Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
November 12, 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 – November 12, 2014**

DATE: **October 31, 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 November 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

Action Item – Vote on 2015 Meeting Dates – See Appendix B

Action Item – Update on Medication Coverage Authorization Unit/Oral Viscous Lidocaine Claims Analysis/Glaucoma Member and Prescriber Mailing Evaluation – See Appendix C

Action Item – Vote to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab) – See Appendix D

Action Item – Vote to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin) – See Appendix E

Action Item – Vote to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine) and Update the Antidepressants Product Based Prior Authorization Category – See Appendix F

30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir) – See Appendix G

Action Item – Annual Review of Fibromyalgia Medications – See Appendix H

Annual Review of Oral Buprenorphine Products and 30-Day Notice to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) – See Appendix I

FDA and DEA Updates – See Appendix J

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – November 12, 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. October 8, 2014 DUR Minutes – Vote
   B. October 8, 2014 DUR Recommendations Memorandum

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

4. **Action Item – Vote on 2015 Meeting Dates – See Appendix B**

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

5. **Update on Medication Coverage Authorization Unit/Oral Viscous Lidocaine Claims Analysis/Glaucoma Member and Prescriber Mailing Evaluation – See Appendix C**
   A. Medication Coverage Activity for October 2014
   B. Pharmacy Help Desk Activity for October 2014
   C. Oral Viscous Lidocaine Claims Analysis
   D. Glaucoma Educational Initiative Mailing Update

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

6. **Action Item – Vote to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab) – See Appendix D**
   A. COP Recommendations

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

7. **Action Item – Vote to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin) – See Appendix E**
   A. COP Recommendations

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

8. **Action Item – Vote to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine) and Update the Antidepressants Product Based Prior Authorization Category – See Appendix F**
   A. COP Recommendations

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

9. 30-Day Notice to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir) – See Appendix G

A. Introduction
B. Market News and Updates
C. Harvoni® (Ledipasvir/Sofosbuvir) Summary
D. COP Recommendations
E. Utilization of Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)
F. Prior Authorization of Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)
G. Utilization Details of Hepatitis C Medications

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

10. Action Item – Annual Review of Fibromyalgia Medications – See Appendix H

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

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

11. Annual Review of Oral Buprenorphine Products and 30-Day Notice to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) – See Appendix I

A. Current Prior Authorization Criteria
B. Key Points
C. Utilization of Oral Buprenorphine Products
D. Prior Authorization of Oral Buprenorphine Products
E. Market News and Updates
F. Zubsolv® and Bunavail™ Summary
G. COP Recommendations
H. Utilization Details of Oral Buprenorphine Products

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

12. FDA and DEA Updates – See Appendix J

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

13. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF OCTOBER 8, 2014

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.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): Steven Caine, Alexander 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	Tricia Hentges, Merck
George Kitchens, Artia Solutions	Phillip Lafferty, Celgene	Jim Fowler, Astra Zeneca
Don Kempin, Novo Novadisk	Roger Grotzinger, BMS	Jim Chapman, Abbvie
Russ Wilson, J&J	Brian Maves, Pfizer	

PRESENT FOR PUBLIC COMMENT:	
Diane Hanna	Celgene

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: DIANE HANNA **AGENDA NO. 9**

ACTION: NONE REQUIRED

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

3A: SEPTEMBER 10, 2014 DUR MINUTES – VOTE

3B: SEPTEMBER 10, 2014 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2014

4B: PHARMACY HELP DESK ACTIVITY FOR SEPTEMBER 2014

4C: OVERVIEW OF SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE VERSACLOZ™ (CLOZAPINE ORAL SUSPENSION)**

5A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE GRASTEK® (TIMOTHY GRASS POLLEN ALLERGEN EXTRACT) AND RAGWITEK™ (SHORT RAGWEED POLLEN ALLERGEN EXTRACT)**

6A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **30-DAY NOTICE TO PRIOR AUTHORIZE SIVEXTRO™ (TEDIZOLID), DALVANCE™ (DALBAVANCIN), AND ORBACTIV™ (ORITAVANCIN)**

7A: INTRODUCTION

7B: PRODUCT SUMMARIES

7C: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

Dr. Muchmore recommends that all 3 antibiotic first recommendations should read as followed "*An Indicated diagnosis or infection known to be susceptible to requested agent and resistant to cephalosporin and other antibiotics commonly used for this class of infections.*"

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE FETZIMA® (LEVOMILNACIPRAN), KHEDEZLA® (DESVENLAFAXINE), AND BRINTELLIX® (VORTIOXETINE)**

8A: CURRENT PRIOR AUTHORIZATION CRITERIA

8B: UTILIZATION OF ANTIDEPRESSANTS

8C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS

8D: MARKET NEWS AND UPDATES

8E: PRODUCT SUMMARIES

8F: COP RECOMMENDATIONS

8G: UTILIZATION DETAILS OF ANTIDEPRESSANTS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF BIOLOGIC PRODUCTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS, PLAQUE PSORIASIS, AND ANKYLOSING SPONDYLITIS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OTEZLA® (APREMILAST) AND ENTYVIO™ (VEDOLIZUMAB)**

9A: CURRENT PRIOR AUTHORIZATION CRITERIA

9B: UTILIZATION OF BIOLOGIC PRODUCTS

9C: PRIOR AUTHORIZATION OF BIOLOGIC PRODUCTS

9D: MARKET NEWS AND UPDATES

9E: PRODUCT SUMMARIES

9F: COP RECOMMENDATIONS

9G: UTILIZATION DETAILS OF BIOLOGIC PRODUCTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF BLADDER CONTROL MEDICATIONS**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF BLADDER CONTROL MEDICATIONS

10C: PRIOR AUTHORIZATION OF BLADDER CONTROL MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: COP RECOMMENDATIONS

10F: UTILIZATION DETAILS OF BLADDER CONTROL MEDICATIONS

Materials included in agenda packet; presented by Dr. Anderson

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **FDA AND DEA UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FUTURE BUSINESS**

12A: ANNUAL REVIEWS

12B: NEW PRODUCT REVIEWS

Materials included in agenda packet; submitted by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ADJOURNMENT**

The meeting was adjourned at 4:51 pm

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

Memorandum

Date: October 09, 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 October 08, 2014

Recommendation 1: Vote to Prior Authorize Versacloz™ (Clozapine Oral Suspension)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Versacloz™ (clozapine oral suspension) to Tier-3 of the Atypical Antipsychotics Product Based Prior Authorization category with the following criteria:

Atypical Antipsychotics*		
Tier-1	**Tier-2**	**Tier-3+**
clozapine (Clozaril®)¥	Supplemental Rebated Products	aripiprazole (Abilify®)
olanzapine (Zyprexa®)		aripiprazole (Abilify Maintena®)
quetiapine (Seroquel®)		asenapine (Saphris®)
risperidone (Risperdal®)		clozapine (Fazaclo®)
risperidone (Risperdal Consta®)		clozapine oral suspension (Versacloz™)
ziprasidone (Geodon®)		iloperidone (Fanapt™)
		lurasidone (Latuda®)
		olanzapine/fluoxetine (Symbyax®)
		paliperidone (Invega®)
		paliperidone (Invega Sustenna®)
		quetiapine ER (Seroquel XR®)

*Mandatory Generic Plan Applies
+ May be rebated to Tier-2 status only
¥ Does not count toward a Tier-1 trial
ER = extended-release

Atypical Antipsychotic Tier-2 Approval Criteria:

1. A trial of two Tier-1 products (not including clozapine), at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
2. Clozapine is available without prior authorization, but does not count towards a Tier-1 trial.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. A trial of two Tier-1 products (not including clozapine), at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
2. A trial of two Tier-2 medications, at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
3. A manual prior authorization may be submitted for consideration of a Tier-3 product when the member has had at least four trials of Tier-1 and Tier-2 products (two trials must be from Tier-1) that did not yield an adequate response or resulted in intolerable adverse effects.
4. Use of Versacloz™ (clozapine oral suspension) and Fazaclo® (clozapine orally disintegrating tablet) requires a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Atypical Antipsychotic for Adjunctive Treatment for Depression Approval Criteria:

1. Use of Abilify® (aripiprazole), Seroquel XR® (quetiapine extended release), or Symbyax® (olanzapine/fluoxetine) for a diagnosis of depression requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and a dual acting antidepressant) that did not yield an adequate response.
2. Tier structure rules still apply.

Current Users or Inpatient Discharge Approval Criteria:

1. Members currently stabilized on a higher tiered medication defined by paid claim(s) for the higher tiered medication in the past 90 days will be approved.
2. Members being released from a hospital and stabilized on a higher tiered medication will be approved.

Clinical Exceptions:

1. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
2. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.
3. Lurasidone (Latuda®) may be approved for pregnant women with appropriate diagnosis.

Second Opinion Process for Children 0 - 4 Years of Age:

1. Children less than 5 years of age will require a "second opinion" prior authorization to be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted child psychiatrist.

Recommendation 2: Vote to Prior Authorize Grastek® (Timothy Grass Pollen Allergen Extract) and Ragwitek™ (Short Ragweed Pollen Allergen Extract)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Grastek® and Ragwitek™ with the following criteria:

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

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

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

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

Recommendation 3: 30-Day Notice to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Plaque Psoriasis, and Ankylosing Spondylitis and 30-Day Notice to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Bladder Control Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Bladder Control Medication Prior Authorization category:

1. Move Ditropan XL® (oxybutynin extended-release) from Tier-2 to Tier-1 based on generic availability and State Maximum Allowable Cost (SMAC).
2. Move Detrol® immediate-release (tolterodine) and Sanctura™ immediate-release (trospium) from Tier-3 to Tier-2 based on generic availability and State Maximum Allowable Cost (SMAC).
3. Move Sanctura XR™ (trospium) from Tier-1 to Tier-3.

Bladder Control Medications		
Tier-1	**Tier-2**	**Tier-3**
oxybutynin (Ditropan®)	tolterodine (Detrol®)	darifenacin (Enablex®)
oxybutynin ER (Ditropan XL®)	trospium (Sanctura™)	fesoterodine (Toviaz™)
		flavoxate (Urispas®)
		mirabegron (Myrbetriq™)
		oxybutynin patch (Oxytrol®)
		oxybutynin gel (Gelnique™)
		solifenacin (Vesicare®)
		tolterodine ER (Detrol LA®)
		trospium ER (Sanctura XR™)

Tier-1 products are available without a prior authorization for all members. Hyoscyamine is available without prior authorization and can be used as adjunctive therapy, but does not count as a Tier-1 trial.

Tier-2 Approval Criteria:

1. Trials of all Tier-1 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique FDA approved indication not covered by Tier-1 medications

Tier-3 Approval Criteria:

1. Trials of all Tier-2 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique FDA approved indication not covered by lower tiered medications

Appendix B

2015 Drug Utilization Review Board Meeting Dates

Oklahoma Health Care Authority
November 2014

Meetings are held the second Wednesday of every month

January 14, 2015

February 11, 2015

March 11, 2015

April 8, 2015

May 13, 2015

June 10, 2015

July 8, 2015

August 12, 2015

September 9, 2015

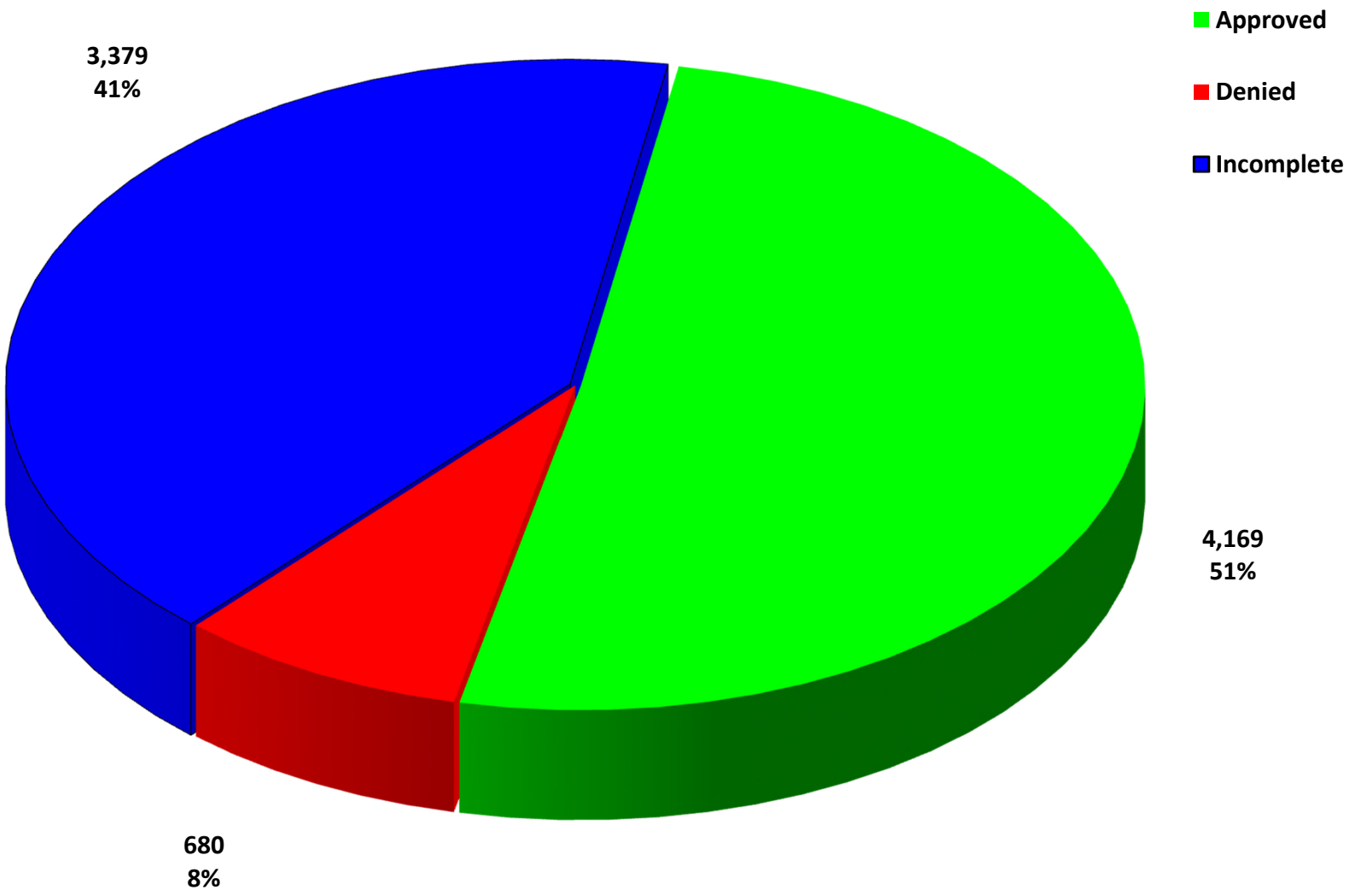
October 14, 2015

November 11, 2015

December 9, 2015

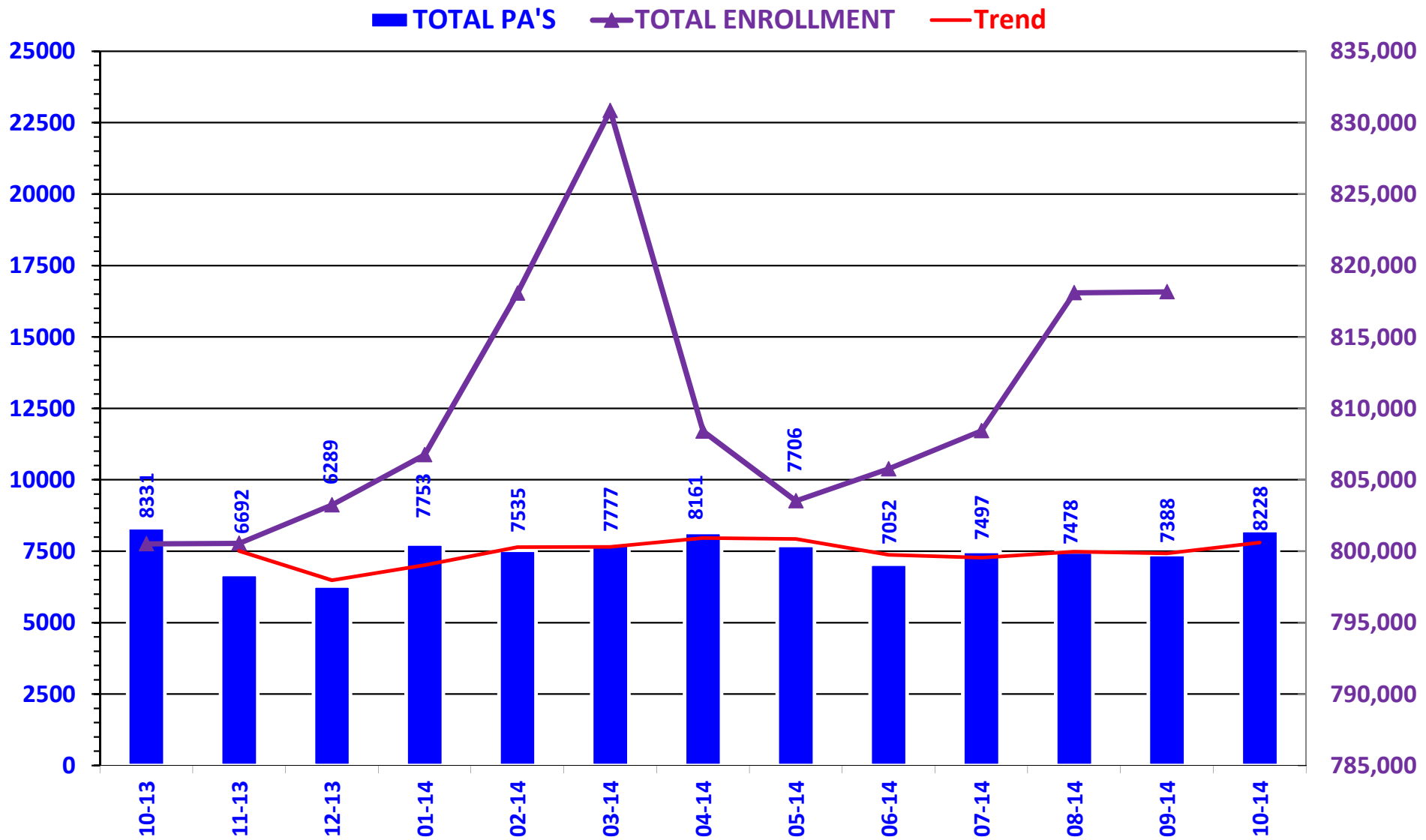
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER



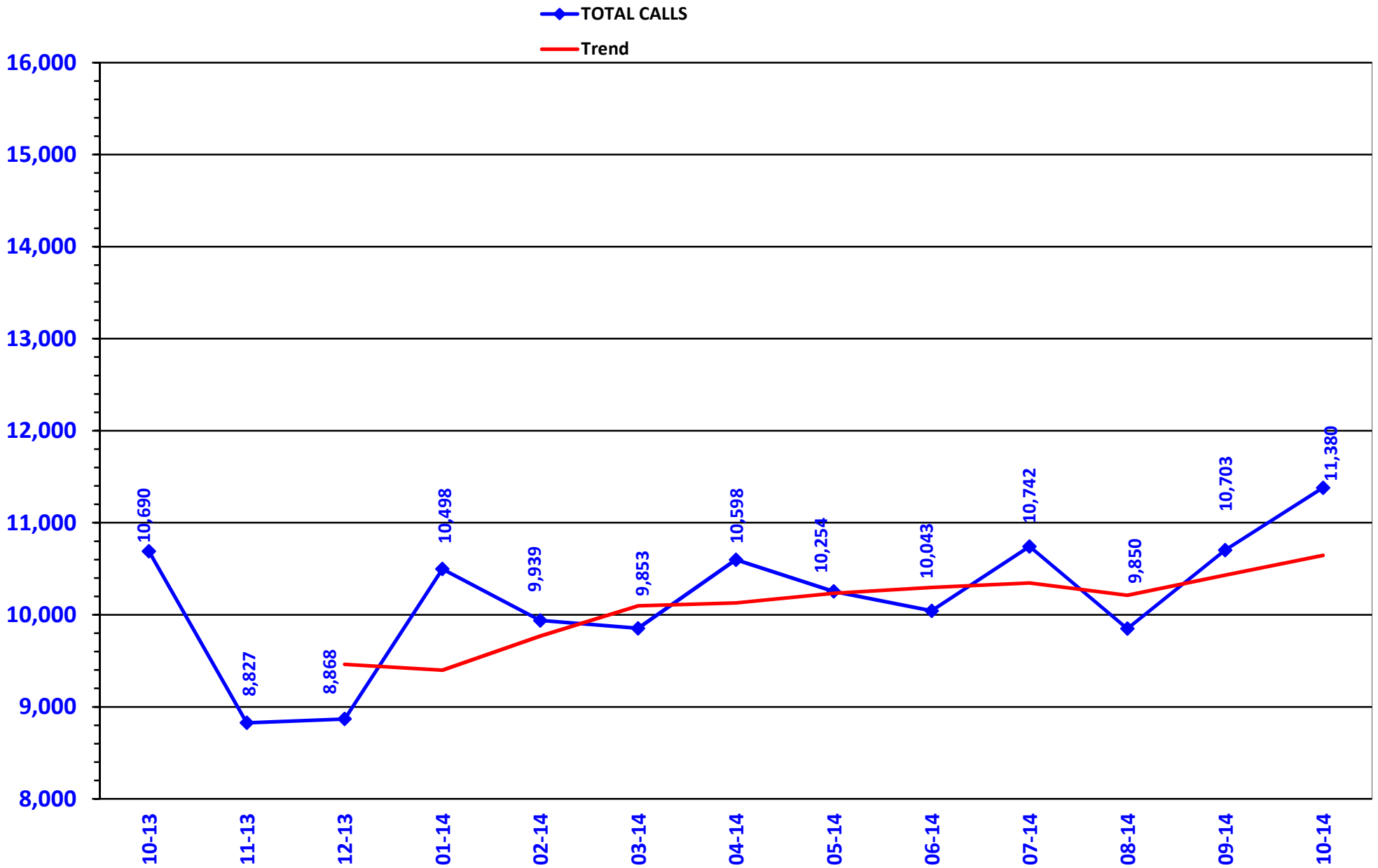
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: OCTOBER 2013 - OCTOBER 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
OCTOBER 2013 – OCTOBER 2014



Prior Authorization Activity

10/1/2014 Through 10/31/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	369	168	11	190	358
Analgesic - NonNarcotic	33	0	8	25	0
Analgesic, Narcotic	448	231	33	184	169
Angiotensin Receptor Antagonist	26	9	3	14	360
Antiasthma	176	67	7	102	339
Antibiotic	30	8	2	20	95
Anticonvulsant	73	43	3	27	324
Antidepressant	208	69	18	121	345
Antidiabetic	149	86	7	56	358
Antifungal	10	1	7	2	28
Antihistamine	265	234	1	30	359
Antimigraine	82	17	6	59	199
Antiulcers	204	52	47	105	139
Anxiolytic	70	50	1	19	304
Atypical Antipsychotics	417	243	9	165	337
Biologics	72	44	6	22	306
Bladder Control	57	11	8	38	175
Blood Thinners	102	69	2	31	329
Botox	26	20	2	4	306
Calcium Channel Blockers	12	4	1	7	93
Cardiovascular	26	10	4	12	269
Cephalosporins	16	4	0	12	9
Chronic Obstructive Pulmonary Disease	22	7	1	14	359
Dermatological	97	10	58	29	82
Endocrine & Metabolic Drugs	43	33	3	7	136
Erythropoietin Stimulating Agents	44	23	1	20	109
Fibromyalgia	142	38	19	85	327
Fish Oils	20	5	1	14	359
Gastrointestinal Agents	55	12	18	25	117
Genitourinary Agents	10	1	4	5	9
Growth Hormones	68	58	1	9	151
Hepatitis C	110	41	24	45	9
HFA Rescue Inhalers	68	17	5	46	339
Insomnia	77	17	13	47	204
Linzess, Amitiza, and Relistor	71	9	10	52	302
Multiple Sclerosis	31	18	1	12	256
Muscle Relaxant	98	28	33	37	60
Nasal Allergy	104	12	25	67	266
Neurological Agents	49	33	7	9	348
Nsaids	179	23	19	137	252
Ocular Allergy	30	7	1	22	150
Ophthalmic Anti-infectives	12	4	0	8	11
Osteoporosis	28	11	4	13	339
Other*	178	35	23	120	219
Otic Antibiotic	27	6	0	21	7
Pediculicide	103	50	5	48	15
Prenatal Vitamins	12	0	2	10	0
Statins	48	15	3	30	358
Stimulant	1,221	587	44	590	334
Suboxone/Subutex	225	174	3	48	82
Synagis	415	168	63	184	143
Testosterone	47	19	3	25	341
Topical Antifungal	45	3	7	35	81

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Corticosteroids	72	3	13	56	184
Vitamin	52	17	23	12	308
Pharmacotherapy	89	75	0	14	316
Emergency PAs	1	1	0	0	
Total	**6,764**	**3,000**	**623**	**3,141**	

Overrides					
Brand	48	34	4	10	288
Cumulative Early Refill	1	1	0	0	180
Dosage Change	418	371	2	45	4
High Dose	3	1	0	2	360
Ingredient Duplication	64	54	0	10	4
Lost/Broken Rx	67	61	1	5	4
NDC vs Age	33	32	0	1	218
Nursing Home Issue	98	95	0	3	3
Opioid Quantity	2	2	0	0	294
Other*	43	38	0	5	3
Quantity vs. Days Supply	608	428	39	141	254
STBS/STBSM	19	19	0	0	67
Stolen	17	10	4	3	11
Temporary Unlock	9	4	4	1	15
Third Brand Request	35	20	3	12	30
Wrong D.S. on Previous Rx	2	2	0	0	14
Overrides Total	**1,464**	**1,169**	**57**	**238**	
Total Regular PAs + Overrides	**8,228**	**4,169**	**680**	**3,379**	

Denial Reasons	
Unable to verify required trials.	2,862
Does not meet established criteria.	658
Lack required information to process request.	525

Other PA Activity	
Duplicate Requests	601
Letters	4,493
No Process	16
Changes to existing PAs	520
Helpdesk Initiated Prior Authorizations	972
PAs Missing Information	65

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

Oral Viscous Lidocaine Claims Analysis

Oklahoma Health Care Authority
November 2014

Background[1]

On June 26, 2014, the FDA issued a Drug Safety Communication regarding the use of oral, viscous lidocaine 2% solution for teething pain in infants and children. Serious adverse events, including seizure, severe brain injury, heart problems and death have occurred due to overdose, and accidental swallowing of lidocaine. The FDA has recommended the addition of a black box warning to the product label. Parents and caregivers are encouraged not to use over-the-counter (OTC) topical medications for teething pain, but to follow the American Academy of Pediatrics' (AAP) recommendations to use a chilled teething ring or gentle rubbing of the gums with a finger.

SoonerCare Claims Analysis

A review of fiscal year 2014 SoonerCare pharmacy claims found 225 members age 1 year or younger with a paid claim for oral, viscous lidocaine. Of these members, 58 or 25.78% had a diagnosis of teething syndrome. An additional analysis was conducted reviewing the first three calendar quarters of 2014. Claims were evaluated for oral, viscous lidocaine use in members 5 years of age or younger.

Calendar Year- Quarter	Number of Paid Claims for Viscous Lidocaine
2014- Q1	159
2014- Q2	298
2014- Q3	235
Average	**231**

Analysis of diagnosis for members 5 years of age or younger receiving oral, viscous lidocaine revealed acute pharyngitis, otitis media, dental carries, and teething pain. Compounded claims were included. The most common prescribers of oral, viscous lidocaine included physician assistants, nurse practitioners, and family practitioners.

Recommendations

Despite FDA recommendations to restrict use of oral, viscous lidocaine in children, utilization in this population remains high. Based on these findings 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.

[1] FDA Drug Safety Communication (viscous lidocaine) available online at http://www.fda.gov/Drugs/DrugSafety/ucm402240.htm Last revised 6/26/2014. Last accessed 10/29/2014

Glaucoma Educational Initiative Mailing Update

Oklahoma Health Care Authority
November 2014

Prescriber and Member Mailing

During the annual review of glaucoma medications in November 2013, the DUR Board recommended an educational initiative consisting of a targeted mailing to prescribers of glaucoma medications and to members with a diagnosis of glaucoma. The goal of the mailing was to increase the appropriate utilization of medications and annual eye examinations in the Oklahoma SoonerCare population.

The mailing targeted members who had a glaucoma diagnosis or a paid claim for a glaucoma medication in SoonerCare claims history from August 1, 2013 to January 31, 2014. Those members were then further evaluated for a dilated, comprehensive eye exam found in medical claims history from August 1, 2012 to January 31, 2014. Letters were mailed to prescribers of members with a glaucoma medication in claims history who did not have a dilated, comprehensive eye examination in the 18-month time period. The prescriber mailing included an optional response form the prescriber could fill out or make additional comments. The prescriber mailing was sent to 149 providers for 195 unique members and was completed in March 2014.

Additionally, educational letters were mailed to all members who were found to have a glaucoma diagnosis or glaucoma medication in claims history but no dilated, comprehensive eye exam. The letter was intended as a reminder of the importance of annual, dilated, comprehensive eye examinations. This mailing included 599 members and was completed in early April 2014.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	149
Total Responses Received	94
Total Members Included	195
Letters/Members	**Count**
Total Letters Mailed	599

Prescriber Response Summary

Response	Total*
I was unaware of this situation and will contact the patient/caregiver.	9
I was unaware of this situation and will schedule patient for follow-up.	13
Member has had an annual dilated eye examination. Date: _____	43
I am no longer seeing this patient.	18
Possible billing error – not my patient.	9
Other, comments.	55

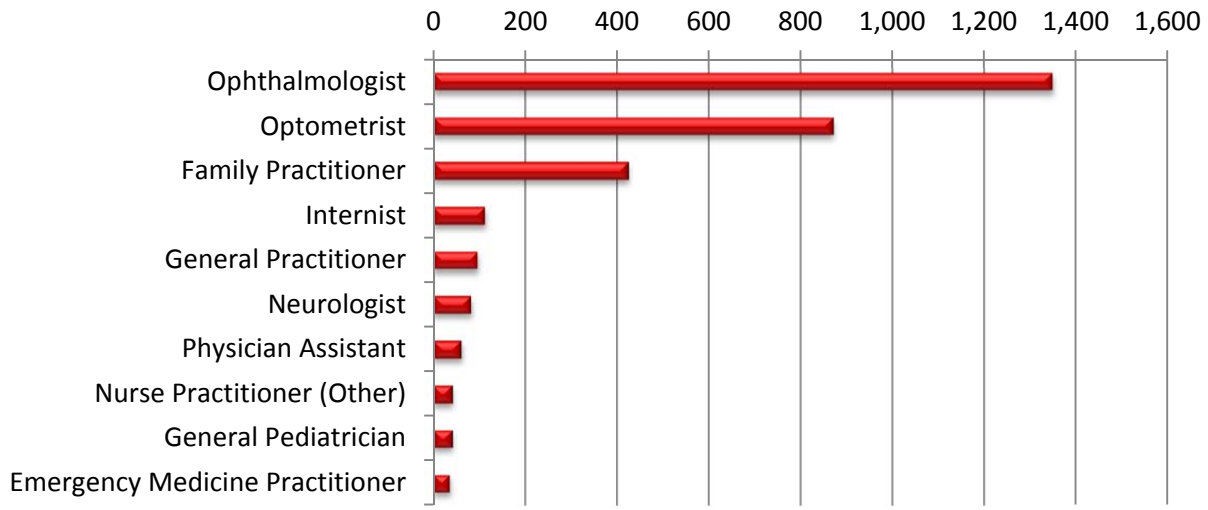
*Responses can be included in multiple categories.

Summary of Additional Comments Provided

Comment Category	Total*
Patient specific information provided.	25
I have scheduled patient for follow-up.	13
Dates of annual dilated eye examination provided.	43
Patient has missed appointments/reports non-compliance.	8
No longer my patient.	11
Not my patient.	6

*Comments can be included in multiple categories, not all comments listed.

Top Prescriber Specialties of Glaucoma Medications by Number of Claims



Results of the Mailing

A recent review of medical claims history was completed to look for dilated, comprehensive eye examinations in order to evaluate the impact of the mailing and to note any improvement in the number of members with dilated, comprehensive eye examinations. The number of dilated, comprehensive eye examinations increased for both members who received a letter only, and for members who received a letter and had a letter sent to their prescriber.

There was an overall increase in the number of dilated, comprehensive eye examinations of 8.32% for the designated time period from May 1, 2014 to September 30, 2014 as compared to the previous 18-month time period, August 1, 2012 to January 31, 2014 (only members included in the mailing were evaluated for an increase in eye exam utilization). For the group of members whose prescriber also received a letter, there was a 12.89% increase in dilated, comprehensive eye examinations, compared to a 6.14% increase in the group of members whose prescriber did not receive a letter. These results are similar to a previous glaucoma educational initiative mailing that showed a greater increase in dilated, comprehensive eye examinations in the group of members who received a letter and had a letter sent to their prescriber.

Copy of Letter and Response Form Mailed to Prescribers

SoonerCare
Oklahoma Health Care Authority

Pharmacy Services
(800) 522-0114, option 4

Dear SoonerCare Provider,

The Oklahoma Health Care Authority is engaged in an effort to improve the quality of care for patients diagnosed or at high risk for glaucoma. The goal is to increase annual dilated eye exams in patients receiving SoonerCare services.

Recent reviews of SoonerCare medical claims revealed some concerning trends as detailed below. We earnestly request your participation to reverse these trends and help promote annual dilated eye examinations as recommended by the National Eye Institute for those diagnosed and at high risk for glaucoma. Those considered at high risk for glaucoma by the National Eye Institute and the American Optometric Association include:

- African-Americans over the age of 40
- Everyone over the age of 60 years, especially Hispanic Americans
- People with diabetes, hypertension, or family history of glaucoma

To assist you in initiating the educational process and raising glaucoma awareness, patient education materials about glaucoma will also be sent to members.

During the review of member diagnosis and medication claim profiles, it was noted that for one or more of your patients, there is **no record of an annual dilated eye examination between 8/1/12 and 1/31/14 as recommended by national guidelines for reevaluation of current medical treatments and status of disease progression.** The patient specific information can be found on the attached provider response form.

Please remember that the findings of the review are based upon the information available in the SoonerCare claims database at the time of review.

We value your response and comments to this information regarding the member's current glaucoma therapy. Please note your comments on the attached provider response form and return the form in the enclosed envelope. This helps us ensure a high standard of quality of care is provided to our members. Thank you for your time and assistance in this review process. We appreciate your service to Oklahoma SoonerCare members.

SoonerCare Pharmacy Services • Pharmacy Management Consultants •
PO Box 26901; ORI W-4403 • Oklahoma City, Oklahoma 73126-0901 •
Phone: (800) 522-0114, option 4 • Fax: (866) 335-3331

SoonerCare
Oklahoma Health Care Authority

Confidential ***Confidential***

Drug Utilization Review Program
Glaucoma
Provider Response Form

Provider Name: Provider NPI Number:

Patient Name: Patient ID Number:

Screening Date:

This information is communicated strictly in confidence to the provider for evaluation and response:

- ☐ I was unaware of this situation and will:
  - ☐ Contact the patient/caregiver
  - ☐ Schedule patient for follow-up
- ☐ Member has had an annual dilated eye examination. Date: _____
- ☐ I am no longer seeing this patient.
- ☐ Possible billing error – not my patient.
- ☐ Other, comments:

_____ _____

Provider Name (please print) Signature

Please return this response page in the enclosed business reply envelope or fax to 866-335-3331.

Confidential ***Confidential***

SoonerCare Pharmacy Services • Pharmacy Management Consultants •
PO Box 26901; ORI W-4403 • Oklahoma City, Oklahoma 73126-0901 •
Phone: (800) 522-0114, option 4 • Fax: (866) 335-3331

Copy of Letter Mailed to Members

SoonerCare
Oklahoma Health Care Authority

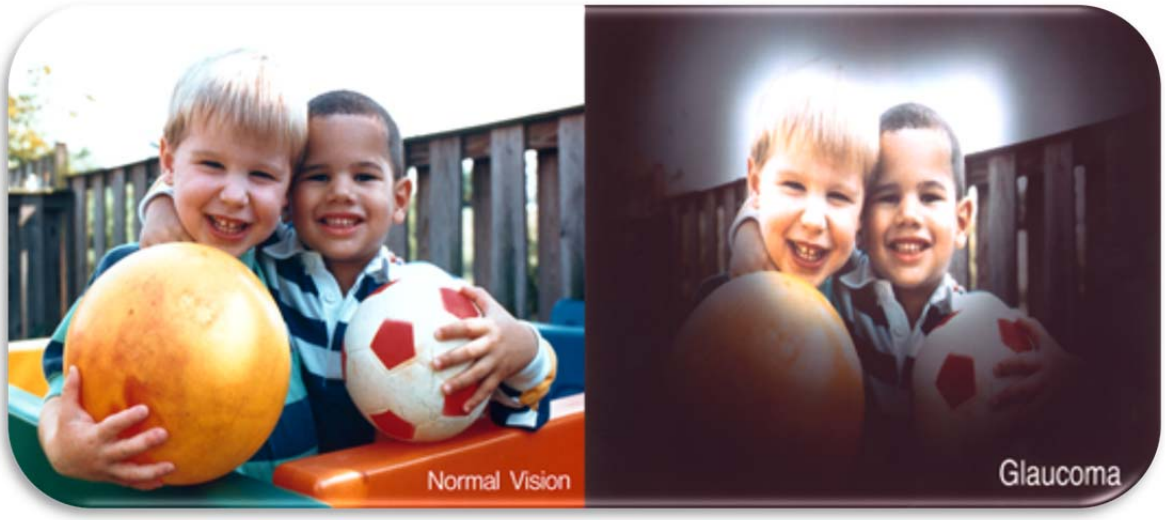
OKC Metro Area: (405)522-6205 option 4
Statewide Toll-free: (800)522-0114 option 4

Pharmacy Services
(800) 522-0114, option 4

Keeping an Eye on Vision

Dear SoonerCare Member,

You or someone you know might have glaucoma. Sight loss from glaucoma cannot be recovered.



Don't skip….

- Yearly dilated eye exams
- Your daily medications
- Early detection and treatment may save your sight.

Check with your eye doctor today. The sooner the better.

Sincerely,

Oklahoma Health Care Authority

Source: www.nei.nih.gov/glaucoma

National Eye Institute
National Institutes of Health

Oklahoma HealthCare Authority

Appendix D

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

Oklahoma Health Care Authority
November 2014

Recommendations

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. A trial of aminosalicylate therapy 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® (adelimumab)
    b. **CD:** Cimzia® (certolizumab), Humira® (adelimumab); and
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. 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.

Appendix E

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

Oklahoma Health Care Authority
November 2014

Recommendations

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.

Appendix F

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

Oklahoma Health Care Authority
November 2014

Recommendations

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

*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).

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.

Appendix G

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

Oklahoma Health Care Authority
November 2014

Introduction[1, 2, 3, 4, 5, 6, 7, 8, 9, 10]

Hepatitis C was covered in the May and June 2014 DUR Board packets. For additional background information, please refer to those documents. Harvoni® (ledipasvir/sofosbuvir) is a fixed-dose combination of a hepatitis C virus (HCV) NS5A inhibitor and an HCV nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection in adults. Harvoni® efficacy has been established in individuals with genotype-1 with compensated liver disease (including cirrhosis). Harvoni® is indicated as monotherapy.

Viral Load

Prior to initiation of HCV therapy, quantitative HCV-RNA testing is necessary to document the baseline level of viremia (viral load). Pretreatment viral load is necessary to select an appropriate treatment regimen and to evaluate an initial viral response. Harvoni® has recommended shortened treatment durations for a baseline viral load less than 6million IU/mL.

Sustained viral response (SVR) is used to evaluate the efficacy of the treatment regimen and is defined as the proportion of patients who experience a decline in HCV-RNA to undetectable levels following completion of antiviral treatment. The current standard marker of successful treatment is an undetectable SVR measured 12 weeks after the patient has completed therapy; this is known as SVR-12. Patients are considered to have relapsed if a patient achieved an undetectable viral load at the last measurement on treatment but subsequently had a detectable viral load post treatment. Patients are considered non-responders to hepatitis C therapy if they did not achieve an undetectable viral load at the end of treatment.

Genotype

Laboratory testing to identify the genotype of the hepatitis C strain should be performed. There are at least six known genotypes of HCV and more than 50 subtypes. Genotype information is necessary for making treatment recommendations. Knowing the genotype can help predict the likelihood of treatment response and determine the duration of treatment. Subtypes can also have unique polymorphisms which further determine response to treatment. In the United States, genotype-1 infection is found in around three-quarters of patients and is associated with a lower response to antiviral treatment than infection with genotypes 2 and 3, which are present in about 20% of patients. Harvoni® is approved to treat genotype-1 only.

Market News and Updates [1, 11, 12, 13, 14, 15, 16]

Guideline Updates:

- **01/2014:** The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) in collaboration with the International Antiviral Society-USA (IAS-USA) issued updated guidelines for *Testing, Managing, and Treating Hepatitis C*.
- **04/2014:** The World Health Organization (WHO) and the European Association for the Study of the Liver (EASL) issued hepatitis C treatment guidelines.
- **08/2014:** The AASLD/IDSA/IAS-USA updated the guidance to include *When and In Whom to Initiate HCV Therapy*.
- **10/2014:** Guidelines have not been updated to incorporate the place in therapy for Harvoni® (ledipasvir/sofosbuvir).

Market and Pipeline Updates:

- **04/2014:** AbbVie submitted a new drug application (NDA) to the FDA for its all-oral interferon free therapy for CHC infection genotype-1. The AbbVie investigational regimen consists of a fixed-dose combination of ABT-450/ritonavir (150/100mg) co-formulated with ombitasvir 25mg, dosed once daily, and dasabuvir 250mg with or without ribavirin (RBV), dosed twice daily. The combination of three different mechanisms of action interrupts the hepatitis C virus replication process with the goal of optimizing sustained virologic response rates across different patient populations.
- **08/2014:** Vertex Pharmaceuticals announced its decision to cease marketing of its hepatitis C medication Incivek® (telaprevir) and to remove Incivek® from the U.S. market by October 2014.
- **10/2014:** Bristol-Myers Squibb (BMS) announced they will not pursue FDA approval of its HCV treatment, a dual regimen of daclatasvir and asunaprevir, and has withdrawn its NDA for asunaprevir, an NS3/4A protease inhibitor. BMS will continue to pursue FDA approval of daclatasvir, a pan-genotypic NS5A complex inhibitor.

Harvoni® (Ledipasvir/Sofosbuvir) Summary [12, 13, 17]

FDA Approved: October 2014

Indications: Harvoni® (ledipasvir/sofosbuvir) is a fixed-dose combination of ledipasvir, an HCV NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of CHC genotype-1 infection in adults.

Dosing:

- Harvoni® is available as an oral tablet containing 90mg of ledipasvir and 400mg of sofosbuvir.
- The recommended dosing of Harvoni® is one tablet taken orally once daily.
- No dose recommendation can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite.

- The recommended treatment duration for Harvoni® depends on baseline host and viral factors. The following table delineates the regimens.

Patient Population	Recommended Treatment Duration
Treatment-naïve without cirrhosis who have pre-treatment HCV-RNA < 6million IU/mL	8 weeks
Treatment-naïve with or without cirrhosis	12 weeks
Treatment-experienced* without cirrhosis	12 weeks
Treatment-experienced* with cirrhosis	24 weeks

*Treatment-experienced patients who have failed treatment with peginterferon alfa + ribavirin or an HCV protease inhibitor + peginterferon alfa + ribavirin

Contraindications: None

Warnings and Precautions:

- The use of Harvoni® with other products containing sofosbuvir (Sovaldi™) is not recommended.
- The concomitant usage of Harvoni® with permeability glycoprotein (P-gp) inducers (e.g., rifampin, St. John's wort) may significantly decrease Harvoni® plasma concentrations and may lead to a reduced therapeutic effect of Harvoni®. Use of Harvoni® with P-gp inducers is not recommended.

Adverse Reactions: The most common adverse reactions (≥5%) experienced with Harvoni® during clinical trials were fatigue, headache, nausea, diarrhea, and insomnia.

Drug Interactions: The following table provides a listing of established or potentially significant drug interactions.

Concomitant Drug Class: Drug Name	Effect on Concentration	Clinical Comment
Antacids: aluminum and magnesium hydroxide	↓ledipasvir	It is recommended to separate antacid and Harvoni® by four hours
Anticonvulsants: carbamazepine, phenytoin, phenobarbital, oxcarbazepine	↓ledipasvir ↓sofosbuvir	Coadministration is not recommended.
Antimycobacterials: rifabutin, rifampin, rifapentine	↓ledipasvir ↓sofosbuvir	Coadministration is not recommended.
HIV Antiretrovirals: elvitegravir, cobicistat, emtricitabine, tenofovir	↑tenofovir	Coadministration is not recommended.
HIV Antiretrovirals: tipranavir/ritonavir	↓ledipasvir ↓sofosbuvir	Coadministration is not recommended.
HCV Medications: simeprevir	↑ledipasvir ↑sofosbuvir	Coadministration is not recommended.
Herbal Supplements: St. John's wort	↓ledipasvir ↓sofosbuvir	Coadministration is not recommended.
HMG-CoA Reductase Inhibitors: rosuvastatin	↑ rosuvastatin	Coadministration is not recommended.

Use in Specific Populations:

- Pregnancy: Harvoni® is pregnancy category B. There are no adequate and well controlled studies with Harvoni® in pregnant women. Harvoni® should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: It is not known whether Harvoni® and its metabolites are present in human breast milk.
- Pediatric Patients: The safety and effectiveness of Harvoni® have not been established in pediatric patients.
- Geriatric Patients: No overall differences in safety or effectiveness with Harvoni® were observed in subjects 65 years and older when compared to younger subjects.
- Renal Impairment: No dosage adjustment of Harvoni® is required for mild or moderate renal impairment. The safety and efficacy of Harvoni® have not been established in patients with severe renal impairment (eGFR <30mL/min/1.73m^2) or ESRD. No dosage recommendation can be given for patients with severe renal impairment or ESRD.
- Hepatic Impairment: No dosage adjustment of Harvoni® is required for patients with mild, moderate, or severe hepatic impairment. The safety and efficacy of Harvoni® have not been established in patients with decompensated cirrhosis.

Mechanism of Action: Ledipasvir is an inhibitor of the HCV NS5A protein, which is required for viral replication. Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication. Sofosbuvir is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate, which can be incorporated into HCV-RNA by the NS5B polymerase and acts as a chain terminator.

Efficacy:

The efficacy of Harvoni® was evaluated in three Phase-3 clinical trials of 1,518 subjects with genotype-1 CHC and compensated liver disease:

- Study ION-3: noncirrhotic treatment-naïve subjects
- Study ION-1: cirrhotic and noncirrhotic treatment-naïve subjects
- Study ION-2: cirrhotic and noncirrhotic subjects who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor

SVR was the primary efficacy endpoint and relapse was a secondary endpoint.

Treatment-Naïve Adults without Cirrhosis – ION-3

Subjects received Harvoni® for 8 weeks or Harvoni® for 12 weeks. Of the 641 treated subjects 81% had baseline HCV-RNA levels ≥800,000 IU/mL. The treatment difference between the 8-week treatment of Harvoni® and 12-week treatment of Harvoni® was –2.3%. Among subjects with a baseline HCV RNA <6 million IU/mL, the SVR was 97% (119/123) with 8-week treatment of Harvoni® and 96% (126/131) with 12-week treatment of Harvoni®.

Treatment-Naïve Adults with or without Cirrhosis – ION-1

Subjects received Harvoni® for 12 weeks. Of the 865 treated subjects, 79% had baseline HCV RNA levels ≥800,000 IU/mL and 16% had cirrhosis. The overall SVR for Harvoni® treatment for 12 weeks without ribavirin was 99%. The relapse rate was <1%. The SVR for noncirrhotic subjects treated was 99% (176/177) versus 94% (32/34) for cirrhotic subjects.

Previously-Treated Adults with or without Cirrhosis – ION-2

Subjects received 12 or 24 weeks of treatment with Harvoni®. Of the 440 treated subjects, 89% had baseline HCV RNA levels ≥800,000 IU/mL, 20% had cirrhosis, and 47% of the subjects failed a prior therapy of pegylated interferon and ribavirin. Fifty-three percent (53%) of the subjects failed a prior therapy of pegylated interferon and ribavirin with an HCV protease inhibitor. The overall SVR was found to be 94% (102/109) for 12 weeks of treatment and 99% (108/109) for 24 weeks of treatment. The SVR for noncirrhotic subjects was 95% (12w) and 99% (24w) versus 86% (12w) and 100% (24w) for cirrhotic subjects.

Cost: The following table shows the cost for each regimen. SVR rates found in clinical studies should not be compared across clinical studies, but can be used as a measure of clinical efficacy for each regimen. Specific regimens are used in specific patient populations depending on pre-treatment viral load, prior hepatitis C treatment experience, and fibrosis score. The table contains only regimens for genotype-1 as Harvoni® is only indicated in genotype-1.

Treatment Regimen	Patient Population (Genotype 1)	Length of Therapy	Total Cost	SVR in Clinical Studies
Sovaldi™ + PEG IFN + RBV	Treatment naïve w/o cirrhosis	12 weeks	$99,544.44	92% (252/273)
Harvoni®	Treatment naïve w/o cirrhosis with a baseline HCV-RNA <6million IU/mL	8 weeks	$66,528.00	97% (119/123)
Sovaldi™ + PEG IFN + RBV	Treatment naïve with cirrhosis	12 weeks	$99,544.44	80% (43/54)
Harvoni®	Treatment naïve with cirrhosis	12 weeks	$99,792.00	94% (32/34)
***Sovaldi™ + Olysio™ ±RBV**	Treatment experienced w/o cirrhosis	12 weeks	$158,780.16 or $159,112.80	96% (26/27) (with RBV) or 93% (13/14)
Harvoni®	Treatment experienced w/o cirrhosis	12 weeks	$99,792.00	95% (83/87)
***Sovaldi™ + Olysio™ ±RBV**	Treatment naïve or experienced with a fibrosis score of F3 or F4 (cirrhosis)	12 weeks	$158,780.16 or $159,112.80	93% (25/27) (with RBV) or 93% (13/14)
Harvoni®	Treatment experienced with cirrhosis	24 weeks	$199,584.00	100% (22/22)
Sovaldi™ + RBV	Treatment naïve and IFN in-eligible or treatment naïve and HIV co-infected	24 weeks	$178,073.28	76% (87/114)

RBV= Ribavirin
PEG IFN= peginterferon alfa
w/o= without
*Not an FDA approved regimen.
RBV Dosing based >75kg patient (1200mg)

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 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.

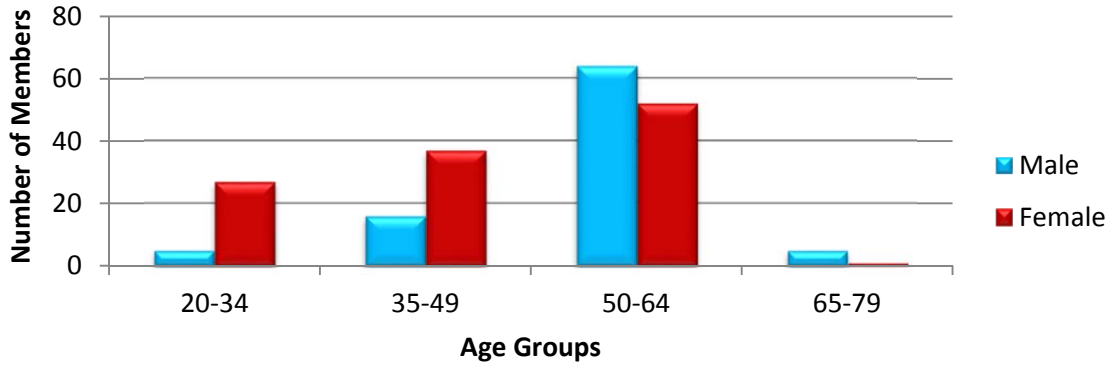
Utilization of Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)

Comparison of Pre and Post Prior Authorization Implementation
(Prior Authorization Implemented 07/01/2014)

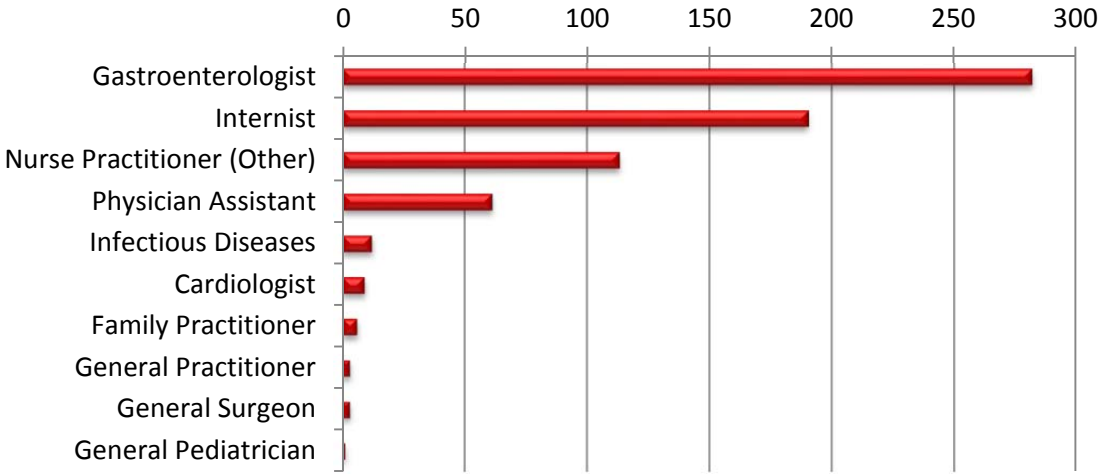
Time Frame	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
Jan 1, 2014-Jun 30, 2014	190	526	$15,305,839.63	$29,098.55	$1,039.23	14,728	14,728
Jul 1, 2014-Oct 1, 2014	79	154	$4,429,360.26	$28,762.08	$1,027.22	4,312	4,312
Total	**207***	**680**	**$19,735,199.89**	**$29,022.35**	**$1,036.51**	**19,040**	**19,040**

*Total number of unduplicated members.

Demographics of Members Utilizing Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)



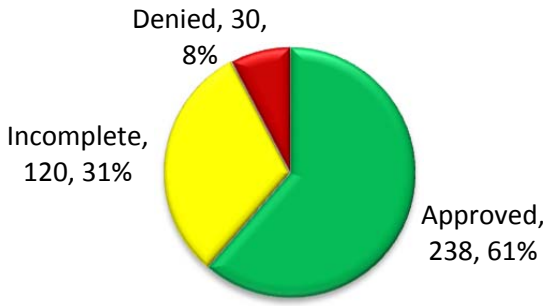
Top Prescriber Specialties of Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)



Prior Authorization of Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir)

There was a total of 388 petitions submitted for a total of 144 unique members for Sovaldi™ (Sofosbuvir) and Olysio™ (Simeprevir) since January 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Care Management Referrals

When a prior authorization is submitted a prescriber or pharmacy can recommend referral of the member to the care management program. Care management nurses will contact the patient and provide support to the member to follow the treatment regimen as prescribed. The nurse will contact the member regularly during their hepatitis C treatment and will continue to follow the patient for up to 12 weeks after the completion of therapy to encourage follow up with lab work to ensure the virus has been cleared. Twelve members utilizing hepatitis C therapies have been referred to the care management program.

Utilization Details of Hepatitis C Medications: 01/01/2014 to 10/01/2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Sofosbuvir Products					
SOVALDI 400MG	621	206	$18,357,006.38	$1,055.73	$29,560.40
Subtotal	**621**	**206**	**$18,357,006.38**	**$1,055.73**	**$29,560.40**
Simeprevir Products					
OLYSIO 150MG	59	25	$1,378,193.51	$834.26	$23,351.21
Subtotal	**59**	**25**	**$1,378,193.51**	**$834.26**	**$23,351.21**
Peginterferon Alfa Products					
PEGASYS INJ PROCLICK	146	54	$480,021.47	$116.45	$3,287.82
PEG-INTRON KIT 120 RP	98	30	$326,422.66	$117.76	$3,330.84
PEGASYS INJ	93	36	$308,180.06	$118.08	$3,313.76
PEG-INTRON KIT 150 RP	63	21	$216,758.85	$122.88	$3,440.62
PEG-INTRON KIT 80MCG RP	22	7	$69,031.51	$112.06	$3,137.80
PEGASYS INJ PROCLICK	8	3	$26,521.69	$118.40	$3,315.21
PEG-INTRON KIT 50MCG RP	6	1	$17,840.28	$106.19	$2,973.38
PEG-INTRON KIT 120MCG	5	1	$12,695.65	$120.91	$2,539.13
PEG-INTRON KIT 150MCG	2	1	$6,866.52	$122.62	$3,433.26
Subtotal	**443**	**148**	**$1,464,338.69**	**$117.74**	**$3,305.50**
Ribavirin Products					
RIBAVIRIN TAB 200MG	257	95	$27,441.48	$3.76	$106.78
RIBASPHERE TAB 200MG	222	83	$23,015.25	$3.71	$103.67
RIBASPHERE CAP 200MG	153	48	$14,767.03	$3.45	$96.52
RIBAVIRIN CAP 200MG	75	32	$7,280.22	$3.44	$97.07
MODERIBA TAB 200MG	26	11	$2,754.42	$3.76	$105.94
REBETOL SOL 40MG/ML	11	2	$5,636.10	$17.72	$512.37
Subtotal	**744**	**242**	**$80,894.50**	**$3.86**	**$108.73**
Total	**1,867**	**264***	**$21,280,433.08**	**$405.94**	**$11,398.20**

*Total number of unduplicated members.

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Appendix H

Fiscal Year 2014 Annual Review of Fibromyalgia Medications

Oklahoma Health Care Authority
November 2014

Current Prior Authorization Criteria

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

Fibromyalgia Medications Tier-2 Approval Criteria:

1. A documented, recent (within the last six months) trial of two Tier-1 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-2 medication.

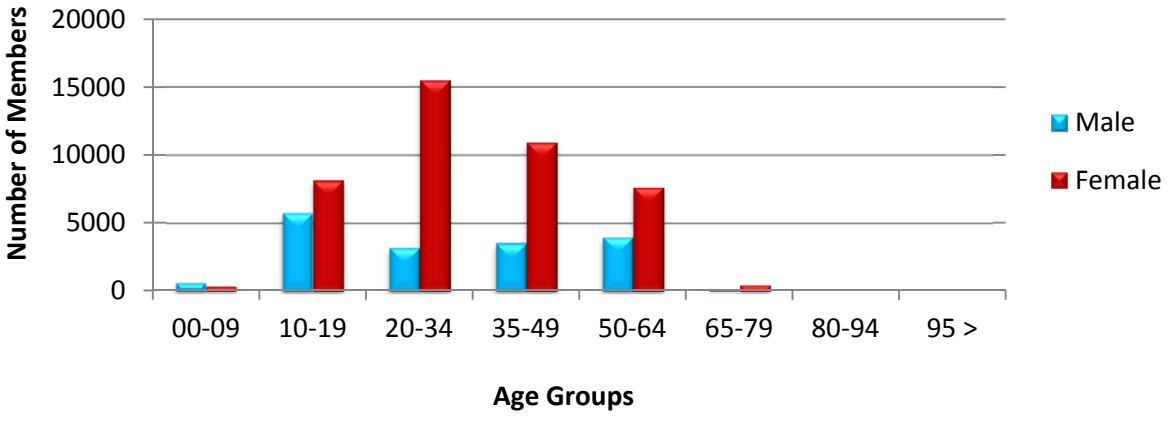
Utilization of Fibromyalgia Medications

Comparison of Fiscal Years

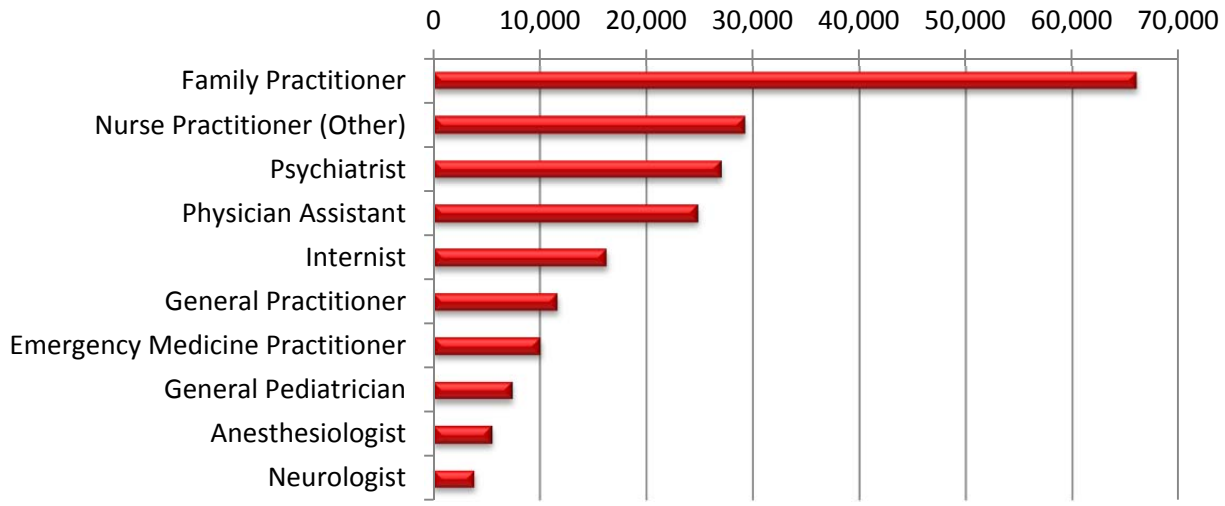
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	62,978	228,144	$8,658,200.63	$37.95	$1.48	12,631,293	5,849,359
2014	60,812	222,290	$9,283,735.64	$41.76	$1.58	12,002,217	5,862,143
% Change	**-3.40%**	**-2.60%**	**7.20%**	**10.00%**	**6.80%**	**-5.00%**	**0.20%**
Change	**-2,166**	**-5,854**	**$625,535.01**	**$3.81**	**$0.10**	**-629,076**	**12,784**

*Total number of unduplicated members.

Demographics of Members Utilizing Fibromyalgia Medications



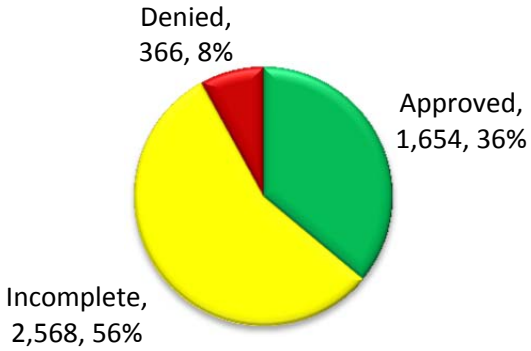
Top Prescriber Specialties of Fibromyalgia Medications by Number of Claims



Prior Authorization of Fibromyalgia Medications

There was a total of 4,588 petitions submitted for the fibromyalgia 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]

Anticipated Patent Expirations:

- Lyrica® (pregabalin)- 12/2018
- Savella® (milnacipran)- 9/2029

Cost Comparison

MEDICATION NAME	DOSING∞	COST/DAY	COST/MONTH
Proposed Tier-1 Medications			
fluoxetine	QD	$0.08 - $1.55*	$2.40 - $46.50
amitriptyline	QD	$0.17 - $1.81*	$5.10 - $54.30
cyclobenzaprine	TID	$0.21 - $0.27*	$6.30 - $8.10
tramadol	8 tablets/day	$0.48*	$14.40
duloxetine	60mg QD	$1.33*	$39.90
Proposed Tier-2 Medications			
Lyrica® (pregabalin)	BID	$9.26 - $10.20+	$277.80 - $306.00
Savella® (milnacipran)	BID	$7.24+	$217.20

∞Dosing is based on FDA approved dosing regimens and/or SoonerCare quantity limits, if applicable.
*State Maximum Allowable Cost (SMAC)
+Estimated Acquisition Cost (EAC)

Recommendations

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.

Utilization Details of Fibromyalgia Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TRAMADOL PRODUCTS						
TRAMADOL HCL TAB 50MG	56,923	22,088	$442,688.59	$0.41	$7.78	4.77%
SUBTOTAL	**56,923**	**22,088**	**$442,688.59**	**$0.41**	**$7.78**	**4.77%**
CYCLOBENZAPRINE PRODUCTS						
CYCLOBENZAPR TAB 10MG	49,165	22,490	$389,820.80	$0.35	$7.93	4.20%
CYCLOBENZAPR TAB 5MG	7,423	4,870	$61,489.77	$0.44	$8.28	0.66%
SUBTOTAL	**56,588**	**27,360**	**$451,310.57**	**$0.36**	**$7.98**	**4.86%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 20MG	30,255	9,612	$219,750.95	$0.22	$7.26	2.37%
FLUOXETINE CAP 40MG	13,161	3,602	$160,800.77	$0.35	$12.22	1.73%
FLUOXETINE CAP 10MG	10,353	3,648	$67,600.50	$0.21	$6.53	0.73%
FLUOXETINE TAB 10MG	2,966	1,062	$17,218.23	$0.19	$5.81	0.19%
FLUOXETINE SOL 20MG/5ML	1,030	247	$8,449.04	$0.28	$8.20	0.09%
FLUOXETINE TAB 20MG	1,007	474	$21,533.03	$0.68	$21.38	0.23%
PROZAC CAP 20MG	21	2	$11,327.33	$18.12	$539.40	0.12%
PROZAC CAP 40MG	12	1	$5,537.58	$15.38	$461.47	0.06%
SUBTOTAL	**58,805**	**18,648**	**$512,217.43**	**$0.27**	**$8.71**	**5.52%**
AMITRIPTYLINE PRODUCTS						
AMITRIPTYLIN TAB 25MG	7,406	2,827	$53,206.38	$0.22	$7.18	0.57%
AMITRIPTYLIN TAB 50MG	5,192	1,720	$38,032.48	$0.21	$7.33	0.41%
AMITRIPTYLIN TAB 10MG	3,590	1,435	$23,309.66	$0.21	$6.49	0.25%
AMITRIPTYLIN TAB 100MG	2,821	749	$27,095.08	$0.28	$9.60	0.29%
AMITRIPTYLIN TAB 150MG	1,101	270	$14,096.05	$0.36	$12.80	0.15%
AMITRIPTYLIN TAB 75MG	1,044	295	$9,303.12	$0.26	$8.91	0.10%
SUBTOTAL	**21,154**	**7,296**	**$165,042.77**	**$0.23**	**$7.80**	**1.78%**
TIER-1 SUBTOTAL	**193,470**	**58,249***	**$1,571,259.36**	**$0.32**	**$8.12**	**16.92%**
DULOXETINE PRODUCTS						
CYMBALTA CAP 60MG	6,573	1,960	$1,896,658.83	$8.48	$288.55	20.43%
DULOXETINE CAP 60MG	5,968	1,836	$1,345,995.15	$6.51	$225.54	14.50%
CYMBALTA CAP 30MG	2,006	744	$633,898.09	$9.74	$316.00	6.83%
DULOXETINE CAP 30MG	1,894	750	$446,180.86	$7.28	$235.58	4.81%
CYMBALTA CAP 20MG	247	91	$71,087.64	$9.17	$287.80	0.77%
DULOXETINE CAP 20MG	198	77	$43,091.93	$6.95	$217.64	0.46%
SUBTOTAL	**16,886**	**5,458**	**$4,436,912.50**	**$7.78**	**$262.76**	**47.79%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
PREGABALIN PRODUCTS						
LYRICA CAP 150MG	3,501	656	$978,410.34	$9.42	$279.47	10.54%
LYRICA CAP 75MG	2,713	726	$704,333.73	$8.87	$259.61	7.59%
LYRICA CAP 100MG	2,106	477	$639,429.11	$10.15	$303.62	6.89%
LYRICA CAP 50MG	1,325	406	$387,852.21	$10.04	$292.72	4.18%
LYRICA CAP 300MG	895	157	$238,192.10	$8.52	$266.14	2.57%
LYRICA CAP 200MG	691	123	$175,152.90	$8.45	$253.48	1.89%
LYRICA CAP 225MG	234	45	$58,793.59	$8.43	$251.25	0.63%
LYRICA CAP 25MG	168	56	$40,726.68	$7.97	$242.42	0.44%
LYRICA SOL 20MG/ML	1	1	$584.24	$19.47	$584.24	0.01%
SUBTOTAL	**11,634**	**2,647**	**$3,223,474.90**	**$9.33**	**$277.07**	**34.72%**
MILNACIPRAN PRODUCTS						
SAVELLA TAB 50MG	165	37	$28,875.43	$5.97	$175.00	0.31%
SAVELLA TAB 100MG	112	21	$19,467.71	$5.79	$173.82	0.21%
SAVELLA TAB 25MG	12	5	$2,099.45	$5.83	$174.95	0.02%
SAVELLA MIS TITR PAK	8	8	$1,319.45	$5.69	$164.93	0.01%
SAVELLA TAB 12.5MG	3	2	$326.84	$3.63	$108.95	0.00%
SUBTOTAL	**300**	**73**	**$52,088.88**	**$5.87**	**$173.63**	**0.56%**
TIER-2 SUBTOTAL	**28,820**	**5,002***	**$7,712,476.28**	**$8.34**	**$267.61**	**83.08%**
TOTAL	**222,290**	**60,812***	**$9,283,735.64**	**$1.58**	**$41.76**	**100.00%**

*Total number of unduplicated members.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 10/21/14. Last accessed 10/22/14.

Appendix I

Fiscal Year 2014 Annual Review of Oral Buprenorphine Products and 30-Day Notice to Prior Authorize Zubsolv® (Buprenorphine/Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films)

Oklahoma Health Care Authority
November 2014

Current Prior Authorization Criteria

Suboxone® (Buprenorphine/Naloxone) and Subutex® (Buprenorphine) 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 Drug Enforcement Agency (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. **Suboxone®** 2mg/0.5mg and 8mg/2mg tablets and 2mg, 4mg, 8mg, and 12mg films: A quantity limit of 90 per 30 days.
    b. **Subutex®** 2mg tablets and 8mg tablets will only be approved if the member is pregnant (product may be used for the duration of the pregnancy only), or has a documented serious allergy or adverse reaction to naloxone.

Key Points[1,2]

- The Drug Addiction Treatment Act of 2000 restricts the ability to prescribe oral buprenorphine products for the maintenance or detoxification of opioid dependence to physicians who have obtained a waiver and a unique Drug Enforcement Agency number beginning with an "X".
- The United States Substance Abuse and Mental Service Clinical Guideline for the Use of Buprenorphine in the Treatment of Opioid Addiction recommends the use of buprenorphine without naloxone only in patients who are pregnant and patients who have a serious allergic reaction to naloxone.
- Buprenorphine in combination with naloxone is recommended for all other patients to minimize the potential diversion associated with buprenorphine monotherapy.
- The target maintenance daily dose is 16mg buprenorphine with a range between 4mg to 24mg per day according to the manufacturers' recommendations and current treatment guidelines. [a]

[a] Zubsolv® 5.7mg/1.4mg and Bunavail™ 4.2mg/0.7mg provides equivalent buprenorphine exposure to Suboxone® and Subutex® 8mg/2mg.

- Some studies have shown doses up to a maximum of 32mg/8mg buprenorphine/naloxone per day may be required in some patients.
- Current treatment guidelines recommend toxicology tests for illicit drugs administered at least monthly.
- Oral buprenorphine products are FDA approved for ages 16 and older.

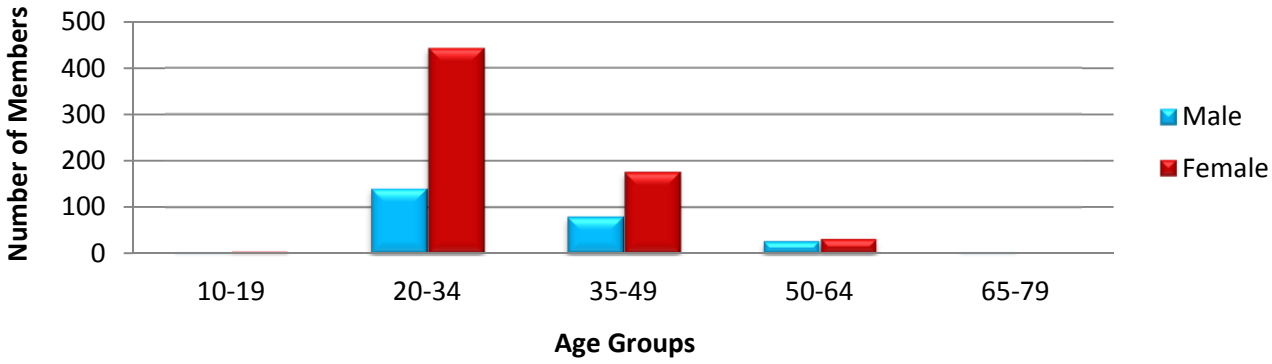
Utilization of Oral Buprenorphine Products

Comparison of Fiscal Years

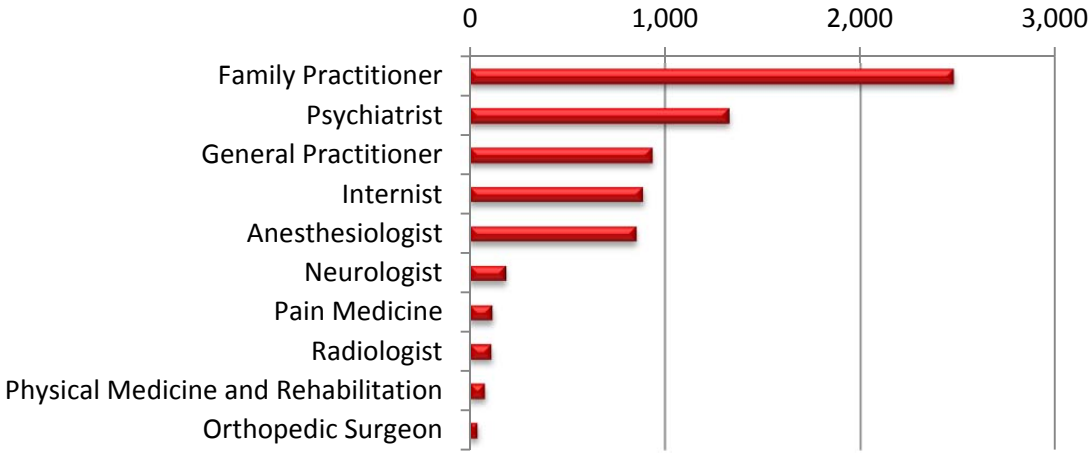
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	867	6,263	$2,678,190.52	$427.62	$16.46	360,275	162,699
2014	915	6,955	$2,696,378.48	$387.69	$14.95	398,615	180,302
% Change	**5.50%**	**11.00%**	**0.70%**	**-9.30%**	**-9.20%**	**10.60%**	**10.80%**
Change	**48**	**692**	**$18,187.96**	**-$39.93**	**-$1.51**	**38,340**	**17,603**

*Total number of unduplicated members.

Demographics of Members Utilizing Oral Buprenorphine Products



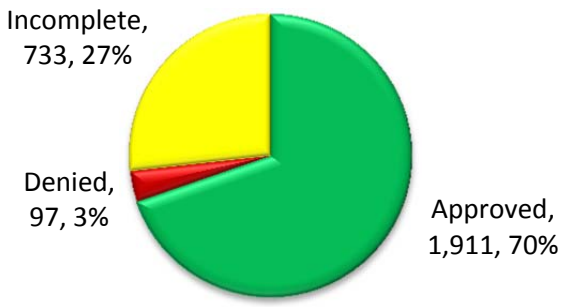
Top Prescriber Specialties of Oral Buprenorphine Products by Number of Claims



Prior Authorization of Oral Buprenorphine Products

There was a total of 2,741 petitions submitted for oral buprenorphine products during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[3]

Anticipated Patent Expirations:

- Suboxone® Sublingual Film (buprenorphine/naloxone)- 2030

New FDA Approvals:

- Zubsolv® (buprenorphine/naloxone sublingual tablet)- July 2013
- Bunavail™ (buprenorphine/naloxone buccal film)- June 2014

Zubsolv® (Buprenorphine/Naloxone Sublingual Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) Summary[4,5]

Indications: Zubsolv® (buprenorphine/naloxone) and Bunavail™ (buprenorphine/naloxone) are partial opioid agonists indicated for the maintenance treatment of opioid dependence. Prescription use of this product is limited under the Drug Addiction Treatment Act.

Zubsolv® Dosing:

- Zubsolv® is available as a sublingual tablet in the following strengths:
  - 1.4mg buprenorphine/0.36mg naloxone
  - 5.7mg buprenorphine/1.4mg naloxone
- Administer Zubsolv® sublingually as a single daily dose.
- The recommended daily dose of Zubsolv® for maintenance treatment is 11.4mg/2.8mg buprenorphine/naloxone.
- Patients should not cut, chew, or swallow Zubsolv®.
- One Zubsolv® 5.7mg/1.4mg sublingual tablet provides equivalent buprenorphine exposure to one Suboxone® 8mg/2mg sublingual tablet.

Bunavail™ Dosing:

- Bunavail™ is available as a buccal film in the following strengths:
  - 2.1mg buprenorphine/0.3mg naloxone
  - 4.2mg buprenorphine/0.7mg naloxone
  - 6.3mg buprenorphine/1mg naloxone
- Apply Bunavail™ buccal film as a single daily dose.
- The recommended daily dose for maintenance is 8.4mg/1.4mg buprenorphine/naloxone.
- One Bunavail™ 4.2mg/0.7mg buccal film provides equivalent buprenorphine exposure to one Suboxone® 8mg/2mg sublingual tablet.

Mechanism of Action: Zubsolv® and Bunavail™ contain buprenorphine and naloxone. Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Naloxone is a potent antagonist at mu-opioid receptors and produces opioid withdrawal signs and symptoms, if administered parenterally, in individuals physically dependent on full opioid agonists.

Contraindications: Hypersensitivity to buprenorphine or naloxone.

Efficacy: The efficacy of Zubsolv® and Bunavail™ is based on trials of other available buprenorphine/naloxone products already available on the market.

Safety:

- Buprenorphine can be abused in a similar manner to other opioids. Clinical monitoring appropriate to the patient's level of stability is essential. Multiple refills should not be prescribed early in treatment or without appropriate patient follow-up visits.
- Significant respiratory depression and death have occurred in association with buprenorphine, particularly when taken by the intravenous route in combination with benzodiazepines or other CNS depressants (including alcohol).
- Consider dose reduction of CNS depressants, buprenorphine, or both, in situations of concomitant prescriptions.
- Store safely out of the sight and reach of children. Buprenorphine can cause severe and fatal respiratory depression in children.
- Chronic administration produces opioid-type physical dependence. Abrupt discontinuation or rapid dose taper may result in opioid withdrawal syndrome.
- Monitor liver function tests prior to initiation and during treatment and evaluate suspected hepatic events.
- Do not administer Bunavail™ or Zubsolv® to patients with known hypersensitivity to buprenorphine or naloxone.
- Opioid withdrawal syndrome is likely to occur with parenteral misuse of Zubsolv® or Bunavail™ by individuals physically dependent on full opioid agonists or by administration before the agonist effects of other opioids have subsided.
- Neonatal withdrawal has been reported following use of buprenorphine by the mother during pregnancy.
- Zubsolv® and Bunavail™ is not appropriate as an analgesic. There have been reported deaths of opioid naïve individuals who received a 2mg sublingual dose of buprenorphine.

- Buprenorphine/naloxone products are not recommended in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment.
- Caution patients about the risk of driving or operating hazardous machinery.

Cost Comparison

MEDICATION NAME	STRENGTH	COST / UNIT	COST / MONTH**
Zubsolv® SL tablets	1.4mg/0.36mg	$3.71+	$906.30
Zubsolv® SL tablets	5.7mg/1.4mg	$7.43+	$445.80
Bunavail™ buccal film	2.1mg/0.3mg	$7.43+	$891.60
Bunavail™ buccal film	4.2mg/0.7mg	$7.43+	$445.80
Bunavail™ buccal film	6.3mg/1mg	$14.86+	$594.40
Suboxone® SL film	8mg/2mg	$7.43+	$445.80
Suboxone® SL film	12mg/3mg	$14.87+	$594.80
Buprenorphine/Nalox SL tablets	8mg/2mg	$6.38*	$382.80
Buprenorphine SL tablets	8mg	$2.22*	$133.20

*State Maximum Allowable Cost (SMAC)
+Estimated Acquisition Cost (EAC)
**Dosed based on FDA target recommended maintenance dose.

- Zubsolv® target maintenance daily dose= 11.4mg/2.8mg
- Bunavail™ target maintenance daily dose= 8.4mg/1.4mg
- Suboxone® SL film, SL tablets, and buprenorphine SL tablets target maintenance daily dose= 16mg/4mg

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.

Utilization Details of Oral Buprenorphine Products: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SUBOXONE PRODUCTS						
SUBOXONE MIS 8-2MG	4,248	659	$1,790,068.69	$16.15	$421.39	66.39%
BUPREN/NALOX SUB 8-2MG	1,713	277	$713,057.62	$15.76	$416.26	26.45%
SUBOXONE MIS 2-0.5MG	129	51	$25,975.51	$8.17	$201.36	0.96%
SUBOXONE MIS 4-1MG	104	29	$38,607.46	$14.57	$371.23	1.43%
BUPREN/NALOX SUB 2-0.5MG	64	27	$11,513.35	$8.32	$179.90	0.43%
SUBOXONE MIS 12-3MG	37	13	$19,395.79	$18.42	$524.21	0.72%
SUBTOTAL	**6,295**	**1,056**	**$2,598,618.42**	**$13.57**	**$352.39**	**96.38%**
SUBUTEX PRODUCTS						
BUPRENORPHIN SUB 8MG	622	109	$91,454.57	$5.99	$147.03	3.39%
BUPRENORPHIN SUB 2MG	30	17	$3,209.43	$6.36	$106.98	0.12%
SUBTOTAL	**652**	**126**	**$94,664.00**	**$6.18**	**$127.01**	**3.51%**
ZUBSOLV PRODUCTS						
ZUBSOLV SUB 5.7-1.4	8	3	$3,096.06	$15.18	$387.01	0.11%
SUBTOTAL	**8**	**3**	**$3,096.06**	**$15.18**	**$387.01**	**0.11%**
TOTAL	**6,955**	**915***	**$2,696,378.4**	**$14.95**	**$387.69**	**100%**

*Total number of unduplicated members.

[1] Therapeutic Class Overview Buprenorphine and Buprenorphine/Naloxone (2014). http://www.medicaid.nv.gov/Downloads/provider/Buprenorphine_and_Buprenorphine_Naloxone_2014-0311.pdf. Last revised March 2014. Last accessed October 2014.

[2]Center for Substance Abuse Treatment. Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction: a treatment improvement protocol TIP 40. Rockville (MD): Substance Abuse and Mental Health Services Administration (SAMHSA); DHHS Publication No. (SMA) 04-3939. 2004.

[3] 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 10/21/14. Last accessed 10/22/2014.

[4]Zubsolv® Product Information. Orexo, Inc. Available online at: http://www.zubsolv.com/pdf/zubsolvFullPI-patient.pdf#1. Last revised 07/2013. Last accessed 10/2014.

[5] Bunavail™ Product Information. BioDelivery Sciences Inc. Available online at: http://www.bdsi.com/siteres.aspx?resid=5a738443-a797-41cd-a39a-a8deb2a4a585. Last revised 06/2014. Last accessed 10/2014.

Appendix J

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

FDA NEWS RELEASE

For Immediate Release: October 10th, 2014
FDA approves first combination pill to treat hepatitis C

The U.S. Food and Drug Administration approved Harvoni (ledipasvir and sofosbuvir) to treat chronic hepatitis C virus (HCV) genotype 1 infection.

Harvoni is the first combination pill approved to treat chronic HCV genotype 1 infection. It is also the first approved regimen that does not require administration with interferon or ribavirin, two FDA-approved drugs also used to treat HCV infection.

Both drugs in Harvoni interfere with the enzymes needed by HCV to multiply. Sofosbuvir is a previously approved HCV drug marketed under the brand name Sovaldi. Harvoni also contains a new drug called ledipasvir.

Harvoni is the third drug approved by the FDA in the past year to treat chronic HCV infection. The FDA approved Olysio (simeprevir) in November 2013 and Sovaldi in December 2013.

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with HCV have no symptoms of the disease until liver damage becomes apparent, which may take decades.

Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections and liver cancer. According to the Centers for Disease Control and Prevention, about 3.2 million Americans are infected with HCV, and without proper treatment, 15-30 percent of these people will go on to develop cirrhosis.

Harvoni's efficacy was evaluated in three clinical trials enrolling 1,518 participants who had not previously received treatment for their infection (treatment-naive) or had not responded to previous treatment (treatment-experienced), including participants with cirrhosis. Participants were randomly assigned to receive Harvoni with or without ribavirin. The trials were designed to measure whether the hepatitis C virus was no longer detected in the blood at least 12 weeks after finishing treatment (sustained virologic response, or SVR), indicating that a participant's HCV infection has been cured.

In the first trial, comprised of treatment-naive participants, 94 percent of those who received Harvoni for eight weeks and 96 percent of those who received Harvoni for 12 weeks achieved SVR. The second trial showed 99 percent of such participants with and without cirrhosis achieved SVR after 12 weeks. And in the third trial, which examined Harvoni's efficacy in treatment-experienced participants with and without cirrhosis, 94 percent of those who received Harvoni for 12 weeks and 99 percent of those who received Harvoni for 24 weeks achieved SVR. In all trials, ribavirin did not increase response rates in the participants.

The most common side effects reported in clinical trial participants were fatigue and headache.

Harvoni is the seventh new drug with breakthrough therapy designation to receive FDA approval. The FDA can designate a drug as a breakthrough therapy at the request of the sponsor if preliminary clinical evidence indicates the drug may demonstrate a substantial improvement over available therapies for patients with serious or life-threatening diseases. Harvoni was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that treat serious conditions and, if approved, would provide significant improvement in safety or effectiveness.

Harvoni and Sovaldi are marketed by Gilead, based in Foster City, California. Olysio is marketed by Janssen Pharmaceutical based in Raritan, New Jersey.

FDA NEWS RELEASE

For Immediate Release: October 10th, 2014

FDA approves Akynzeo for nausea and vomiting associated with cancer chemotherapy

The U.S. Food and Drug Administration approved Akynzeo (netupitant and palonosetron) to treat nausea and vomiting in patients undergoing cancer chemotherapy.

Akynzeo is a fixed combination capsule comprised of two drugs. Oral palonosetron, approved in 2008, prevents nausea and vomiting during the acute phase (within the first 24 hours) after the start of cancer chemotherapy. Netupitant, a new drug, prevents nausea and vomiting during both the acute phase and delayed phase (from 25 to 120 hours) after the start of cancer chemotherapy.

Akynzeo's effectiveness was established in two clinical trials of 1,720 participants receiving cancer chemotherapy. Participants were randomly assigned to receive Akynzeo or oral palonosetron. The trials were designed to measure whether the study drugs prevented any vomiting episodes in the acute, delayed and overall phases after the start of cancer chemotherapy.

Results of the first trial showed that 98.5 percent, 90.4 percent and 89.6 percent of Akynzeo-treated participants did not experience any vomiting or require rescue medication for nausea during the acute, delayed and overall phases, respectively. In contrast, 89.7 percent, 80.1 percent and 76.5 percent of participants treated with oral palonosetron did not experience any vomiting or require rescue medication for nausea during the acute, delayed and overall phases, respectively. The second trial showed similar results.

Common side effects of Akynzeo in the clinical trials were headache, weakness (asthenia), fatigue, indigestion (dyspepsia) and constipation.

Akynzeo is distributed and marketed by Eisai Inc. of Woodcliff Lake, New Jersey, under license from Lugano, Switzerland-based Helsinn Healthcare S.A.

FDA NEWS RELEASE

For Immediate Release: October 15th, 2014

FDA approves Ofev to treat idiopathic pulmonary fibrosis

The U.S. Food and Drug Administration approved Ofev (nintedanib) for the treatment of idiopathic pulmonary fibrosis (IPF).

Idiopathic pulmonary fibrosis is a condition in which the lungs become progressively scarred over time. As a result, patients with IPF experience shortness of breath, cough, and have difficulty participating in everyday physical activities. Current treatments for IPF include oxygen therapy, pulmonary rehabilitation, and lung transplant.

The FDA granted Ofev fast track, priority review, orphan product, and breakthrough designations. Ofev is being approved ahead of the product's prescription drug user fee goal date of Jan. 2, 2015, the date the agency was scheduled to complete the review of the drug application.

Ofev is a kinase inhibitor that blocks multiple pathways that may be involved in the scarring of lung tissue. Its safety and effectiveness were established in three clinical trials of 1,231 patients with IPF. The decline in forced vital capacity – the amount of air which can be forcibly exhaled from the lungs after taking the deepest breath possible – was significantly reduced in patients receiving Ofev compared to patients receiving placebo.

Ofev is not recommended for patients who have moderate to severe liver problems. Ofev can cause birth defects or death to an unborn baby. Women should not become pregnant while taking Ofev. Women who are able to get pregnant should use adequate contraception during and for at least three months after the last dose of Ofev.

The most common side effects of Ofev are diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, decreased weight, and high blood pressure.

Ofev is distributed by Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut.

FDA NEWS RELEASE

For Immediate Release: October 15th, 2014

FDA approves Esbriet to treat idiopathic pulmonary fibrosis

The U.S. Food and Drug Administration approved Esbriet (pirfenidone) for the treatment of idiopathic pulmonary fibrosis (IPF).

The FDA granted Esbriet fast track, priority review, orphan product, and breakthrough designations. Esbriet is being approved ahead of the product's prescription drug user fee goal date of Nov. 23, 2014, the date the agency was scheduled to complete the review of the drug application.

Esbriet acts on multiple pathways that may be involved in the scarring of lung tissue. Its safety and effectiveness were established in three clinical trials of 1,247 patients with IPF. The decline in forced vital capacity was significantly reduced in patients receiving Esbriet compared to patients receiving placebo.

Esbriet is not recommended for patients who have severe liver problems, end-stage kidney disease, or who require dialysis. Esbriet should be taken with food to minimize the potential for nausea and dizziness.

Patients should avoid or minimize exposure to sunlight and sunlamps and wear sunscreen and protective clothing, as Esbriet may cause patients to sunburn more easily.

The most common side effects of Esbriet are nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, decreased/loss of appetite, gastro-esophageal reflux disease, sinusitis, insomnia, decreased weight, and arthralgia.

Esbriet is manufactured for InterMune, Inc., Brisbane, California.

FDA NEWS RELEASE

For Immediate Release: October 17th, 2014

FDA approves labeling with abuse-deterrent features for third extended-release opioid analgesic

The U.S. Food and Drug Administration approved new labeling for Embeda (morphine sulfate and naltrexone hydrochloride) extended-release (ER) capsules, an 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. Embeda is the third ER opioid analgesic to be approved with labeling describing the product's abuse-deterrent properties consistent with the FDA's 2013 draft guidance. The new labeling includes a claim indicating that Embeda has properties that are expected to reduce oral abuse when the product is crushed.

Embeda has properties that are expected to reduce, but not totally prevent, abuse of the drug when crushed and taken orally or snorted. Embeda works by releasing only the morphine in the capsule when taken properly. When crushed, the naltrexone in Embeda blocks some of the euphoric effects of the morphine and can precipitate withdrawal in persons dependent on opioids.

When swallowed intact, however, Embeda can still be abused or misused because the naltrexone is not expected to substantially block the euphoric effects of the morphine. It is unknown whether the abuse-deterrent properties of Embeda will result in a reduction in abuse by the intravenous route until additional postmarketing data are available.

Embeda can still be abused or misused by any of these routes, and such abuse or misuse can cause an overdose that may result in death. If abused, it can also cause withdrawal in people who are dependent on, or tolerant to, opioids.

Embeda is not approved, and should not be used, for as-needed pain relief. Given Embeda'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.

Embeda was first approved on August 13, 2009, but was voluntarily withdrawn from the market in March 2011, due to testing that found stability concerns in the manufacturing process. The FDA confirmed that these issues were resolved with its approval of a manufacturing supplement in November 2013.

When Embeda was first approved, the drug was evaluated in a clinical trial of 547 osteoarthritis patients. Additional data from abuse liability studies conducted in laboratories and in people demonstrated the abuse-deterrent features of Embeda for certain types of abuse (oral and snorting), when the product was crushed. The abuse potential for the intravenous route was studied by simulating the amount of morphine and

naltrexone that would be released upon crushing Embeda. This study demonstrated that Embeda was less attractive to abusers or less likely to produce a high compared with morphine alone. However, it is unknown whether these results with simulated crushed Embeda predict a reduction in abuse by the intravenous route until additional postmarketing data are available.
The FDA is requiring postmarketing studies of Embeda to further assess the effects of the abuse-deterrent features on the risk for abuse of Embeda and the consequences of that abuse. In addition, Embeda 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.
Embeda is marketed by New York City-based Pfizer, Inc.

Safety Announcements

FDA Drug Safety Communication: Lidocaine HCl Injection, USP 10 MG Per ML, 30 ML Single-Dose, Preservative-Free, by Hospira: Recall - Particulate Matter

[October 17th, 2014] **ISSUE:** Hospira announced it will initiate a voluntary recall of one lot of 1% Lidocaine HCl for Injection, USP, 10 mg per mL, 30 mL Single-dose, Preservative-Free to the user level due to a confirmed customer report of particulate in a single unit. Hospira has identified the particulate as a human hair, embedded in and attached to a pinched area of the stopper. To date, Hospira has not received reports of any adverse events associated with this issue for this lot. In the unlikely event that the particulate breaks and pieces are able to pass through the intravenous catheter, injected particulate material may result in local inflammation, phlebitis, and/or low-level allergic response to the particulate or microembolic effects. This lot (NDC 0409-4279-02; Lot 40-316-DK, Expiry 1APRIL2016) was distributed nationwide from May 2014 through June 2014. Hospira has initiated an investigation to determine the root cause and corrective and preventive actions.
Anyone with an existing inventory of the recalled lot should stop use and distribution and quarantine the product immediately. This recall is being carried out to the medical facility/retail level (both human and veterinary). Please notify all users in your facility. If you have further distributed the recalled product please notify any accounts or additional locations which may have received the recalled product from you and instruct them if they have redistributed the product to notify their accounts, locations or facilities to the medical facility/retail level. In addition, customers should inform potential users of these products in their organizations of this notification. Hospira will be notifying its direct customers via a recall letter and will arrange for impacted product to be returned to Stericycle. For additional assistance, call Stericycle at 1-877-546-5069 between the hours of 8am to 5pm ET, Monday through Friday.

Current Drug Shortages Index (as of October 31, 2014):

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

Amikacin Injection	***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	***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***
Cidofovir 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) CR	***Currently in Shortage***
Doxorubicin (Adriamycin) Lyophilized Powder	***Currently in Shortage***
Ephedrine Sulfate Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)13	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
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***
Fortaz 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***
Methazolamide (Neptazane) Tablets	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets14	***Currently in Shortage***
Methylphenidate Hydrochloride 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***
Rifampin for Injection	***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***
Verapamil Hydrochloride Injection, USP	***Currently in Shortage***
Zinc Injection	***Currently in Shortage***