Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
December 10, 2014
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 – December 10, 2014

DATE: December 1, 2014

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 December 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/SoonerPsych Program Update/ Drug Rebate Program Review – See Appendix B

Action Item – Vote to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir) – See Appendix C

Action Item – Vote to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) – See Appendix D

Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease Medications and 30-Day Notice to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol) – See Appendix E

30-Day Notice to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone) – See Appendix F

Annual Review of Testosterone Products and 30-Day Notice to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel) – See Appendix G

Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene) – See Appendix H

FDA and DEA Updates – See Appendix I

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – December 10, 2014 @ 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. November 12, 2014 DUR Minutes – Vote
   B. November 12, 2014 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/SoonerPsych Program Update/Drug Rebate Program Review – See Appendix B**
   A. Medication Coverage Activity for November 2014
   B. Pharmacy Help Desk Activity for November 2014
   C. Update on Medication Coverage Authorization Unit
   D. SoonerPsych Program Update
   E. Drug Rebate Program Review

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

5. **Action Item – Vote to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir) – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease Medications and 30-Day Notice to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol) – See Appendix E**

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

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

8. 30-Day Notice to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone) – See Appendix F

A. Introduction
B. Drug Product Summaries
C. College of Pharmacy Recommendations

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

9. Annual Review of Testosterone Products and 30-Day Notice to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel) – See Appendix G

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

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

10. Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene) – See Appendix H

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

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

11. FDA and DEA Updates – See Appendix I

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

12. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF NOVEMBER 12, 2014

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.		x
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 Winegardener, 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): Charlie Nguyen, Mai Tran	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
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Medicaid Director	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Melvin Nwamadi, Abbott	Mark DeClerk, Lilly	Jim Chapman, Abbvie
Nick Casale, Reckitt Benckiser	David Williams, Actavis	Carolyn Savini , Gilead
Brent Hildebrand, Gilead	Hayley Endicott, Gilead	Ron Cain, Pfizer
Russ Wilson, J&J	Brian Maves, Pfizer	Ashley Weber, Astellas
Mark Welburn, Intermune	Toby Thompson, Pfizer	Tony Esposito , UCB
Janie Huff, Takeda	Charlene Kaiser, Amgen	Minesh Jariwala, Pfizer
Warren Tayes, Merck	Joe Summers, UCB	
Ric Uhles, Actavis	Pat Harvey, Walgreens	
Hampton Mansion, Reckitt Benckiser	Jim Fowler, AstraZeneca	

PRESENT FOR PUBLIC COMMENT:	
Hampton Mansion	Reckitt Benckiser
Carolyn Savini	Gilead

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: CAROLYN SAVINI **AGENDA NO. 9**

2B: HAMPTON MANSION **AGENDA NO. 11**

ACTION: NONE REQUIRED

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

3A: OCTOBER 8, 2014 DUR MINUTES – VOTE

3B: OCTOBER 8, 2014 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **VOTE ON 2015 MEETING DATES**

4A: 2015 MEETING DATES – VOTE

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS/GLAUCOMA MEMBER AND PRESCRIBER MAILING EVALUATION**

5A: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2014

5B: PHARMACY HELP DESK ACTIVITY FOR OCTOBER 2014

5C: ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS

5D: GLAUCOMA EDUCATIONAL INITIATIVE MAILING UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE OTEZLA® (APREMILAST) AND ENTYVIO™ (VEDOLIZUMAB)**

6A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Muchmore recommends that *"add history of failure of mesalamine."*

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE SIVEXTRO™ (TEDIZOLID), DALVANCE™ (DALBAVANCIN), AND ORBACTIV™ (ORITAVANCIN)**

7A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE FETZIMA® (LEVOMILNACIPRAN), KHEDEZLA® (DESVENLAFAXINE), AND BRINTELLIX® (VORTIOXETINE) AND UPDATE THE ANTIDEPRESSANTS PRODUCT BASED PRIOR AUTHORIZATION CATEGORY**

8A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **30-DAY NOTICE TO PRIOR AUTHORIZE HARVONI® (LEDIPASVIR/SOFOSBUVIR)**

9A: INTRODUCTION

9B: MARKET NEWS AND UPDATES

9C: HARVONI® (LEDIPASVIR/SOFOSBUVIR) SUMMARY

9D: COP RECOMMENDATIONS

9E: UTILIZATION OF SOVALDI™ (SOFOSBUVIR) AND OLYSIO™ (SIMEPREVIR)

9F: PRIOR AUTHORIZATION OF SOVALDI™ (SOFOSBUVIR) AND OLYSIO™ (SIMEPREVIR)

9G: UTILIZATION DETAILS OF HEPATITIS C MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Muchmore requested additional information, when available, regarding preferred treatment after previous failure and post liver transplant.

Dr. Osborne recommended tracking hepatitis C cost per cure.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF FIBROMYALGIA MEDICATIONS**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF FIBROMYALGIA MEDICATIONS

10C: PRIOR AUTHORIZATION OF FIBROMYALGIA MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: COP RECOMMENDATIONS

10F: UTILIZATION DETAILS OF FIBROMYALGIA MEDICATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ORAL BUPRENORPHINE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZUBSOLV® (BUPRENORPHINE/NALOXONE TABLETS) AND BUNAVAIL™ (BUPRENORPHINE/NALOXONE BUCCAL FILMS)**

11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: KEY POINTS
11C: UTILIZATION OF ORAL BUPRENORPHINE PRODUCTS
11D: PRIOR AUTHORIZATION OF ORAL BUPRENORPHINE PRODUCTS
11E: MARKET NEWS AND UPDATES
11F: ZUBSOLV® AND BUNAVAIL™ SUMMARY
11G: COP RECOMMENDATIONS
11H: UTILIZATION DETAILS OF ORAL BUPRENORPHINE PRODUCTS

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

AGENDA ITEM NO. 12: **FDA AND DEA UPDATES**
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **FUTURE BUSINESS**
13A: ANNUAL REVIEWS
13B: NEW PRODUCT REVIEWS
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ADJOURNMENT**
The meeting was adjourned at 4:57PM.

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

Memorandum

Date: November 13, 2014

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

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

Subject: DUR Board Recommendations From Meeting of November 12, 2014

Recommendation 1: Educational Initiative to Recent Prescribers of Oral Viscous Lidocaine

NO ACTION REQUIRED.

The College of Pharmacy recommends an educational initiative to recent prescribers of oral viscous lidocaine in children 5 years of age or younger. The initiative would consist of a targeted mailing to prescribers outlining the FDA recommendations. Following the mailing, a review of utilization will be conducted to determine if the intervention was effective in reducing prescribing in this population.

Recommendation 2: Vote to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Entyvio™ (vedolizumab) and Otezla® (apremilast) to Tier-3 of the Targeted Immunomodulator Agent Product Based Prior Authorization category with the following criteria:

Entyvio™ (Vedolizumab) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of moderate-to-severely active Crohn's disease (CD) or moderate-to-severely active ulcerative colitis (UC); and
3. History of failure of a mesalamine product (does not have to be within the last 90 days) and a trial of one Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; and
4. A minimum of a 4 week trial of a Tier-2 tumor necrosis factor (TNF) blocker indicated for the treatment of CD or UC that did not yield adequate relief of symptoms or resulted in intolerable adverse effects. Current Tier-2 products include the following:
    a. **UC:** Humira® (adalimumab)
    b. **CD:** Cimzia® (certolizumab), Humira® (adalimumab); or
5. Prior stabilization on the medication documented within the last 100 days.
6. A quantity limit of 300mg every 8 weeks will apply. Approvals will be granted for titration quantities required for initial dosing.
7. Initial approvals will be for the duration of 14 weeks as Entyvio™ should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.

Otezla® (Apremilast) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of active psoriatic arthritis (PsA) or moderate-to-severe plaque psoriasis (Ps); and
3. Current Tier-3 approval criteria will apply.
4. A quantity limit of 60 tablets for 30 days will apply. Approvals will be granted for titration quantities required for initial dosing.

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

Tier structure based on supplemental rebate participation.
DMARDs= Disease modifying antirheumatic drugs
*Supplemental rebated products
+ May be rebated to Tier-2 status only

Tier-2 Approval Criteria:

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

Tier-3 Approval Criteria:

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

Recommendation 3: Vote to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Sivextro™, Dalvance™, and Orbactiv™ with the following criteria:

Sivextro™ (Tedizolid Phosphate) Tablet Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use Zyvox® (linezolid), or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of six tablets per six days will apply.

Dalvance™ (Dalbavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid), or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of two vials per seven days will apply.

Orbactiv™ (Oritavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid), or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of three vials per 30 days will apply.

Recommendation 4: Vote to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine) and Update the Antidepressants Product Based Prior Authorization Category

MOTION CARRIED by unanimous approval.

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

1. Place Khedezla®, Fetzima®, and Brintellix® into Tier-3.
2. Move duloxetine to Tier-1 based on generic availability and State Maximum Allowable Cost (SMAC).
3. Change the approval criteria for Tier-2 medications to include a required trial of duloxetine as one of the Tier-1 trials.
4. Create a Special PA category to include special dosage forms that are similar to currently available, cost-effective Tier-1 products. This category would include the following:
    a. Fluoxetine 60mg tablets, Prozac Weekly®, Luvox CR®, Paxil CR®, Pexeva®, Aplenzin®, Forfivo XL®, Oleptro®, and venlafaxine ER tablets
    b. Medications in the special PA category require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications.
5. Tier-2 will include supplemental rebated products. If no products rebate to Tier-2, then Tier-2 will include the lowest cost Tier-3 product(s).

Antidepressants Tier-2 Approval Criteria:

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

Antidepressants Tier-3 Approval Criteria:

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

Antidepressants Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA product will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists.
3. Tier structure rules still apply.

Recommendation 5: 30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Fibromyalgia Medications

MOTION CARRIED by unanimous approval.

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

1. Move duloxetine to Tier-1 based on generic availability and State Maximum Allowable Cost (SMAC).
2. Change the approval criteria for Tier-2 medications to include a required trial of duloxetine as one of the Tier-1 trials, based on its FDA approved indications.
3. Tier-2 will include supplemental rebated products. If no products rebate to Tier-2, then Tier-2 will include the lowest cost Tier-3 product(s).

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

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

Fibromyalgia Medications Tier-2 Approval Criteria:

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

Fibromyalgia Medications Tier-3 Approval Criteria:

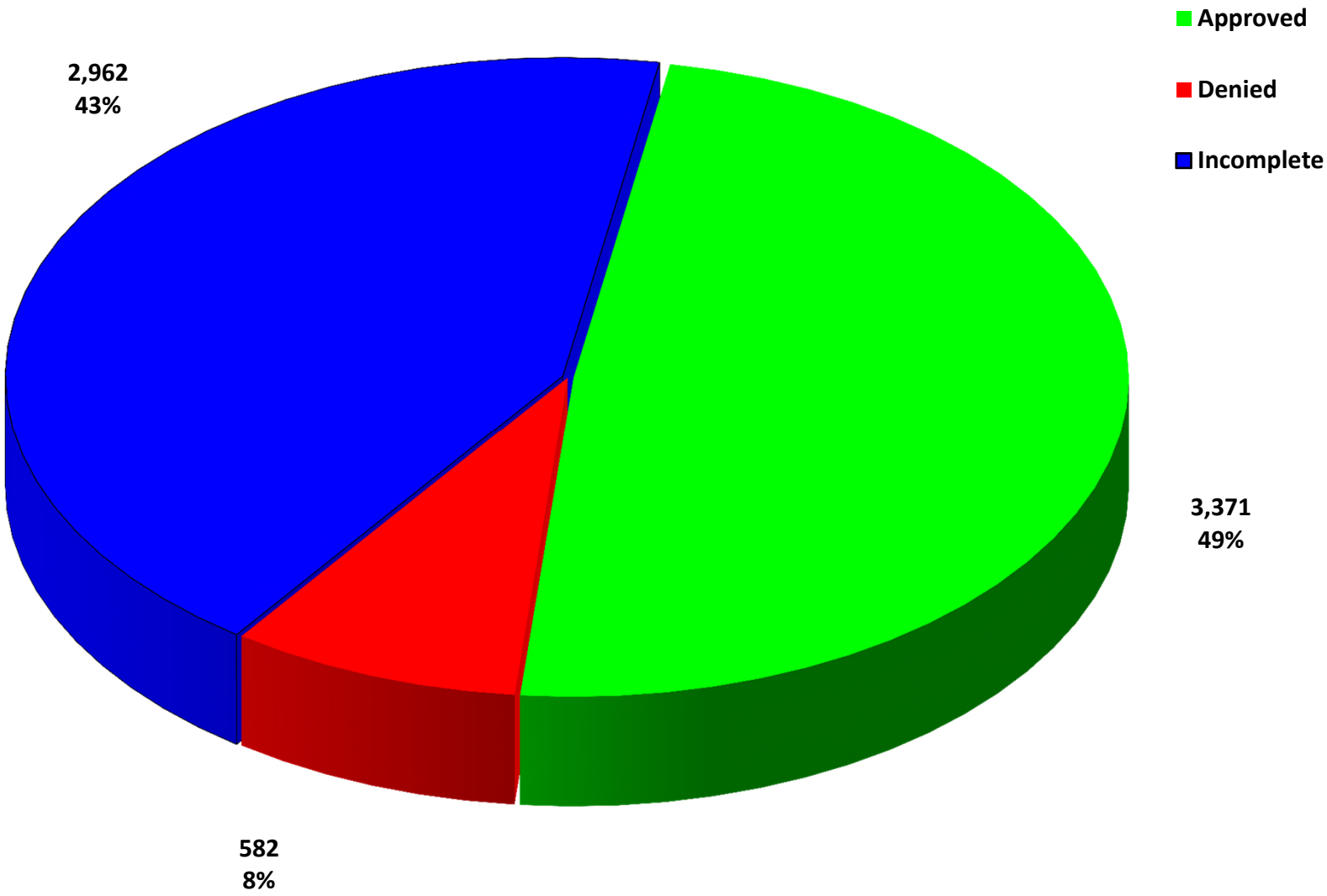
1. A documented, recent (within the last six months) trial of two Tier-1 medications (must include one trial with duloxetine) and all available Tier-2 medications at least three weeks in duration that did not provide an adequate response or resulted in intolerable adverse effects; or
2. Contraindication(s)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

Recommendation 7: Annual Review of Oral Buprenorphine Products and 30-Day Notice to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films)

NO ACTION REQUIRED.

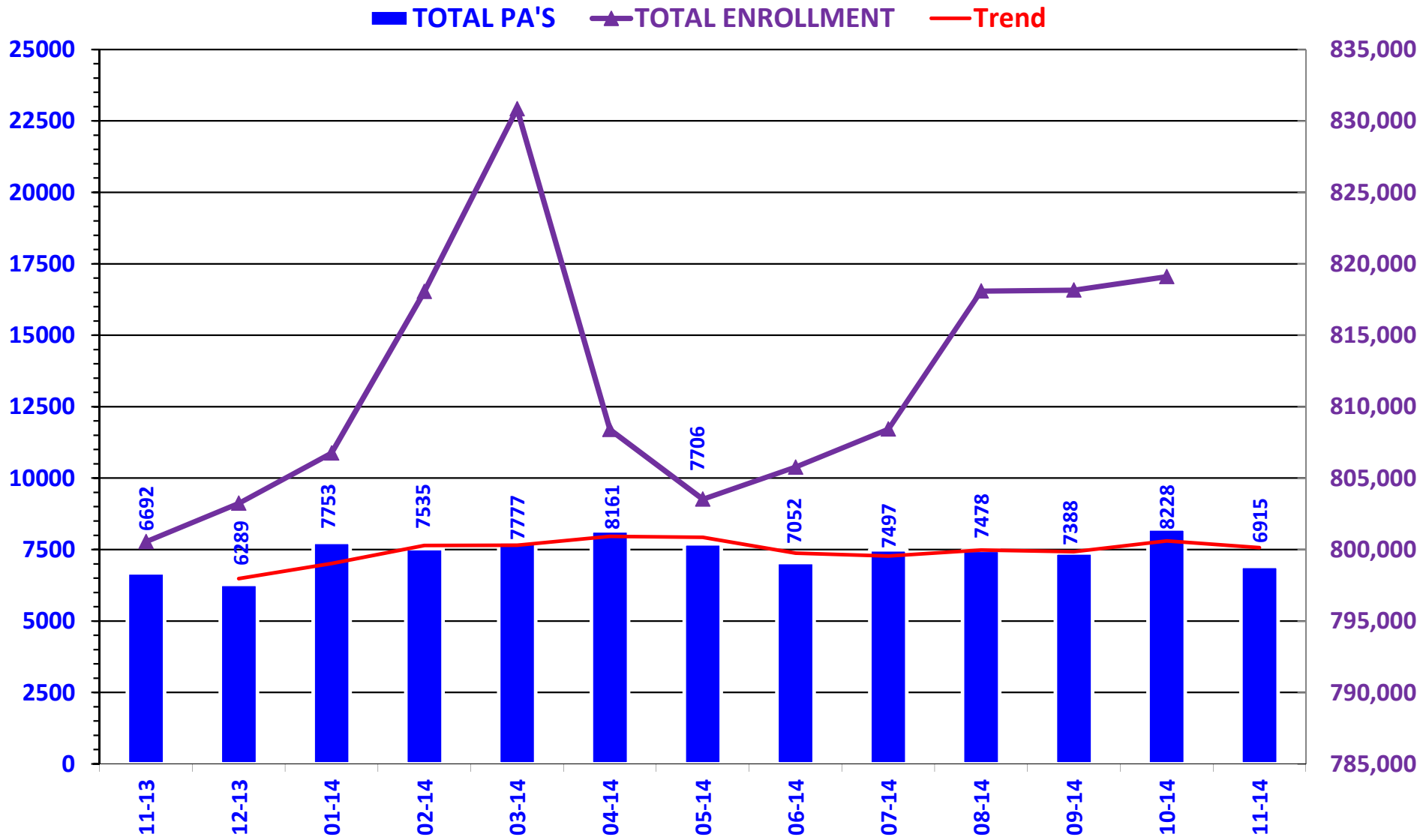
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER



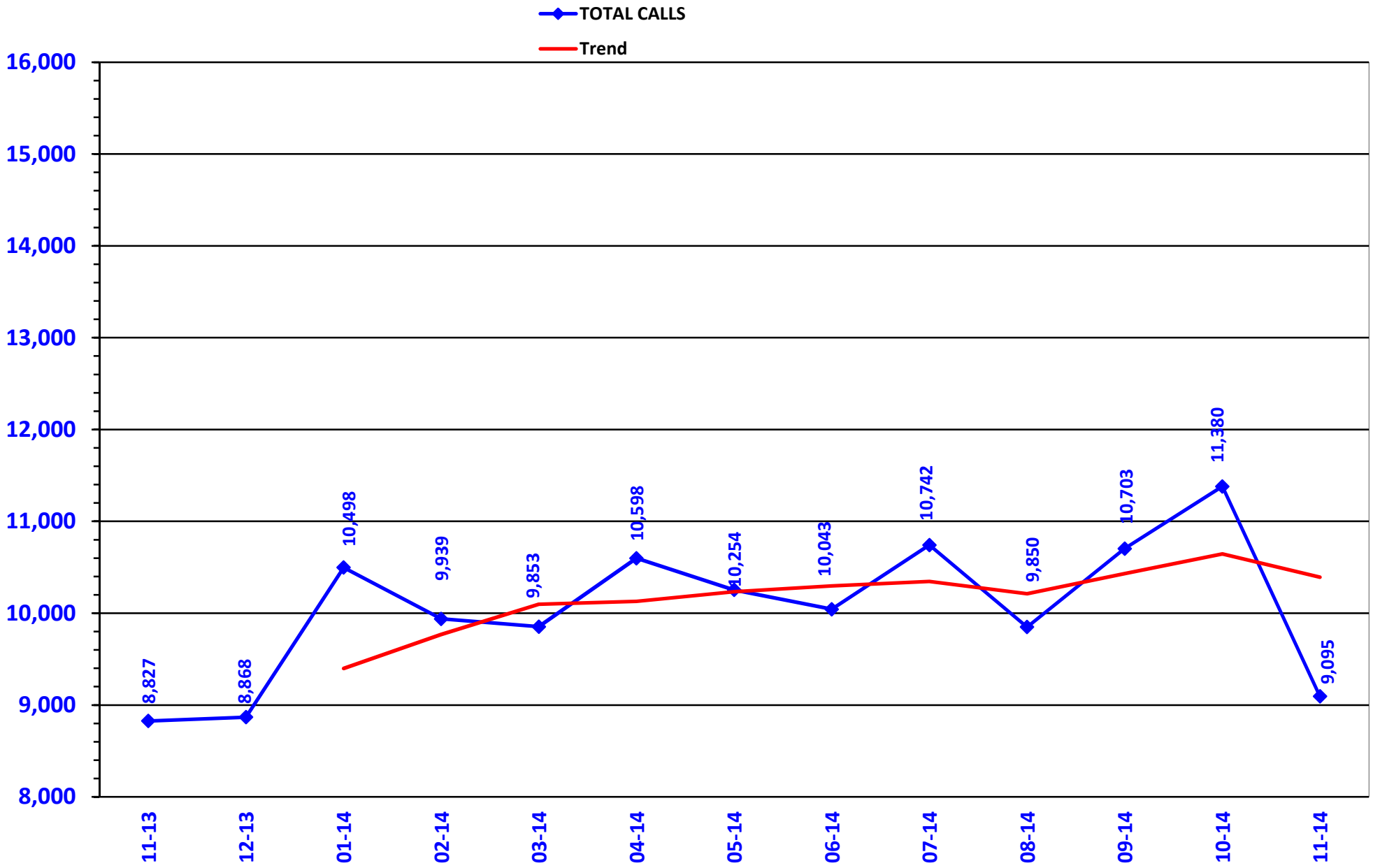
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2013 – NOVEMBER 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
NOVEMBER 2013 – NOVEMBER 2014



Prior Authorization Activity

11/1/2014 Through 11/30/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	314	128	6	180	351
Analgesic - NonNarcotic	18	0	5	13	0
Analgesic, Narcotic	422	199	31	192	144
Angiotensin Receptor Antagonist	14	2	1	11	359
Antiasthma	152	76	10	66	346
Antibiotic	29	4	1	24	119
Anticonvulsant	69	44	1	24	306
Antidepressant	162	50	14	98	285
Antidiabetic	118	52	6	60	357
Antifungal	10	3	2	5	26
Antigout	13	6	1	6	220
Antihistamine	162	135	5	22	356
Antimigraine	43	8	9	26	144
Antiulcers	182	40	44	98	176
Anxiolytic	63	37	6	20	209
Atypical Antipsychotics	343	196	7	140	345
Biologics	61	28	3	30	333
Bladder Control	43	7	3	33	358
Blood Thinners	107	75	1	31	273
Botox	10	7	1	2	359
Cardiovascular	22	15	1	6	287
Cephalosporins	15	1	1	13	6
Chronic Obstructive Pulmonary Disease	16	6	0	10	313
Dermatological	87	9	45	33	82
Endocrine & Metabolic Drugs	45	28	4	13	128
Erythropoietin Stimulating Agents	26	12	2	12	106
Fibromyalgia	119	39	16	64	305
Fish Oils	11	6	1	4	359
Gastrointestinal Agents	46	11	12	23	110
Glaucoma	13	1	1	11	88
Growth Hormones	89	63	4	22	145
Hepatitis C	98	41	23	34	9
HFA Rescue Inhalers	59	26	2	31	327
Insomnia	40	8	4	28	180
Linzess, Amitiza, and Relistor	63	15	13	35	250
Multiple Sclerosis	33	19	2	12	158
Muscle Relaxant	84	23	26	35	49
Nasal Allergy	71	5	12	54	148
Neurological Agents	74	51	4	19	333
Nsaids	142	16	12	114	230
Ocular Allergy	34	11	4	19	283
Ophthalmic Anti-infectives	25	7	2	16	59
Osteoporosis	18	6	1	11	359
Other*	172	32	33	107	215
Otic Antibiotic	24	7	1	16	7
Pediculicide	84	33	1	50	12
Prenatal Vitamins	17	0	2	15	0
Statins	40	15	4	21	339
Stimulant	961	442	47	472	344
Suboxone/Subutex	163	128	4	31	75
Synagis	330	156	53	121	136
Testosterone	34	9	1	24	359
Topical Antifungal	43	1	8	34	25
Topical Corticosteroids	74	2	17	55	234

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Vitamin	49	21	20	8	320
Pharmacotherapy	50	41	2	7	260
Emergency PAs	0	0	0	0	
Total	**5,606**	**2,403**	**542**	**2,661**	
Overrides					
Brand	43	37	0	6	246
Cumulative Early Refill	3	3	0	0	121
Dosage Change	330	294	1	35	6
High Dose	3	2	0	1	192
Ingredient Duplication	49	41	0	8	5
Lost/Broken Rx	71	56	3	12	4
NDC vs Age	40	40	0	0	271
Nursing Home Issue	50	50	0	0	5
Other*	30	26	0	4	19
qua	1	1	0	0	360
Quantity vs. Days Supply	626	383	25	218	250
STBS/STBSM	13	11	0	2	76
Stolen	19	9	9	1	6
Temporary Unlock	8	5	0	3	8
Third Brand Request	27	14	2	11	31
Overrides Total	**1,309**	**968**	**40**	**301**	
Total Regular PAs + Overrides	**6,915**	**3,371**	**582**	**2,962**	

Denial Reasons	
Unable to verify required trials.	2,491
Does not meet established criteria.	575
Lack required information to process request.	460

Other PA Activity	
Duplicate Requests	470
Letters	3,957
No Process	7
Changes to existing PAs	477
Helpdesk Initiated Prior Authorizations	822
PAs Missing Information	31

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

SoonerPsych Program Update

Oklahoma Health Care Authority
December 2014

Prescriber Mailing: Appropriate Diagnosis

In order to reach more prescribers and streamline mailings, the SoonerPsych program has changed its mailing style to a quarterly "report card" for prescribers. The mailing includes a gauge showing prescribers how their prescribing compares to other prescribers of atypical antipsychotics regarding potential differences from generally accepted evidence-based prescribing practices.

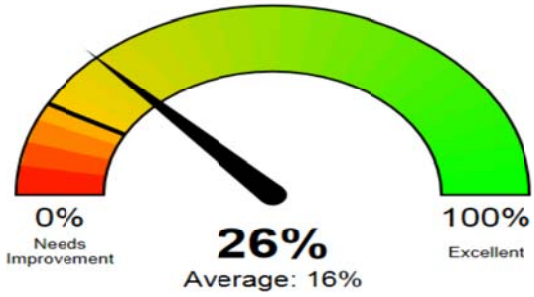
The first report-card style mailing was processed in April and addressed appropriate diagnosis for pediatric and adult members receiving an atypical antipsychotic. Prescribers were eligible for inclusion in the mailing if they had prescribed antipsychotics for members whose recent twelve month medical claims history lacked a diagnosis with a strong indication for prescribing an antipsychotic medication. The review period was for one year and was prevalent in nature (not based on a new start of an atypical antipsychotic). A total of 1,665 prescribers were flagged for having at least one patient without a target diagnosis. These prescribers had 11,865 flagged patients without a target diagnosis. A total of 200 prescribers were included in the mailing which included 8,069 flagged patients without a target diagnosis.

Prescribers received a letter with a gauge showing the percent of their prescribing of atypical antipsychotic medications in patients with a strongly indicated diagnosis in comparison to the average percentage for all other SoonerCare antipsychotic prescribers. The mailing also included an informational page with a list of diagnoses consistent with generally accepted evidence-based prescribing practices.

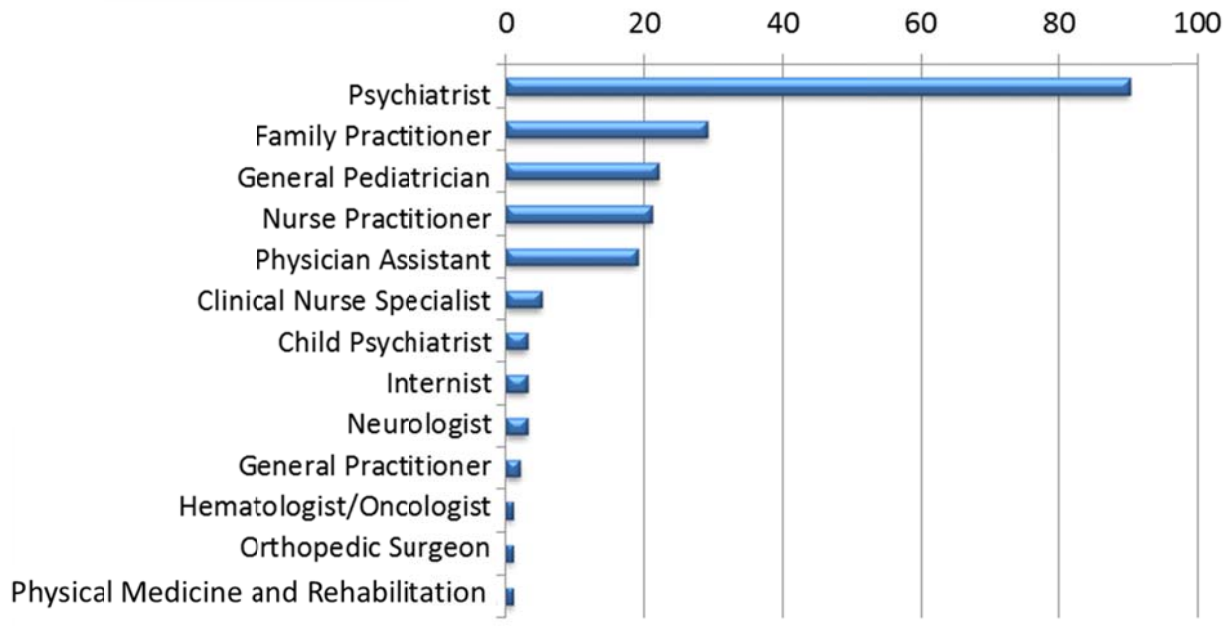
Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	200
Members	**Count**
Total Members Included	8,069

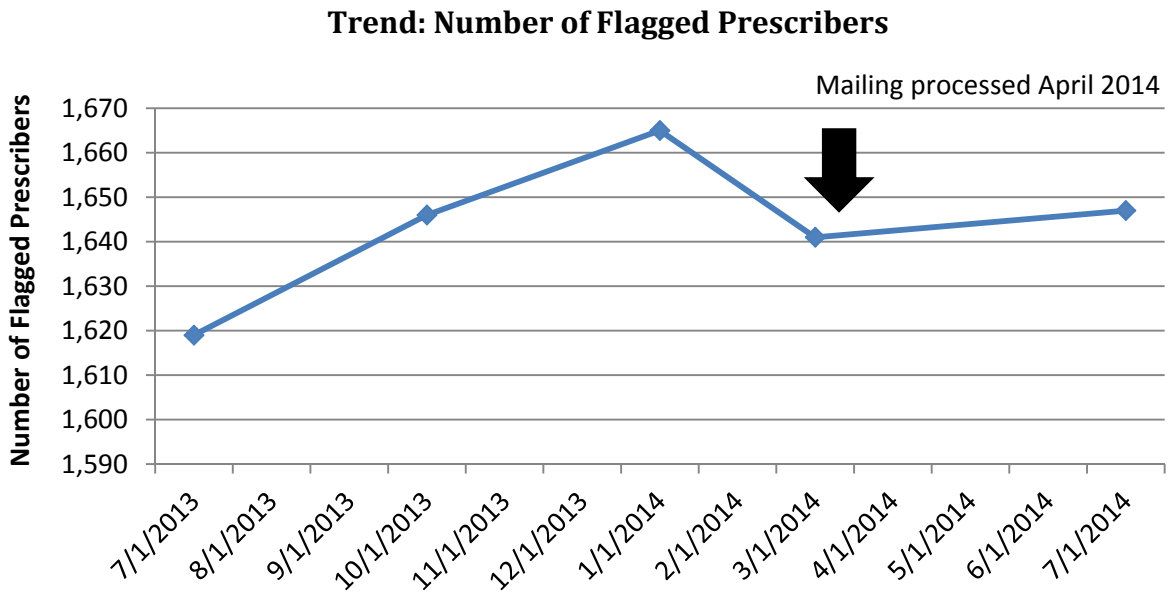
Example Gauge

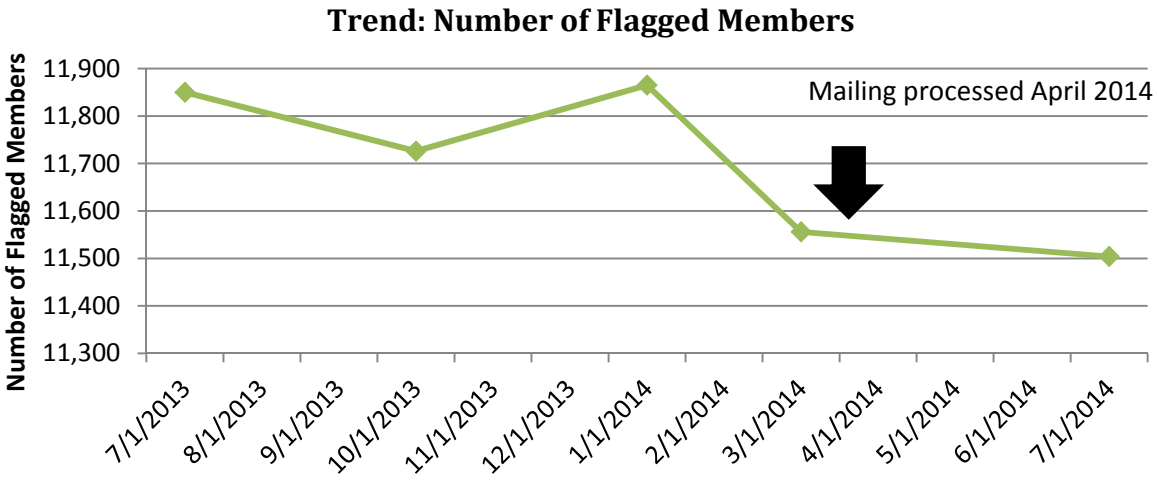


Top Prescriber Specialties of Atypical Antipsychotics Included in Mailing



Diagnosis Consistent with Antipsychotic Prescription Trends





Diagnosis Consistent with Antipsychotic Prescription Informational Page

Diagnoses consistent with a strong indication for antipsychotic use:

- Schizophrenia
- Bipolar disorders
- Severe depression with or without psychotic features
- Delusional disorders
- Other nonorganic psychoses
- Obsessive-compulsive disorders
- Autistic disorder
- Mood disorder*

All other mental health-related diagnoses or non-mental health-related diagnoses are considered weak or not-indicated for antipsychotic use.

The two most common diagnoses inconsistent with receipt of antipsychotics for SoonerCare were Attention Deficit Hyperactivity Disorder (ADHD) and Conduct/Disruptive Behavioral Disorders.

Medications indicated for treatment of ADHD:

- Psychostimulants: Methylphenidate HCl, Dextroamphetamine sulfate, and D- and L-amphetamine racemic mixture.
- Non-stimulants: Atomoxetine HCl, guanfacine, and clonidine.[1]

Medications indicated for treatment of Conduct/Disruptive Behavioral Disorders:

- Methylphenidate, Dextroamphetamine sulfate, Bupropion HCl, Fluoxetine HCl, Phenytoin, Carbamazepine, Valproic Acid, Lithium Carbonate, and Clonidine HCl.[2]

References
1. Pliszka S. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2007; 46(7):894-921
2. Searight HR, Rottnek F, & Abby SL. Conduct disorder: diagnosis and treatment in primary care. *Am Fam Physician.* 2001; 63(8):1579-1588.
*Mood disorder added based on input from Oklahoma providers and psychiatrists.

Appendix C

Vote to Prior Authorize
Harvoni® (Ledipasvir/Sofosbuvir)

Oklahoma Health Care Authority
December 2014

Recommendations

The College of Pharmacy recommends the prior authorization of Harvoni® (ledipasvir/sofosbuvir) with the following criteria:

Harvoni® (Ledipasvir/Sofosbuvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1** with a METAVIR fibrosis score of **F2** or greater; and
3. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
4. Hepatitis C Virus (HCV) genotype 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, baseline viral load, and cirrhosis will apply:
   a. **Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA less than 6 million IU/mL:**
      i. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 8 weeks
   b. **Treatment-naïve with or without cirrhosis:**
      i. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA greater than 6 million IU/mL
      ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 12 weeks
   c. **Treatment-experienced without cirrhosis**
      i. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
      ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 12 weeks
   d. **Treatment-experienced with cirrhosis**
      i. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
      ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 24 weeks
   e. New regimens will apply as approved by the FDA
7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and

9. 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
10. 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
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis; and
13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy; and
15. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease.
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
19. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, 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, due to superior SVR rates and shortened treatment durations with Harvoni®, authorization of Sovaldi™ or Olysio™ for genotype-1 will require a patient-specific, clinically significant reason why Harvoni® is not an option.

Appendix D

Vote to Prior Authorize
Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films)

Oklahoma Health Care Authority
December 2014

Recommendations

The College of Pharmacy recommends the prior authorization of Zubsolv® and Bunavail™ with the following criteria:

Zubsolv® (Buprenorphine/Naloxone Sublingual Tablets) and
Bunavail™ (Buprenorphine/Naloxone Buccal Films) Approval Criteria:

1. Oral buprenorphine products must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a DEA (X) number; and
2. Member must have an FDA approved diagnosis of opiate abuse/dependence; and
3. Concomitant treatment with opioids (including tramadol) will be denied; and
4. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
5. The following limitations will apply:
    a. **Zubsolv®** sublingual tablets: A quantity limit of 90 tablets per 30 days.
    b. **Bunavail™** 2.1mg/0.3mg and 4.2mg/0.7mg buccal films: A quantity limit of 90 films per 30 days.
    c. **Bunavail™** 6.3mg/1mg buccal films: A quantity limit of 60 films per 30 days.

Additionally, the College of Pharmacy recommends the addition of detailed criteria for high-dose oral buprenorphine regimens:

High Dose Buprenorphine Products Criteria:

1. Each request for greater than 24mg bioequivalent buprenorphine per day should be evaluated on a case-by-case basis.
2. A taper schedule should be documented on the petition or dates of an attempted taper with reason for failure should be documented or a patient-specific, clinically significant reason a taper schedule or attempt is not appropriate for the member; and
3. Opioid urine drug screens should be submitted with high-dose requests that plan to continue high-dose treatment longer than the duration of one month.
    a. Urine drug screens must show the absence of opioid medications other than buprenorphine products for continued approval; or

    b. Prescriber must document a patient-specific reason the member should continue therapy, reason for opioid use, and document a plan for member to discontinue opioid use; and
4. Symptoms associated with withdrawal at lower doses or symptoms requiring high doses should be listed on petition; and
5. Each approval will be for the duration of one month. If urine drug screen and other documentation are submitted indicating high-dose therapy is necessary an approval can be granted for the duration of three months.
6. Continued high-dose authorization after the three month approval will require a new (recent) urine drug screen.

Appendix E

Fiscal Year 2014 Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease Medications and 30-Day Notice to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol)

Oklahoma Health Care Authority
December 2014

Current Prior Authorization Criteria

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Anticholinergics (LAMA)	
Tier-1	**Tier-2**
Long Acting Beta$_2$ Agonists* (LABA)	
Serevent® (salmeterol inhalation powder)	Perforomist® (formoterol nebulizer solution)
Foradil® (formoterol aerosolized powder)	Brovana® (arformoterol nebulizer solution)
	Arcapta® (indacaterol inhalation powder
Long Acting Anticholinergics (LAMA)	
Spiriva® (tiotropium inhalation powder)	Tudorza® (aclidinium inhalation powder)

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

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

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

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

1. An FDA approved diagnosis of Chronic Obstructive Pulmonary Disease (COPD); or
2. An FDA approved diagnosis of Asthma:
    a. Medication must be indicated for member's age; and
    b. Member must have used an inhaled corticosteroid (ICS) product for at least one month immediately prior to request for authorization; and
    c. Member's asthma must be considered uncontrolled by prescriber:
        i. Member requires rescue inhaler more than two days per week for reasons other than prevention of exercise induced bronchospasms; or
        ii. Member requires oral systemic corticosteroids; or

d. Clinical situation warranting initiation with combination therapy due to severity of asthma.

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

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

Daliresp® (Roflumilast) Approval Criteria:

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

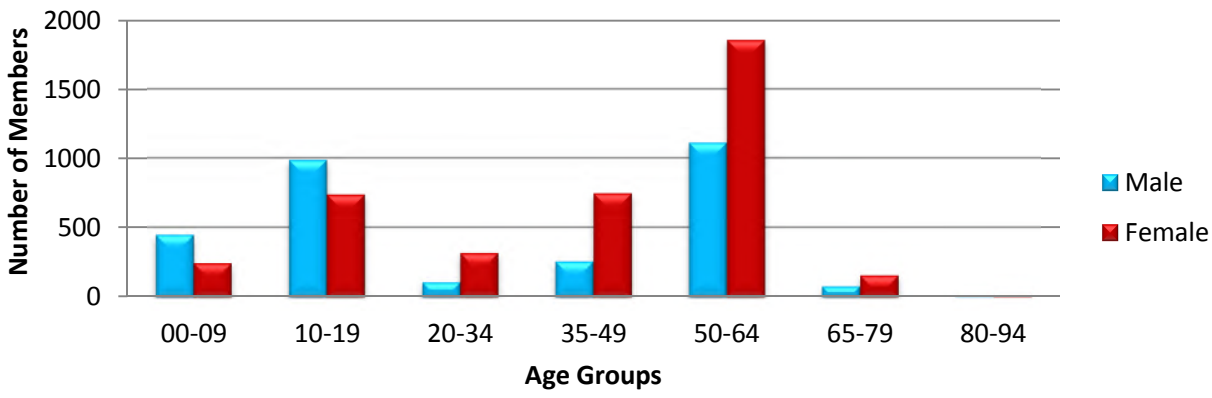
Utilization of Maintenance Asthma and COPD Medications

Comparison of Fiscal Years

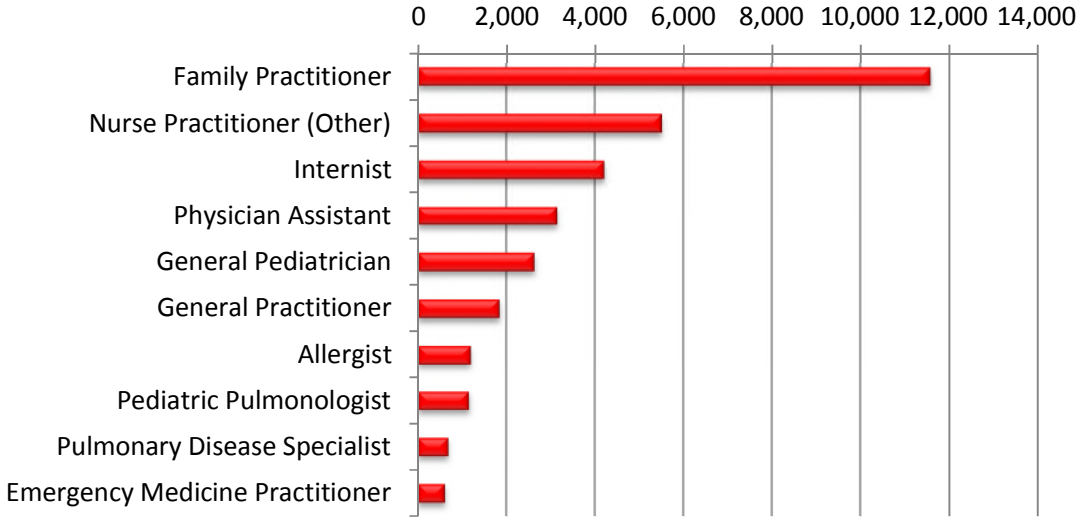
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	7,417	35,117	$9,029,331.81	$257.12	$8.46	1,410,875	1,067,042
2014	7,065	33,809	$9,588,011.79	$283.59	$9.30	1,267,320	1,031,345
% Change	**-4.70%**	**-3.70%**	**6.20%**	**10.30%**	**9.90%**	**-10.20%**	**-3.30%**
Change	**-352**	**-1,308**	**$558,679.98**	**$26.47**	**$0.84**	**-143,555**	**-35,697**

*Total number of unduplicated members.

Demographics of Members Utilizing Maintenance Asthma and COPD Medications



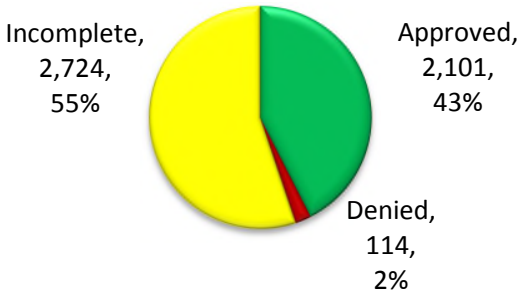
Top Prescriber Specialties of Maintenance Asthma and COPD Medications by Number of Claims



Prior Authorization of Maintenance Asthma and COPD Medications

There were a total of 4,939 petitions submitted for maintenance asthma and COPD medications during fiscal year 2014. Computer edits are in place to detect Tier-1 medications in members' recent claims history and generate automated prior authorizations where possible. Computer edits are also in place to detect a COPD diagnosis in a member's recent diagnosis history and generate automated prior authorizations for Tier-1 combination long-acting beta$_2$-adrenergic agonist (LABA)/corticosteroid products. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1]

Anticipated Patent Expirations:

- Advair® (fluticasone propionate/salmeterol)- 08/2016
- Serevent® (salmeterol)- 08/2016
- Dulera® (mometasone/formoterol)- 05/2020
- Foradil® (formoterol)- 11/2020
- Perforomist® (formoterol)- 06/2021
- Brovana® (arformoterol)- 11/2021
- Daliresp® (roflumilast)- 03/2024

- Spiriva® (tiotropium)- 03/2027
- Tudorza® (aclidinium)- 04/2027
- Striverdi® Respimat® (olodaterol)- 03/2028
- Spiriva® Respimat® (tiotropium)- 03/2028
- Arcapta® (indacaterol)- 11/2028
- Symbicort® (budesonide/formoterol)- 04/2029
- Breo® Ellipta™ (fluticasone furoate/vilanterol)- 10/2030

New FDA Approvals:

- Anoro™ Ellipta® (umeclidinium/vilanterol inhalation powder)- 12/18/2013
- Incruse™ Ellipta® (umeclidinium inhalation powder)- 04/30/2014
- Striverdi® Respimat® (olodaterol inhalation spray)- 07/31/2014
- Arnuity™ Ellipta® (fluticasone furoate inhalation powder)- 08/20/2014
- Spiriva® Respimat® (tiotropium soft mist inhaler)- 09/25/2014

Anoro™ Ellipta® (Umeclidinium/Vilanterol Inhalation Powder)[2]

Indications: Anoro™ Ellipta® (umeclidinium/vilanterol inhalation powder) is a combination of umeclidinium, an anticholinergic, and vilanterol, a long-acting beta$_2$-adrenergic agonist (LABA), indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD. Anoro™ Ellipta® is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Anoro™ Ellipta® Dosing:

- Anoro™ Ellipta® is available as an inhalation powder. The inhaler contains two double-foil blister strips of powder formulation for oral inhalation. Each strip contains 62.5mcg of umeclidinium per blister and 25mcg of vilanterol per blister.
- The recommended maintenance treatment is one inhalation once daily.
- Anoro™ Ellipta® is for oral inhalation only.

Mechanism of Action:

- Umeclidinium is one of the active ingredients in Anoro™ Ellipta®. Umeclidinium is a long-acting antimuscarinic agent (LAMA), which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3 receptor at the smooth muscle leading to bronchodilation.
- Vilanterol is a LABA and an active ingredient in Anoro™ Ellipta®. *In vitro* tests have shown the functional selectivity of vilanterol was similar to salmeterol. The clinical relevance of this *in vitro* finding is unknown. The pharmacologic effects of beta$_2$-adrenergic agonist drugs, including vilanterol, are at least in part attributable to stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels cause relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

Contraindications: Severe hypersensitivity to milk proteins or any ingredients.

Incruse™ Ellipta® (Umeclidinium Inhalation Powder)[3]

Incruse™ Ellipta® (umeclidinium inhalation powder) is a LAMA , also known as an anticholinergic, indicated for the long-term, once-daily maintenance treatment of airflow obstruction in patients with COPD.

Incruse™ Ellipta® Dosing:

- Incruse™ Ellipta® is available as an inhalation powder. The inhaler contains one double-foil blister strip of powder formulation for oral inhalation. Each strip contains 62.5mcg of umeclidinium per blister.
- The recommended maintenance treatment for COPD is one inhalation once daily.
- Incruse™ Ellipta® is for oral inhalation only.

Mechanism of Action:

- Umeclidinium is the active ingredient in Incruse™ Ellipta®. Umeclidinium is a LAMA, and has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3 receptor at the smooth muscle leading to bronchodilation.

Contraindications: Severe hypersensitivity to milk proteins or any ingredients.

Spiriva® Respimat® (Tiotropium Soft Mist Inhaler)[4]

Spiriva® Respimat® (tiotropium soft mist inhaler) is a LAMA, also known as an anticholinergic, indicated as maintenance bronchodilator treatment to relieve symptoms of patients with COPD.

Spiriva® Respimat® Dosing:

- Spiriva® Respimat® is available as an inhalation spray. Each actuation contains 2.5mcg of tiotropium. Two actuations equal one dose.
- The recommended dose is two inhalations of the spray once daily.
- Spiriva® Respimat® is for oral inhalation only.

Mechanism of Action:

- Tiotropium is a LAMA and an active ingredient in Spiriva® Respimat®. It has similar affinity to the subtypes of muscarinic receptors, M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3-receptors at the smooth muscle leading to bronchodilation.

Contraindications:

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

Striverdi® Respimat® (Olodaterol Inhalation Spray)[5]

Striverdi® Respimat® (olodaterol inhalation spray) is a LABA indicated for the long-term, once-daily, maintenance bronchodilator treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

Striverdi® Respimat® Dosing:

- Striverdi® Respimat® is available as an inhalation spray. Each actuation contains 2.5mcg olodaterol per actuation. Two actuations equal one dose
- The recommended dose is two inhalations of the spray once daily. Doses should be taken at the same time of day.
- Striverdi® Respimat® is for oral inhalation only.

Mechanism of Action:

- Olodaterol is a LABA and the active ingredient in Striverdi® Respimat®. The compound exerts its pharmacological effects by binding and activation of beta$_2$-adrenoceptors after topical administration by inhalation. Activation of these receptors in the airways results in a stimulation of intracellular adenyl cyclase, an enzyme that mediates the synthesis of cyclic-3', 5' adenosine monophosphate (cAMP). Elevated levels of cAMP induce bronchodilation by relaxation of airway smooth muscle cells.

Contraindications:

- All LABA medications are contraindicated in patients with asthma without use of a long-term asthma control medication.
- Striverdi® Respimat® is not indicated for treatment of asthma.

Cost Comparison

Medication Name	Strength	Cost/ Month
Combination LAMA/LABA		
Anoro™ Ellipta® (umeclidinium/vilanterol)	62.5mcg/25mcg	$296.40
Individual Component LAMA		
Incruse™ Ellipta® (umeclidinium)	62.5mcg	Not Available
Spiriva® Respimat® (tiotropium)	2.5mcg	$314.48
Spiriva® Handihaler® (tiotropium)	18mcg	$314.10
Individual Component LABA		
Striverdi® Respimat® (olodaterol)	2.5mcg	$164.40
Serevent® (salmeterol)	50mcg	$234.00
Foradil® (formoterol)	12mcg	$234.00

+Estimated Acquisition Cost (EAC)
Rebated prices are not included in the above stated costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Anoro™ Ellipta® (umeclidinium/vilanterol inhalation powder) with the following criteria:

Anoro™ Ellipta® (Umeclidinium/Vilanterol Inhalation Powder) Approval Criteria:

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

Additionally, the College of Pharmacy recommends placement of Incruse™ Ellipta® (umeclidinium inhalation powder), Spiriva® Respimat® (tiotropium soft mist inhaler), and Striverdi® Respimat® (olodaterol inhalation spray) in the Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Anticholinergics (LAMA) product based prior authorization category. Current criteria for this category will apply.

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

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

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

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

Utilization Details of Maintenance Asthma and COPD Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
COMBINATION LABA/ICS PRODUCTS						
ADVAIR DISKUS AER 250/50	7,881	1,964	$2,259,878.63	$9.51	$286.75	23.57%
SYMBICORT AER 160-4.5	3,846	999	$980,467.66	$7.98	$254.93	10.23%
ADVAIR DISKUS AER 500/50	2,739	615	$1,031,017.78	$12.53	$376.42	10.75%
ADVAIR DISKUS AER 100/50	2,680	699	$619,589.29	$7.65	$231.19	6.46%
ADVAIR HFA AER 115/21	2,212	676	$621,554.39	$9.02	$280.99	6.48%
SYMBICORT AER 80-4.5	917	270	$202,480.68	$7.07	$220.81	2.11%
DULERA AER 100-5MCG	774	223	$187,420.67	$7.92	$242.15	1.95%
DULERA AER 200-5MCG	717	251	$172,328.35	$7.88	$240.35	1.80%
ADVAIR HFA AER 230/21	669	219	$248,345.83	$12.20	$371.22	2.59%
ADVAIR HFA AER 45/21	138	67	$30,558.12	$7.12	$221.44	0.32%
SUBTOTAL	**22,573**	**5,983**	**$6,353,641.40**	**$8.89**	**$272.63**	**66.26%**
INDIVIDUAL COMPONENT LABA PRODUCTS						
TIER-1						
SEREVENT DIS AER 50MCG	396	164	$82,531.74	$6.95	$208.41	0.86%
FORADIL CAP AEROLIZE	208	67	$40,545.81	$6.41	$194.93	0.42%
TIER-2						
BROVANA NEB 15MCG	78	17	$41,030.45	$16.38	$526.03	0.43%
PERFOROMIST NEB 20MCG	44	11	$22,490.75	$17.04	$511.15	0.23%
SUBTOTAL	**726**	**259**	**$186,598.75**	**$11.70**	**$360.13**	**1.94%**
INDIVIDUAL COMPONENT LAMA PRODUCTS						
TIER-1						
SPIRIVA CAP HANDIHLR	10,142	2,462	$2,965,519.88	$9.67	$292.40	30.93%
TIER-2						
TUDORZA PRES AER 400/ACT	82	23	$19,614.18	$7.97	$239.20	0.20%
SUBTOTAL	**10,224**	**2,485**	**$2,985,134.06**	**$8.82**	**$265.80**	**31.13%**
COMBINATION LABA/LAMA PRODUCTS						
ANORO ELLIPTA AER 62.5-25	1	1	$297.20	$4.95	$297.20	0.00%
SUBTOTAL	**1**	**1**	**$297.20**	**$4.95**	**$297.20**	**0.00**
PHOSPHODIESTERASE-4 ENZYEME INHIBITOR						
DALIRESP TAB 500MCG	285	51	$62,340.38	$7.25	$218.74	0.65%
SUBTOTAL	**285**	**51**	**$62,340.38**	**$7.25**	**$218.74**	**0.65%**
TOTAL	**33,809**	**7,065***	**$9,588,011.79**	**$9.30**	**$289.68**	**100%**

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 10/14. Last accessed 11/2014.

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Appendix F

30-Day Notice to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone)

Oklahoma Health Care Authority
December 2014

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

Idiopathic pulmonary fibrosis (IPF) is a chronic, incurable lung condition that is characterized by varying degrees of fibrosis, collagen deposits, and distortion of the pulmonary architecture. Although the specific initiating factor(s) leading to IPF are unknown, lung injury progresses due to interaction with growth factors, cytokines, and other mediators, leading to fibroblast proliferation and excessive extracellular matrix deposition in the lungs.

Clinical manifestations include progressive symptoms of dyspnea and cough and worsening pulmonary function. Over time, fibrosis of the lungs increases until the lungs can no longer provide enough oxygen to the body's organs and tissues. The natural progression of IPF varies among individuals; however, prognosis is poor, with a median survival of approximately three years after diagnosis. The most common cause of death related to IPF is respiratory failure. Other causes of death related to IPF include pulmonary hypertension, heart failure, pulmonary embolism, pneumonia, and lung cancer.

It is estimated that IPF affects approximately 100,000 individuals in the United States, with 30,000-40,000 new cases being diagnosed each year.[8] IPF is usually diagnosed in adults over the age of 50 years and is more common in men than in women. Approximately 1-4% of patients with IPF have a family history of this disease, so these patients may be diagnosed at a younger age. IPF occurring in multiple members of the same family is known as familial pulmonary fibrosis.

Pharmacologic treatments for IPF are limited. Prior to the FDA approval of Ofev® (nintedanib) and Esbriet® (pirfenidone), no medications were approved for the treatment of IPF. Traditional approaches to treat IPF have included prednisone, azathioprine, and N-acetylcysteine, either alone or in combination; however, this approach does not seem to be effective and there is not adequate evidence to support the use of these medications. Treatment has predominantly been limited to supportive care (e.g., oxygen therapy, pulmonary rehabilitation), with lung transplantation an option for selected patients.

The FDA granted approval through a process of fast track, orphan product, breakthrough designation, and priority review to two new products for the treatment of IPF, Ofev® (nintedanib) and Esbriet® (pirfenidone), in October 2014. Ofev® and Esbriet® slow the rate of progressive lung function decline, but do not cure IPF or lead to improvement of lung function.

Ofev® (Nintedanib Capsules) Summary[9,10,11,12]

Indications: Ofev® (nintedanib) is indicated for the treatment of IPF in adult patients.

Dosing:

- Ofev® is available as 100mg and 150mg oral capsules.
- The recommended dosage of Ofev® is 150mg by mouth twice daily, administered approximately 12 hours apart.
- Ofev® capsules should be taken with food and swallowed whole with liquid. Ofev® capsules should not be chewed or crushed because of a bitter taste. The effect of chewing or crushing of the capsule on the pharmacokinetics of Ofev® is not known.
- In addition to symptomatic treatment, if applicable, the management of adverse reactions of Ofev® may require dose reduction or temporary interruption until the specific adverse reaction resolves to levels that allow continuation of therapy.
- Dose modifications or interruptions may be necessary for liver enzyme elevations (for aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than three times to less than five times the upper limit of normal (ULN) without signs of severe liver damage). Ofev® should be discontinued for AST or ALT elevations greater than five times ULN or greater than three times ULN with signs or symptoms of severe liver damage.

Mechanism of Action: Ofev® is a kinase inhibitor shown to inhibit fibroblast growth factor receptor (FGFR), platelet-derived growth factor receptor (PDGFR), and vascular endothelial growth factor receptor (VEGFR), all of which have been implicated in IPF pathogenesis. Competitive binding to these receptors block the intracellular signaling that is necessary for the proliferation, migration, and transformation of fibroblasts.

Contraindications: None

Efficacy:

- The efficacy of Ofev® for the treatment of IPF was established in one phase-2 and two phase-3 randomized, double-blind, placebo-controlled studies comparing treatment with Ofev® 150mg twice daily to placebo for 52 weeks in a total of 1,231 patients.
- The primary endpoint was the annual rate of decline in forced vital capacity (FVC). Time to first acute IPF exacerbation, change from baseline in percent predicted forced vital capacity (%FVC), and survival were secondary endpoints.
- A statistically significant reduction in the annual rate of decline of FVC was demonstrated in patients receiving Ofev® compared to patients receiving placebo. The treatment effect on FVC was consistent in all 3 studies.
- The time to first acute IPF exacerbation was significantly reduced in patients receiving Ofev® compared to placebo in two of the three studies, with no difference between the treatment groups in one study. For the change from baseline in %FVC, the proportion of patients declining was lower on Ofev® than on placebo. All-cause mortality was assessed irrespective of cause of death and whether patients continued treatment, and did not show a statistically significant difference between the treatment groups.

Safety:

- In clinical trials, administration of Ofev® was associated with elevations of liver enzymes, which were reversible with dose modification or interruption and not associated with

clinical signs or symptoms of liver injury. Liver function tests should be conducted prior to initiating treatment with Ofev®, monthly for three months, every three months thereafter, and as clinically indicated. Dosage modifications or interruption may be necessary for liver enzyme elevations.

- Ofev® can cause fetal harm when administered during pregnancy. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Ofev® and to use adequate contraception during treatment and at least 3 months after the last dose of Ofev®.
- Ofev® may increase the risk of bleeding due to inhibition of VEGFR. Monitor patients on full anticoagulation therapy closely for bleeding and adjust anticoagulation treatment as necessary.
- Ofev® is a substrate of P-glycoprotein (P-gp) and, to a minor extent, CYP3A4. Concomitant use of P-gp and CYP3A4 inhibitors (e.g., ketoconazole, erythromycin) may increase exposure to Ofev®. In such cases, patients should be monitored closely for tolerability of Ofev®. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with Ofev®. Concomitant use of P-gp and CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's Wort) with Ofev® should be avoided, as these drugs may decrease exposure to Ofev®.
- The most common adverse reactions leading to discontinuation of Ofev® were diarrhea, nausea, and decreased appetite. The most common adverse reaction that led to permanent dose reduction in patients treated with Ofev® was diarrhea. Other common adverse reactions include abdominal pain, liver enzyme elevation, vomiting, decreased weight, headache, and hypertension.

Cost:

Medication Name	Cost/Capsule*	Cost/Month	Cost/Year
Ofev® (nintedanib)	$140.80	$8,448.00	$101,376.00

*Cost based on Estimated Acquisition Cost (EAC)

Utilization: There has been no utilization of Ofev® in the SoonerCare population since its approval in October 2014.

Esbriet® (Pirfenidone Capsules) Summary[13,14,15,16]

Indications: Esbriet® (pirfenidone) is indicated for the treatment of IPF in adult patients.

Dosing:

- Esbriet® is available as 267mg oral capsules.
- Upon initiation of treatment, Esbriet® dosage should be titrated over a 14-day period as follows: one capsule (267mg) three times a day on days 1-7, then two capsules (534mg) three times a day on days 8-14, then three capsules (801mg) three times a day on day 15 onward.
- The recommended daily maintenance dosage of Esbriet® is 801mg (three 267mg capsules) by mouth three times daily for a total of 2,403mg per day. Doses greater than 2,403mg per day are not recommended for any patient.
- Esbriet® should be taken with food, and doses should be taken at the same time each day.

- If patients experience significant adverse reactions (e.g., gastrointestinal, photosensitivity reaction or rash), consider temporary dosage reductions or interruptions of Esbriet® to allow for resolution of symptoms.
- Dosage modifications or interruptions may be necessary for liver enzyme elevations (for AST or ALT greater than three times to less than or equal to five times ULN without symptoms of hyperbilirubinemia) and for bilirubin elevations. Esbriet® should be permanently discontinued for AST or ALT elevations greater than five times ULN or greater than three times to less than or equal to five times ULN with symptoms of hyperbilirubinemia, and the patient should not be rechallenged with Esbriet®.

Mechanism of Action: Esbriet® belongs to the pyridone chemical class; however, the mechanism of action for the treatment of IPF has not been established. In in-vitro and animal models, it has been shown to regulate the activity of transforming growth factor (TGF) beta and tumor necrosis factor (TNF) alpha and inhibit fibroblast proliferation and collagen synthesis.

Contraindications: None

Efficacy:
- The efficacy of Esbriet® for the treatment of IPF was evaluated in three phase-3, randomized, double-blind, placebo-controlled, multicenter trials comparing treatment with Esbriet® to placebo in a total of 1,247 patients. One trial was for a duration of 52 weeks, while the other two trials were for a duration of 72 weeks.
- The primary endpoint was change in %FVC from baseline to study end.
- A statistically significant treatment effect in the change in %FVC from baseline was demonstrated in patients receiving Esbriet® compared to patients receiving placebo in two of the three studies. There was no statistically significant difference in one of the three studies.
- Mean change from baseline in FVC was evaluated, and a reduction in the mean decline in FVC was observed in two of the three studies, but there was no statistically significant difference in one of the three studies.
- Survival was evaluated for Esbriet® compared to placebo in all three studies as an exploratory analysis to support the primary endpoint. All-cause mortality was assessed over the study duration and available follow-up period, irrespective of cause of death and whether patients continued treatment, and did not show a statistically significant difference between the treatment groups.

Safety:
- Increases in ALT and AST greater than three times ULN have been reported in patients treated with Esbriet®, which were reversible with dose modification or treatment discontinuation, and rarely were associated with concomitant elevations in bilirubin. Liver function tests should be conducted prior to initiating treatment with Esbriet®, monthly for the first six months, and every three months thereafter. Dosage modifications or interruption may be necessary for liver enzyme elevations.
- Esbriet® is metabolized primarily by CYP1A2, with minor contributions from other CYP isoenzymes including CYP2C9, CYP2C19, CYP2D6, and CYP2E1. The concomitant administration of Esbriet® and strong CYP1A2 inhibitors (e.g., fluvoxamine) is not recommended because it significantly increases exposure to Esbriet®. The concomitant

use of Esbriet® and a CYP1A2 inducer may decrease the exposure of Esbriet® and may lead to loss of efficacy; therefore, the use of strong CYP1A2 inducers should be discontinued prior to Esbriet® treatment and concomitant use should be avoided.

- In clinical studies, patients treated with Esbriet® had a higher incidence of photosensitivity reactions compared with patients treated with placebo. The majority of the photosensitivity reactions occurred during the initial six months, and patients were instructed to avoid or minimize exposure to sunlight, to use a sunblock, to wear clothing that protects against sun exposure, and to avoid concomitant medications known to cause photosensitivity. Dosage reduction or discontinuation may be necessary in some cases of photosensitivity reaction or rash.
- The most common adverse reactions leading to discontinuation of Esbriet® were rash and nausea. The most common adverse reactions that led to dose reduction or interruption in patients treated with Esbriet® were rash, nausea, diarrhea, and photosensitivity reaction. Other common adverse reactions include abdominal pain, upper respiratory tract infection, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastroesophageal reflux disease, sinusitis, insomnia, decreased weight, and arthralgia.

Cost:

Medication Name	Cost/Capsule*	Cost/Month	Cost/Year
Esbriet® (pirfenidone)	$30.51	$8,237.70	$98,852.40

*Cost based on Estimated Acquisition Cost (EAC)

Utilization: There has been no utilization of Esbriet® in the SoonerCare population since its approval in October 2014.

Recommendations

The College of Pharmacy recommends prior authorization of Ofev® (nintedanib) and Esbriet® (pirfenidone) with the following criteria:

Ofev® (Nintedanib) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. A quantity limit of 60 capsules per 30 days will apply.

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. A quantity limit of 270 capsules per 30 days will apply.

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[15] Micromedex 2.0: Esbriet® Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 10/31/14. Last accessed 11/19/14.
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Appendix G

Fiscal Year 2014 Annual Review of Testosterone Products and 30-Day Notice to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel)

Oklahoma Health Care Authority
December 2014

Current Prior Authorization Criteria

Testosterone Products		
Tier-1*	**Tier-2**	**Special PA**
methyltestosterone powder	testosterone patch (Androderm®)	fluoxymesterone oral tablet (Androxy®)
testosterone cypionate injection (Depo-Testosterone®)	testosterone topical gel (Fortesta®)	methyltestosterone oral tablet/capsule (Android®, Methitest® ,Testred®)
testosterone enanthate injection	testosterone topical solution (Axiron®)	testosterone buccal tablet (Striant®)
testosterone topical gel (Androgel®, Testim®)		testosterone (Testopel Pellets®)

* Tier-1 products include generic injectable products and supplemental rebated topical products.

Initial Approval Criteria for All Testosterone Products:

1. An FDA approved diagnosis:
   a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome; or orchidectomy; or
   b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation; or
   c. Delayed puberty; or
   d. Advanced inoperable metastatic mammary cancer in females one to five years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and
2. Must include two labs showing pre-medication, morning testosterone levels below 300ng/dL; and
3. Must include one lab showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis.

Testosterone Products Tier-2 Authorization Criteria:

1. All diagnoses and laboratory requirements listed above must be met; and
2. A trial of at least two Tier-1 products (must include at least one injectable and one topical formulation) at least 12 weeks in duration; or
3. A patient-specific, clinically significant reason why member cannot use all available Tier-1 medications; or

4. Prior stabilization on a Tier-2 medication (within the past 180 days).
5. Approvals will be for the duration of one year.

Testosterone Products Special Prior Authorization Criteria:

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

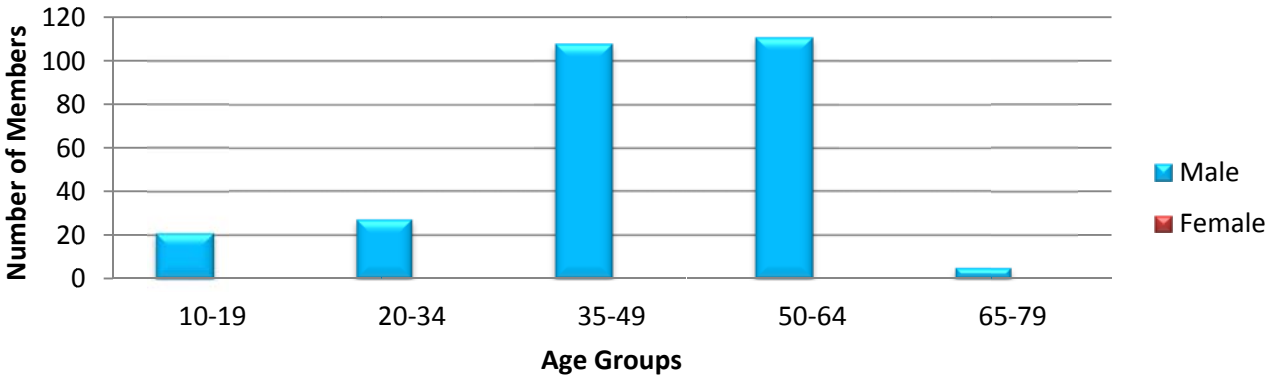
Utilization of Testosterone Products

Comparison of Fiscal Years

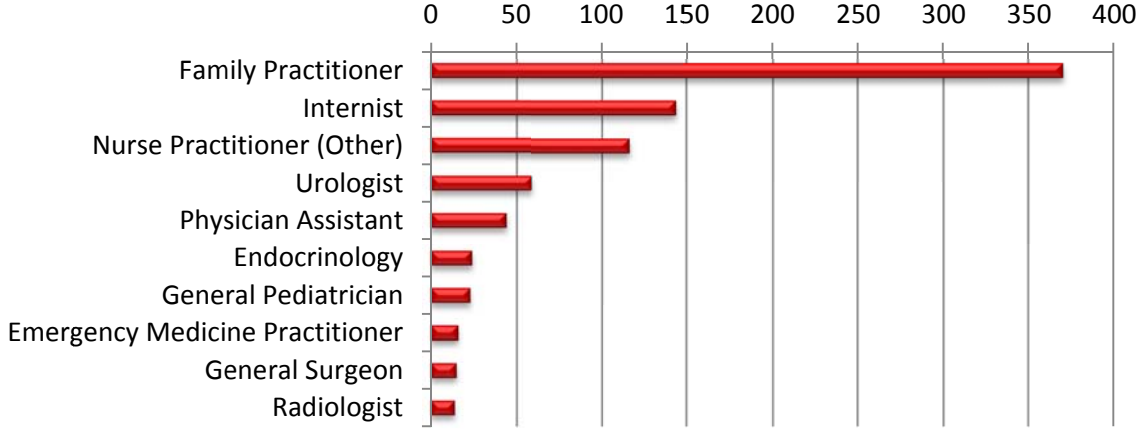
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	347	1,044	$279,749.30	$267.96	$5.55	77,032	50,418
2014	273	863	$245,426.29	$284.39	$5.90	63,693	41,624
% Change	**-21.30%**	**-17.30%**	**-12.30%**	**6.10%**	**6.30%**	**-17.30%**	**-17.40%**
Change	**-74**	**-181**	**-$34,323.01**	**$16.43**	**$0.35**	**-13,339**	**-8,794**

*Total number of unduplicated members.

Demographics of Members Utilizing Testosterone Products



Top Prescriber Specialties of Testosterone Products by Number of Claims



Prior Authorization of Testosterone Products

There was a total of 941 petitions submitted for the testosterone products category during fiscal year 2014.

Status of Petitions

Market News and Updates[1,2,3]

Anticipated Patent Expirations:

- Androderm® (testosterone transdermal patch)- 10/2014
- Axiron® (testosterone topical solution)- 02/2017
- Striant® (testosterone buccal tablet)- 08/2019
- Androgel® (testosterone topical gel)- 03/2021
- Testim® (testosterone topical gel)- 01/2025

New FDA Approvals:

- Natesto™ (testosterone nasal gel)- 05/2014
- Aveed® (testosterone undecanoate injection)- 06/2014
- Vogelxo™ (testosterone gel 1%) and its exclusive generic- 06/2014
- Testosterone topical gel 2% (generic for Fortesta®)- 08/2014

FDA Safety Alert:

- June 2014: The FDA has mandated a new general warning in the drug labeling regarding the risk of venous thromboembolisms (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) with the use of testosterone.
- November 2014: A study presented by Intermountain Medical Center Heart Institute has found that taking supplemental testosterone does not increase the risk of experiencing a major adverse cardiac event, such as heart attack or stroke.

Natesto™ (Testosterone Nasal Gel)[4]

Indications: Natesto™ (testosterone nasal gel) is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone (congenital or acquired primary hypogonadism and congenital or acquired hypogonadotropic hypogonadism).

Dosing:

- Natesto™ is available as a metered dose pump. One pump actuation delivers 5.5mg of testosterone.

- The recommended dose of Natesto™ is 11mg (2 pump actuations, one per nostril) three times daily.
- Serum total testosterone concentrations should be checked periodically, starting one month after initiating Natesto™. If total testosterone concentrations consistently exceed 1050ng/dL, therapy with Natesto™ should be discontinued. If total testosterone concentrations are consistently less than 300ng/dL, an alternative treatment should be considered.

Mechanism of Action: Testosterone is an endogenous androgen responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; the development of male hair distribution, such as facial, pubic, chest, and axillary hair; laryngeal enlargement, vocal cord thickening, alterations in the body musculature, and fat distribution. Testosterone and dihydrotestosterone (DHT) are necessary for the normal development of secondary sex characteristics.

Contraindications:
- Men with carcinoma of the breast or known or suspected prostate cancer
- Pregnant or breast-feeding women. Testosterone may cause fetal harm.

Efficacy:
- The efficacy of Natesto™ was evaluated in a 90-day, open-label, multicenter trial of 306 hypogonadal men 18 years of age and older (mean age 54 years) who had morning serum total testosterone concentrations less than 300ng/dL. Patients were instructed to self-adminsiter Natesto™ either two or three times daily.
- A total of 78 hypogonadal men received Natesto™ three times daily. Of these, 73 patients were included in the statistical evaluation of efficacy on Day 90; 90% of these patients had an average serum concentration (C_{AVG}) within the normal range (300 to 1050ng/dL), 10% had a C_{AVG} less than 300ng/dL, and no patients had a C_{AVG} greater than 1050ng/dL.

Safety:
- The most common adverse effects reported with Natesto™ during clinical trials were prostate specific antigen (PSA) increased, headache, rhinorrhea, epistaxis, nasal discomfort, nasopharyngitis, bronchitis, upper respiratory tract infection, sinusitis, and nasal scab.
- Natesto™ is not recommended for use in patients with chronic nasal conditions or alterations in nasal anatomy.
- Venous thromboembolisms, including DVT and PE have been reported in patients using testosterone products. Evaluate patients with signs or symptoms consistent with DVT or PE.

Aveed® (Testosterone Undecanoate Injection)[5]

Indications: Aveed® (testosterone undecanoate injection) is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone (congenital or acquired primary hypogonadism and congenital or acquired hypogonadotropic hypogonadism).

Dosing:

- Aveed® is available as 750mg/3mL sterile injectable solution.
- The recommended dosing for Aveed® is 3mL to be injected intramuscularly at initiation, at four weeks, and every ten weeks thereafter.
- Following each injection of Aveed®, patients should be observed in the healthcare setting for 30 minutes in order to provide appropriate medical treatment in the event of serious pulmonary oil microembolism (POME) reactions or anaphylaxis.

Mechanism of Action: Testosterone is an endogenous androgen responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics.

Contraindications:

- Men with carcinoma of the breast or known or suspected carcinoma of the prostate.
- Pregnant or breastfeeding women. Testosterone may cause fetal harm.
- Known hypersensitivity to Aveed® or its ingredients (testosterone undecanoate, refined castor oil, benzyl benzoate).

Efficacy:

- The efficacy of Aveed® was evaluated in an 84-week, single-arm, open-label, multicenter study of 130 hypogonadal men weighing at least 65kg, who were 18 years of age and older (mean age (54.2 years), and who had a morning serum testosterone concentration less than 300ng/dL.
- All patients received injections of Aveed® 750mg at baseline, four weeks, and then every ten weeks thereafter. A total of 117 patients completed the study through Week 24. Approximately 94% of patients maintained a C_{AVG} within normal range (300 to 1000ng/dL), 5.1% of patients had a C_{AVG} below the normal range (less than 300ng/dL), and 0.9% had a C_{AVG} greater than 1000ng/dL.

Safety:

- Aveed® has a black box warning regarding serious POME reactions and anaphylaxis and is available only through a restricted program called the Aveed® REMS Program. Serious POME reactions, involving urge to cough, dyspnea, throat tightening, chest pain, dizziness, and syncope; and episodes of anaphylaxis, including life-threatening reactions, have been reported to occur during or immediately after the administration of testosterone undecanoate injection. These reactions can occur after any injection of testosterone undecanoate during the course of therapy, including after the first dose.
- Venous thromboembolisms, including DVT and PE have been reported in patients using testosterone products. Evaluate patients with signs or symptoms consistent with DVT or PE.
- The most commonly reported adverse effects during clinical trials of Aveed® were acne, injection site pain, PSA increased, estradiol increased, hypogonadism, fatigue, irritability, hemoglobin increased, insomnia, and mood swings.

Vogelxo™ (Testosterone Topical Gel)[6]

Indications: Vogelxo™ (testosterone topical gel) is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone (congenital or acquired primary hypogonadism and congenital or acquired hypogonadotropic hypogonadism).

Dosing:

- Vogelxo™ is available as 50mg unit-dose tube, 50mg unit-dose packet, and 12.5mg per actuation metered-dose pump.
- The recommended starting dose for Vogelxo™ is 50mg applied topically once daily at the same time each day. Apply to clean, dry, intact skin of the shoulders and/or upper arms.
- If morning pre-dose serum testosterone concentration is below the normal range, increase dose to 100mg. Pre-dose serum testosterone concentration should be assessed periodically.

Mechanism of Action: Testosterone is an endogenous androgen responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics.

Contraindications:

- Men with known carcinoma of the breast or known or suspected carcinoma of the prostate.
- Pregnant or breastfeeding women. Testosterone may cause fetal harm.

Efficacy:

- The efficacy of Vogelxo™ was evaluated in a randomized multicenter, multi-dose, active and placebo controlled 90-day study in 406 adult males with morning testosterone levels less than or equal to 300ng/dL. During the first 60 days, patients were evenly randomized to testosterone gel 50mg, testosterone gel 100mg, placebo gel, or testosterone transdermal system. At day 60, patients receiving testosterone gel were maintained, titrated up, or titrated down within their treatment group, based on C_{AVG} levels obtained on day 30.
- Of the 192 patients who were titrated with testosterone gel and who had sufficient data for analysis, 74% achieved an average serum testosterone level within the normal range (300 to 1000ng/dL) on day 90.

Safety:

- Vogelxo™ has a black box warning for secondary exposure to testosterone. Avoid unintentional exposure of women or children to Vogelxo™. Secondary exposure to testosterone can produce signs of virilization. Children should avoid contact with unwashed or unclothed application sites in men using testosterone gel.
- Venous thromboembolisms, including DVT and PE have been reported in patients using testosterone products. Evaluate patients with signs or symptoms consistent with DVT or PE.
- The most common adverse reactions reported during clinical trials were application site reactions and increased hematocrit.

Cost Comparison

Medication	Dosing∞	Cost/Day	Cost/Month
Natesto™	TID	Not Available	Not Available
Vogelxo™	QD	$10.90 - $27.40+	$327.00 - $822.00
Aveed®	Every 10 weeks*	$11.61+	$348.48
Testosterone Enanthate Inj	Every 2 - 4 weeks	$0.49 - $1.99+	$14.95 - $59.80

∞Dosing is based on FDA approved dosing regimens and/or SoonerCare quantity limits, if applicable.
*Following dose at initiation and at week 4.
+Estimated Acquisition Cost (EAC)

Recommendations

The College of Pharmacy recommends the following changes to the Testosterone Product Based Prior Authorization category:

1. Place Natesto™, Aveed®, Testim®, and Vogelxo™ into Tier-2.
2. Tier-1 includes supplemental rebated topical product(s) and generic injectable products.

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

*Tier-1 products include generic injectable products and supplemental rebated product(s).

Initial Approval Criteria for All Testosterone Products:

1. An FDA approved diagnosis:
   a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome; or orchidectomy; or
   b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation; or
   c. Delayed puberty; or
   d. Advanced inoperable metastatic mammary cancer in females one to five years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and
2. Must include two labs showing pre-medication, morning testosterone (total testosterone) levels below 300ng/dL; and

3. Must include one lab showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis.

Testosterone Products Tier-2 Authorization Criteria:

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

Testosterone Products Special Prior Authorization Criteria:

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

Utilization Details of Testosterone Products: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
PROPOSED TIER-1 PRODUCTS						
DEPO-TESTOST INJ 100MG/ML	8	5	$585.02	$0.60	$73.13	0.24%
DEPO-TESTOST INJ 200MG/ML	44	23	$2,495.81	$1.31	$56.72	1.02%
METHYLTESTOS POW USP	2	2	$11.55	$0.26	$5.78	0.00%
TESTOST CYP INJ 100MG/ML	4	3	$210.21	$0.48	$52.55	0.09%
TESTOST CYP INJ 200MG/ML	305	138	$21,914.05	$0.96	$71.85	8.93%
TESTOST ENAN INJ 200MG/ML	16	7	$1,309.88	$1.11	$81.87	0.53%
SUBTOTAL	**379**	**178**	**$26,526.52**	**$0.97**	**$69.99**	**10.8%**
PROPOSED TIER-2 PRODUCTS						
ANDRODERM DIS 2MG/24HR	16	3	$5,666.15	$10.81	$354.13	2.31%
ANDRODERM DIS 4MG/24HR	10	5	$4,591.86	$12.76	$459.19	1.87%
ANDROGEL GEL 1%(25MG)	6	2	$2,161.66	$12.01	$360.28	0.88%
ANDROGEL GEL 1%(50MG)	87	21	$41,292.07	$16.29	$474.62	16.82%
ANDROGEL GEL 1.62%	173	38	$84,419.08	$16.79	$487.97	34.40%
ANDROGEL GEL 1.62%	8	2	$4,653.56	$19.39	$581.70	1.90%
ANDROGEL GEL 1.62%	1	1	$728.67	$24.29	$728.67	0.30%
ANDROGEL GEL PUMP 1%	100	28	$40,470.68	$13.54	$404.71	16.49%
AXIRON SOL 30MG/ACT	40	8	$15,838.94	$13.20	$395.97	6.45%
FORTESTA GEL 10MG/ACT	3	2	$1,070.90	$11.90	$356.97	0.44%
TESTIM GEL 1%(50MG)	39	16	$17,642.17	$15.41	$452.36	7.19%
TESTOSTERONE GEL 1%(50MG)	1	1	$364.03	$12.13	$364.03	0.15%
SUBTOTAL	**484**	**127**	**$218,899.77**	**$15.25**	**$452.27**	**89.2%**
TOTAL	**863**	**273**	**$245,426.29**	**$5.90**	**$284.39**	**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 11/17/14. Last accessed 11/18/14.

[2]FDA: Drug Safety and Availability: FDA adding general warning to testosterone products about potential for venous blood clots. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm401746.htm. Last revised 6/25/14. Last accessed 11/18/14.

[3]Intermountain Medical Center. "Testosterone replacement therapy does not increase cardiovascular risks in men with low testosterone levels." ScienceDaily. ScienceDaily, 18 November 2014. www.sciencedaily.com/releases/2014/11/141118104843.htm

[4]Natesto™ Prescribing Information. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205488s000lbl.pdf. Last revised 5/2014. Last accessed 11/18/14.

[5]Aveed® Prescribing Information. Available online at: http://www.endo.com/File%20Library/Products/Prescribing%20Information/AVEED_prescribing_information.html. Last revised 9/2014. Last accessed 11/18/14.

[6]Vogelxo™ Prescribing Information. Available online at: http://www.upsher-smith.com/wp-content/uploads/Vogelxo-MI.pdf. Last revised 6/2014. Last accessed 11/18/14.

Appendix H

Fiscal Year 2014 Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene)

Oklahoma Health Care Authority
December 2014

Current Prior Authorization Criteria

Osteoporosis Medications		
Tier-1	**Tier-2***	**Special PA**
alendronate (Fosamax®)	alendronate + D (Fosamax® +D)	alendronate effervescent tablets (Binosto®)
calcium + vitamin D	ibandronate (Boniva®)	denosumab (Prolia®)
	risedronate (Actonel®)	ibandronate (Boniva® IV)
		risedronate 30mg tablet (Actonel®)
		risedronate delayed release tablets (Atelvia®)
		teriparatide (Forteo®)
		zoledronic acid (Reclast®)

*Tier-2 placement based on state maximum allowable cost (SMAC), estimated acquisition cost (EAC), or rebate participation.

Osteoporosis Medications Tier-2 Approval Criteria:

1. A trial of at least one Tier-1 medication, compliantly used for at least six months concomitantly with calcium + vitamin D, that failed to prevent fracture, or improve BMD scores; or
2. Hypersensitivity to or intolerable adverse effects with all Tier-1 medications.
3. Quantity limits apply based on FDA approved maximum doses.

Osteoporosis Medications Special Prior Authorization Approval Criteria:

1. **Forteo® (Teriparatide)**:
    a. A Bone Mineral Density test (T-score) at or below -2.5 within the last month; and
    b. A minimum of a 12 month trial with a bisphosphonate plus adequate calcium and vitamin D; or
    c. A 12 month trial of Prolia™ (Denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results.
    d. The diagnosis of non-healing fracture may be approved for six months.
    e. Approval will be for a maximum of 2 years of therapy.

2. **Prolia® (Denosumab), Reclast® (Zoledronic Acid), Boniva® (Ibandronate IV)**:
    a. A minimum of a 12 month trial with a Tier-1 or Tier-2 bisphosphonate plus adequate calcium and vitamin D; or
    b. Contraindication to or intolerable adverse effects with Tier-1 and Tier-2 medications.

c. Clinical exceptions may apply for members with:
    i. Severe esophageal disease (e.g., ulcerations, strictures)
    ii. Inability to take anything by mouth
    iii. Inability to sit or stand for prolonged periods
    iv. Inability to take bisphosphonates orally or other special medical circumstances that justify this method of administration

3. **Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets) , and Actonel® (Risedronate 30mg Tablets):**
    a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 medications.
    b. Members with diagnosis in history of Paget's disease will not require prior authorization.
4. Quantity limits apply based on FDA approved maximum doses.

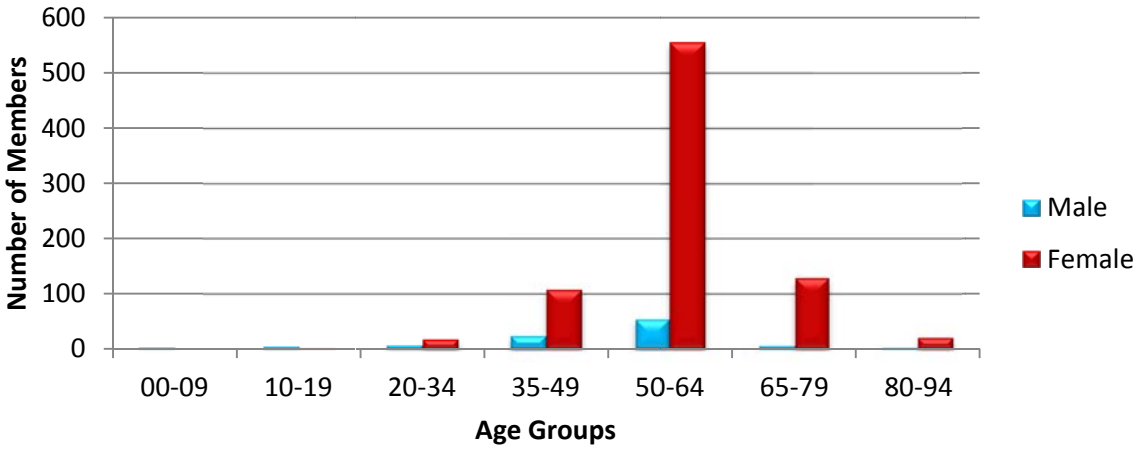
Utilization of Osteoporosis Medications

Comparison of Fiscal Years

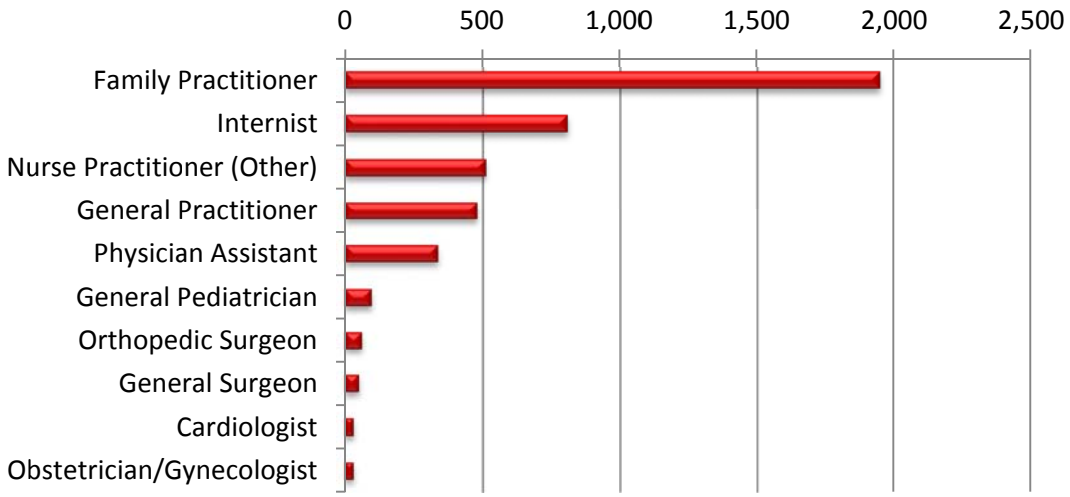
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	1,044	5,262	$277,620.25	$52.76	$1.72	25,307	161,473
2014	934	4,598	$259,570.64	$56.45	$1.83	23,261	141,893
% Change	**-10.50%**	**-12.60%**	**-6.50%**	**7.00%**	**6.40%**	**-8.10%**	**-12.10%**
Change	**-110**	**-664**	**-$18,049.61**	**$3.69**	**$0.11**	**-2,046**	**-19,580**

*Total number of unduplicated members.

Demographics of Members Utilizing Osteoporosis Medications



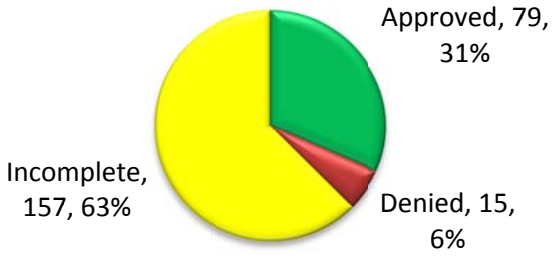
Top Prescriber Specialties of Osteoporosis Medications by Number of Claims



Prior Authorization of Osteoporosis Medications

There was a total of 251 petitions submitted for the osteoporosis medication category during fiscal year 2014. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates [1, 2]

Anticipated Patent Expirations:

- Fosamax® Plus D (alendronate/cholecalciferol)- There are no unexpired patents however there are not currently any generic products available.
- Prempro® (conjugated estrogens/medroxyprogesterone)- 01/2015
- Actonel® (risedronate)- 150mg tablets are available as a generic however the remaining strengths are anticipated to stay on patent until 06/2018
- Forteo® (teriparatide)- 08/2019
- Binosto® (alendronate effervescent tablets)- 08/2023
- Reclast® (zoledronic acid)- 02/2028

FDA Approvals:

- Duavee® (conjugated estrogens/bazedoxifene): FDA approved 10/2013

Duavee® (Conjugated Estrogens/Bazedoxifene) Product Summary[3]

FDA Approved: October 2013

Indications: Duavee® (conjugated estrogens/bazedoxifene) is a combination of conjugated estrogens with an estrogen agonist/antagonist indicated for treatment of the following conditions in women with a uterus:

- Treatment of moderate to severe vasomotor symptoms associated with menopause
- Prevention of postmenopausal osteoporosis

Important limitations of use:

- Use Duavee® for the shortest duration consistent with treatment goals and risks for the individual woman. Postmenopausal women should be re-evaluated periodically as clinically appropriate to determine if treatment is still necessary.
- When prescribed solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medication should be carefully considered.

Dosing: Duavee® is available as an oral tablet containing 0.45mg conjugated estrogens and 20mg bazedoxifene.

- The recommended dosing is one tablet by mouth once daily for both FDA approved indications.
- Duavee® can be taken without regard to meals.
- Tablets should be swallowed whole.
- Women taking Duavee® for prevention of postmenopausal osteoporosis should add supplemental calcium and/or vitamin D to their diet if daily intake is inadequate.

Mechanism of Action: Duavee® pairs conjugated estrogens with bazedoxifene, an estrogen agonist/antagonist that acts as an agonist in some estrogen-sensitive tissues and an antagonist in others (e.g., uterus). The bazedoxifene component reduces the risk of endometrial hyperplasia that can occur with the conjugated estrogens component.

Black Box Warning: Endometrial Cancer, Cardiovascular Disorders, and Probable Dementia

- Women taking Duavee® should not take additional estrogens.
- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Duavee® has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.
- Estrogen therapy should not be used for the prevention of cardiovascular disease or dementia.
- The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (0.625 mg)-alone, relative to placebo.
- The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older during 5.2 years of treatment with daily conjugated estrogens (0.625 mg)-alone,

relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.
- In the absence of comparable data, these risks should be assumed to be similar for other doses of conjugated estrogens and other dosage forms of estrogens.
- Estrogens should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Contraindications: Duavee® is contraindicated in women with any of the following conditions:
- Undiagnosed abnormal uterine bleeding
- Known, suspected, or past history of breast cancer
- Known, or suspected estrogen-dependent neoplasia
- Active deep venous thrombosis, pulmonary embolism, or history of these conditions
- Active thromboembolic disease (for example: stroke, myocardial infarction) or history of these conditions
- Hypersensitivity (for example: anaphylaxis, angioedema) to estrogens, bazedoxifene, or any ingredients
- Known hepatic impairment or disease
- Known protein C, protein S, or antithrombin deficiency or other known thromboembolic disorders
- Pregnancy, women who may become pregnant, and nursing mothers

Warnings and Precautions:
- Estrogen agonist/antagonists and estrogens individually are known to increase the risk of venous thromboembolism (VTE). An increased risk of stroke and deep vein thrombosis (DVT) has been reported with estrogen-alone therapy.
- An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in women with a uterus.
- A 2- to 4-fold increase in the risk of gallbladder disease requiring surgery in postmenopausal women receiving estrogens has been reported.
- Retinal vascular thrombosis has been reported in patients receiving estrogens. Discontinue medication pending examination if there is sudden partial or complete loss of vision, or a sudden onset of proptosis, diplopia, or migraine.
- In women with pre-existing hypertriglyceridemia, treatment with estrogens may be associated with elevations of plasma triglycerides leading to pancreatitis.
- Estrogens may cause some degree of fluid retention. Because of this, patients who have conditions that might be influenced by this factor, such as cardiac dysfunction or renal impairment, warrant careful observation when estrogens are prescribed.
- Estrogen therapy should be used with caution in women with hypoparathyroidism as estrogen-induced hypocalcemia may occur.
- Exogenous estrogens may exacerbate symptoms of angioedema in women with hereditary angioedema.
- Estrogens may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine or porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions.

Use in Special Populations:

- Pregnancy: Duavee® is pregnancy category X. Duavee® must not be used in women who are or may become pregnant.
- Nursing Mothers: Duavee® should not be used by lactating women. It is not known whether this drug is excreted in human milk.
- Pediatric Patients: Duavee® is not indicated for use in pediatric patients.
- Geriatric Patients: Duavee® has not been studied in women older than 75 years of age. Use in women older than 75 years of age is not recommended.
    - An increased risk of probable dementia in women older than 65 years of age was reported in the WHI Memory ancillary studies.
- Renal Impairment: The pharmacokinetics, safety, and efficacy of Duavee® have not been evaluated in patients with renal impairment. Use in patients with renal impairment is not recommended.
- Hepatic Impairment: Duavee® is contraindicated in patients with hepatic impairment.

Efficacy:

Moderate to Severe Vasomotor Symptoms Associated with Menopause: The safety and efficacy of Duavee® as a treatment for moderate to severe vasomotor symptoms associated with menopause was established in a 12-week randomized, double-blind, placebo-controlled study. The study enrolled a total of 318 women, age 42–64 (mean age of 53 years), who had at least 7 moderate to severe hot flushes per day or at least 50 per week at baseline. The mean number of years since menopause was 4.5 years with all women undergoing natural menopause. Duavee® significantly reduced the number and severity of moderate to severe hot flushes, as measured by the daily severity score, compared with placebo at weeks four and twelve. The change in baseline frequency for Duavee® was -5.9 at week four and -7.6 at week twelve versus -0.6 at week four and -0.9 at week twelve for placebo.

Prevention of Postmenopausal Osteoporosis in Women with a Uterus: The safety and efficacy of Duavee® for the prevention of postmenopausal osteoporosis was demonstrated in a 24-month, double-blind, randomized, placebo- and active-controlled study. The primary endpoint of the study was the incidence of endometrial hyperplasia at Year-1. Bone mineral density change at the lumbar spine at Year-2 was the key secondary endpoint, assessed in two subsets of patients (Substudy I and Substudy II). Patients enrolled into Substudy I had to be more than 5 years postmenopausal, have a lumbar spine or total hip T-score of -1 to -2.5, and have at least one additional risk factor for osteoporosis (e.g., Caucasian race, family history of osteoporosis, early menopause, thin/small frame, inactive lifestyle, tobacco abuse). Those enrolled into Substudy II had to be 1–5 years postmenopausal with at least one additional risk factor for osteoporosis. In these substudies, treatment with Duavee® significantly increased lumbar spine bone mineral density (BMD) at 24 months compared to placebo in both groups of postmenopausal women. The percent mean change in lumbar spine bone mineral density for Duavee® in women between one and five years postmenopausal was 1.72 versus -1.90 for placebo and 1.64 for Duavee® and -1.47 for placebo in women more than five years post-menopausal.

Cost Comparison

The following table contains the cost estimates for Duavee®, Prempro®, and aldendronate treatment. It is important to note that rebates are not included in the costs listed below. Additionally, the patent for Prempro® is expected to expire January 2015.

Drug Name	Cost per Unit	Cost per Year
Duavee® (Conjugated estrogens/Bazedoxifene) 0.45mg/20mg tablets	$3.92*	$1,411.20
Prempro® (conjugated estrogens/medroxyprogesterone) 0.45mg/1.5mg tablets	$4.29*	$1,544.40
Alendronate 10mg daily tablets	$0.17+	$61.20
Alendronate 70mg weekly tablets	$0.65+	$33.80

*Estimated Acquisition Cost (EAC)
+ State Maximum Allowable Cost (SMAC)
Cost based on FDA approved dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Duavee® (conjugated estrogens/bazedoxifene) with the following criteria:

Duavee® (Conjugated estrogens/Bazedoxifene) Approval Criteria:

1. An FDA approved diagnosis of moderate to severe vasomotor symptoms associated with menopause or for prevention of postmenopausal osteoporosis; and
2. Member must be a female with an intact uterus; and
3. For a diagnosis of moderate to severe vasomotor symptoms associated with menopause:
    a. Member must have at least 7 moderate to severe hot flushes per day or at least 50 per week prior to treatment; and
4. For a diagnosis of prevention of postmenopausal osteoporosis:
    a. A trial of Fosamax® (alendronate), Actonel® (risedronate), Boniva® (ibandronate) or Reclast® (zoledronic acid) compliantly used for at least 6 months concomitantly with calcium + vitamin D, that failed to prevent fracture or improve BMD scores; or
    b. Contraindication to, hypersensitivity to, or intolerable adverse effects with all bisphosphonates indicated for prevention of postmenopausal osteoporosis; and
5. Member must not have any of the contraindications for use of Duavee®; and
6. Members greater than 65 years of age will generally not be approved without supporting information.
7. Approvals will be for the duration of 6 months to ensure the need for continued therapy is reassessed periodically and the medication is being used for the shortest duration possible.
8. A quantity limit of 30 tablets per 30 days will apply.

Utilization Details of Osteoporosis Medications: Fiscal Year 2014

Pharmacy Claims: Fiscal Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Alendronate Products					
ALENDRONATE TAB 70MG	3,392	683	$20,154.23	$0.21	$5.94
ALENDRONATE TAB 35MG	468	117	$2,261.46	$0.17	$4.83
ALENDRONATE TAB 10MG	83	18	$747.66	$0.31	$9.01
ALENDRONATE TAB 5MG	48	7	$396.28	$0.28	$8.26
ALENDRONATE TAB 40MG	14	5	$1,365.67	$2.47	$97.55
ALENDRONATE SOL 70MG/75ML	4	1	$332.88	$2.97	$83.22
Subtotal	**4,009**	**820**	**$25,258.18**	**$0.22**	**$6.30**
Tier-1 Subtotal	**4,009**	**820**	**$25,258.18**	**$0.22**	**$6.30**
Ibandronate Products					
IBANDRONATE TAB 150MG	248	55	$22,685.69	$2.04	$91.47
BONIVA TAB 150MG	1	1	$143.10	$4.77	$143.10
IBANDRONATE TAB 150MG	1	1	$58.19	$1.94	$58.19
Subtotal	**250**	**57**	**$22,886.98**	**$2.05**	**$91.55**
Risedronate Products					
ACTONEL TAB 35MG	156	18	$27,295.94	$6.21	$174.97
ACTONEL TAB 5MG	24	2	$4,029.33	$5.82	$167.89
Subtotal	**180**	**20**	**$31,325.27**	**$6.15**	**$174.03**
Tier-2 Subtotal	**430**	**75**	**$54,212.25**	**$3.34**	**$126.08**
Teriparatide Products					
FORTEO SOL 600MG/2.4ML	89	16	$127,944.86	$50.45	$1,437.58
Subtotal	**89**	**16**	**$127,944.86**	**$50.45**	**$1,437.58**
Denosumab Products					
PROLIA SOL 60MG/ML	36	24	$32,226.34	$5.14	$895.18
Subtotal	**36**	**24**	**$32,226.34**	**$5.14**	**$895.18**
Risedronate Products					
ACTONEL TAB 30MG	13	2	$12,435.41	$18.84	$956.57
Subtotal	**13**	**2**	**$12,435.41**	**$18.84**	**$956.57**
Alendronate Products					
BINOSTO TAB 70MG	13	1	$1,862.90	$5.12	$143.30
Subtotal	**13**	**1**	**$1,862.90**	**$5.12**	**$143.30**
Ibandronate Products					
BONIVA INJ 3MG/3ML	4	2	$1,869.57	$6.27	$467.39
Subtotal	**4**	**2**	**$1,869.57**	**$6.27**	**$467.39**
Zoledronic Acid Products					
ZOLEDRONIC INJ 5/100ML	3	3	$2,637.21	$2.41	$879.07
RECLAST INJ 5/100ML	1	1	$1,123.92	$3.08	$1,123.92
Subtotal	**4**	**4**	**$3,761.13**	**$2.58**	**$940.28**
Special PA Subtotal	**159**	**48**	**$180,100.21**	**$15.54**	**$1,132.71**
Total	**4,598**	**934***	**$259,570.64**	**$1.83**	**$56.45**

*Total number of unduplicated members.

Medical Claims: Fiscal Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Units
Denosumab Products				
DENOSUMAB INJECTION 1MG	14	11	$6,779.26	840
Total	**14**	**11***	**$6,779.26**	**840**

*Total number of unduplicated members.

Only medical claims used for osteoporosis indications are included in the above table.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 11/24/14. Last accessed 11/24/14.

[2] FDA: FDA Approves Duavee to Treat Hot Flashes and Prevent Osteoporosis. Available online at: http://www.fda.gov/Drugs/NewsEvents/ucm370679.htm. Last revised 10/03/2013. Last accessed 11/24/14.

[3] Duavee® Prescribing Information, Wyeth Pharmaceuticals Company, a subsidiary of Pfizer Inc. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=1174. Last revised 10/2013. Last accessed 11/24/14.

Appendix I

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

FDA NEWS RELEASE

For Immediate Release: December 3rd, 2014

FDA approves Blincyto to treat a rare form of acute lymphoblastic leukemia

The U.S. Food and Drug Administration approved Blincyto (blinatumomab) to treat patients with Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukemia (B-cell ALL), an uncommon form of ALL.

Precursor B-cell ALL is a rapidly growing type of cancer in which the bone marrow makes too many B-cell lymphoblasts, an immature type of white blood cell. The Philadelphia chromosome is an abnormality that sometimes occurs in the bone marrow cells of leukemia patients. The National Cancer Institute estimates that 6,020 Americans will be diagnosed with ALL and 1,440 will die from the disease in 2014.

Blincyto is an example of immunotherapy, a treatment that uses certain parts of a person's immune system to fight diseases such as cancer. Blincyto is the first approved drug that engages the body's T-cells, a type of white blood cell or lymphocyte, to destroy leukemia cells. The drug acts as a connector between a protein called CD19, which is found on the surface of most B-cell lymphoblasts, and CD3, a protein on T-cell lymphocytes. It is intended for patients whose cancer returned after treatment (relapsed) or did not respond to previous treatment (refractory).

"Recognizing the potential of this novel therapy, the FDA worked proactively with the sponsor under our breakthrough therapy designation program to facilitate the approval of this novel agent."

The FDA granted Blincyto breakthrough therapy designation, priority review and orphan product designation because the sponsor demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies; the drug had the potential, at the time the application was submitted, to be a significant improvement in safety or effectiveness in the treatment of a serious condition; and the drug is intended to treat a rare disease, respectively. Blincyto is being approved more than five months ahead of the prescription drug user fee goal date of May 19, 2015, the date the agency was scheduled to complete review of the application.

The safety and effectiveness of Blincyto were evaluated in a clinical study involving 185 adults with Philadelphia chromosome-negative relapsed or refractory precursor B-cell ALL. All participants were treated with Blincyto for at least four weeks via infusion. Results showed 32 percent of participants had complete remission for approximately 6.7 months.

Blincyto 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 FDA is requiring Blincyto's manufacturer to conduct a study to verify that the drug improves survival in participants with relapsed or refractory Philadelphia-negative precursor B-cell ALL.

Blincyto carries a boxed warning alerting patients and health care professionals that some clinical trial participants had problems with low blood pressure and difficulty breathing (cytokine release syndrome) at the start of the first treatment, experienced a short period of difficulty with thinking (encephalopathy) or other side effects in the nervous system. The most common side effects seen in Blincyto-treated participants were fever (pyrexia), headache, swelling of tissues (peripheral edema), fever with a low number of white blood cells (febrile neutropenia), nausea, low potassium (hypokalaemia), fatigue, constipation, diarrhea and tremor.

The FDA approved Blincyto with a Risk Evaluation and Mitigation Strategy (REMS), which consists of a communication plan to inform health care providers about the serious risks and the potential for preparation and administration errors.

Blincyto is marketed by Thousand Oaks, California-based Amgen Inc.

FDA NEWS RELEASE

For Immediate Release: November 20th, 2014

FDA approves extended-release, single-entity hydrocodone product with abuse-deterrent properties

The U.S. Food and Drug Administration approved Hysingla ER (hydrocodone bitartrate), an extended-release (ER) opioid analgesic to treat pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Hysingla ER has approved labeling describing the product's abuse-deterrent properties consistentwith the FDA's 2013 draft guidance for industry, Abuse-Deterrent Opioids – Evaluation and Labeling.

Hysingla ER has properties that are expected to reduce, but not totally prevent, abuse of the drug when chewed and then taken orally, or crushed and snorted or injected. The tablet is difficult to crush, break or dissolve. It also forms a viscous hydrogel (thick gel) and cannot be easily prepared for injection. The FDA has determined that the physical and chemical properties of Hysingla ER are expected to make abuse by these routes difficult. However, abuse of Hysingla ER by these routes is still possible. It is important to note that taking too much Hysingla ER, whether by intentional abuse or by accident, can cause an overdose that may result in death.

Quote from the FDA: "Preventing prescription opioid abuse is a top public health priority for the FDA, and encouraging the development of opioids with abuse-deterrent properties is just one component of a broader approach to reducing abuse and misuse, and will better enable the agency to balance addressing this problem with ensuring that patients have access to appropriate treatments for pain."

Hysingla ER is not approved for, and should not be used for, as-needed pain relief. Given Hysingla ER's risks for abuse, misuse and addiction, it should only be prescribed to people for whom alternative treatment options are ineffective, not tolerated or would be otherwise inadequate to provide sufficient pain management. As a single-entity opioid, Hysingla ER does not carry the serious liver toxicity risks associated with hydrocodone combination products containing acetaminophen. The FDA encourages health care professionals to review and consider all available information as part of their decision-making when prescribing opioid analgesics.

Strengths of Hysingla ER contain 20, 30, 40, 60, 80, 100 and 120 milligrams (mg) of hydrocodone to be taken every 24 hours. Doses of 80 mg per day and higher should not be prescribed to people who have not previously taken an opioid medication (opioid non-tolerant). While Hysingla ER contains larger amounts of hydrocodone compared to immediate-release hydrocodone combination products, the range of tablet strengths of Hysingla ER is comparable to existing approved ER opioids.

The safety and effectiveness of Hysingla ER were evaluated in a clinical trial of 905 people with chronic low back pain. Additional data from studies conducted in laboratories and in people demonstrated the abuse-deterrent features of Hysingla ER for certain types of abuse (oral, snorting and injection). The most common side effects of Hysingla ER are constipation, nausea, fatigue, upper respiratory tract infection, dizziness, headache and drowsiness (somnolence).

The FDA is requiring postmarketing studies of Hysingla ER to assess the effects of the abuse-deterrent features on the risk for abuse of Hysingla ER and the consequences of that abuse in the community. In addition, Hysingla ER is part of the ER/LA Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS), which requires companies to make available to health care professionals educational programs on how to safely prescribe ER/LA opioid analgesics and to provide Medication Guides and patient counseling documents containing information on the safe use, storage, and disposal of ER/LA opioids.

Hysingla ER is manufactured by Stamford-based Purdue Pharma L.P.

Safety Announcements

FDA Drug Safety Communication: FDA reviews long-term antiplatelet therapy as preliminary trial data shows benefits but a higher risk of non-cardiovascular death

[November 16th, 2014] FDA is evaluating preliminary data from a clinical trial showing that treatment for 30 months with dual antiplatelet blood-thinning therapy decreased the risk of heart attacks and clot formation in stents, but there was an increased overall risk of death compared to 12 months of treatment. The clinical trial compared 30 months versus 12 months of treatment with dual antiplatelet therapy consisting of aspirin plus either clopidogrel (Plavix) or prasugrel (Effient), following implantation of drug-eluting coronary stents. These

stents are small, medicine-coated tubes inserted into narrowed arteries in the heart to keep them open and maintain blood flow to the heart. Clopidogrel and prasugrel are important medicines used to prevent heart attacks, strokes, and other clot-related diseases.
FDA believes the benefits of clopidogrel (Plavix) and prasugrel (Effient) therapy continue to outweigh their potential risks when used for approved uses. Patients should not stop taking these drugs because doing so may result in an increased risk of heart attacks, blood clots, strokes, and other major cardiovascular problems. Health care professionals should not change the way they prescribe these drugs at this time.
The Dual Antiplatelet Therapy (DAPT) trial was published in the New England Journal of Medicine on November 16, 2014. FDA has not reviewed the trial results or reached any conclusions based on the findings from this clinical trial. We are communicating this safety information while we continue to evaluate the results from this trial and other available data. We will communicate our final conclusions and recommendations when our evaluation is complete.
The DAPT trial is a public-private collaboration to study the optimal duration of antiplatelet therapy after stent placement. The trial examined the effects of dual antiplatelet therapy for 12 months compared to 30 months in approximately 10,000 patients with an implanted drug-eluting coronary stent. The risks of stent thrombosis and heart attacks in the group receiving treatment for 30 months was reduced compared to 12 months; however, there was a higher rate of death in the 30-month treatment group. The higher rate of death was largely explained by an increase in deaths from non-cardiovascular causes, primarily cancer and trauma deaths. The increased risk of death with longer treatment was seen in the patients given clopidogrel, but not those given prasugrel. It should be noted that increases in non-cardiovascular death have not been reported in previous large trials examining clopidogrel for other cardiovascular diseases.

Safety Announcements

FDA Drug Safety Communication: FDA warns about case of rare brain infection PML with MS drug Tecfidera (dimethyl fumarate)

[November 25th, 2014] The U.S. Food and Drug Administration (FDA) is warning that a patient with multiple sclerosis (MS) who was being treated with Tecfidera (dimethyl fumarate), developed a rare and serious brain infection called PML, and later died. As a result, information describing this case of PML, or progressive multifocal leukoencephalopathy, is being added to the Tecfidera drug label. Patients taking Tecfidera should contact their health care professionals right away if they experience symptoms that concern them, such as new or worsening weakness; trouble using their arms or legs; or changes to thinking, eyesight, strength or balance. Health care professionals should stop Tecfidera if PML is suspected.
Tecfidera has been shown to benefit patients with relapsing forms of MS. This type of MS causes attacks or relapses – periods of time when symptoms get distinctly worse.
The patient who died was not taking any other drugs that affect the immune system or drugs that are thought to be associated with PML. This is the only confirmed case of this rare and serious brain infection reported in patients taking Tecfidera.
PML is a rare and serious brain infection caused by the John Cunningham (JC) virus. The JC virus is a common virus that is harmless in most people but can cause PML in some patients who have weakened immune systems. Symptoms of PML are diverse and may include progressive weakness on one side of the body, clumsiness, vision problems, confusion, and changes in thinking, personality, memory, and orientation. The progression of deficits can lead to severe disability or death.
The drug manufacturer, Biogen Idec, notified FDA when the MS patient died after developing PML. The patient had taken Tecfidera for more than four years. Prior to developing PML, the patient had a very low number of lymphocytes, a type of white blood cell, in her blood. Reduced lymphocyte counts can weaken the immune system, which increases the risk for PML. It is unknown whether the low lymphocyte count contributed to the development of PML in this patient, or if low lymphocyte counts are a risk factor for PML development in Tecfidera-treated patients.
We urge health care professionals and patients to report side effects involving Tecfidera to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Current Drug Shortages Index (as of December 3, 2014):

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***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Clindamycin Phosphate (Cleocin) Injection	***Currently in Shortage***
Clonidine HCL Injection (Duraclon)	***Currently in Shortage***
Cyanocobalamin (Vitamin B12) Injection	***Currently in Shortage***
Daunorubicin Hydrochloride Solution for 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***
Dihydroergotamine Mesylate 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)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Erythrocin Lactobionate Lyophilized Powder for Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Sodium Injection	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Heparin Sodium Injection	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Irrigation Solutions	***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***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets	***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***
Nitroglycerin (Nitronal) Injection	***Currently in Shortage***
Nitroglycerin in 5% Dextrose Injection	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Papaverine Hydrochloride Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phenylephrine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Phosphate (Glycophos) Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Radium RA-223 Dichloride (Xofigo) Injection	***Currently in Shortage***
Ranitidine Hydrochloride (Zantac) 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***
Succinylcholine (Anectine, Quelicin) Injection	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sulfamethoxazole and Trimethoprim (Bactrim) Oral Suspension	***Currently in Shortage***
Technetium tc99m Exametazime Injection (Ceretec Kit)	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Solution for 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***
Verapamil Hydrochloride Injection, USP	***Currently in Shortage***
Zinc Injection	***Currently in Shortage***