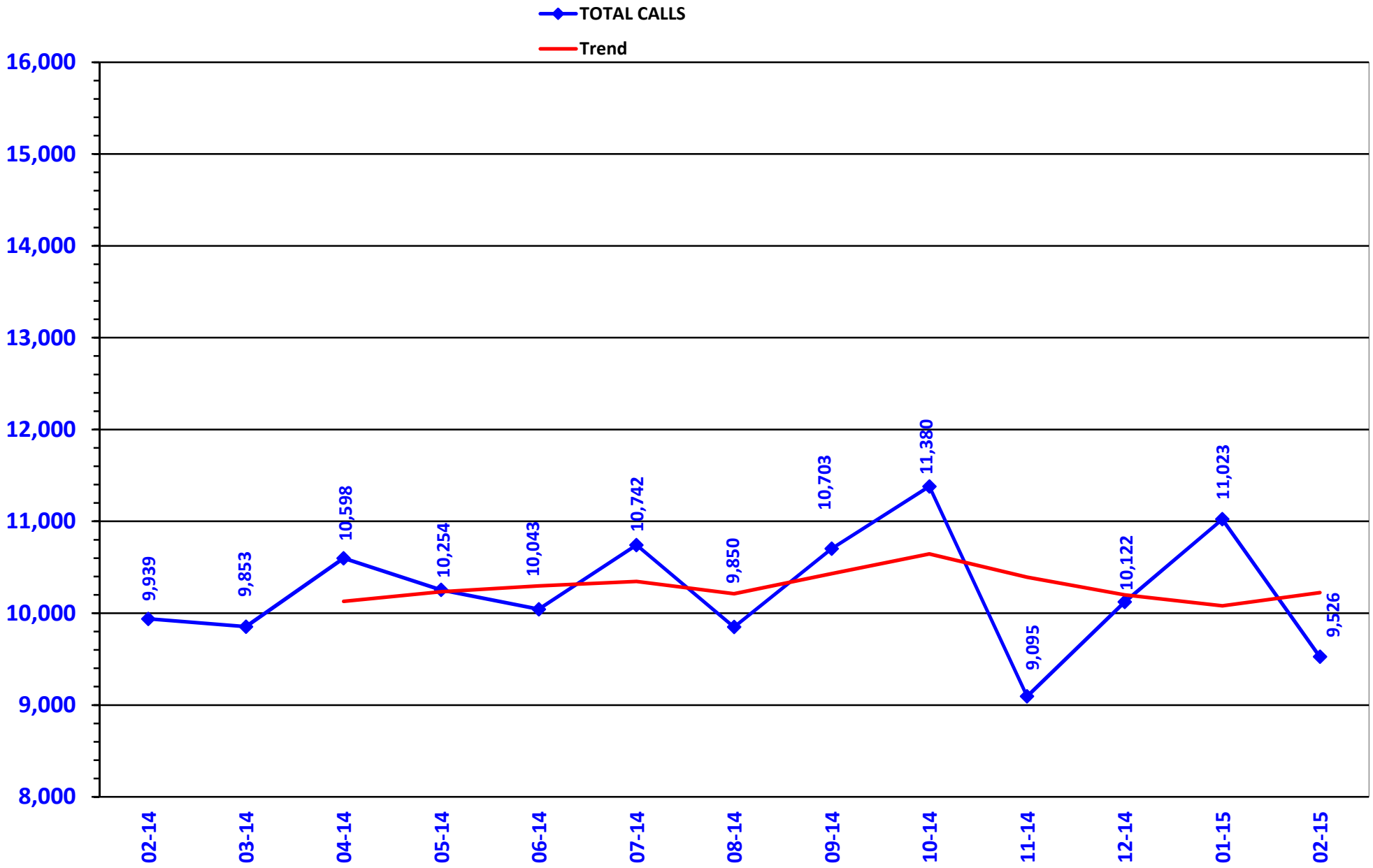
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: FEBRUARY 2014 – FEBRUARY 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
FEBRUARY 2014 – FEBRUARY 2015



Prior Authorization Activity

2/1/2015 Through 2/28/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	375	174	10	191	356
Analgesic - NonNarcotic	18	0	2	16	0
Analgesic, Narcotic	525	318	21	186	164
Angiotensin Receptor Antagonist	34	6	7	21	359
Antiasthma	198	84	13	101	347
Antibiotic	83	30	8	45	95
Anticonvulsant	86	26	7	53	328
Antidepressant	74	14	3	57	342
Antidiabetic	247	106	11	130	359
Antifungal	10	2	2	6	181
Antigout	11	7	0	4	272
Antihistamine	139	107	7	25	356
Antimigraine	40	10	1	29	191
Antiulcers	170	40	28	102	180
Anxiolytic	88	53	6	29	271
Atypical Antipsychotics	346	222	3	121	334
Biologics	71	46	1	24	332
Bladder Control	141	81	10	50	351
Blood Thinners	111	70	2	39	313
Botox	26	11	4	11	329
Cardiovascular	47	22	2	23	357
Cephalosporins	14	2	0	12	9
Chronic Obstructive Pulmonary Disease	11	2	0	9	356
Contraceptive	13	7	1	5	209
Dermatological	106	22	50	34	89
Endocrine & Metabolic Drugs	49	34	4	11	127
Erythropoietin Stimulating Agents	32	19	2	11	109
Fibromyalgia	143	44	26	73	347
Gastrointestinal Agents	66	10	14	42	58
Glaucoma	14	1	3	10	360
Growth Hormones	90	62	6	22	152
Hepatitis C	165	84	27	54	8
HFA Rescue Inhalers	48	20	2	26	313
Insomnia	61	11	5	45	192
Linzess, Amitiza, and Relistor	72	10	7	55	228
Multiple Sclerosis	33	23	0	10	214
Muscle Relaxant	99	31	29	39	50
Nasal Allergy	91	5	16	70	359
Neurological Agents	58	41	5	12	353
NSAIDs	133	11	12	110	268
Ocular Allergy	30	4	3	23	192
Ophthalmic Anti-infectives	37	5	5	27	35
Osteoporosis	22	6	1	15	359
Other*	207	37	38	132	177
Pediculicide	74	33	7	34	12
Prenatal Vitamins	10	0	2	8	0
Statins	55	15	4	36	358
Stimulant	920	401	35	484	343
Suboxone/Subutex	163	124	6	33	76
Synagis	103	66	4	33	70
Testosterone	52	18	3	31	345
Topical Antifungal	47	3	11	33	63
Topical Corticosteroids	131	2	50	79	177
Vitamin	56	12	20	24	320
Pharmacotherapy	45	43	0	2	229

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Emergency PAs	0	0	0	0	
Total	**6,090**	**2,637**	**546**	**2,907**	
Overrides					
Brand	39	31	1	7	327
Cumulative Early Refill	2	2	0	0	180
Dosage Change	347	318	2	27	6
High Dose	3	3	0	0	124
Ingredient Duplication	30	24	1	5	4
Lost/Broken Rx	62	52	5	5	4
NDC vs Age	35	32	0	3	268
Nursing Home Issue	40	36	0	4	4
Opioid Quantity	2	2	0	0	174
Other*	35	30	2	3	8
Quantity vs. Days Supply	661	442	42	177	265
STBS/STBSM	8	8	0	0	47
Stolen	8	5	1	2	24
Temporary Unlock	2	2	0	0	24
Third Brand Request	23	8	6	9	6
Overrides Total	**1,293**	**991**	**60**	**242**	
Total Regular PAs + Overrides	**7,383**	**3,628**	**606**	**3,149**	

Denial Reasons	
Unable to verify required trials.	2,569
Does not meet established criteria.	609
Lack required information to process request.	546

Other PA Activity	
Duplicate Requests	443
Letters	4,905
No Process	5
Changes to existing PAs	504
Helpdesk Initiated Prior Authorizations	796
PAs Missing Information	36

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

Retrospective Drug Evaluation: Focus on Safety

Overview of FDA Safety Alerts

Oklahoma Health Care Authority
March 2015

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

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

Date	Drug	Issue
9/26/2014	**omalizumab (Xolair®)**	**Risk of compromised blood supply to brain**
Issue Details: A review of a 5-year safety study found a slightly higher rate of heart and brain blood vessel problems in patients treated with omalizumab, compared to non-omalizumab treated patients. Problems include transient ischemic attacks (TIA's), heart attacks, sudden unexpected chest pain, pulmonary hypertension, pulmonary emboli, and deep vein thrombosis. An additional review of 25 randomized, placebo-controlled trials did not show this increased risk, but further study is warranted. **FDA Recommendations:** Safety data has been added to product label to reflect the additional risk. **Pharmacy Claims Evaluation:** During calendar year 2014, 15 members utilized omalizumab. No adverse effects related to omalizumab use were reported among these members.		

Date	Drug	Issue
11/14/2014	**leflunomide (Arava®), teriflunomide (Aubagio®)**	**Risk of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)**
Issue Details: Rare cases of DRESS have been reported in post-marketing surveillance of patients receiving leflunomide. **FDA Recommendations**: The package labeling has been modified to include contraindications for leflunomide use in patients with hypersensitivity, and a warning that if symptoms of DRESS occur, the drug should be discontinued and a drug elimination procedure (cholestyramine washout or activated charcoal administration) should be initiated. Teriflunomide (Aubagio®), the active metabolite of leflunomide, should not be co-administered with leflunomide. **Pharmacy Claims Evaluation:** In calendar year 2014, 133 SoonerCare members utilized leflunomide and eight members utilized teriflunomide. Claims analysis did not reveal any concomitant use of leflunomide and teriflunomide.		

Date	Drug	Issue
11/16/2014	**Long-term dual antiplatelet therapy**	**Risk of non-cardiovascular death**

Issue Details: Preliminary clinical trial data indicates that treatment for 30 months with dual antiplatelet therapy with aspirin plus either clopidogrel or prasugrel, following placement of drug-eluting stents, decreased risk of heart attacks or clots in stents, but appeared to increase the overall risk of death, compared to the same treatment for 12 months. The increased risk of death was reported in the clopidogrel arm of the study, and not in the prasugrel arm. The Dual Antiplatelet Therapy (DAPT) trial was published in the New England Journal of Medicine.
FDA Recommendations: The FDA continues to evaluate the results of the trial prior to making recommendations. Prescribers are advised not to discontinue these medications because it is believed that the benefits continue to outweigh potential risks.
Pharmacy Claims Evaluation: In fiscal year 2014, 2,851 SoonerCare members utilized one of these medications; 2,674 of these members utilized clopidogrel. Since aspirin is available over-the-counter concomitant utilization cannot be evaluated.

Date	Drug	Issue
11/17/2014	**ampicillin-sulbactam (Unasyn®)**	**Hepatic dysfunction**

Issue Details: Hepatic dysfunction, including hepatitis and cholestatic jaundice, has been reported in patients utilizing ampicillin-sulbactam. These conditions are generally reversible, however deaths have been reported.
FDA Recommendations: The package labeling has been updated to reflect this potential adverse effect. The update to the labeling was approved by the FDA Center for Drug Evaluation and Research (CDER).
Pharmacy Claims Evaluation: Ampicillin-sulbactam is administered via intravenous infusion and therefore typically given in an inpatient or hospital setting. In calendar year 2014, 12 SoonerCare members had a total of 30 paid pharmacy claims for ampicillin-sulbactam. No adverse effects related to ampicillin-sulbactam use were reported among these members.

Date	Drug	Issue
12/3/2014	**All prescription drugs and biological products**	**Labeling for use during pregnancy and breastfeeding.**

Issue Details: The FDA published a final rule regarding the labeling of medications used during pregnancy and while breastfeeding.
FDA Recommendations: The current letter categories, A, B, C, D and X, are to be replaced to provide a more consistent way to define the risks and benefits of medications used during pregnancy and breastfeeding. The three new subsections are “Pregnancy”, “Lactation”, and “Females and Males of Reproductive Potential”. Each category will provide risk information of medications for the specific population. The “Pregnancy” and “Lactation” subsections will have three subheadings: risk summary, clinical considerations, and data. The subheadings will provide more detailed information. This new rule will go into effect as of June 30, 2015.
SoonerCare action: The College of Pharmacy will follow the changes and utilize them in prior authorization evaluations and drug utilization reviews going forward.

Date	Drug	Issue
12/11/2014	**ziprasidone (Geodon®)**	**Rare but potential fatal skin reactions**

Issue Details: An FDA safety communication was issued regarding the risk of development of a skin reaction that can progress to other parts of the body in patients utilizing ziprasidone. Patients who develop fever with a rash and/or swollen lymph nodes while taking ziprasidone should be advised to seek medical treatment and discontinue the drug immediately.
FDA Recommendations: The FDA required the drug manufacturer to add a warning to the package label of all formulations regarding this potential reaction.
Pharmacy Claims Evaluation: In calendar year 2014, there were 1,653 SoonerCare members utilizing ziprasidone. No adverse effects related to ziprasidone use were reported among these members.

Date	Drug	Issue
1/9/2015	**Analgesics, over-the-counter (OTC) & prescription**	**Safety in pregnancy**

Issue Details: The FDA reviewed numerous published studies that evaluated the use of prescription and OTC pain medications during pregnancy; these included non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and acetaminophen (APAP).
Potential risks for each class of analgesic include:

1. NSAIDs: miscarriage in first half of pregnancy
2. Opioids: risk of birth defects of the brain, spine, or spinal cord when taken in first trimester
3. APAP: risk of attention deficit hyperactivity disorder (ADHD)

FDA Recommendations: The FDA determined that the studies were too limited to make recommendations, but encouraged prescribers to weigh the benefits and the risks of any pain medications for their pregnant patients.
Pharmacy Claims Evaluation: Previously evaluated SoonerCare data from January 1, 2014 to April 23, 2014 revealed that 14.8% of pregnant SoonerCare members filled a prescription for an opioid. Opioid analgesic claims accounted for 32.6% of the prescriptions filled by pregnant members. OTC medication data is unavailable.
Follow Up Data: Additional claims evaluation from October 1, 2014 to December 31, 2014 found 2,851 pharmacy claims for any medication for 928 SoonerCare members with a diagnosis indicator for pregnancy. Of those claims, 384 were for an opioid medication for 267 pregnant SoonerCare members. Approximately 13% of all claims for pregnant SoonerCare members were for an opioid medication, and approximately 28.7% of pregnant SoonerCare members who had a paid claim for any medication utilized an opioid medication.

[1] FDA Drug Safety Communication (omalizumab) available online at http://www.fda.gov/Drugs/DrugSafety/ucm414911.htm Last revised: 10/9/2014. Last accessed: 2/16/2015.
[2] Drug Safety Communication (leflunomide) available online at http://www.fda.gov/safety/medwatch/safetyinformation/ucm230245.htm Last revised: 12/11/2014. Last accessed: 2/16/2015.
[3] FDA Drug Safety Communication (antiplatelet) available online at http://www.fda.gov/Drugs/DrugSafety/ucm423079.htm Last revised: 12/2/2014. Last accessed. 2/16/2015.
[4] FDA Drug Safety Communication (Ampicillin-sulbactam) available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm426034.htm Last revised: 12/11/2014. Last accessed: 2/16/2015.
[5] FDA Drug Safety Communication (prescription drugs and biological products) available online at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm425317.htm Last revised: 12/12/2014. Last accessed: 2/16/2015.
[6] Label revision (ziprasidone) available online at http://www.fda.gov/Drugs/DrugSafety/DrugSafetyPodcasts/ucm426740.htm Last revised: 12/12/2014. Last accessed: 2/16/2015.
[7] FDA Drug Safety Communication (analgesics) available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm429604.htm Last revised: 1/20/2015. Last accessed: 2/16/2015.

Appendix C

Vote to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a)

Oklahoma Health Care Authority
March 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Lemtrada™ (alemtuzumab) with the following criteria:

Lemtrada™ (Alemtuzumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Member must have had an inadequate response to two or more drugs indicated for the treatment of Multiple Sclerosis; and
3. Lemtrada™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for two hours after each infusion; and
4. The prescriber must agree to monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose of Lemtrada™; and
5. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada™ therapy; and
6. Member, prescriber, pharmacy, and healthcare facility must all enroll in the Lemtrada™ REMS Program and maintain enrollment throughout therapy.

Additionally the College of Pharmacy recommends placement of Plegridy™ (peginterferon β-1a) into Tier-2 of the Multiple Sclerosis Interferon Prior Authorization category. Current criteria for this category will apply.

Multiple Sclerosis Interferon Approval Criteria:

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

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

*Tier structure based on supplemental rebate participation.

Appendix D

Vote to Prior Authorize Brisdelle® (Paroxetine Mesylate)

Oklahoma Health Care Authority
March 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Brisdelle® (paroxetine mesylate) with the following criteria:

Brisdelle® (Paroxetine Mesylate) Approval Criteria:

1. An FDA approved diagnosis of moderate to severe vasomotor symptoms associated with menopause; and
2. Approvals for Brisdelle® will not be granted for psychiatric indications; and
3. Member must not have any of the contraindications for use of Brisdelle®; and
4. Two previous trials with either a selective serotonin reuptake inhibitor (SSRI) or a selective serotonin norepinephrine reuptake inhibitor (SNRI) or both, or a patient-specific, clinically significant reasoning why a SSRI or SNRI is not appropriate for the member; and
5. Authorization requires a patient-specific, clinically significant reason why paroxetine 10mg is not appropriate for the member; and
6. A quantity limit of 30 capsules per 30 days will apply.

Appendix E

Vote to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Suspension)

Oklahoma Health Care Authority
March 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Orenitram™ (treprostinil) and Revatio® (sildenafil) suspension with the following criteria:

Orenitram™ (Treprostinil) Approval Criteria:

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

Revatio® (Sildenafil Suspension) Approval Criteria:

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

Additionally, the College of Pharmacy recommends updating the current criteria for Adcirca® (tadalafil) with the following criteria:

Adcirca® (Tadalafil) Approval Criteria:

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

Appendix F

Vote to Prior Authorize Myalept™ (Metreleptin)

Oklahoma Health Care Authority
March 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Myalept™ (metreleptin) with the following criteria:

Myalept™ (Metreleptin) Approval Criteria:

1. An FDA approved diagnosis of leptin deficiency in patients with congenital or acquired generalized lipodystrophy; and
2. Approvals will not be granted for the following diagnoses:
    a. Metabolic disease without current evidence of generalized lipodystrophy
    b. HIV-related lipodystrophy
    c. General obesity not associated with congenital leptin deficiency
3. Myalept™ must be prescribed by an endocrinologist; and
4. Prescriber must agree to test for neutralizing antibodies in patients who experience severe infections or if they suspect Myalept™ is no longer effective.
    a. Baseline HbA1c, fasting glucose, and fasting triglycerides must be stated on prior authorization request
    b. Re-approvals will require recent lab values (HbA1c, fasting glucose, and fasting triglycerides) to ensure neutralizing antibodies have not developed; and
5. Prescriber and pharmacy must be enrolled in the Myalept™ REMS program; and
6. Approvals will be for the duration of three months to evaluate compliance and ensure the prescriber is assessing continued efficacy; and
7. A quantity limit of one vial per day will apply.

Appendix G

Fiscal Year 2014 Annual Review of Ilaris® (Canakinumab)

Oklahoma Health Care Authority
March 2015

Introduction[1,2,3]

Systemic Juvenile Idiopathic Arthritis (SJIA) is a subset of Juvenile Idiopathic Arthritis (JIA) defined as arthritis in one or more joints for at least six weeks in a child less than 16 years old, preceded by daily fever for at least two weeks, and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis. SJIA accounts for approximately 4% to 15% of JIA and typically affects both sexes equally. The most common complications of SJIA are severe growth retardation, osteoporosis, and macrophage activation syndrome (MAS) which can be life-threatening.

In 2011, the American College of Rheumatology (ACR) published the first treatment recommendations specific to pediatric rheumatic disease that included recommendations for systemic manifestations. Current treatment options include disease modifying anti-rheumatic drugs (DMARDs) such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), oral steroids, and methotrexate and some biologic products such as Tumor Necrosis Factor (TNF) inhibitors, anakinra and canakinumab. NSAIDs, glucocorticoids, and anakinra are considered first-line therapy options, whereas methotrexate or leflunomide and the other biologic agents are considered second and third line options. Step therapy can be additive with the exception of the biologics which should not be used in combination with another biologic.

Current Prior Authorization Criteria

Ilaris® (Canakinumab) Approval Criteria:

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

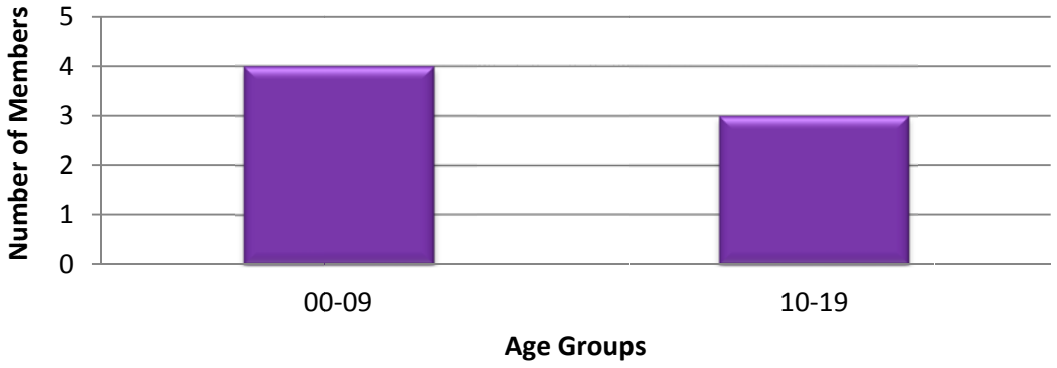
Utilization of Ilaris® (Canakinumab)

Comparison of Fiscal Years

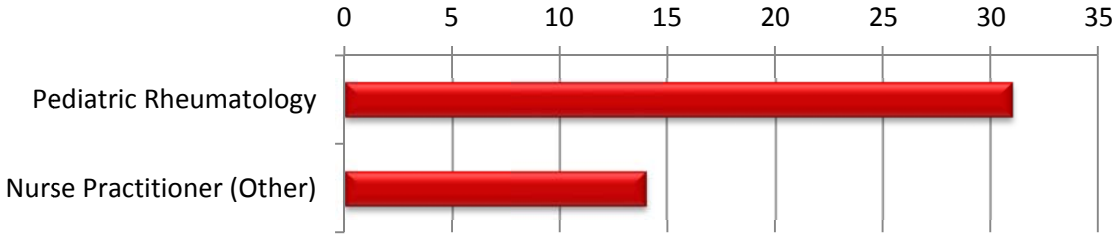
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	4	16	$270,861.60	$16,928.85	$312.05	16	868
2014	7	45	$763,114.95	$16,958.11	$421.38	45	1,811
% Change	**75.00%**	**181.30%**	**181.70%**	**0.20%**	**35.00%**	**181.30%**	**108.60%**
Change	**3**	**29**	**$492,253.35**	**$29.26**	**$109.33**	**29**	**943**

*Total number of unduplicated members.

Demographics of Members Utilizing Ilaris® (Canakinumab)



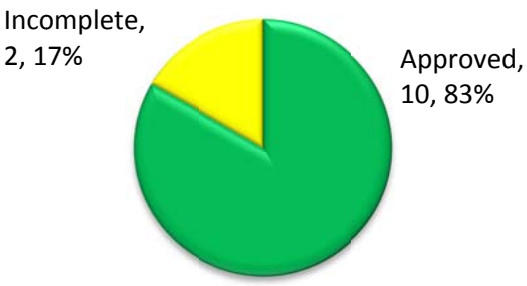
Top Prescriber Specialties of Ilaris® (Canakinumab) by Number of Claims



Prior Authorization of Ilaris® (Canakinumab)

There were 12 petitions submitted for Ilaris® (canakinumab) during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,4,5]

FDA Approvals:

- May 2013: The FDA approved a new indication for Ilaris® (canakinumab) for Systemic Juvenile Idiopathic Arthritis (SJIA) for children ages 2 years and older.

Guideline Updates:

- October 2013: The American College of Rheumatology (ACR) updated its *2011 Recommendations for the Treatment of Juvenile Idiopathic Arthritis* to include canakinumab, rilonacept, and tocilizumab as additional treatment options. Previously recommended treatment options include NSAIDs, glucocorticoids, methotrexate, leflunomide, Intravenous Immunoglobulin (IVIG), cyclosporine, tacrolimus, TNF inhibitors, abatacept, rituximab, and anakinra.

FDA Safety Alerts:

- October 2014: Ilaris® (canakinumab) has been associated with an increased risk of serious infections. Predominantly, upper respiratory tract infections have been reported in patients using canakinumab. An increased incidence of serious infections has been associated with administration of an IL-1 blocker in combination with TNF inhibitors. Co-administration of canakinumab with TNF inhibitors is not recommended due to the increased risk of serious infections.

Recommendations

The College of Pharmacy recommends the addition of Ilaris® (canakinumab) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization category for the diagnosis of Systemic Juvenile Idiopathic Arthritis (SJIA) with the following criteria:

Ilaris® (Canakinumab) Approval Criteria for Systemic Juvenile Idiopathic Arthritis (SJIA):

1. An FDA approved indication of Systemic Juvenile Idiopathic Arthritis; and
2. Ilaris® will not be approved for concurrent use with a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, or 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. Dosing should not be more often than once every 4 weeks.
    a. Two years of age and older and body weight greater than 7.5kg: 4mg/kg every 4 weeks; max dose 300mg/dose; and
5. Recent trials of one Tier-1 product and all appropriate Tier-2 products that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
6. Prior stabilization on Ilaris® documented within the last 100 days.
7. Approvals will be for the duration of one year.

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®)
mesalamine		golimumab (Simponi® Aria™)
6-mercaptopurine		infliximab (Remicade®)
azathioprine		rituximab (Rituxan®)
NSAIDs		tocilizumab (Actemra®)
		tofacitinib (Xeljanz®)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

Tier structure based on supplemental rebate participation.
DMARDs= Disease Modifying Anti-Rheumatic Drugs
*Supplemental rebated products
+ May be rebated to Tier-2 status only

Utilization Details of Ilaris® (Canakinumab): Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
ILARIS 180 MG/1.2 VIAL	45	7	$763,114.95	$421.38	$16,958.11	100.00%
TOTAL	**45**	**7***	**$763,114.95**	**$421.38**	**$16,958.11**	**100.00%**

*Total number of unduplicated members.

[1] American College of Rheumatology, "2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis," 2013

[2] UpToDate. Systemic Juvenile Idiopathic Arthritis: Clinical Manifestations and Diagnosis. Available online at: http://www.uptodate.com/contents/systemic-juvenile-idiopathic-arthritis-clinical-manifestations-and-diagnosis?source=search_result&search=SJIA&selectedTitle=2%7E10. Last revised 9/9/14. Last accessed 2/24/15.

[3] UpToDate. Systemic Juvenile Idiopathic Arthritis: Course, Prognosis, and Complications. Available online at: http://www.uptodate.com/contents/systemic-juvenile-idiopathic-arthritis-course-prognosis-and-complications?source=see_link. Last revised 12/11/14. Last accessed 2/24/15.

[4] FDA: Safety Information: Ilaris (canakinumab). Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm327827.htm. Last revised 11/17/14. Last accessed 2/9/15.

[5] Ilaris® Prescribing Information. Available online at: http://pharma.us.novartis.com/product/pi/pdf/ilaris.pdf. Last revised 10/2014. Last accessed 2/9/15.

Appendix H

30-Day Notice to Prior Authorize Sylvant™ (Siltuximab)

Oklahoma Health Care Authority
March 2015

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

Castleman's disease (CD) is a rare disease of lymph nodes and related tissues. CD is not cancer, but a lymphoproliferative disorder or an abnormal overgrowth of cells of the lymph system.

There are two main classifications of CD, localized and multicentric. Localized Castleman's disease (LCD) is the more common type. LCD is usually confined to lymph nodes in the chest or abdomen and is often cured when the affected lymph nodes are removed. Multicentric Castleman's disease (MCD) affects more than one group of lymph nodes and can also affect other organs containing lymphoid tissue. MCD is strongly associated with immunosuppression and Human Immunodeficiency Virus (HIV) or Human Herpesvirus-8 (HHV-8) infections. MCD is considered to be mediated by the interplay among deregulated inflammatory mediators, particularly interleukin (IL)-6, which may be driven by HHV-8 in some cases, resulting in lymphovascular proliferation and systemic manifestations of the disease.

Symptoms of MCD include fever, night sweats, fatigue, anorexia, weight loss, organomegaly, diffuse polyadenopathy, and edema. A number of laboratory abnormalities are seen, including thrombocytosis, thrombocytopenia, anemia, leukocytosis, hypoalbuminemia, hypergammaglobulinemia, and increases in acute-phase proteins like C-reactive protein (CRP), sedimentation rates, fibrinogen, and interleukin (IL)-6. MCD can progress to severe pancytopenia, multi-organ failure, and lymphoma.

The United States 10-year prevalence of MCD has been estimated to be 2.4 per million. MCD typically presents later in the fifth to sixth decade of life (mean age of 53 years), and is found most commonly in Caucasian males.

Patients with MCD require systemic treatment and their prognosis is unfavorable. Treatment selection is based on HIV/HHV-8 status and the clinical aggressiveness of the disease. Sylvant™ (siltuximab) is the first FDA approved therapy indicated for treating patients with MCD. Other treatments commonly used for MCD include oral steroids (prednisone), immunotherapy with monoclonal antibodies rituximab or tocilizumab, chemotherapy with etoposide, or antiviral therapy with ganciclovir.

Sylvant™ (Siltuximab) Product Summary[6,7]

FDA Approved: April 2014

Indications: Sylvant™ (siltuximab) is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with MCD who are HIV negative and HHV-8 negative.

Limitations of Use: Siltuximab was not studied in patients with MCD who are HIV positive or HHV-8 positive because siltuximab did not bind to virally produced IL-6 in a nonclinical study.

Dosing: Siltuximab is administered via intravenous (IV) infusion every three weeks until treatment failure.

- Siltuximab is available as 100mg and 400mg lyophilized powder in a single-use vial for IV infusion.
- The recommended dosing of siltuximab is 11mg/kg given over one hour IV every three weeks.
- Hematology laboratory tests should be performed prior to each dose of siltuximab therapy for the first 12 months and every three dosing cycles thereafter. If treatment criteria outlined in the table below are not met, consideration should be given to delaying treatment with siltuximab. It is not recommended to reduce the dose of siltuximab.

Laboratory Parameter	Requirements before 1st Siltuximab Dose	Retreatment Criteria
Absolute Neutrophil Count	≥1.0 x 10^9/L	≥1.0 x 10^9/L
Platelet Count	≥75 x 10^9/L	≥50 x 10^9/L
Hemoglobin*	<17 g/dL	<17 g/dL

*Siltuximab may increase hemoglobin levels in MCD patients.

Mechanism of Action: Siltuximab binds human IL-6 and prevents the binding of IL-6 to both soluble and membrane bound IL-6 receptors. IL-6 has been shown to be involved in diverse normal physiologic processes such as induction of immunoglobulin secretion. Overproduction of IL-6 has been linked to systemic manifestations in patients with MCD.

Contraindications: Severe hypersensitivity reaction to siltuximab or any of the excipients in the siltuximab product.

Warnings and Precautions:

- Concurrent Active Severe Infections: Siltuximab should not be administered to patients with severe infections until the infection resolves. Siltuximab may mask signs and symptoms of acute inflammation including suppression of fever.
- Vaccinations: Live vaccines should not be administered to patients receiving siltuximab.
- Infusion Related Reactions and Hypersensitivity: Siltuximab therapy should be discontinued if the member develops signs of anaphylaxis. If the patient develops a mild to moderate infusion reaction and the reaction resolves, siltuximab may be restarted at a lower infusion rate. Consider pre-medication with antihistamines, acetaminophen, and corticosteroids. Siltuximab should be administered in a setting that provides resuscitation equipment, medication, and personnel trained to provide resuscitation.
- Gastrointestinal Perforation: Gastrointestinal (GI) perforation has been reported in clinical trials with siltuximab although not in MCD trials. Use with caution in patients who may be at increased risk for GI perforation.
- Cytochrome P450 Substrates: Cytochrome P450s in the liver are down regulated by infection and inflammation stimuli including cytokines such as IL-6. Inhibition of IL-6 signaling in patients treated with siltuximab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates. Patients being treated with CYP450 substrates with a narrow therapeutic index should be monitored closely.

Adverse Reactions:

- The most common adverse reactions (>10% compared to placebo) reported during clinical trials included pruritus, increased weight, rash, hyperuricemia, and upper respiratory tract infection.

Efficacy:

- The efficacy of siltuximab for the treatment of patients with MCD was established in a phase 2 randomized, double blind, placebo-controlled study. The study included 53 patients who were randomized to Best Supportive Care (BSC) and siltuximab 11mg/kg every three weeks and 26 patients who were randomized to BSC and placebo. The median age of the patients included was 48 years (range 20 to 78), and treatment was continued until treatment failure (defined as disease progression based on increase in symptoms, radiologic progression, or deterioration in performance status).
- The major efficacy outcome of the study was durable tumor and symptomatic response, defined as tumor response assessed by independent review and complete resolution or stabilization of MCD symptoms.
- The durable tumor and symptomatic response in the siltuximab arm was 34% compared to 0% in the placebo arm (95% Confidence Interval: 11.1, 54.8; *p*= 0.0012).

Cost:

Medication Name	Cost/Vial+	Cost/Dose*	Cost/Year*
Sylvant™ (siltuximab)	$3,518.59	$7,037.18	$119,632.06

+ Estimated acquisition cost for 400mg vial.

*Dosing based on recommended dose of 11mg/kg for a 70kg patient.

Utilization:

- There have been no medical or pharmacy claims for Sylvant™ (siltuximab) since its approval in April 2014.

Recommendations

The College of Pharmacy recommends the prior authorization of Sylvant™ (siltuximab) with the following criteria:

Sylvant™ (Siltuximab) Approval Criteria:

1. An FDA approved diagnosis of Multicentric Castleman's Disease (also known as giant lymph node hyperplasia); and
2. Member must be Human Immunodeficiency Virus (HIV) and Human Herpesvirus-8 (HHV-8) negative; and
3. Member must be 18 years of age or older; and
4. The following FDA approved dosing restrictions will apply:
    a. 11 mg/kg via intravenous (IV) infusion every 3 weeks until treatment failure (defined as disease progression based on increase in symptoms, radiologic progression, or deterioration in performance status); and
5. Sylvant™ must be administered in a clinical setting able to provide resuscitation equipment, medications, and trained personnel; and
6. The prescriber must verify that a complete blood count (CBC) will be done prior to each dose for the first 12 months and for an additional three doses thereafter; and
7. Approvals will be for the duration of six months.

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[1] American Cancer Society. Castleman Disease. Available online at: http://www.cancer.org/cancer/castlemandisease/detailedguide/castleman-disease-what-is-castleman-disease. Last revised 07/07/14. Last accessed 02/23/15.

[2] El-Osta HE, Kurzrock R. Castleman's Disease: From Basic Mechanisms to Molecular Therapeutics. *The Oncologist.* 2011; 16:497-511.

[3] UpToDate. Multicentic Castleman's Disease. Available online at: http://www.uptodate.com/contents/multicentric-castlemans-disease?source=search_result&search=multicentric+castleman+disease&selectedTitle=1%7E17. Last revised 01/05/2015. Last accessed 02/23/15.

[4] Robinson D, Reynolds M, Casper C, et al. Clinical Epidemiology and Treatment Patterns of Patients with Multicentric Castleman Disease: Results from Two US Treatment Centres. *British Journal of Haematology.* 2014; 165:39-48.

[5] Johnson and Johnson. European Commision Approves Sylvant® (Siltuximab) as a Treatment for Patients with Multicentric Castleman's Disease (MCD). Available online at: http://www.investor.jnj.com/releasedetail.cfm?ReleaseID=852821. Last revised 06/05/14. Last accessed 02/23/15.

[6] Food and Drug Administration. FDA approves Sylvant for Rare Castleman's Disease. Available on line at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm394522.htm. Last revised 04/24/14. Last accessed 02/23/15.

[7] Sylvant™ Prescribing Information. Janssen Biotech Inc. Available online at: http://www.sylvant.com/shared/product/sylvant/sylvant-prescribing-information.pdf. Last revised 06/2014. Last accessed 02/23/15.

Appendix I

Fiscal Year 2014 Annual Review of Topical Antifungal Medications and 30-Day Notice to Prior Authorize Ecoza™ (Econazole Nitrate), Jublia® (Efinaconazole), and Kerydin™ (Tavaborole)

Oklahoma Health Care Authority
March 2015

Current Prior Authorization Criteria

Topical Antifungal Medications	
Tier-1	**Tier-2**
ciclopirox cream	butenafine (Mentax®)
clotrimazole (Rx) cream, solution	ciclopirox solution, shampoo, gel, suspension (Penlac® and Loprox®)
clotrimazole (OTC)* cream	clotrimazole/betamethasone cream, lotion
econazole cream	ketoconazole foam (Extina®)
ketoconazole cream, shampoo	ketoconazole gel (Xolegel™)
nystatin cream, ointment, powder	luliconazole cream (Luzu™)
terbinafine (OTC)* cream	miconazole/zinc oxide/white petrolatum (Vusion®)
tolnaftate (OTC)*cream	naftifine (Naftin®)
	nystatin/triamcinolone cream, ointment
	oxiconazole (Oxistat®)
	salicylic acid (Bensal HP®)
	sertaconazole nitrate (Ertaczo®)
	sulconazole (Exelderm®)

*Over-the-counter (OTC) antifungal products are covered for pediatric members 0-20 years of age without prior authorization.

Topical Antifungal Tier-2 Approval Criteria:

1. Documented trials of at least two Tier-1 topical antifungal products within the last 30 days.
2. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).
3. Authorization of combination products nystatin/triamcinolone or clotrimazole/betamethasone requires a patient-specific, clinically significant reason why the member cannot use the individual components separately.

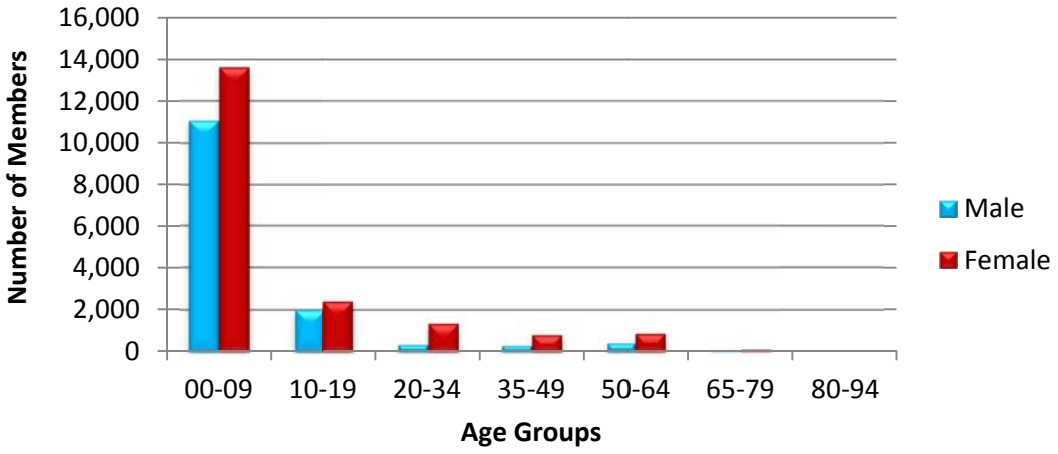
Utilization of Topical Antifungal Medications

Comparison of Fiscal Years

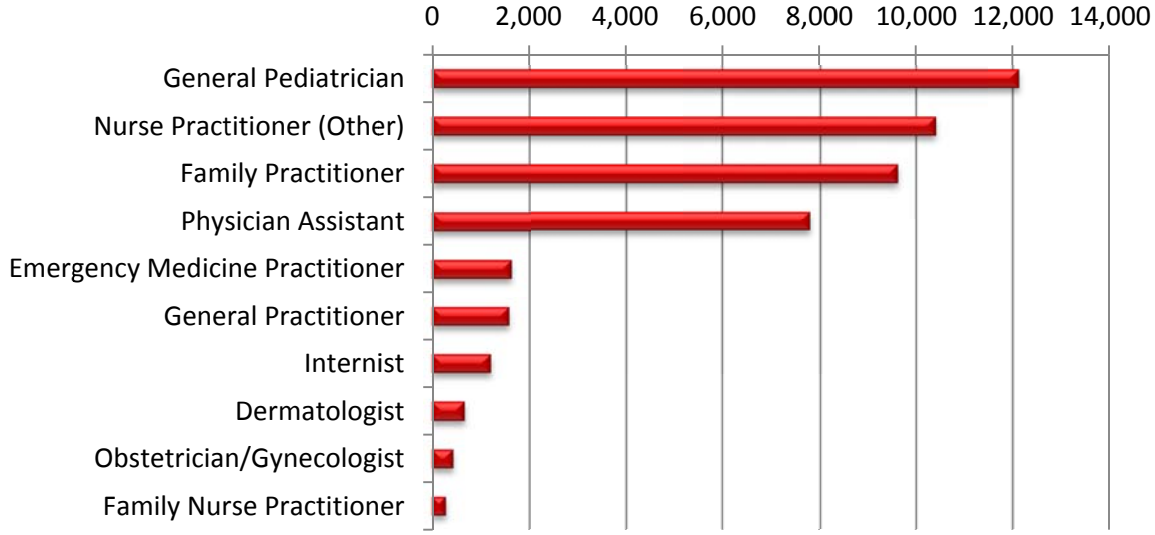
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	33,839	48,036	$1,403,256.20	$29.21	$2.15	1,782,303	653,669
2014	33,286	47,313	$1,026,715.52	$21.70	$1.55	1,699,293	660,633
% Change	**-1.60%**	**-1.50%**	**-26.80%**	**-25.70%**	**-27.90%**	**-4.70%**	**1.10%**
Change	**-553**	**-723**	**-$376,540.68**	**-$7.51**	**-$0.60**	**-83,010**	**6,964**

*Total number of unduplicated members.

Demographics of Members Utilizing Topical Antifungal Medications

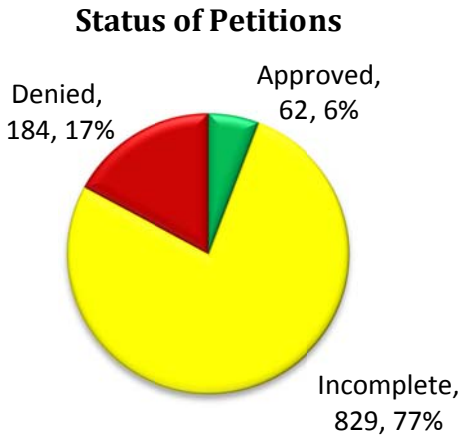


Top Prescriber Specialties of Topical Antifungal Medications by Number of Claims



Prior Authorization of Topical Antifungal Medications

There were 1,075 petitions submitted for the Topical Antifungal Medication Product Based Prior Authorization category during fiscal year 2014. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expirations:

- Loprox® Gel (ciclopirox): September 2018
- Extina® (ketoconazole foam 2%): October 2018
- Luzu™ (luliconazole): November 2018
- Xolegel™ (ketoconazole gel): December 2018
- Vusion® (miconazole/zinc oxide/white petrolatum): March 2028
- Naftin® (naftifine gel 2%): January 2033

New FDA Approvals:

- October 2013: The FDA approved approved Ecoza™ (econazole nitrate topical foam 1%) for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older. Ecoza™ foam is the first and only FDA approved prescription econazole nitrate foam in the United States.
- June 2014: The FDA approved Jublia® (efinaconazole 10% topical solution), the first topical triazole approved for the treatment of onychomycosis of the toenails.
- July 2014: The FDA approved Kerydin™ (tavaborole 5% solution), the first oxaborole-class topical antifungal approved for the treatment of onychomycosis of the toenails. Tavaborole is indicated specifically for onychomycosis caused by *Trichophyton rubrum* or *Trichophyton mentagrophytes*.

Ecoza™ (Econazole Nitrate) Product Summary[5]

Indications: Ecoza™ (econazole nitrate) is an azole antifungal indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum* in patients 12 years of age and older.

Dosing: Econazole nitrate is available as 1% topical foam. Each gram of the foam contains 10mg of econazole nitrate.

- Econazole nitrate is administered topically; it is not indicated for oral, ophthalmic, or vaginal use.
- The recommended dosing of econazole nitrate is topical application to affected areas once daily for 4 weeks.

Mechanism of Action: Econazole nitrate, an azole antifungal agent, inhibits fungal cytochrome P-450-mediated 14 alpha-lanosterol demethylase enzyme. This enzyme functions to convert lanosterol to ergosterol. The accumulation of sterols contributes to the loss of ergosterol in the fungal cell wall.

Contraindications: None

Warnings and Precautions:

- Flammability: Econazole nitrate topical foam is flammable. Avoid heat, flame, and smoking during and immediately following application.

Adverse Reactions: The most common adverse drug reactions experienced during clinical trials with econazole nitrate topical foam were application site reactions.

Use in Special Populations:

- Pregnancy: Econazole nitrate topical foam is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- Nursing Mothers: It is not known whether econazole nitrate topical foam is excreted in human milk.
- Pediatric Patients: The safety and effectiveness of econazole nitrate topical foam have not been established in pediatric patients younger than 12 years of age. The safety findings for subjects 12 to 17 years were similar to those in the adult population.
- Geriatric Patients: The safety and effectiveness of econazole nitrate topical foam were similar in clinical trials between geriatric patients and younger patients.

Efficacy:

- In two multi-center, randomized, double-blind, vehicle-controlled clinical trials a total of 505 subjects with interdigital tinea pedis were randomized 1:1 to econazole topical foam or vehicle; subjects applied the assigned medication once daily for 4 weeks.
- The severity of erythema, scaling, fissuring, maceration, vesiculation, and pruritus were graded using a 4-point scale (none, mild, moderate, severe).
- A total of 339 subjects with positive fungal cultures were evaluated for efficacy. Efficacy was evaluated on Day 43, two weeks post-treatment with treatment success being

defined as complete cure (negative KOH and fungal culture and no evidence of clinical disease).

	Trial 1		Trial 2	
	Econazole Topical Foam N = 82 n(%)	**Foam Vehicle N = 83 n(%)**	**Econazole Topical Foam N = 91 n(%)**	**Foam Vehicle N = 83 n(%)**
Complete Cure[a]	19 (23.2%)	2 (2.4%)	23 (25.3%)	4 (4.8%)
Effective Treatment[b]	40 (48.8%)	9 (10.8%)	44 (48.4%)	9 (10.8%)
Mycological Cure[c]	56 (68.3%)	13 (15.7%)	61 (67.0%)	15 (18.1%)

[a] Mycological cure and an absence of clinical signs and symptoms (erythema, scaling, fissuring, maceration, vesiculation, or pruritus).

[b] Mycological cure and no or mild erythema and/or scaling with all other signs and symptoms absent.

[c] Negative KOH and fungal culture.

Cost:

Medication Name	Cost/Gram	Cost/Canister or Tube
Clotrimazole 1% Cream	[+]$0.97	[+]$14.55
Ecoza™ (econazole nitrate)	***$5.73**	***$401.10**

[+]Cost based on state maximum allowable cost (SMAC) and 15gram tube.

*Cost based on estimated acquisition cost (EAC) and 70gram canister.

Julia® (Efinaconazole) Product Summary[6]

Indications: Julia® (efinaconazole) is an azole antifungal indicated for the topical treatment of onychomycosis of the toenails due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

Dosing: Efinaconazole is available as 10% topical solution.

- Efinaconazole is for topical use only.
- The recommended dosing for efinaconazole is a once daily application to the affected toenails for 48 weeks using the brush applicator.
- When applying efinaconazole, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate, should be completely covered.

Mechanism of Action: Efinaconazole is an azole antifungal. Efinaconazole inhibits fungal lanosterol 14α-demethylase involved in the biosynthesis of ergosterol, a constituent of fungal cell membranes.

Contraindications: None

Warnings and Precautions: None

Adverse Reactions: The most common (at least 1% of subjects) adverse drug reactions experienced during clinical trials with efinaconazole were ingrown toenail, application site dermatitis, application site vesicles, and application site pain.

Use in Special Populations:

- Pregnancy: Efinaconazole is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- Nursing Mothers: It is not known whether efinaconazole is excreted in human milk.
- Pediatric Patients: The safety and effectiveness of efinaconazole have not been established in pediatric patients.
- Geriatric Patients: The safety and effectiveness of efinaconazole were similar in clinical trials between geriatric patients and younger patients.

Efficacy:

- The safety and efficacy of efinaconazole for the treatment of onychomycosis of the toenail were assessed in two 52-week prospective, multi-center, randomized, double-blind clinical trials in patients 18 years and older with 20% to 50% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement. The trials compared 48-weeks of treatment with efinaconazole to the vehicle solution.
- The Complete Cure rate was assessed at Week 52 (4-weeks after completion of therapy). Complete cure was defined as 0% involvement of the target toenail (no clinical evidence of onychomycosis of the target toenail) in addition to Mycologic Cure, defined as both negative fungal culture and negative KOH.

	Trial 1		Trial 2	
	Efinaconazole N = 656 n(%)	**Vehicle N = 214 n(%)**	**Efinaconazole N = 580 n(%)**	**Vehicle N = 201 n(%)**
Complete Cure[a]	117 (17.8%)	7 (3.3%)	88 (15.2%)	11 (5.5%)
Complete or Almost Complete Cure[b]	173 (26.4%)	15 (7.0%)	136 (23.4%)	15 (7.5%)
Mycological Cure[c]	362 (55.2%)	36 (16.8%)	310 (53.4%)	34 (16.9%)

[a] Complete cure defined as 0% clinical involvement of the target toenail plus negative KOH and negative culture.

[b] Complete or almost complete cure defined as ≤5% affected target toenail area involved and negative KOH and culture.

[c] Mycologic cure defined as negative KOH and negative culture.

Cost:

Medication Name	*Cost/mL or Tablet	*Cost/Bottle or Regimen
Terbinafine 250mg Oral Tablets	+$0.18	∞$15.12 (84 tablets)
Penlac® (ciclopirox) Topical Solution 8%	+$5.37	+$35.42 (6.6mL)
Jublia® (efinaconazole) Topical Solution 10%	***$118.54**	***$474.16 (4mL)**

+Cost based on state maximum allowable cost (SMAC).

∞ Cost per 12 weeks of oral therapy.

*Cost based on estimated acquisition cost (EAC).

Kerydin™ (Tavaborole) Product Summary[7]

Indications: Kerydin™ (tavaborole) is an oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*.

Dosing: Tavaborole is available as 5% topical solution.

- Tavaborole is for topical use only. It is not for oral, ophthalmic, or intravaginal use.
- The recommended dosing for tavaborole is a once daily application to the affected toenails for 48 weeks.
- Tavaborole should be applied to the entire toenail surface and under the tip of each toenail being treated.

Mechanism of Action: Tavaborole inhibits fungal protein synthesis by inhibition of an aminoacyl-transfer ribonucleic acid (tRNA) synthetase (AARS).

Contraindications: None

Warnings and Precautions: None

Adverse Reactions: The most common (at least 1% of subjects) adverse drug reactions experienced during clinical trials with tavaborole were application site exfoliation, ingrown toenail, application site erythema, and application site dermatitis.

Use in Special Populations:

- Pregnancy: Tavaborole is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- Nursing Mothers: It is not known whether tavaborole is excreted in human milk.
- Pediatric Patients: The safety and effectiveness of tavaborole have not been established in pediatric patients.
- Geriatric Patients: The safety and effectiveness of tavaborole were similar in clinical trials between geriatric patients and younger patients.

Efficacy:

- The efficacy and safety of tavaborole was evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. Tavaborole or vehicle was applied once daily for 48 weeks in subjects with 20% to 60% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement. A total of 1,194 participated in these two trials.
- Efficacy assessments were made at 52 weeks following a 48-week treatment period. The complete cure efficacy endpoint included negative mycology (negative KOH wet mount and negative fungal culture) and completely clear nail (no clinical evidence of onychomycosis as evidenced by a normal toenail plate, no onycholysis, and no subungual hyperkeratosis).

	Trial 1		Trial 2	
	Tavaborole N=399 n(%)	Vehicle N=194 n(%)	Tavaborole N=396 n(%)	Vehicle N=205 n(%)
Complete Cure[a]	26 (6.5%)	1 (0.5%)	36 (9.1%)	3 (1.5%)
Complete or Almost Complete Cure[b]	61 (15.3%)	3 (1.5%)	71 (17.9%)	8 (3.9%)
Mycological Cure[c]	124 (31.1%)	14 (7.2%)	142 (35.9%)	25 (12.2%)

[a] Complete cure defined as 0% clinical involvement of the target toenail plus negative KOH and negative culture.

[b] Complete or almost complete cure defined as ≤10% affected target toenail area involved and negative KOH and culture.

[c] Mycologic cure defined as negative KOH and negative culture.

Cost:

Medication Name	*Cost/mL or Tablet	*Cost/Bottle or Regimen
Terbinafine 250mg Oral Tablets	+$0.18	∞$15.12 (84 tablets)
Penlac® (ciclopirox) Topical Solution 8%	+$5.37	+$35.42 (6.6mL)
Kerydin™ (tavaborole) Topical Solution 5%	***$129.68**	***$518.72 (4mL)**

+Cost based on state maximum allowable cost (SMAC).

∞ Cost per 12 weeks of oral therapy.

*Cost based on estimated acquisition cost (EAC).

Recommendations

The College of Pharmacy recommends the prior authorization of Julia® (efinaconazole), and Kerydin™ (tavaborole) with the following criteria:

Julia® (Efinaconazole) and Kerydin™ (Tavaborole) Approval Criteria:

1. An FDA approved diagnosis of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes;* and
2. A trial of oral antifungals (12 weeks for toenails); and
3. A patient-specific, clinically significant reason why member cannot use Penlac® (ciclopirox solution).

Additionally the College of Pharmacy recommends the addition of Ecoza™ (econazole nitrate) to Tier-2 of the Topical Antifungal Product Based Prior Authorization category. Current criteria for this category will apply.

Topical Antifungal Tier-2 Approval Criteria:

1. Documented trials of at least two Tier-1 topical antifungal products within the last 30 days.
2. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).

3. Authorization of combination products nystatin/triamcinolone or clotrimazole/betamethasone requires a patient-specific, clinically significant reason why the member cannot use the individual components separately.

Topical Antifungal Medications	
Tier-1	**Tier-2**
ciclopirox cream	butenafine (Mentax®)
clotrimazole (Rx) cream, solution	ciclopirox solution, shampoo, gel, suspension (Penlac® and Loprox®)
clotrimazole (OTC)* cream	clotrimazole/betamethasone cream, lotion
econazole cream	**econazole Nitrate (Ecoza™)**
ketoconazole cream, shampoo	**efinaconazole (Jublia®)**
nystatin cream, ointment, powder	ketoconazole foam (Extina®)
terbinafine (OTC)* cream	ketoconazole gel (Xolegel™)
tolnaftate (OTC)*cream	luliconazole cream (Luzu™)
	miconazole/zinc oxide/white petrolatum (Vusion®)
	naftifine (Naftin®)
	nystatin/triamcinolone cream, ointment
	oxiconazole (Oxistat®)
	salicylic acid (Bensal HP®)
	sertaconazole nitrate (Ertaczo®)
	sulconazole (Exelderm®)
	tavaborole (Kerydin™)

*Over-the-counter (OTC) antifungal products are covered for pediatric members 0-20 years of age without prior authorization.

Utilization Details of Topical Antifungal Medications: Fiscal Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Nystatin Products					
NYSTATIN CREAM 100000	17,489	13,447	$332,450.13	$1.62	$19.01
NYSTATIN OIN 100000	6,715	5,562	$175,463.55	$2.28	$26.13
NYSTOP POW 100000	1,893	1,326	$65,385.94	$2.64	$34.54
NYAMYC POW 100000	1,545	804	$57,224.47	$2.40	$37.04
NYSTATIN POW 100000	588	323	$18,943.12	$2.27	$32.22
Subtotal	**28,230**	**20,288**	**$649,467.21**	**$1.91**	**$23.01**
Clotrimazole Products					
CLOTRIMAZOLE CREAM 1%	9,345	7,727	$210,314.08	$1.56	$22.51
CLOTRIMAZOLE SOL 1%	189	172	$2,400.71	$0.88	$12.70
ATHLETE FOOT CREAM 1%	27	27	$208.51	$0.48	$7.72
CLOTRIMAZOLE POW	13	10	$112.45	$0.43	$8.65
CLOTRIMAZOLE CRYSTALS	2	2	$13.20	$0.26	$6.60
Subtotal	**9,576**	**7,921**	**$213,048.95**	**$1.54**	**$22.25**
Ketoconazole Products					
KETOCONAZOLE CRE 2%	4,312	3,658	$73,119.25	$1.08	$16.96
KETOCONAZOLE SHA 2%	2,539	1,614	$40,898.83	$0.53	$16.11
Subtotal	**6,851**	**5,117**	**$114,018.08**	**$0.79**	**$16.64**
Econazole Products					
ECONAZOLE CREAM 1%	1,238	1,005	$22,403.93	$1.21	$18.10
Subtotal	**1,238**	**1,005**	**$22,403.93**	**$1.21**	**$18.10**
Ciclopirox Products					
CICLOPIROX CREAM 0.77%	888	735	$17,667.87	$1.50	$19.90
Subtotal	**888**	**735**	**$17,667.87**	**$1.50**	**$19.90**
Terbinafine Products					
TERBINAFINE CREAM 1%	368	326	$4,910.33	$0.94	$13.34
LAMISIL AT CREAM 1%	80	74	$1,267.80	$1.17	$15.85
ATHLETE FOOT CREAM 1%	19	18	$284.47	$1.21	$14.97
ATHLETE FOOT CREAM AF	7	7	$94.45	$1.29	$13.49
Subtotal	**474**	**423**	**$6,557.05**	**$0.99**	**$13.83**
Tolnaftate Products					
TOLNAFTATE CREAM 1%	7	7	$95.34	$0.66	$13.62
SM ANTIFUNGL CREAM 1%	1	1	$9.36	$0.31	$9.36
ANTIFUNGAL CREAM 1%	1	1	$8.41	$0.84	$8.41
Subtotal	**9**	**9**	**$113.11**	**$0.61**	**$12.57**
Miconazole Products					
MICONAZOLE POW NITRATE	6	5	$173.07	$0.96	$28.85
ANTIFUNGAL CREAM 2%	5	1	$38.80	$1.11	$7.76
BAZA ANTIFUN CREAM 2%	1	1	$4.63	$0.31	$4.63
MICONAZOLE CREAM 2%	1	1	$2.37	$0.34	$2.37
Subtotal	**13**	**8**	**$218.87**	**$0.92**	**$16.84**
Tier-1 Subtotal	**47,279**	**35,506**	**$1,023,495.07**	**$1.18**	**$21.65**
Clotrimazole/Betamethasone Products					
CLOTRIM/BETA CREAM DIPROP	10	8	$429.67	$2.70	$42.97
CLOTRIM/BETA CREAM 1-0.05%	3	2	$78.42	$2.24	$26.14
CLOTRIM/BETA LOT DIPROP	2	2	$72.20	$1.81	$36.10

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Subtotal	**15**	**12**	**$580.29**	**$2.48**	**$38.69**
Ciclopirox Products					
CICLOPIROX SHA 1%	5	2	$399.41	$2.94	$79.88
CICLOPIROX SOL 8%	3	2	$115.39	$0.77	$38.46
Subtotal	**8**	**4**	**$514.80**	**$1.80**	**$64.35**
Nystatin/Triamcinolone Products					
NYSTAT/TRIAM CREAM	4	3	$426.06	$7.22	$106.52
NYSTAT/TRIAM OIN	4	1	$288.16	$7.20	$72.04
Subtotal	**8**	**4**	**$714.22**	**$7.21**	**$89.28**
Naftifine Products					
NAFTIN CREAM 2%	2	1	$1,224.06	$20.40	$612.03
Subtotal	**2**	**1**	**$1,224.06**	**$20.40**	**$612.03**
Oxiconazole Products					
OXICONAZOLE NITRATE LOTION 1%	1	1	$187.08	$6.24	$187.08
Subtotal	**1**	**1**	**$187.08**	**$6.24**	**$187.08**
Tier-2 Subtotal	**34**	**22**	**$3,220.45**	**$7.63**	**$94.72**
Total	**47,313**	**33,286***	**$1,026,715.52**	**$1.55**	**$21.70**

*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 02/24/2015. Last accessed 02/25/2015.

[2] Quinnova Pharmaceuticals. Quinnova Pharmaceuticals Announces the Launch of ECOZA™ (econazole nitrate) topical foam, 1%. Available online at: http://exeltis.com/quinnova-pharmaceuticals-announces/. Last revised 03/26/2014. Last accessed 02/25/2015.

[3] Valeant Pharmaceuticals. Valeant Pharmaceuticals Announces FDA Approval Of Jublia® for the Treatment of Onychomycosis. Available online at: http://ir.valeant.com/investor-relations/news-releases/news-release-details/2014/Valeant-Pharmaceuticals-Announces-FDA-Approval-Of-Jublia-for-the-Treatment-of-Onychomycosis/default.aspx. Last revised 06/09/2014. Last accessed 02/25/2015.

[4] Lowes, Robert: Medscape. FDA Oks Another Topical Drug for Onychomycosis (Kerydin). Available online at: http://www.medscape.com/viewarticle/828035. Last revised 07/09/2014. Last accessed 02/25/2015.

[5] Ecoza™ Product Information. Quinnova Pharmaceuticals, LLC. Available online at: http://dermatology.exeltisusa.com/. Last revised 10/2013. Last accessed 02/25/2015.

[6] Jublia® Product Information. Valeant Pharmaceuticals North America LLC. Available online at: http://www.jubliarx.com/. Last revised 06/2014. Last accessed 02/25/2015.

[7] Kerydin™ Product Information. Anacor Pharmaceuticals Inc. Available online at: http://www.kerydin.com/. Last revised 07/2014. Last accessed 02/25/15.

Appendix J

Fiscal Year 2014 Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Izba® (Travoprost Ophthalmic Solution)

Oklahoma Health Care Authority
March 2015

Current Prior Authorization Criteria

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must attempt at least three Tier-1 trials of a minimum of four weeks duration each within the last 120 days. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 products; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 products.
5. The member must have had a comprehensive, dilated eye exam within the last 365 day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

*A detailed tier chart can be found in the recommendations section at the end of this report.

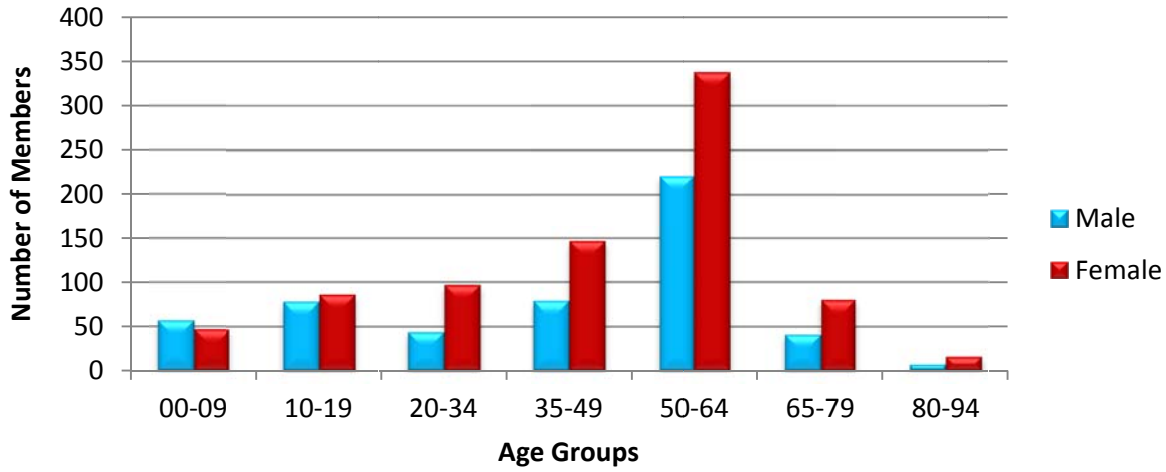
Utilization of Glaucoma Medications

Comparison of Fiscal Years

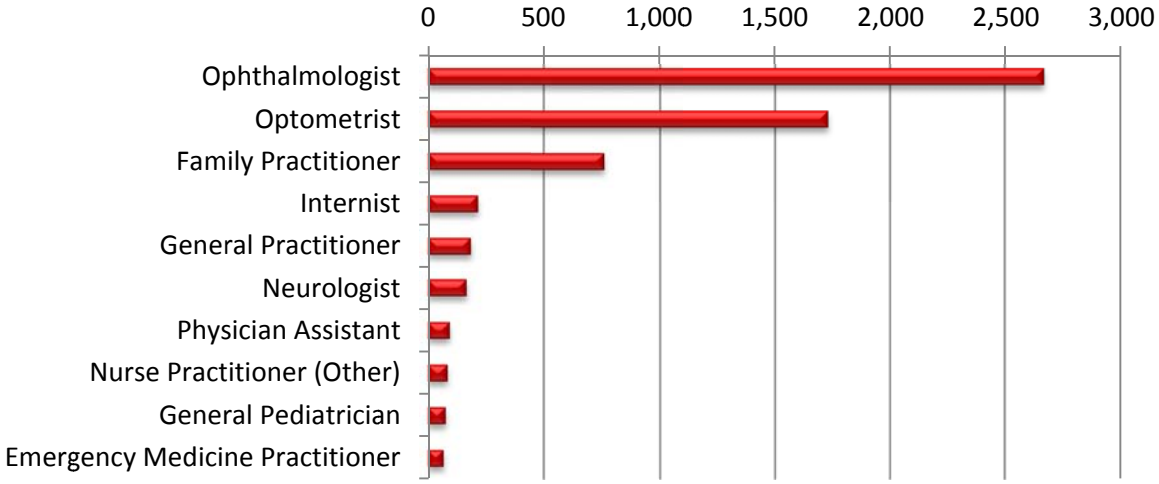
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	1,327	6,407	$465,386.09	$72.64	$2.31	81,984	201,507
2014	1,338	6,381	$453,007.37	$70.99	$2.27	79,681	199,504
% Change	**0.80%**	**-0.40%**	**-2.70%**	**-2.30%**	**-1.70%**	**-2.80%**	**-1.00%**
Change	**11**	**-26**	**-$12,378.72**	**-$1.65**	**-$0.04**	**-2,303**	**-2,003**

*Total number of unduplicated members.

Demographics of Members Utilizing Glaucoma Medications



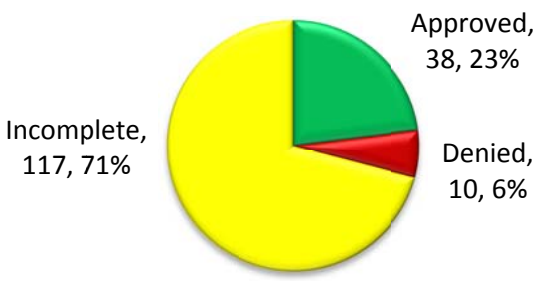
Top Prescriber Specialties of Glaucoma Medications by Number of Claims



Prior Authorization of Glaucoma Medications

There were 165 petitions submitted for glaucoma medications during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1]

Anticipated Patent Expirations:

- Cosopt PF® (dorzolamide/timolol): February 2015
- Zioptan™ (tafluprost): December 2017
- Istalol® (timolol): November 2018
- Simbrinza™ (brinzolamide/brimonidine): December 2019
- Rescula® (unoprostone): July 2021
- Combigan® (brimonidine/timolol): April 2022
- Alphagan-P® (brimonidine): March 2024

New FDA Approvals:

- Izba® (travoprost): May 2014

Izba® (Travoprost Ophthalmic Solution)[2]

Indications: Izba® (travoprost ophthalmic solution) is a prostaglandin analog indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Dosing:

- Izba® is available as an ophthalmic solution containing 0.03mg/mL travoprost (0.003%).
- The recommended dosing of travoprost is one drop in the affected eye(s) once daily in the evening.
- Contact lenses should be removed prior to installation of travoprost and may be reinserted 15 minutes following administration.

Mechanism of Action:

- Travoprost free acid, a prostaglandin analog is a selective Prostaglandin F (FP) receptor agonist which is believed to reduce intraocular pressure by increasing uveoscleral outflow. The exact mechanism of action is unknown at this time.

Warnings and Precautions:

- Pigmentation: Pigmentation of the iris, periorbital tissue (eyelid), and eyelashes can occur. Iris pigmentation is likely to be permanent.
- Eyelash changes: Gradual change to eyelashes including increased length, thickness, and number of lashes may occur. This effect is usually reversible.
- Intraocular Inflammation: Travoprost should be used with caution in patients with active intraocular inflammation because the inflammation may be exacerbated.
- Macular edema: Macular edema, including cystoid macular edema, has been reported during treatment with travoprost ophthalmic solution. Travoprost should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.
- Bacterial keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Adverse Reactions:

- Ocular hyperemia: Most common adverse reaction reported in 12% of patients.

Clinical Studies:

- A single three month trial was conducted to compare the intraocular lowering effect of Izba® (travoprost 0.003%) to Travatan® (travoprost 0.004%) with both dosed once daily in the evening in adult patients with open angle glaucoma or ocular hypertension.
- The differences in mean intraocular pressure at all visits and time points were within +/- 1 mmHg, demonstrating equivalence of Izba® to Travtan® in lowering intraocular pressure.
- The mean intraocular pressure reduction from baseline in the Izba® group ranged from 7.1 to 8.2 mmHg and in the Travatan® group ranged from 7.1 to 8.4 mmHg.

Cost Comparison:

- Izba® cost and launch date information is currently unavailable.

Recommendations

The College of Pharmacy recommends the placement of Izba® (travoprost) into Tier-2 of the Glaucoma Medications Product Based Prior Authorization (PBPA) category. The existing criteria for this category will apply.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must attempt at least three Tier-1 trials of a minimum of four weeks duration each within the last 120 days. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 products; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 products.
5. The member must have had a comprehensive, dilated eye exam within the last 365 day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Glaucoma Medications*	
Tier-1	**Tier-2**
Beta-Blockers	
betaxolol (Betoptic® 0.5%)	betaxolol (Betoptic-S®)
carteolol 1% soln (Ocupress®)	brimonidine/timolol (Combigan®)
dorzolamide/timolol (Cosopt®)	timolol maleate (Timoptic Ocudose®)
levobunolol (Betagan®)	
metipranolol (OptiPranolol®)	
timolol maleate (Betimol®, Istalol®, Timoptic®, Timoptic-XE®)	
Prostaglandin Analogs	
travoprost 0.004% (Travatan-Z®)	bimatoprost (Lumigan®)
latanoprost (Xalatan®)	tafluprost (Zioptan™)
	travoprost 0.004% (Travatan®)
	unoprostone (Rescula®)
	travoprost 0.003% (Izba®)
Adrenergic Agonists	
dipivefrin (Propine®)	
Alpha-2 Adrenergic Agonists	
brimonidine 0.2%	brimonidine (Alphagan-P® 0.1%, 0.15%)
brinzolamide/brimonidine (Simbrinza™)	apraclonidine (Iopidine®)
	brimonidine/timolol (Combigan®)
Carbonic Anhydrase Inhibitors	
dorzolamide/timolol (Cosopt®)	
dorzolamide (Trusopt®)	
brinzolamide (Azopt®)	
brinzolamide/brimonidine (Simbrinza™)	
acetazolamide (Diamox®)+	
methazolamide (Neptazane®)+	
(+Indicates Available Oral Products)	
Cholinergic Agonists/Cholinesterase Inhibitors	
pilocarpine (Isopto® Carpine®, Pilopine HS®)	carbachol (Isopto®, Miostat® 1.5%, 3%)
	echothiophate iodide (Phospholine Iodide®)

*Tier structure based on supplemental rebate participation.

Utilization Details of Glaucoma Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 UTILIZATION						
BETA-BLOCKERS						
DORZOLAMIDE/TIMOL SOL	507	151	$10,811.06	$0.57	$21.32	2.39%
TIMOLOL MAL SOL 0.5% OP	502	202	$4,376.96	$0.23	$8.72	0.97%
TIMOLOL GEL SOL 0.5% OP	108	39	$6,238.67	$1.69	$57.77	1.38%
TIMOLOL MAL SOL 0.25% OP	80	36	$595.73	$0.21	$7.45	0.13%
COSOPT PF SOL	22	5	$1,788.37	$2.71	$81.29	0.39%
LEVOBUNOLOL SOL 0.5% OP	20	7	$298.37	$0.40	$14.92	0.07%
BETIMOL SOL 0.5%	19	6	$1,376.11	$2.84	$72.43	0.30%
COSOPT SOL 2-0.5%OP	13	5	$279.18	$0.72	$21.48	0.06%
BETAXOLOL SOL 0.5% OP	8	4	$263.16	$0.95	$32.90	0.06%
TIMOLOL GEL SOL 0.25% OP	5	3	$166.65	$1.72	$33.33	0.04%
BETIMOL SOL 0.25%	3	3	$330.91	$7.35	$110.30	0.07%
CARTEOLOL SOL 1% OP	1	1	$18.20	$0.61	$18.20	0.00%
ISTALOL SOL 0.5% OP	1	1	$230.18	$5.75	$230.18	0.05%
PROSTAGLANDIN ANALOGS						
LATANOPROST SOL 0.005%	1,569	402	$25,920.72	$0.58	$16.52	5.72%
TRAVATAN Z DRO 0.004%	1,324	349	$188,883.02	$4.65	$142.66	41.70%
ALPHA-2 ADRENERGIC AGONISTS						
BRIMONIDINE SOL 0.2% OP	349	126	$4,967.59	$0.48	$14.23	1.10%
BRIMONIDINE SOL 0.15%	158	34	$22,625.05	$4.80	$143.20	4.99%
SIMBRINZA SUS 1-0.2%	35	14	$3,347.50	$3.17	$95.64	0.74%
CARBONIC ANHYDRASE INHIBITORS						
ACETAZOLAMID TAB 250MG	485	140	$31,458.07	$2.20	$64.86	6.94%
DORZOLAMIDE SOL 2% OP	188	63	$5,589.13	$0.90	$29.73	1.23%
ACETAZOLAMID CAP 500MG ER	164	76	$24,819.09	$5.43	$151.34	5.48%
ACETAZOLAMID TAB 125MG	55	9	$2,358.61	$1.46	$42.88	0.52%
METHAZOLAMID TAB 25MG	21	8	$981.76	$2.98	$46.75	0.22%
TIER-1 SUBTOTAL	**5,637**	**1,684**	**$337,724.09**	**$2.28**	**$63.40**	**74.55%**
TIER-2 UTILIZATION						
BETA-BLOCKERS						
COMBIGAN SOL 0.2/0.5%	294	55	$37,549.57	$4.28	$127.72	8.29%
BETOPTIC-S SUS 0.25% OP	14	5	$2,822.57	$5.71	$201.61	0.62%
TIMOPTIC OCU SOL 0.25% OP	1	1	$294.81	$9.83	$294.81	0.07%
PROSTAGLANDIN ANALOGS						
LUMIGAN SOL 0.01%	245	55	$41,871.18	$5.13	$170.90	9.24%
TRAVOPROST DRO 0.004%	11	3	$1,715.02	$5.20	$155.91	0.38%
ZIOPTAN DRO 0.0015%	5	3	$1,424.40	$3.65	$284.88	0.31%
LUMIGAN SOL 0.03%	1	1	$106.43	$3.55	$106.43	0.02%
ALPHA-2 ADRENERGIC AGONISTS						
ALPHAGAN P SOL 0.1%	142	35	$24,235.61	$5.28	$170.67	5.35%
ALPHAGAN P SOL 0.15%	30	4	$5,181.81	$5.08	$172.73	1.14%
CHOLINERIC AGONISTS/CHOLINESTERASE INHIBITORS						
PHOSPHOLINE SOL 0.125%OP	1	1	$81.88	$2.21	$81.88	0.02%
TIER-2 SUBTOTOAL	**744**	**101**	**$115,283.28**	**$4.99**	**$176.75**	**25.44%**
TOTAL	**6,381**	**1,338***	**$453,007.37**	**$2.27**	**$97.75**	**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 02/2015. Last accessed 02/2015.

[2] Izba® Product Information. Alcon®. Available online at: hhttp://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204822s000lbl.pdf. Last revised 05/2014. Last accessed 2/2015.

Appendix K

Fiscal Year 2014 Annual Review of Soliris® (Eculizumab)

Oklahoma Health Care Authority
March 2015

Indication[1]

Soliris® (eculizumab) is a complement inhibitor indicated for:

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Limitation of Use: Eculizumab is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

Current Prior Authorization Criteria

Soliris® (Eculizumab) Approval Criteria:

1. An established diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) or atypical hemolytic uremic syndrome via ICD-9 coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply; and
3. For members younger than 18 years of age, approval may be granted with a documented diagnosis of atypical hemolytic uremic syndrome.

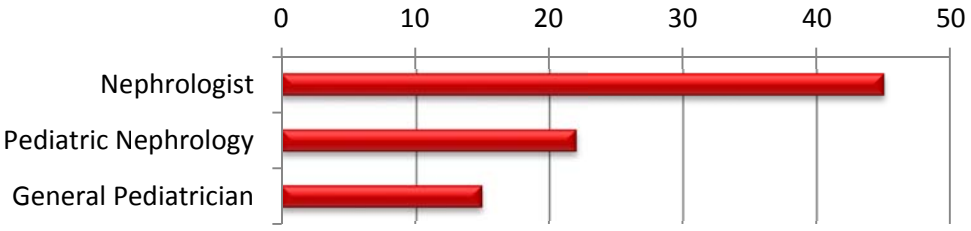
Utilization of Soliris® (Eculizumab): Pharmacy Claims

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	2	34	$565,172.86	$16,622.73	$1,302.24	7,220	434
2014	3	82	$1,580,192.48	$19,270.64	$1,519.42	11,860	1,040
% Change	**50.00%**	**141.20%**	**179.60%**	**15.90%**	**16.70%**	**64.30%**	**139.60%**
Change	**1**	**48**	**$1,015,019.62**	**$2,647.91**	**$217.18**	**4,640**	**606**

*Total number of unduplicated members.

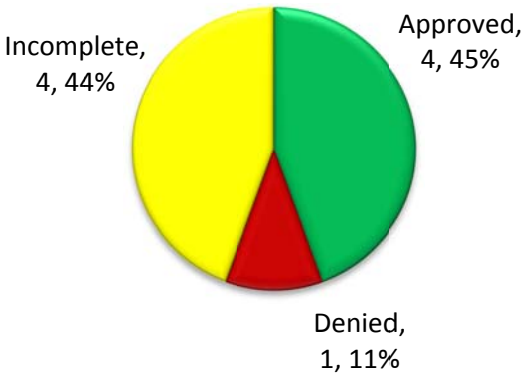
Top Prescriber Specialties of Soliris® (Eculizumab) by Number of Pharmacy Claims



Prior Authorization of Soliris® (Eculizumab)

There were 9 petitions submitted for Soliris® (eculizumab) during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Recommendations

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

Utilization Details of Soliris® (Eculizumab): Fiscal Year 2014

Pharmacy Claims: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
SOLIRIS INJ 10MG/ML	82	3	$1,580,192.48	$1,519.42	$19,270.64
TOTAL	**82**	**3***	**$1,580,192.48**	**$1,519.42**	**$19,270.64**

*Total number of unduplicated members.

Medical Claims: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
SOLIRIS INJ 10MG/ML (J1300)	32	4	$575,675.76	$17,989.87
TOTAL	**32**	**4***	**$575,675.76**	**$17,989.87**

*Total number of unduplicated members.

[1] Soliris® Product Information. Alexion Pharmaceuticals Inc. Available online at: http://www.soliris.net/sites/default/files/assets/soliris_pi.pdf. Last revised 04/2014. Last accessed 02/25/2015.

Appendix L

Fiscal Year 2014 Annual Review of Botulinum Toxins

Oklahoma Health Care Authority
March 2015

Current Prior Authorization Criteria

Botulinum Toxins Approval Criteria:

1. Cosmetic indications will not be covered.
2. A diagnosis of chronic migraine (tension headaches are not a covered diagnosis), non-neurogenic overactive bladder, and neurogenic overactive bladder will require manual review (see specific criteria below).
3. The following indications listed below have been determined to be appropriate and are covered:

Covered Indications
▪ Spasticity associated with: o Cerebral Palsy o Paralysis o Generalized weakness/incomplete paralysis o Larynx o Anal fissure o Esophagus (achalasia and cardiospasms) o Eye and eye movement disorders ▪ Cervical Dystonia

Botulinum toxins are billed through the medical claims system. They are denied if submitted through the pharmacy point of sale system. There are four covered products in this class: Botox®, Dysport®, Xeomin®, and Myobloc®.

During fiscal year 2013, there was an increase in the number of prior authorizations received for the diagnosis of migraine for Botox®. As a result, the review process by the Oklahoma Health Care Authority physician was enhanced. Specific criteria were developed and dispersed to the prior authorization department at the College of Pharmacy. Prior authorization requests were first reviewed by a clinical pharmacist and if necessary, the prior authorization request was sent to OHCA for a second review from an OHCA physician. At the same time, the prior authorization of Botox® for any covered diagnosis was changed to require a manual prior authorization to ensure appropriate reimbursement for the billing provider.

The botulinum toxin approval criteria for the prevention of chronic migraine headaches, non-neurogenic overactive bladder, and neurogenic overactive bladder were developed internally at OHCA. Medical staff at OHCA then reached out to two SoonerCare contracted neurologists to review the criteria. After consultation, the criteria were altered to incorporate the changes suggested by the neurologists.

Cost Comparison:

Medication	Cost (Based on 3 Months of Therapy)
Migraine Prophylaxis	
amitriptyline 25-150mg/day	$38.13 – $174.03*
venlafaxine 75-150mg/day	$32.73 – $54.33*
propranolol 80-240mg/day	$18.33 – $32.73*
topiramate 50-200mg/day	$21.93 - $25.53*
Botox® 155 units	$975.49+
Overactive Bladder	
oxybutynin ER 5-15mg/day	$97.53-$105.63*
tolterodine ER 2-4mg/day	$483.63*
Botox® 100 units	$673.70+

*Includes monthly dispensing fee.
+One dose of Botox® and the administration fee is $125. If the procedure is done in a facility, there may be additional associated costs.

Place in Therapy:
Due to the modest effect, high cost, and potential for severe adverse reactions, Botox® should be reserved for patients who have failed all available recommended therapies.

Approval Criteria for Botox® for Prevention of Migraine Headaches (other botulinum toxins will not be approved for this diagnosis):

1. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes but is not limited to:
    a. Increased intracranial pressure (e.g. tumor, pseudotumor cerebri, central venous thrombosis, etc.)
    b. Decreased intracranial pressure (e.g. post-lumbar puncture headache, dural tear after trauma, etc.)
2. Migraine headache exacerbation secondary to other medication conditions or therapies have been ruled out and/or treated. This includes but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives
    b. Chronic insomnia
    c. Obstructive sleep apnea
3. Member has no contraindications to Botox® injections; and
4. FDA indications are met:
    a. Member is 18 years of age or older
    b. Member has documented chronic migraine headaches
        i. Frequency of 15 or more days per month; and
        ii. Duration of 4 hours per day or longer
5. The member has failed medical migraine preventative therapy including at least 3 agents in 3 or more categories, but not limited to:
    a. Select antihypertensive therapy such as beta-blocker therapy
    b. Select anticonvulsant therapy
    c. Select antidepressant therapy (e.g. TCA or SNRI)
6. Member is not frequently taking medications which are known to cause medication overuse headaches (MOH or rebound headache) in the absence of intractable conditions

known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes but is not limited to:
    a. Decongestants (alone or in combination products)
    b. Combination analgesics containing caffeine and/or butalbital (>5 days/month)
    c. Narcotics
    d. Analgesic medications including acetaminophen or NSAIDs
    e. Ergotamine-containing medications (>8 days/month)
    f. Triptans (>8 days/month)
7. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last six months by a neurologist for chronic migraine headaches and Botox® recommended as treatment (not necessarily prescribed or administered by a neurologist); and
9. Members who smoke or use tobacco products will not be approved.

Approval Criteria for Botox® for Non-Neurogenic Overactive Bladder (other botulinum toxins will not be approved for this diagnosis):

1. Member must have severe disease (>6 urinary incontinence episodes per day) and specific pathology determined via urodynamic studies; and
2. Member must have participated in behavioral therapy for at least 12 weeks that did not yield adequate clinical results; and
3. Member must have had compliant use of at least three anti-muscarinic or beta-3 adrenoceptor agonist medications for at least 12 weeks each, alone or in combination with behavioral therapy, that did not yield adequate clinical results. One of those trials must have been an extended-release formulation; and
4. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
5. Botox® must be administered by urologist.

Approval Criteria for Botox® for Neurogenic Overactive Bladder (other botulinum toxins will not be approved for this diagnosis):

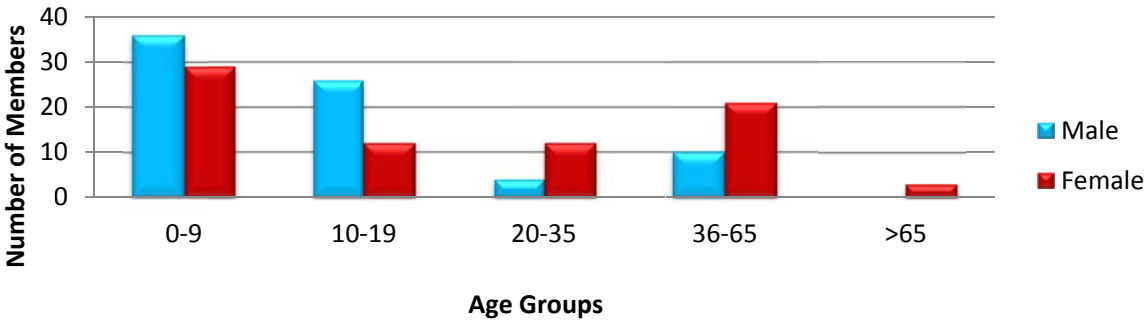
1. Diagnosis of neurogenic bladder including underlying pathological dysfunction subtype confirmed by:
    a. Urodynamic studies to determine pathology and serve to provide objective evidence of bladder and external sphincter function; and
    b. A diary of fluid intake, incontinence, voiding, and catheterization times and amounts to provide a record of actual occurrences.
2. Member must have a clinically significant reason why anticholinergic medications are no longer an option for the member; and
3. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
4. Botox® must be administered by urologist.

Utilization of Botulinum Toxins

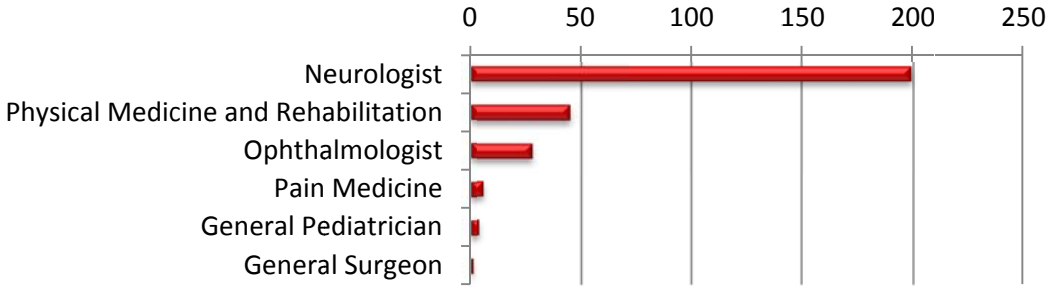
Comparison of Fiscal Years

Fiscal Year	Total Members	Total Claims	Total Cost	Cost/ Claim
2013	188	367	$429,521.87	$1,170.36
2014	153	295	$368,017.00	$1,247.52
% Change	**-18.6%**	**-19.6%**	**-14.3%**	**6.2%**
Change	**-35**	**-72**	**-$61,504.87**	**$77.16**

Demographics of Members Utilizing Botulinum Toxins



Top Prescriber Specialties of Botulinum Toxins by Number of Claims



Prior Authorization of Botulinum Toxins

There were 320 petitions submitted for the Botulinum Toxins category during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions

Market News and Updates[1]

May 2014: The American Urological Association announced a revision to its 2012 *Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults* clinical guidelines. This amendment includes beta-3 adrenoceptor agonists as an additional oral therapy option. The approval criterion for Botox® has been updated to include the change.

Recommendations

The College of Pharmacy recommends no changes at this time.

Utilization Details of Botulinum Toxins: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	PERCENT COST
BOTOX® PRODUCTS					
BOTOX	284	146	$358,227.70	$1,261.37	97.4%
MYOBLOC® PRODUCTS					
MYOBLOC	8	4	$8,512.50	$1,064.06	2.3%
XEOMIN® PRODUCTS					
XEOMIN	3	3	$1,276.80	$425.60	0.3%
TOTAL	**295**	**153***	**$368,017.00**	**$1,247.52**	**100%**

*Total number of unduplicated members.

[1] AUA: News: AUA Announces Amendments to Overactive Bladder, Clinical Practice Guideline. Available online at: http://www.auanet.org/press-media/press_releases/article.cfm?articleNo=380. Last revised 05/18/14. Last accessed 2/16/15.

Appendix M

Annual Review of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)

Oklahoma Health Care Authority
March 2015

Introduction

Singulair® was FDA approved in 1998 as adjunctive therapy for asthma. After receiving additional indications for use in allergic rhinitis in 2004, Singulair® utilization rose dramatically to become one of the top reimbursed medications in the SoonerCare pharmacy program, totaling over $13 million in fiscal year 2007, and $16 million in 2008. The prior authorization of Singulair® was implemented in January of 2009. The patent on Singulair® expired in the spring of 2012 and by August 2012 a state maximum allowable cost was applied. The Drug Utilization Review board voted to remove the majority of the prior authorization restrictions in June 2013. The following utilization report reflects the drop in pricing due to generic availability and an increase in utilization due to the prior authorization removal.

Current Prior Authorization Criteria

Singulair® (Montelukast) Approval Criteria:

1. Asthma Diagnosis:
    a. Montelukast tablets and chewable tablets are available without prior authorization for members 21 years and younger.
    b. A prior authorization is required for members 21 years and older; however the claim will process automatically if the member has a recent diagnosis of mild or moderate persistent asthma, and/or exercise induced asthma in the member's SoonerCare diagnosis claims history.
2. Allergic Rhinitis Diagnosis:
    a. Montelukast tablets and chewable tablets are available without prior authorization for members 21 years and younger.
    b. A prior authorization is required for members 21 years and older, and authorization requires a trial of an oral antihistamine of 14 day duration within the last 30 days.
    c. Allergy medications are not a covered benefit for Insure Oklahoma members.

Singulair® (Montelukast) Granules Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use montelukast tablets or chewable tablets.

Zyflo CR® (Zileuton Extended-Release) Approval Criteria:

1. Member must be 12 years of age or older; and
2. An FDA approved diagnosis of mild or moderate persistent asthma; and
3. Previous trials of an inhaled corticosteroid (ICS) and an ICS/Long-Acting Beta$_2$ Agonist (LABA) combination product within the previous six months with reasoning for trial failure; and
4. Recent trials with at least one other available leukotriene modifier that did not yield an adequate response.

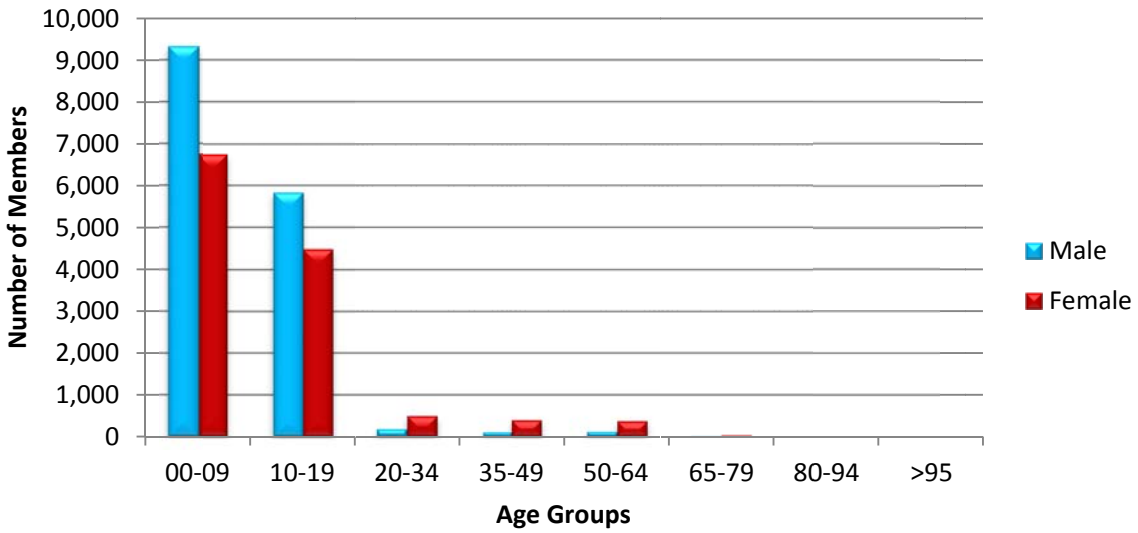
Utilization of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)

Comparison of Fiscal Years

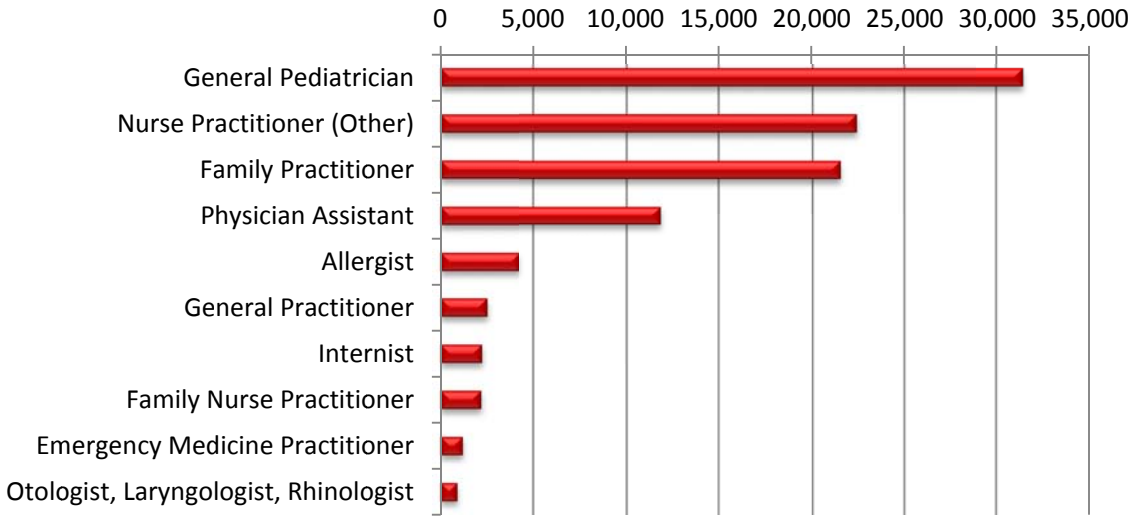
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	20,038	84,487	$3,528,508.78	$41.76	$1.39	2,532,088	2,532,200
2014	28,116	103,160	$1,849,335.98	$17.93	$0.60	3,089,467	3,092,914
% Change	**40.31%**	**22.10%**	**-47.59%**	**-24.80%**	**-0.57%**	**22.01%**	**22.14%**
Change	**8,078**	**18,673**	**-$1,679,172.80**	**-$23.84**	**-$0.79**	**557,379**	**560,714**

*Total number of unduplicated members.

Demographics of Members Utilizing Singulair® & Zyflo CR®



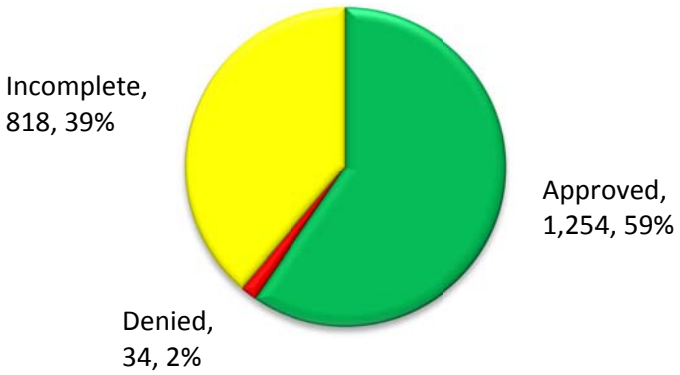
Top Prescriber Specialties of Singulair® & Zyflo CR® by Number of Claims



Prior Authorization of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release)

There were 2,106 petitions submitted for Singulair® and Zyflo CR® during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1]

FDA Update:

- November 2014: The addition of "enuresis in children" was added to the adverse drug reaction section of the package labeling of Singulair®.

Recommendations

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

Utilization Details of Singulair® (Montelukast) and Zyflo CR® (Zileuton Extended-Release): Fiscal Year 2014

PRODUCT UTILIZED	CLAIMS	MEMBERS	COST	COST/ DAY	% COST	COST/ CLAIM
Montelukast Products						
MONTELUKAST CHW 5MG	44,041	12,146	$658,884.96	$0.50	35.63%	$14.96
MONTELUKAST CHW 4MG	29,302	8,935	$485,731.73	$0.55	26.27%	$16.58
MONTELUKAST TAB 10MG	26,853	7,499	$380,960.42	$0.47	20.60%	$14.19
MONTELUKAST GRA 4MG	1,973	920	$283,368.33	$4.76	15.32%	$143.62
MONTELUKAST TAB 10MG	887	253	$13,103.03	$0.49	0.71%	$14.77
SINGULAIR GRA 4MG	32	16	$5,614.77	$5.85	0.30%	$175.46
SINGULAIR CHW 5MG	31	22	$2,323.00	$2.50	0.13%	$74.94
SINGULAIR CHW 4MG	29	7	$3,833.99	$4.55	0.21%	$132.21
SINGULAIR TAB 10MG	4	4	$60.62	$0.51	0.00%	$15.16
Subtotal	**103,152**	**29,802**	**$1,833,880.85**	**$20.18**	**99.17%**	**$601.88**
Zileuton Extended-Release Products						
ZYFLO CR TAB 600MG	8	2	$15,455.13	$64.40	0.84%	$1,931.8
Subtotal	**8**	**2**	**$15,455.13**	**$64.40**	**0.84%**	**$1,931.8**
Total	**103,160**	**29,804***	**$1,849,335.98**	**$0.60**	**100%**	**$2,533.7**

*Total number of unduplicated members.

[1] FDA. Safety Labeling Changes Approved by FDA Center for Drug Evaluation and Research: Singulair montelukast sodium. MedWatch The FDA Safety Information and Adverse Event Reporting Program. Available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm285264.htm. Last revised 12/11/14. Last accessed: 02/17/15.

Appendix N

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

FDA NEWS RELEASE

For Immediate Release: February 25th, 2015
FDA approves new antibacterial drug Avycaz

The U.S. Food and Drug Administration approved Avycaz (ceftazidime-avibactam), a new antibacterial drug product, to treat adults with complicated intra-abdominal infections (cIAI), in combination with metronidazole, and complicated urinary tract infections (cUTI), including kidney infections (pyelonephritis), who have limited or no alternative treatment options.
Avycaz is a fixed-combination drug containing ceftazidime, a previously approved cephalosporin antibacterial drug, and avibactam, a new beta-lactamase inhibitor.
Avycaz is the fifth approved antibacterial drug product designated as a Qualified Infectious Disease Product (QIDP). This designation is given to antibacterial products to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act.
As part of its QIDP designation, Avycaz was given priority review, which provides an expedited review of the drug's application. The QIDP designation also qualifies Avycaz for an additional five years of marketing exclusivity to be added to the five-year exclusivity period provided by the Food, Drug, and Cosmetic Act.
The determination of efficacy of Avycaz was supported in part by the findings of the efficacy and safety of ceftazidime for the treatment of cIAI and cUTI. The contribution of avibactam to Avycaz was based on data from in vitro studies and animal models of infection. Avycaz was studied in two Phase 2 trials, one each in cIAI and cUTI. Both trials were not designed with any formal hypotheses for inferential testing against the active comparators.
The most common side effects include vomiting, nausea, constipation and anxiety. Health care professionals should inform patients of these risks and also advise that decreased efficacy, seizures and other neurologic events were seen in patients with renal impairment. Serious skin reactions and anaphylaxis may occur in patients with penicillin allergies.
Avycaz is distributed by Forest Pharmaceuticals Inc., a subsidiary of Forest Laboratories Inc. based in Cincinnati, Ohio.

FDA NEWS RELEASE

For Immediate Release: February 6th, 2015
FDA approves Lucentis to treat diabetic retinopathy in patients with diabetic macular edema

The U.S. Food and Drug Administration expanded the approved use for Lucentis (ranibizumab injection) 0.3 mg to treat diabetic retinopathy (DR) in patients with diabetic macular edema (DME).
Diabetic retinopathy is the most common diabetic eye disease and is a leading cause of blindness in adults in the United States. According to the Centers for Disease Control and Prevention, diabetes (type 1 and type 2) affects more than 29 million people in the United States and is the leading cause of new blindness among people ages 20 to 74 years. In 2008, 33 percent of adults with diabetes aged 40 years or older had some form of DR. In some cases of DR with DME, abnormal new blood vessels grow on the surface of the retina. Severe vision loss or blindness can occur if the new blood vessels break.
Lucentis is administered by a physician as an injection into the eye once a month. It is intended to be used along with appropriate interventions to control blood sugar, blood pressure and cholesterol.
The drug's safety and efficacy to treat DR with DME were established in two clinical studies involving 759 participants who were treated and followed for three years. In the two studies, participants being treated with Lucentis showed significant improvement in the severity of their DR at two years compared to patients who did not receive an injection.
The most common side effects include bleeding of the conjunctiva, the tissue that lines the inside of the eyelids and covers the white part of the eye; eye pain; floaters; and increased pressure inside the eye (intraocular pressure). Serious side effects include infection within the eyeball (endophthalmitis) and retinal detachments.
The FDA granted Lucentis for DR with DME breakthrough therapy designation. The FDA can designate a drug a breakthrough therapy at the request of the sponsor if preliminary clinical evidence indicates the drug may demonstrate a substantial improvement over available therapies for patients with serious or life-threatening conditions. The FDA also reviewed the new use for Lucentis under the agency's priority review program, which provides for an expedited review of drugs that demonstrate the potential to be a significant improvement in safety or effectiveness in the treatment of a serious condition.
The FDA previously had approved Lucentis to treat DME and macular edema secondary to retinal vein occlusions, both of which cause fluid to leak into the macula resulting in blurred vision. Lucentis also is approved to treat wet (neovascular) age-related macular degeneration (AMD), a condition in which abnormal blood vessels grow and leak fluid into the macula.
Lucentis is marketed by South San Francisco, California-based Genentech, a subsidiary of Roche.

FDA NEWS RELEASE

For Immediate Release: February 23rd, 2015
FDA approves Farydak for treatment of multiple myeloma

The U.S. Food and Drug Administration approved Farydak (panobinostat) for the treatment of patients with multiple myeloma.
Multiple myeloma is a form of blood cancer that arises from plasma cells, a type of white blood cell, found in bone marrow. According to the National Cancer Institute, approximately 21,700 Americans are diagnosed with multiple myeloma and 10,710 die from the disease annually.
Primarily affecting older adults, multiple myeloma causes plasma cells to rapidly multiply and crowd out other healthy blood cells from the bone marrow. When the bone marrow has too many plasma cells, the cells may move to other parts of the body, which can weaken the body's immune system, lead to anemia and cause other bone and kidney problems.
Farydak works by inhibiting the activity of enzymes, known as histone deacetylases (HDACs). This process may slow the over-development of plasma cells in multiple myeloma patients or cause these dangerous cells to die.
Farydak is the first HDAC inhibitor approved to treat multiple myeloma. It is intended for patients who have received at least two prior standard therapies, including bortezomib and an immunomodulatory agent. Farydak is to be used in combination with bortezomib, a type of chemotherapy, and dexamethasone, an anti-inflammatory medication.
In November 2014, the FDA's Oncologic Drugs Advisory Committee advised the agency that, based on the data reviewed, the drug's benefits did not outweigh its risks for patients with relapsed multiple myeloma. After the meeting, the company submitted additional information supporting Farydak's use for a different indication: patients with multiple myeloma who have received at least two prior standard therapies, including bortezomib and an immunomodulatory agent.
The safety and efficacy of Farydak in combination with bortezomib and dexamethasone was demonstrated in 193 clinical trial participants with multiple myeloma who received at least two prior treatments that included bortezomib and an immunomodulatory agent. Participants were randomly assigned to receive a combination of Farydak, bortezomib and dexamethasone, or bortezomib and dexamethasone alone.
Study results showed participants receiving the Farydak combination saw a delay in their disease progression (progression-free survival) for about 10.6 months, compared to 5.8 months in participants treated with bortezomib and dexamethasone alone. Additionally, 59 percent of Farydak-treated participants saw their cancer shrink or disappear after treatment (response rate), versus 41 percent in those receiving bortezomib and dexamethasone.
Farydak carries a Boxed Warning alerting patients and health care professionals that severe diarrhea and severe and fatal cardiac events, arrhythmias and electrocardiogram (ECG) changes have occurred in patients receiving Farydak. Because of these risks, Farydak is being approved with a Risk Evaluation and Mitigation Strategy (REMS) consisting of a communication plan to inform health care professionals of these risks and how to minimize them.
The most common side effects of Farydak were diarrhea, tiredness, nausea, swelling in the arms or legs, decreased appetite, fever, vomiting and weakness. The most common laboratory abnormalities were low levels of phosphorus in the blood (hypophosphatemia), hypokalemia, low levels of salt in the blood (hyponatremia), increased creatinine, low platelets (thrombocytopenia), leukopenia and anemia. Healthcare professionals should also inform patients of the risk of bleeding in the gastrointestinal tract and the lungs, and hepatotoxicity.
The FDA granted Farydak priority review and orphan product designation. Priority review provides for an expedited review of drugs that are intended to treat a serious disease or condition and may provide a significant improvement over available therapy. Orphan product designation is given to drugs intended to treat rare diseases.
The FDA action was taken under the agency's accelerated approval program, which allows 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. The accelerated approval program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials. An improvement in survival or disease-related symptoms has not yet been established for Farydak. The company is now required to conduct confirmatory trials to verify and describe the clinical benefit of Farydak.
Farydak is marketed by East Hanover, New Jersey-based Novartis Pharmaceuticals.

FDA NEWS RELEASE

For Immediate Release: February 13th, 2015
FDA approves Lenvima for a type of thyroid cancer

The U.S. Food and Drug Administration granted approval to Lenvima (lenvatinib) to treat patients with progressive, differentiated thyroid cancer (DTC) whose disease progressed despite receiving radioactive iodine therapy (radioactive iodine refractory disease).
The most common type of thyroid cancer, DTC is a cancerous growth of the thyroid gland which is located in the neck and helps regulate the body's metabolism. The National Cancer Institute estimates that 62,980 Americans were diagnosed with thyroid cancer and 1,890 died from the disease in 2014. Lenvima is a kinase inhibitor, which works by blocking certain proteins from helping cancer cells grow and divide.

Lenvima was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that, if approved, would provide significant improvement in safety or effectiveness in the treatment of a serious condition. The drug also received orphan product designation because it is intended to treat a rare disease. Lenvima is being approved approximately two months ahead of the prescription drug user fee goal date of April 14, 2015, the date when the agency was scheduled to complete its review of the application.

Lenvima's efficacy was demonstrated in 392 participants with progressive, radioactive iodine-refractory DTC who were randomly assigned to receive either Lenvima or a placebo. Study results showed Lenvima-treated participants lived a median of 18.3 months without their disease progressing (progression-free survival), compared to a median of 3.6 months for participants who received a placebo. Additionally, 65 percent of participants treated with Lenvima saw a reduction in tumor size, compared to the two percent of participants who received a placebo. A majority of participants randomly assigned to receive the placebo were treated with Lenvima upon disease progression.

The most common side effects of Lenvima were hypertension, fatigue, diarrhea, arthralgia/myalgia, decreased appetite, decreased weight, nausea, inflammation of the lining of the mouth (stomatitis), headache, vomiting, proteinuria, swelling and pain in the palms, hands and/or the soles of the feet (palmar-plantar erythrodysesthesia syndrome), abdominal pain and changes in voice volume or quality (dysphonia).

Lenvima may cause serious side effects, including cardiac failure, blood clot formation (arterial thromboembolic events), hepatotoxicity, renal failure and impairment, an opening in the wall of the stomach or intestines (gastrointestinal perforation) or an abnormal connection between two parts of the stomach or intestines (fistula formation), changes in the heart's electrical activity (QT Interval Prolongation), hypocalcemia, the simultaneous occurrence of headache, confusion, seizures and visual changes (Reversible Posterior Leukoencephalopathy Syndrome), hemorrhage, risks to an unborn child if a patient becomes pregnant during treatment, and impairing suppression of the production of thyroid-stimulating hormone.

Lenvima is marketed by Woodcliff Lake, New Jersey-based Eisai Inc.

FDA NEWS RELEASE

For Immediate Release: February 3rd, 2015

FDA approves Ibrance for postmenopausal women with advanced breast cancer

The U.S. Food and Drug Administration granted accelerated approval to Ibrance (palbociclib) to treat advanced (metastatic) breast cancer.

Breast cancer in women is the second most common type of cancer in the United States. It forms in the breast tissue and in advanced cases, spreads to surrounding normal tissue. The National Cancer Institute estimates that 232,670 American women were diagnosed with breast cancer and 40,000 died from the disease in 2014.

Ibrance works by inhibiting molecules, known as cyclin-dependent kinases (CDKs) 4 and 6, involved in promoting the growth of cancer cells. Ibrance is intended for postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have not yet received an endocrine-based therapy. It is to be used in combination with letrozole, another FDA-approved product used to treat certain kinds of breast cancer in postmenopausal women.

The FDA granted Ibrance breakthrough therapy designation because the sponsor demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies. It also received a priority review, which provides for an expedited review of drugs intended to provide a significant improvement in safety or effectiveness in the treatment of a serious condition or meet an unmet medical need. Ibrance is being approved more than two months ahead of the prescription drug user fee goal date of April 13, 2015, the date when the agency was scheduled to complete its review of the application.

Ibrance is being approved under the FDA's accelerated approval program, which allows 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.

The drug's efficacy was demonstrated in 165 postmenopausal women with ER-positive, HER2-negative advanced breast cancer who had not received previous treatment for advanced disease. Clinical study participants were randomly assigned to receive Ibrance in combination with letrozole or letrozole alone. Participants treated with Ibrance plus letrozole lived about 20.2 months without their disease progressing (progression-free survival), compared to about 10.2 months seen in participants receiving only letrozole. Information on overall survival is not available at this time.

The most common side effects of the drug were a decrease in neutrophils (neutropenia), low levels of white blood cells (leukopenia), fatigue, anemia, upper respiratory infection, nausea, inflammation of the lining of the mouth (stomatitis), hair loss (alopecia), diarrhea, low blood platelet counts (thrombocytopenia), decreased appetite, vomiting, lack of energy and strength (asthenia), damage to the peripheral nerves (peripheral neuropathy) and nosebleed (epistaxis). Healthcare professionals should inform patients of these risks.

It is recommended that treatment begin with a 125 milligram dose for 21 days, followed by seven days without treatment. Healthcare professionals are advised to monitor complete blood count prior to start of therapy and at the beginning of each cycle, as well as on Day 14 of the first two cycles, and as clinically indicated.

Ibrance is marketed by New York City-based Pfizer, Inc.

Safety Announcements

FDA Drug Safety Communication: FDA requires label warnings to prohibit sharing of multi-dose diabetes pen devices among patients

[February 25th, 2015] In an effort to reduce the serious risk of infection spread through sharing of multi-dose diabetes pen devices intended for single patient use only, the U.S. Food and Drug Administration (FDA) is requiring additional label warnings prohibiting sharing of these injectable medicines. Insulin pens and pens for other injectable diabetes medicines should never be shared among patients, even if the needle is changed. Sharing pens can result in the spread of serious infections from one patient to another. To promote safe use, we are requiring that pens and packaging containing multiple doses of insulin and other injectable diabetes medicines display a warning label stating "For single patient use only."

Insulin and other injectable diabetes medicines are used to help lower or regulate blood sugar, which, when uncontrolled, can increase the risk for serious complications, including blindness, nerve and kidney damage, and heart disease. Injectable diabetes medicines can come in pen-shaped devices with either a reservoir or cartridge containing multiple doses of medicine. Each pen is designed to be safe for just one patient to use multiple times with a new, fresh needle for each injection. Pens must never be used for more than one patient because blood may be present in the pen after use. Sharing pens can lead to transmission of infections such as the human immunodeficiency virus (HIV) and hepatitis viruses.

Since 2008, we have learned of thousands of patients possibly exposed to infections that are transmitted through blood from the sharing of multi-dose pen devices for insulin and other injectable diabetes medicines. No confirmed cases of actual infection transmission have been reported, but sources of infection are often difficult to identify and may go unreported. In response to the reports of potential exposure, FDA and other organizations have issued multiple safety alerts, including a 2009 FDA Health Care Professional Sheet, and launched campaigns warning against the sharing of insulin pens.

The "For single patient use only" warning will appear on the labels affixed to the pens and on the pen cartons. Additional warnings against sharing pens will also be added to the prescribing information and to the patient Medication Guides, Patient Package Inserts, and Instructions for Use.

Safety Announcements

FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use

[March 3rd, 2015] The U.S. Food and Drug Administration (FDA) cautions that prescription testosterone products are approved only for men who have low testosterone levels caused by certain medical conditions. The benefit and safety of these medications have not been established for the treatment of low testosterone levels due to aging, even if a man's symptoms seem related to low testosterone. We are requiring that the manufacturers of all approved prescription testosterone products change their labeling to clarify the approved uses of these medications. We are also requiring these manufacturers to add information to the labeling about a possible increased risk of heart attacks and strokes in patients taking testosterone. Health care professionals should prescribe testosterone therapy only for men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests.

Testosterone is FDA-approved as replacement therapy only for men who have low testosterone levels due to disorders of the testicles, pituitary gland, or brain that cause a condition called hypogonadism. Examples of these disorders include failure of the testicles to produce testosterone because of genetic problems, or damage from chemotherapy or infection. However, FDA has become aware that testosterone is being used extensively in attempts to relieve symptoms in men who have low testosterone for no apparent reason other than aging. The benefits and safety of this use have not been established.

In addition, based on the available evidence from published studies and expert input from an Advisory Committee meeting, FDA has concluded that there is a possible increased cardiovascular risk associated with testosterone use. These studies included aging men treated with testosterone. Some studies reported an increased risk of heart attack, stroke, or death associated with testosterone treatment, while others did not.

Based on our findings, we are requiring labeling changes for all prescription testosterone products to reflect the possible increased risk of heart attacks and strokes associated with testosterone use. Health care professionals should make patients aware of this possible risk when deciding whether to start or continue a patient on testosterone therapy. We are also requiring manufacturers of approved testosterone products to conduct a well-designed clinical trial to more clearly address the question of whether an increased risk of heart attack or stroke exists among users of these products. We are encouraging these manufacturers to work together on a clinical trial, but they are allowed to work separately if they so choose.

Patients using testosterone should seek medical attention immediately if symptoms of a heart attack or stroke are present, such as:

- Chest pain
- Shortness of breath or trouble breathing

- Weakness in one part or one side of the body
- Slurred speech

Current Drug Shortages Index (as of March 3rd, 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***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***Currently in Shortage***
Barium Sulfate for Suspension	***Currently in Shortage***
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection[12]	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmethylphenidate Hydrochloride (Focalin) Tablet	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Dimercaprol (Bal-in-Oil) Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Lyophilized Powder	***Currently in Shortage***
Ephedrine Sulfate Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)[13]	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Sodium Injection	***Currently in Shortage***
Fluoxymesterone (Androxy) Tablets, USP	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Irrigation Solutions	***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***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Memantine Hydrochloride (Namenda) XR Capsules	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylene Blue Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets[14]	***Currently in Shortage***
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride (Nubain) Injection	***Currently in Shortage***
Nebivolol (BYSTOLIC) Tablets	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Papaverine Hydrochloride Injection	***Currently in Shortage***

Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Phosphate (Glycophos) Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Quazepam (Doral) Tablets	***Currently in Shortage***
Radium RA-223 Dichloride (Xofigo) Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Secretin Synthetic Human (ChiRhoStim) Injection	***Currently in Shortage***
Selenium Injection	***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***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Water for Injection Solutions	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trace Elements	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Trypan Blue (Membraneblue)	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***