Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
April 9, 2014
4 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln
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 – April 9, 2014

DATE: April 1, 2014

NOTE: The DUR Board will meet at 4:00 p.m. The meeting will be held at the Oklahoma Health Care Authority Offices on Lincoln.

Enclosed are the following items related to the April meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

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

Update on DUR/Medication Coverage Authorization/Narcotic RetroDUR -See Appendix B

Fiscal Year 2013 Annual Report -See Appendix C

30-Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications -See Appendix D

Annual Review of Anti-Diabetic Medications and 30-Day Notice to Prior Authorize Farxiga™ (Dapagliflozin) and Invokana™ (Canagliflozin) -See Appendix E

Annual Review of Topical Antifungals and 30-Day Notice to Prior Authorize Luzu® (Luliconazole) -See Appendix F

Annual Review of Nonsteroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Zorvolex™ (Diclofenac) and Tivorbex™ (Indomethacin) -See Appendix G

Annual Review of Benign Prostatic Hyperplasia Medications -See Appendix H

Annual Review of Muscle Relaxants and 30-Day Notice to Prior Authorize Lorzone™ (Chlorzoxazone) - See Appendix I

FDA and DEA Updates -See Appendix J

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – April 9, 2014 @ 4:00 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln
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. March 12, 2014 DUR Minutes – Vote
   B. March 12, 2014 DUR Recommendation Memorandum

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

4. **Update on DUR / Medication Coverage Authorization Unit – See Appendix B**
   A. Medication Coverage Activity for March 2014
   B. Pharmacy Help Desk Activity for March 2014
   C. Narcotic RetroDUR

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

5. **Fiscal Year 2013 Annual Report – See Appendix C**
   A. Utilization Details

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

6. **30-Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications – See Appendix D**
   A. Introduction
   B. Recommendations

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

7. **Annual Review of Anti-Diabetic Medications and 30-Day Notice to Prior Authorize Farxiga™ (Dapagliflozin) and Invokana™ (Canagliflozin) – See Appendix E**
   A. Current Authorization Criteria
   B. Utilization of Anti-Diabetic Medications
   C. Prior Authorization
   D. Market News and Updates
   E. Summary
   F. Recommendations
   G. Utilization Details
   H. Product Details

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

8. Annual Review of Topical Antifungals and 30-Day Notice to Prior Authorize Luzu® (Luliconazole) – See Appendix F

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

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

9. Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Zorvolex™ (Diclofenac) and Tivorbex™ (Indomethacin) – Appendix G

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

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

10. Annual Review of Benign Prostatic Hyperplasia Medications – Appendix H

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

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

11. Annual Review of Muscle Relaxants and 30-Day Notice to Prior Authorize Lorzone™ (Chlorzoxazone) – See Appendix I

A. Current Authorization Criteria
B. Utilization of Muscle Relaxants
C. Prior Authorization
D. Market News and Updates
E. COP Recommendations
F. Utilization Details
G. Product Details

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

12. FDA and DEA Updates – See Appendix J

13. Future Business

A. Annual Reviews
B. New Product Reviews

14. Adjournment

Appendix A

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

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.		x
Anetta Harrell, Pharm.D.	x	
Evie Knisely, Pharm.D.	x	
John Muchmore, M.D., Ph.D.; Chairman	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	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison		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
Jennifer Sipols, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Graduate Students: Tim Pham	x	
Visiting Pharmacy Student(s): Dianna Nguyen & Samantha Sepulveda	x	

	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Nico Gomez, Chief Executive Officer	x	
Chris Le, Pharm.D.; Clinical Pharmacist Consultant	x	
Sylvia Lopez, M.D., FAAP; Chief Medical Officer	x	
Ed Long, Chief Communications Officer	x	
Jennie Melendez, 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.; Pharmacy Specialist	x	
Garth Splinter, M.D., M.B.A.; Medicaid Director	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Clint Degner, Novartis	Jim Chapman, Abbvie	Holly Turner, Merck
Brian Maves, Pfizer	Bob Gustafson, Lundbeck	Sharon Jackson, GSK
Toby Thompson, Pfizer	Ben Liniger, Alcon	
Mark DeClerk, Lilly	David Williams, Forest	
Roger Grotzinger, BMS	Charlene Kaiser, Amgen	

PRESENT FOR PUBLIC COMMENT:	
Actelion	George Yasutake Pharm.D.

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: George Yasutake; Pharm.D. Agenda No. 5

ACTION: NONE REQUIRED

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

3A: FEBRUARY 12, 2014 DUR MINUTES-VOTE

3B: FEBRUARY 12, 2014 DUR RECOMMENDATION MEMORANDUM

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR FEBRUARY 2014

4B: PHARMACY HELP DESK ACTIVITY FOR FEBRUARY 2014

4C: UPDATES ON FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE ADEMPAS® (RIOCIGUAT) AND OPSUMIT® (MACITENTAN)

5A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE SELECT CEPHALOSPORINS

6A: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Le.

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF ERYTHROPOIESIS STIMULATING AGENTS**

7A: INTRODUCTIONS
7B: UTILIZATION OF ERYTHROPOESIS STIMULATING AGENTS
7C: PRIOR AUTHORIZATION REVIEW
7D: MARKET NEWS AND UPDATES
7E: DISCUSSION
7F: RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Le

ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF INSOMNIA MEDICATIONS**

8A: CURRENT AUTHORIZATION CRITERIA
8B: UTILIZATION OF INSOMNIA MEDICATIONS
8C: PRIOR AUTHORIZATION REVIEW
8D: MARKET NEWS AND UPDATES
8E: COP RECOMMENDATIONS
8F: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF ORAL ANTIHISTAMINES**

9A: CURRENT AUTHORIZATION CRITERIA
9B: UTILIZATION OF ORAL ANTIHISTAMINES
9C: PRIOR AUTHORIZATION REVIEW
9D: MARKET NEWS AND UPDATES
9E: COP RECOMMENDATIONS
9F: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Teel

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF SMOKING CESSATION PRODUCTS**

10A: CURRENT AUTHORIZATION CRITERIA
10B: UTILIZATION REVIEW
10C: PRIOR AUTHORIZATION REVIEW
10D: MARKET NEWS AND UPDATES
10E: DISCUSSION
10F: COP RECOMMENDATIONS
10G: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF BENZODIAZEPINE MEDICATIONS**

11A: CURRENT AUTHORIZATION CRITERIA
11B: UTILIZATION OF BENZODIAZEPINES
11C: PRIOR AUTHORIZATION REVIEW
11D: MARKET NEWS AND UPDATES
11E: COP RECOMMENDATIONS
11F: UTILIZATION DETAILS

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

AGENDA ITEM NO. 12: **60-DAY NOTICE TO PRIOR AUTHORIZE OPHTHALMIC ANTI-INFLAMMATORY MEDICATIONS**

12A: INTRODUCTION
12B: ECONOMIC IMPACT
12C: MARKET ANALYSIS
12D: COP RECOMMENDATIONS

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

AGENDA ITEM NO. 13: **UPDATES REGARDING OHCA**

Presented by Nico Gomez

AGENDA ITEM NO. 14: **FDA AND DEA UPDATES**

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

AGENDA ITEM NO. 15: **FUTURE BUSINESS**

15A: ANNUAL REVIEWS
15B: NEW PRODUCT REVIEWS

Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **ADJOURNMENT**

The meeting was adjourned at 5:24 pm

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

Memorandum

Date: March 13, 2014

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

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

Subject: DUR Board Recommendations from Meeting of March 12, 2014

Recommendation 1: Vote to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of the following medications:

Adempas® (Riociguat) Approval Criteria:

1. FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension
    a. Members with a diagnosis of pulmonary arterial hypertension must have previous failed trials of at least one of each of the following categories:
        i. Revatio® (sildenafil) or Adcirca® (tadalafil); and
        ii. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    b. Members with a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) must currently be on anticoagulation therapy; and
2. Medical supervision by a pulmonary specialist and/or cardiologist; and
3. Member must not be on concurrent PDE-5 inhibitor therapy; and

4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Adempas® REMS program.
5. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

1. FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan), or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist and/or cardiologist; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Opsumit® REMS program.
5. A quantity limit of 30 tablets per 30 days will apply.

Recommendation 2: Vote to Prior Authorize Select Cephalosporins

MOTION CARRIED by unanimous approval.

Prior authorize cefixime (Suprax®), ceftibuten (Cedax®), and cefditoren (Spectracef®) with the criteria presented below. A pre-emptive educational initiative will be sent to medical as well as pharmacy providers before these prior authorizations become effective.

Suprax® (Cefixime), Cedax® (Ceftibuten), and Spectracef® (Cefditoren) Approval Criteria:

1. Indicated diagnosis or infection known to be susceptible to requested agent; and
2. Patient specific, clinically significant reason why member cannot use cephalexin and cefdinir, or other cost effective therapeutic equivalent medication(s).

Recommendation 3: Annual Review of Eyrthropoiesis Stimulating Agents

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Insomnia Medications

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Oral Antihistamines

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Smoking Cessation Products

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Benzodiazepine Medications

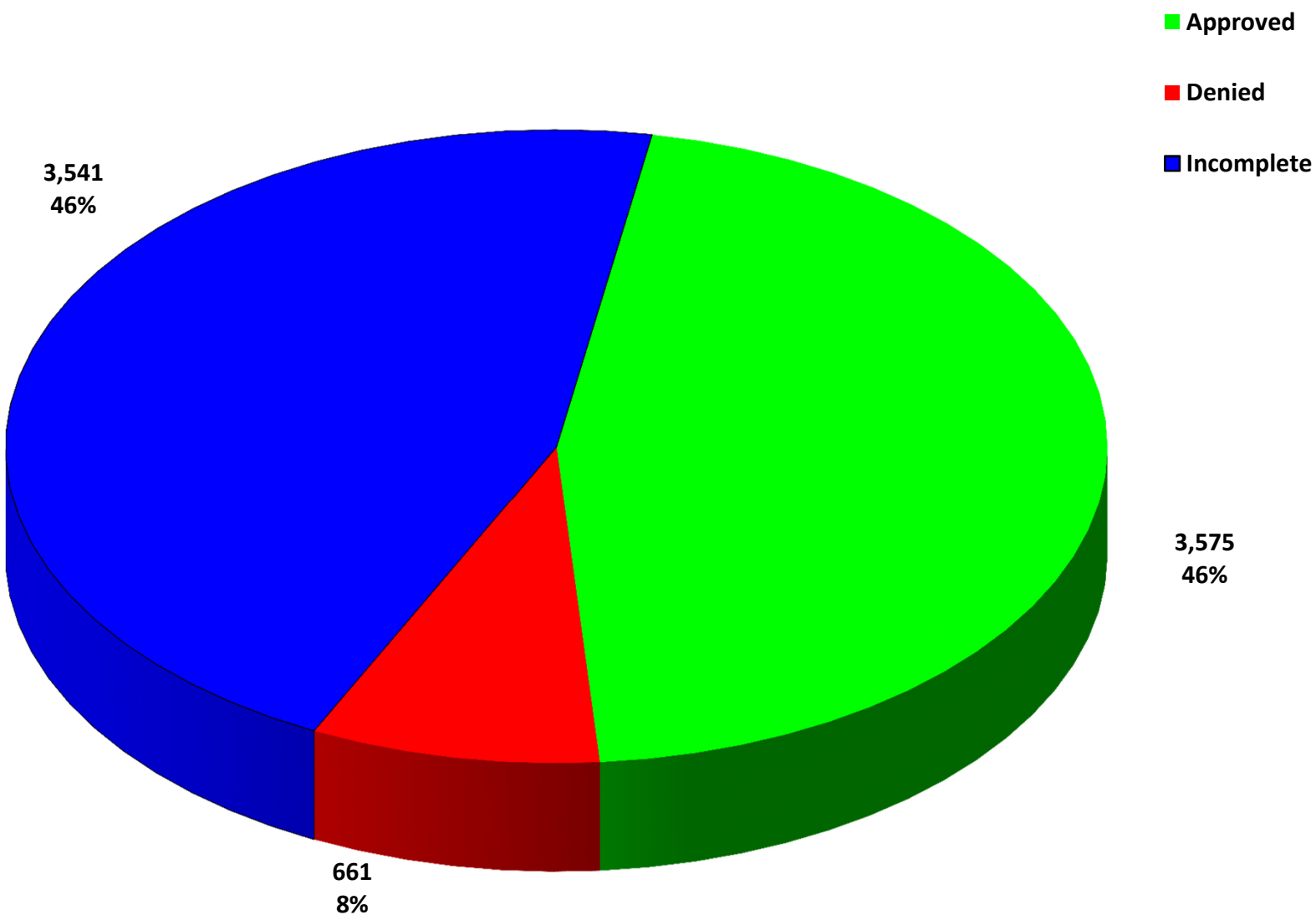
NO ACTION REQUIRED.

Recommendation 8: 60-Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications

NO ACTION REQUIRED.

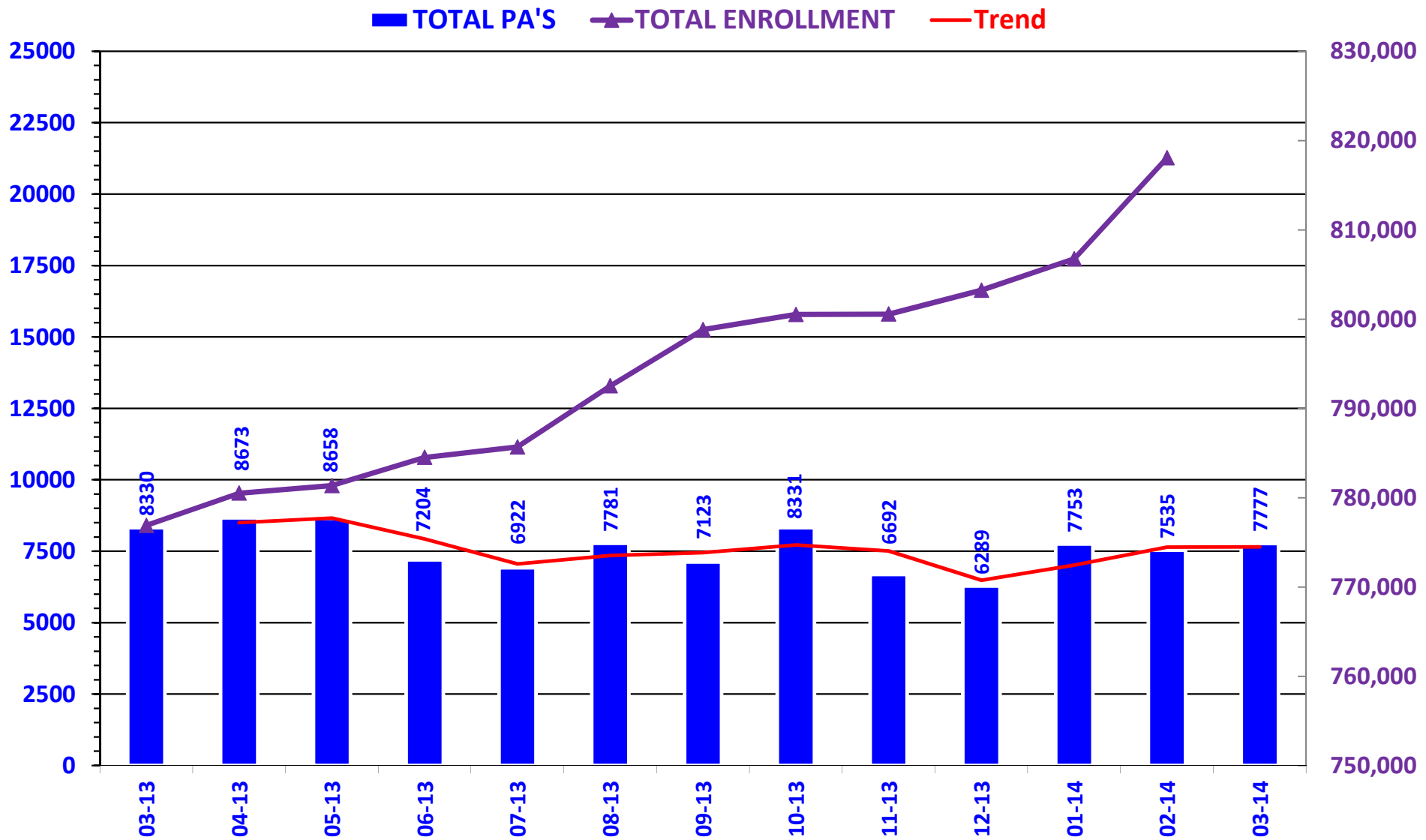
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MARCH



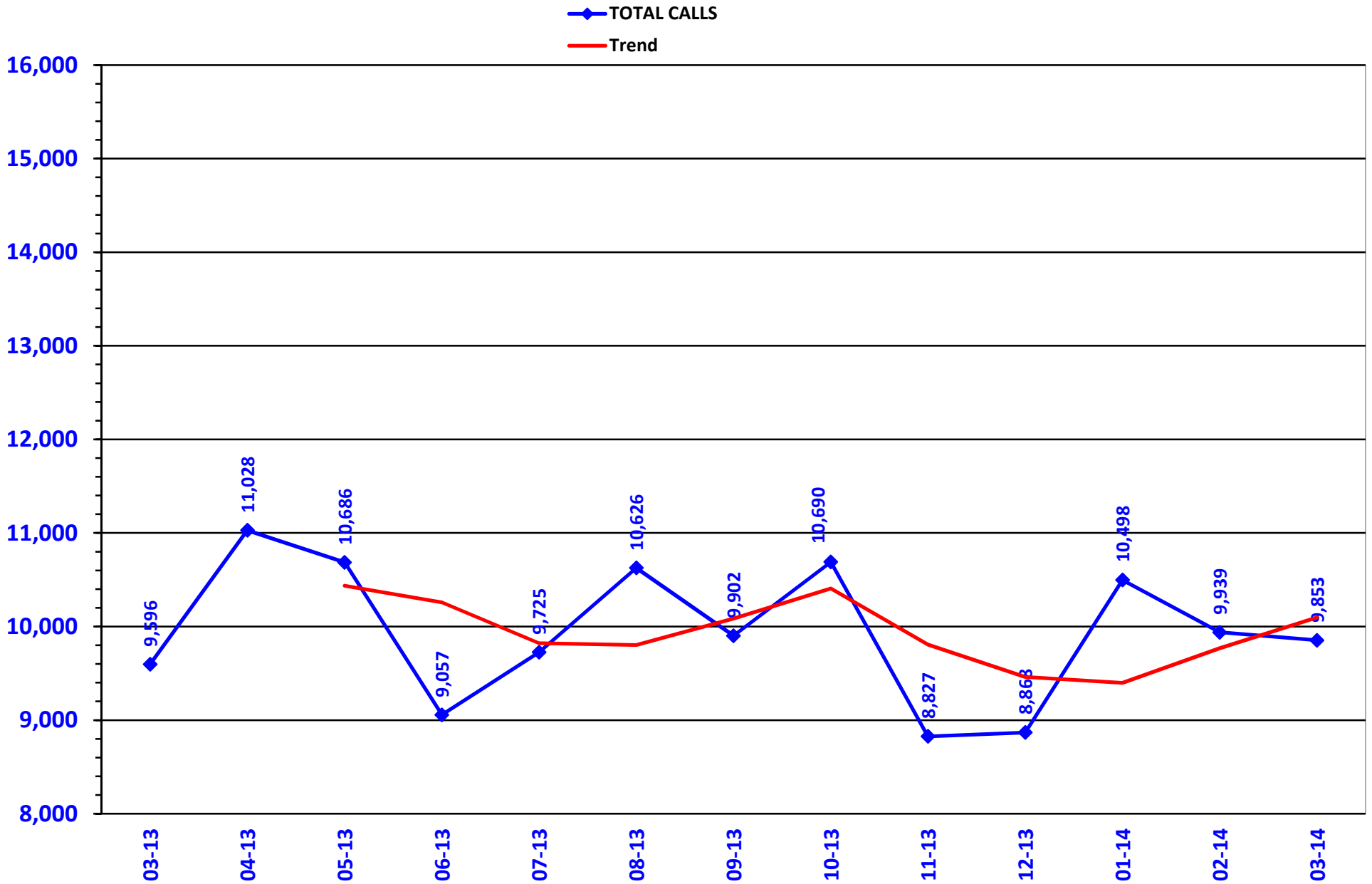
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MARCH 2013– MARCH 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MARCH 2013- MARCH 2014



Prior Authorization Activity
3/1/2014 Through 3/31/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	409	172	8	229	353
Analgesic, Narcotic	412	208	16	188	234
Angiotensin Receptor Antagonist	22	3	3	16	298
Antiasthma	299	159	5	135	302
Antibiotic	22	3	2	17	7
Anticoagulant	90	52	3	35	319
Anticonvulsant	86	44	5	37	318
Antidepressant	260	65	26	169	344
Antidiabetic	126	52	4	70	359
Antifungal	17	1	5	11	54
Antihistamine	176	139	6	31	346
Antihyperlipidemic	22	3	1	18	360
Antimigraine	71	22	13	36	328
Antiparkinsons	11	3	1	7	288
Antiplatelet	17	11	2	4	360
Antiulcers	250	53	65	132	174
Anxiolytic	95	68	0	27	252
Atypical Antipsychotics	402	192	12	198	343
Biologics	63	36	3	24	290
Bladder Control	61	6	10	45	358
Botox	25	14	4	7	321
Calcium Channel Blockers	16	2	2	12	222
Cardiovascular	42	17	2	23	314
Chronic Obstructive Pulmonary Disease	30	6	2	22	329
Dermatological	120	20	47	53	90
Endocrine & Metabolic Drugs	40	31	2	7	130
Erythropoietin Stimulating Agents	32	18	0	14	106
Fibromyalgia	151	31	11	109	350
Gastrointestinal Agents	132	29	18	85	164
Glaucoma	10	2	0	8	190
Growth Hormones	72	53	2	17	159
Hematopoietic Agents	13	7	0	6	85
HFA Rescue Inhalers	63	18	2	43	353
Insomnia	69	17	8	44	171
Multiple Sclerosis	32	19	1	12	245
Muscle Relaxant	112	26	44	42	49
Nasal Allergy	120	15	38	67	188
Neurological Agents	37	31	1	5	360
Nsaids	153	18	26	109	321
Ocular Allergy	51	8	4	39	104
Ophthalmic Anti-infectives	25	5	3	17	9
Osteoporosis	27	6	3	18	361
Other*	147	24	16	107	219
Otic Antibiotic	22	7	0	15	14
Pediculicide	92	42	5	45	18
Prenatal Vitamins	11	0	1	10	0
Statins	93	36	12	45	359
Stimulant	1,104	447	68	589	330
Suboxone/Subutex	166	129	6	31	81
Synagis	70	45	13	12	24
Testosterone	66	15	8	43	325
Topical Antifungal	54	1	6	47	84
Topical Corticosteroids	114	3	11	100	268
Vitamin	76	18	38	20	296
Pharmacotherapy	74	61	0	13	71
Emergency PAs	3	3	0	0	
Total	**6,375**	**2,516**	**594**	**3,265**	

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Overrides					
Brand	103	77	2	24	161
Cumulative Early Refill	11	11	0	0	180
Dosage Change	353	325	2	26	6
High Dose	3	3	0	0	177
Ingredient Duplication	51	35	3	13	4
Lost/Broken Rx	81	74	0	7	5
NDC vs Age	5	4	0	1	360
Nursing Home Issue	60	58	0	2	4
Other*	44	41	0	3	4
Quantity vs. Days Supply	618	392	39	187	253
STBS/STBSM	18	16	1	1	97
Stolen	6	1	4	1	3
Temporary Unlock	19	13	5	1	19
Third Brand Request	41	20	11	10	50
Overrides Total	**1,402**	**1,059**	**67**	**276**	
Total Regular PAs + Overrides	**7,777**	**3,575**	**661**	**3,541**	

Denial Reasons	
Unable to verify required trials.	3,050
Does not meet established criteria.	660
Lack required information to process request.	485

Other PA Activity	
Duplicate Requests	481
Letters	4,024
No Process	8
Changes to existing PAs	488
Partials	869

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

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

Duplication of Narcotic Therapy

October, November, December 2013, and January 2014

Pharmacy claims were reviewed over a four month period for duplication of immediate release opioid medications. Member profiles were flagged if the computer edit detected two or more claims for a narcotic analgesic with overlapping day supplies during that month. A total of 1,229 messages were reviewed for 1,213 members, and 541 letters were sent to providers. The details are below:

Parameters	Total Messages	Messages Reviewed	Members Reviewed	Members Intervened
Males and Females Age 36-59	25,021	1,229	1,213	93

Letters		
Prescribers: 371	Pharmacies: 170	Total Letters: 541

	Top 25 Narcotic Combination Messages Arranged by Total Messages Reviewed	Messages Flagged	Messages Reviewed	Members Reviewed	Members Intervened
1	Tramadol 50 MG and Hydro/APAP 7.5-750 MG	7754	416	410	28
2	Oxyco/APAP 7.5-500 MG and Hydro/APAP 7.5-500 MG	5334	163	159	15
3	Oxycodone 5 MG and Hydro/APAP 7.5-500 MG	2222	125	124	15
4	Hydro/APAP 7.5-750 MG and Hydro/APAP 5-325 MG	2091	61	61	1
5	Tramadol 50 MG and Oxycodone/APAP 7.5-500	992	56	55	4
6	Oxycodone 5 MG and Oxycodone/APAP 7.5-500	630	33	33	4
7	APAP/Codeine 300-60 MG and Hydro/APAP 7.5-500 MG	936	22	22	4
8	Methadone 5 MG and Hydro/APAP 7.5-500 MG	536	36	34	2
9	Methadone 5 MG and Oxycodone 5 MG	466	23	23	0
10	Tramadol 50 MG and APAP/Codeine 300-60 MG	428	22	22	1
11	Oxycodone 5 MG and Tramadol 50 MG	338	28	28	1
12	Morphine Sulfate 30 MG and Hydro/APAP 7.5-500 MG	312	22	22	3
13	Hydromorphone 8 MG and Hydro/APAP 7.5-750 MG	290	20	20	0
14	Oxyco/APAP 7.5-500 MG and Oxyco/APAP 10-325 MG	417	9	9	0
15	Methadone 5 MG and Oxyco/APAP 10-325 MG	214	16	15	0
16	Oxycodone 5 MG and Oxycodone 30 MG	204	10	10	1
17	Hydromorphone 8 MG and Oxycodone 30 MG	140	13	13	2
18	Tramadol 50 MG and Hydro/IBU 7.5/200 MG	138	7	7	0
19	Hydromorphone 8 MG and Oxyco/APAP 10-325 MG	126	14	13	2
20	Pentaz/Nalox 50-0.5 MG and Hydro/APAP 7.5-500 MG	96	4	4	0
21	Meperidine 50 MG and Hydro/APAP 7.5-650 MG	94	3	3	0
22	Methadone 5 MG and Morphine 15 MG	92	8	8	0
23	Oxycodone/APAP 7.5-325MG and APAP/Codeine 300-30 MG	135	3	3	2
24	But/APAP/Caff/Cod and Hydro/APAP 7.5-500 MG	111	8	8	0
25	Hydro/APAP 7.5-750 MG and Tramadol/APAP 37.5-325 MG	102	3	3	0

Appendix C

Top 100 Reimbursed Drugs By Fiscal Year		2013		2012	
Generic Name	Brand Name*	Rank	Amount Paid	Rank	Amount Paid
Aripiprazole	Abilify	1	$21,541,780.91	1	$19,940,503.62
Methylphenidate	Multiple Products	2	$13,748,669.91	4	$12,831,920.11
Albuterol Sulfate	Multiple Products	3	$12,702,955.21	5	$10,306,566.54
Amphetamine-Dextroamphetamine	Multiple Products	4	$9,989,373.00	6	$7,063,949.57
Dexmethylphenidate	Focalin*	5	$7,030,450.79	12	$5,615,652.94
Guanfacine	Intuniv	6	$6,761,516.28	38	$2,393,436.18
Budesonide Inhalation	Pulmicort*	7	$6,625,612.10	8	$6,213,529.98
Lisdexamfetamine	Vyvanse	8	$6,607,918.96	9	$6,075,124.89
Paliperidone Injection	Invega	9	$6,482,708.44	20	$3,997,876.67
Fluticasone Inhalation	Flovent	10	$6,078,312.48	14	$4,957,448.46
Insulin Glargine	Lantus	11	$5,678,523.15	16	$4,407,843.88
Oxycodone	Multiple Products	12	$5,286,506.19	11	$5,643,226.41
Palivizumab	Synagis	13	$5,170,145.65	10	$5,953,551.87
Atomoxetine	Strattera	14	$5,139,098.12	19	$4,071,107.37
Somatropin	Genotropin	15	$4,990,611.57	17	$4,268,525.02
Fluticasone-Salmeterol	Advair	16	$4,959,132.10	15	$4,801,370.72
Quetiapine	Seroquel *	17	$4,838,947.21	2	$13,318,444.01
Hydrocodone-APAP	Multiple Products	18	$4,600,895.11	18	$4,217,227.69
Duloxetine	Cymbalta	19	$4,510,264.74	26	$3,285,597.82
Antihemophilic Factor (Recombinant)	Multiple Products	20	$4,194,450.42	13	$5,113,193.83
Adalimumab	Humira	21	$4,105,502.73	30	$2,769,100.17
Oseltamivir	Tamiflu	22	$4,062,607.39	69	$1,346,929.29
Cefixime	Suprax	23	$4,039,124.70	31	$2,719,785.34
Insulin Aspart	Novolog	24	$4,028,857.67	25	$3,307,969.18
Antiinhibitor Coagulant Complex	Feiba	25	$3,784,799.02	24	$3,483,793.05
Montelukast	Singulair*	26	$3,482,006.24	3	$13,318,433.03
Cefdinir	Omnicef*	27	$3,225,407.41	48	$1,900,081.85
Etanercept	Enbrel	28	$3,115,173.09	34	$2,504,496.20
Efavirenz-Emtricitabine-Tenofovir	Atripla	29	$3,047,213.16	29	$2,882,774.42
Telaprevir	Incivek	30	$2,928,956.99	22	$3,617,297.87
Enoxaparin	Lovenox *	31	$2,801,476.41	27	$3,008,308.38
Azithromycin	Zithromax*	32	$2,731,057.26	28	$2,991,078.09
Tiotropium	Spiriva	33	$2,631,911.08	39	$2,257,594.06
Buprenorphine-Naloxone	Multiple Products	34	$2,572,886.59	47	$1,902,437.54
Glatiramer Acetate	Copaxone	35	$2,504,753.02	42	$2,169,545.26
Paliperidone Oral	Invega	36	$2,487,073.16	32	$2,578,649.17
Pregabalin	Lyrica	37	$2,444,485.94	40	$2,195,146.48
Insulin Detemir	Levemir	38	$2,409,195.86	53	$1,770,855.66
Antihemophilic Factor rAHF-PFM	Advate	39	$2,329,323.87	21	$3,936,546.80
Amoxicillin	Amoxil*	40	$2,314,896.28	44	$2,048,376.91
Dornase Alfa	Pulmozyme	41	$2,254,993.26	35	$2,416,997.87
Tobramycin	Tobi	42	$2,207,347.12	37	$2,395,189.69

Top 100 Reimbursed Drugs By Fiscal Year		2013		2012	
Generic Name	Brand Name*	Rank	Amount Paid	Rank	Amount Paid
Peginterferon Alfa-2a	Pegasys	43	$2,142,681.94	36	$2,402,680.98
Amoxicillin & K Clavulanate	Augmentin*	44	$2,118,424.33	51	$1,831,632.27
Insulin Lispro	Humalog	45	$2,075,563.81	52	$1,800,816.22
Clozapine	Multiple Products	46	$2,058,516.68	41	$2,180,312.29
Fluticasone Nasal	Flonase*	47	$2,056,676.73	45	$2,013,942.33
Ipratropium-Albuterol	Multiple Products	48	$2,032,376.98	46	$1,987,165.63
Epinephrine	Twinject	49	$1,989,500.14	68	$1,368,329.15
Interferon Beta-1a	Rebif	50	$1,972,276.02	54	$1,754,666.18
Levalbuterol	Xopenex	51	$1,793,211.89	49	$1,879,535.70
Emtricitabine-Tenofovir	Truvada	52	$1,791,736.87	65	$1,438,277.90
Sitagliptin	Januvia	53	$1,621,840.82	66	$1,391,667.38
Cetirizine	Multiple Products	54	$1,594,015.24	70	$1,312,599.91
Gabapentin	Neurontin*	55	$1,588,162.08	59	$1,522,518.36
Oxcarbazepine	Trileptal	56	$1,551,624.40	60	$1,495,729.43
Fentanyl	Duragesic*	57	$1,541,108.45	63	$1,452,578.11
Etonogestrel-Ethinyl Estradiol Ring	Nuvaring	58	$1,520,572.46	57	$1,529,356.89
Lacosamide	Vimpat	59	$1,479,775.15	86	$1,022,884.43
Prednisolone	Multiple Products	60	$1,476,467.09	83	$1,124,884.19
Memantine	Namenda	61	$1,456,558.38	79	$1,150,310.15
Deferasirox	Exjade	62	$1,450,036.99	61	$1,487,759.41
Pancrelipase	Multiple Products	63	$1,384,481.70	67	$1,384,944.49
Imatinib	Gleevec	64	$1,378,669.74	64	$1,442,430.51
Iloperidone	Fanapt	65	$1,371,038.63	88	$941,827.32
Lurasidone	Latuda	66	$1,364,394.95	123	$623,027.70
Ziprasidone	Geodon*	67	$1,337,594.81	23	$3,507,889.89
Levetiracetam	Keppra*	68	$1,323,203.91	56	$1,588,797.23
Coagulation Factor VIIa	Novoseven RT	69	$1,312,823.64	50	$1,872,184.42
Hydroxyprogesterone	Makena	70	$1,294,693.10	161	$454,466.61
Omeprazole	Multiple Products	71	$1,289,841.48	72	$1,299,783.05
Risperidone Injection	Risperdal*	72	$1,269,069.30	62	$1,453,550.50
Spacer/Aerosol-Holding Chambers	Multiple Products	73	$1,262,599.09	82	$1,126,660.70
Oxycodone with APAP	Multiple Products	74	$1,258,219.54	77	$1,173,705.74
Norgestimate-Ethinyl Estradiol	Multiple Products	75	$1,246,942.16	78	$1,152,533.18
Risperidone Oral	Risperidal*	76	$1,242,681.56	73	$1,296,298.92
Lamotrigine	Lamictal*	77	$1,213,142.37	75	$1,232,883.23
Linezolid	Zyvox	78	$1,100,112.82	89	$941,090.85
Beclomethasone	Qvar	79	$1,051,845.69	111	$680,326.32
Alprazolam	Xanax*	80	$1,035,138.78	71	$1,300,476.21
Divalproex	Depakote*	81	$1,034,649.22	76	$1,213,056.97
Asenapine	Saphris	82	$1,031,200.17	167	$448,937.20
Norelgestromin-Ethinyl Estradiol	Ortho Evra	83	$1,025,358.58	93	$872,827.41
Sapropterin	Kuvan	84	$1,004,126.88	84	$1,106,731.09

Top 100 Reimbursed Drugs By Fiscal Year		2013		2012	
Generic Name	Brand Name*	Rank	Amount Paid	Rank	Amount Paid
Diazepam	Diastat	85	$998,888.10	81	$1,133,803.45
Immune Globulin	Gamunex-C	86	$982,256.18	135	$569,549.79
Permethrin	Multiple Products	87	$949,247.08	97	$818,409.30
Budesonide-Formoterol	Symbicort	88	$947,631.53	94	$856,503.89
Loratadine	Multiple Products	89	$936,201.25	95	$851,401.77
C1 Esterase Inhibitor	Cinryze	90	$935,786.03	43	$2,137,463.15
Boceprevir	Victrelis	91	$931,082.04	121	$624,301.48
Desmopressin	Multiple Products	92	$927,812.46	92	$888,608.44
Mometasone	Asmanex	93	$902,374.96	96	$846,607.53
Darunavir	Prezista	94	$869,070.62	131	$583,373.26
Antihemophilic Factor/VWF	Wilate	95	$863,606.39	102	$764,496.78
Acyclovir	Zovirax*	96	$853,078.44	118	$628,431.81
Morphine	Multiple Products	97	$839,169.10	90	$913,478.92
Varenicline	Chantix	98	$826,542.72	98	$811,813.60
Imiglucerase	Cerezyme	99	$817,475.06	113	$668,404.35
Coagulation Factor IX	Benefix	100	$810,913.13	74	$1,267,247.86

*Includes brand and generic where applicable.

Top 50 Medications by Total Number of Claims										
Rank	Generic Name	Claims	Units	Days	Members	Cost	Units/Day	Claims/Client	Cost/Day	% Cost
1	Hydrocodone-APAP	334,390	22,510,677	5,149,593	110,633	$4,601,335.27	4.37	3.02	$0.89	3.97%
2	Albuterol	268,128	15,023,670	5,689,583	116,175	$12,706,444.37	2.64	2.31	$2.23	10.97%
3	Amoxicillin	227,186	24,986,782	2,188,331	164,165	$2,315,850.77	11.42	1.38	$1.06	2.00%
4	Cetirizine	184,266	16,538,006	5,514,290	82,704	$1,594,503.08	3	2.23	$0.29	1.38%
5	Azithromycin	174,042	2,709,388	870,599	128,148	$2,731,928.68	3.11	1.36	$3.14	2.36%
6	Alprazolam	112,819	7,492,445	3,182,735	21,980	$1,035,226.54	2.35	5.13	$0.33	0.89%
7	Omeprazole	100,674	4,234,551	3,362,527	28,784	$1,289,915.33	1.26	3.5	$0.38	1.11%
8	Methylphenidate	92,515	3,528,343	2,754,052	14,881	$13,750,341.70	1.28	6.22	$4.99	11.87%
9	Ibuprofen	91,745	6,107,706	1,449,012	64,136	$713,149.73	4.22	1.43	$0.49	0.62%
10	Loratadine	88,929	6,770,185	2,720,736	40,917	$936,330.93	2.49	2.17	$0.34	0.81%
11	Fluticasone Propionate Nasal	85,585	1,369,156	2,796,569	48,517	$2,056,915.61	0.49	1.76	$0.74	1.78%
12	Montelukast	84,345	2,525,309	2,527,940	20,003	$3,482,117.20	1	4.22	$1.38	3.01%
13	Clonidine	76,426	3,483,630	2,367,421	14,095	$609,031.60	1.47	5.42	$0.26	0.53%
14	Risperidone	74,983	3,380,078	2,303,085	14,563	$1,243,133.29	1.47	5.15	$0.54	1.07%
15	Sulfamethoxazole-Trimethoprim	73,957	6,173,760	796,520	58,100	$661,002.31	7.75	1.27	$0.83	0.57%
16	Lisinopril	67,456	2,963,436	2,707,350	16,869	$437,872.06	1.09	4	$0.16	0.38%
17	Tramadol	66,914	5,008,464	1,218,064	25,852	$534,466.42	4.11	2.59	$0.44	0.46%
18	Amphetamine-	66,823	2,492,234	1,989,831	11,077	$9,989,858.85	1.25	6.03	$5.02	8.63%
19	Amoxicillin & K Clavulanate	65,322	5,538,638	652,623	53,586	$2,118,944.34	8.49	1.22	$3.25	1.83%
20	Gabapentin	64,043	6,156,288	2,002,101	15,463	$1,588,250.92	3.07	4.14	$0.79	1.37%
21	Sertraline	63,860	2,458,329	2,076,899	16,170	$565,728.18	1.18	3.95	$0.27	0.49%
22	Citalopram	63,489	2,172,069	2,153,865	17,923	$450,683.97	1.01	3.54	$0.21	0.39%
23	Clonazepam	63,447	3,842,941	1,818,193	13,967	$519,309.53	2.11	4.54	$0.29	0.45%
24	Prednisolone	61,216	2,286,862	340,648	44,433	$1,477,023.15	6.71	1.38	$4.34	1.28%
25	Trazodone	60,585	2,402,526	1,929,794	15,341	$555,146.73	1.24	3.95	$0.29	0.48%
26	Oxycodone with APAP	58,489	3,505,174	785,134	30,489	$1,258,810.91	4.46	1.92	$1.60	1.09%
27	Cyclobenzaprine	57,865	2,988,447	1,246,960	27,608	$475,194.91	2.4	2.1	$0.38	0.41%
28	Cefdinir	55,863	3,914,625	555,834	44,056	$3,226,462.48	7.04	1.27	$5.80	2.79%
29	Levothyroxine	54,738	2,220,026	2,209,930	11,400	$679,469.24	1	4.8	$0.31	0.59%
30	Fluoxetine	53,917	2,263,604	1,767,778	13,885	$495,997.90	1.28	3.88	$0.28	0.43%
31	Promethazine	53,469	2,055,500	399,143	34,669	$597,459.69	5.15	1.54	$1.50	0.52%
32	Cephalexin	50,993	4,070,712	460,107	43,733	$521,462.20	8.85	1.17	$1.13	0.45%
33	Prednisone	50,833	1,067,844	503,221	36,882	$248,273.16	2.12	1.38	$0.49	0.21%
34	Ondansetron	49,223	468,263	1,233,876	39,362	$406,363.47	0.38	1.25	$0.33	0.35%

Top 50 Medications by Total Number of Claims										
Rank	Generic Name	Claims	Units	Days	Members	Cost	Units/Day	Claims/Client	Cost/Day	% Cost
35	Metformin	48,721	3,263,285	1,571,398	11,224	$424,878.88	2.08	4.34	$0.27	0.37%
36	Dexmethylphenidate	46,933	1,509,294	1,393,840	7,182	$7,032,657.53	1.08	6.53	$5.05	6.07%
37	Ranitidine	41,767	3,695,083	1,257,788	17,699	$369,012.44	2.94	2.36	$0.29	0.32%
38	Zolpidem	41,378	1,189,640	1,198,586	9,895	$393,114.08	0.99	4.18	$0.33	0.34%
39	Triamcinolone	41,293	2,869,319	609,954	29,646	$547,456.33	4.7	1.39	$0.90	0.47%
40	Fluticasone Propionate HFA	39,741	455,601	1,251,178	17,310	$6,079,865.82	0.36	2.3	$4.86	5.25%
41	Lisdexamfetamine	38,617	1,153,291	1,148,906	6,428	$6,609,333.20	1	6.01	$5.75	5.71%
42	Diazepam	37,061	2,265,843	984,374	9,654	$323,193.05	2.3	3.84	$0.33	0.28%
43	Meloxicam	36,436	1,415,601	1,239,391	16,640	$271,058.00	1.14	2.19	$0.22	0.23%
44	APAP with Codeine	35,639	2,452,586	246,545	28,061	$302,228.81	9.95	1.27	$1.23	0.26%
45	Mupirocin	34,675	810,802	384,627	29,063	$568,483.15	2.11	1.19	$1.48	0.49%
46	Quetiapine	34,432	1,539,652	1,069,397	6,122	$4,838,934.02	1.44	5.62	$4.52	4.18%
47	Guanfacine ER	34,080	1,002,477	1,001,998	6,403	$6,763,382.85	1	5.32	$6.75	5.84%
48	Simvastatin	32,073	1,353,451	1,363,536	7,599	$301,364.72	0.99	4.22	$0.22	0.26%
49	Divalproex	31,927	2,502,843	962,666	5,090	$1,034,701.94	2.6	6.27	$1.07	0.89%
50	Oseltamivir	31,570	1,538,700	189,232	30,272	$4,063,039.84	8.13	1.04	$21.47	3.51%
Total		**3,804,878**	**213,727,136**	**85,597,760**		**$115,796,709.18**	**2.5**	**7.2**	**$1.35**	**100%**

Top Traditional Therapeutic Classes by Fiscal Year

Antipsychotics and Antimanic Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Antipsychotics		200,210	$57,872,977.69	204,764	$46,495,507.37
	Total:	**200,210**	**$57,872,977.69**	**204,764**	**$46,495,507.37**

Antiasthmatic and Bronchodilator Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Antiasthmatic and Bronchodilator Agents		459,478	$49,418,353.62	493,623	$44,825,718.42
	Total:	**459,478**	**$49,418,353.62**	**493,623**	**$44,825,718.42**

Anti-Infectives		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Antiviral		36,942	$19,032,871.55	59,723	$22,672,070.60
Cephalosporins		136,700	$6,367,588.97	142,493	$9,428,725.94
Anti-Infectives		122,976	$4,408,775.67	119,054	$5,007,442.78
Penicillins		297,156	$4,191,754.50	309,458	$4,792,277.57
Macrolide Antibiotics		170,774	$3,370,362.20	179,897	$3,238,500.62
Aminoglycosides		944	$2,414,460.42	868	$2,245,382.37
Antifungals		30,791	$970,558.65	30,863	$1,088,255.04
Fluoroquinolones		29,590	$445,365.53	29,480	$433,507.68
Tetracyclines		27,880	$281,342.52	27,143	$721,649.57
Anthelmintic		4,203	$79,980.17	2,778	$238,163.72
Antimalarial		3,081	$43,942.08	3,622	$57,150.72
Antimycobacterial Agents		649	$37,166.87	614	$31,101.58
Sulfonamides		2	$593.79	6	$4,072.11
Amebicides		0	$0.00	0	$0.00
	Total:	**861,688**	**$41,644,762.92**	**905,999**	**$49,958,300.30**

ADHD Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
ADHD/Anti-Narcolepsy/Anti-Obesity/Anorexiants		266,451	$39,146,909.47	307,779	$50,596,512.93
	Total:	**266,451**	**$39,146,909.47**	**307,779**	**$50,596,512.93**

Pain Products		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Analgesics - Narcotic		590,830	$18,574,349.52	575,989	$18,657,975.16
Analgesics - Anti-Inflammatory		187,295	$2,220,318.18	188,996	$2,465,121.09
Migraine Products		11,230	$622,719.20	11,893	$669,832.04
Analgesics - Non-narcotic		35,526	$374,583.62	29,626	$367,323.36
Gout		4,844	$160,983.19	4,950	$98,712.03
Local Anesthetics-Parenteral		1,113	$6,295.60	1,189	$9,488.69
General Anesthetics		80	$1,715.20	189	$4,063.63
	Total:	**830,918**	**$21,960,964.51**	**812,832**	**$22,272,516.00**
Anti-Diabetics		**2012**		**2013**	
		Total Claims	Total Paid	Total Claims	Total Paid
Anti-Diabetics		146,488	$19,427,062.18	148,413	$22,153,072.31
	Total:	**146,488**	**$19,427,062.18**	**148,413**	**$22,153,072.31**
Endocrine Drugs		**2012**		**2013**	
		Total Claims	Total Paid	Total Claims	Total Paid
Contraceptives		163,342	$8,851,859.32	150,869	$9,150,878.87
Misc. Endocrine		22,344	$5,856,523.97	22,132	$5,139,907.50
Corticosteroids		152,600	$2,357,219.82	170,424	$2,901,030.67
Estrogens		17,088	$978,994.01	16,664	$1,087,159.65
Thyroid		55,571	$657,577.96	57,567	$745,807.00
Progestins		5,272	$347,630.17	5,648	$347,313.85
Androgen-Anabolic		1,048	$222,667.68	1,052	$280,423.75
Oxytocics		675	$8,920.10	639	$16,102.89
	Total:	**417,940**	**$19,281,393.03**	**424,995**	**$19,668,624.18**
Anticonvulsants		**2012**		**2013**	
		Total Claims	Total Paid	Total Claims	Total Paid
Anticonvulsant		320,725	$15,580,510.61	320,300	$16,378,564.74
	Total:	**320,725**	**$15,580,510.61**	**320,300**	**$16,378,564.74**
Cardiovascular Agents		**2012**		**2013**	
		Total Claims	Total Paid	Total Claims	Total Paid
Antihyperlipidemics		88,708	$4,255,724.03	91,406	$3,470,124.42

Antihypertensives		218,998	$2,952,750.20	225,490	$2,827,471.01
Beta Blockers		87,327	$1,655,222.70	89,731	$1,841,312.64
Vasopressors		7,758	$1,386,445.96	8,526	$2,013,125.77
Calcium Channel Blockers		41,878	$767,061.46	43,408	$775,222.17
Diuretics		67,513	$609,247.00	66,642	$615,417.65
Antianginal Agents		9,131	$517,236.80	9,359	$637,306.94
Cardiovascular Agents		682	$183,545.38	484	$115,824.32
Cardiotonics		4,707	$103,256.64	4,748	$87,338.30
Antiarrhythmic		2,345	$92,587.12	2,483	$99,546.54
	Total:	**529,047**	**$12,523,077.29**	**542,277**	**$12,482,689.76**
Topical Products		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological		207,082	$7,876,756.46	204,592	$8,577,680.80
Ophthalmic		66,449	$1,894,558.29	66,512	$1,970,317.65
Otic		50,451	$873,192.17	50,885	$853,886.10
Mouth/Throat/Dental Agents		28,019	$459,001.46	28,476	$460,696.74
Anorectal		1,722	$68,866.10	1,740	$70,372.92
	Total:	**353,723**	**$11,172,374.48**	**352,205**	**$11,932,954.21**
Antidepressants		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antidepressants		379,650	$9,552,976.30	397,541	$9,710,483.85
	Total:	**379,650**	**$9,552,976.30**	**397,541**	**$9,710,483.85**
Gastrointestinal Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Ulcer Drugs		208,994	$4,568,791.19	215,819	$4,465,659.70
GI Agents		16,530	$1,571,747.73	16,185	$1,785,048.93
Digestive Aids		1,603	$1,384,944.49	1,583	$1,384,481.70
Antiemetics		55,618	$905,103.18	76,889	$1,210,461.76
Laxatives		34,962	$851,434.21	37,746	$1,029,116.89
Antidiarrheals		3,551	$40,912.36	3,888	$47,760.19
Antacids		459	$4,947.53	377	$2,559.27
	Total:	**321,717**	**$9,327,880.69**	**352,487**	**$9,925,088.44**

Antineoplastic Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Antineoplastics		12,973	$7,483,054.36	13,885	$8,243,815.52
	Total:	**12,973**	**$7,483,054.36**	**13,885**	**$8,243,815.52**
Allergy Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antihistamines		312,651	$2,946,594.19	334,677	$3,283,342.63
Systemic And Topical Nasal Products		86,221	$2,385,490.72	93,072	$2,491,335.47
Cough/Cold/Allergy		2,056	$107,658.12	2,114	$74,722.04
	Total:	**400,928**	**$5,439,743.03**	**429,863**	**$5,849,400.14**
Non-Therapeutic Products		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Assorted Classes		5,446	$2,027,194.89	5,894	$2,207,561.50
Antidotes		1,404	$1,592,233.36	1,364	$1,595,163.21
Medical Devices		21,861	$1,130,176.23	23,824	$1,265,053.20
Pharmaceutical Adjuvants		7,897	$268,066.43	7,071	$509,300.28
Chemicals		10,189	$58,302.46	15,337	$116,451.01
Diagnostic Products		43	$14,005.56	53	$7,328.31
Antiseptics & Disinfectants		190	$5,622.10	218	$7,174.38
Alternative Medicines		0	$0.00	0	$0.00
	Total:	**47,030**	**$5,095,601.03**	**53,761**	**$5,708,031.89**
Psychotherapeutic/Neurologic Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Psychotherapeutic And Neurological Agents		19,473	$3,394,208.32	19,335	$4,058,479.48
	Total:	**19,473**	**$3,394,208.32**	**19,335**	**$4,058,479.48**
Genitourinary Products		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Urinary Anti-Infectives		20,429	$1,184,602.09	19,878	$1,109,601.92
Urinary Antispasmodics		13,073	$993,772.05	13,190	$815,437.78
Vaginal Products		7,754	$436,368.78	7,714	$490,920.25
Genitourinary Products		14,589	$398,772.07	14,853	$487,701.62
	Total:	**55,845**	**$3,013,514.99**	**55,635**	**$2,903,661.57**

Nutritional Products		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Multivitamins		56,748	$2,527,760.50	46,807	$1,211,089.79
Minerals & Electrolytes		33,627	$1,023,369.88	31,890	$830,364.56
Vitamins		796	$76,697.71	646	$92,804.05
Dietary Products		123	$40,662.44	116	$34,927.34
Nutrients		298	$32,647.45	333	$28,119.61
	Total:	**91,592**	**$3,701,137.98**	**79,792**	**$2,197,305.35**

Antianxiety Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Antianxiety Agents		311,621	$2,978,457.94	262,369	$2,646,512.27
	Total:	**311,621**	**$2,978,457.94**	**262,369**	**$2,646,512.27**

Hematological Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Hematological Agents		14,999	$3,190,351.46	15,820	$1,098,837.65
Anticoagulants		11,811	$292,573.92	12,195	$422,633.54
Hematopoietic Agents		16,782	$133,620.18	17,666	$248,912.17
Hemostatics		191	$36,017.18	282	$51,710.18
	Total:	**43,783**	**$3,652,562.74**	**45,963**	**$1,822,093.54**

Specialized Respiratory Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Specialized Respiratory Agents		1,036	$2,416,997.87	868	$2,254,993.26
	Total:	**1,036**	**$2,416,997.87**	**868**	**$2,254,993.26**

Neuromuscular Drugs		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Musculoskeletal Therapy Agents		116,226	$1,301,020.75	119,409	$1,487,612.24
Antiparkinsonian		25,774	$435,060.04	26,260	$588,916.75
Antimyasthenic Agents		221	$14,881.12	209	$17,879.25
Neuromuscular Agents		8	$8,556.25	17	$23,860.69
	Total:	**142,229**	**$1,759,518.16**	**145,895**	**$2,118,268.93**

Hypnotics		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Hypnotics		91,230	$1,115,134.48	75,826	$969,674.35
	Total:	**91,230**	**$1,115,134.48**	**75,826**	**$969,674.35**

Biologicals		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Vaccines		4,398	$96,956.82	4,870	$140,825.71
Passive Immunizing Agents		4	$5,063.30	7	$43,092.48
Toxoids		34	$1,450.11	11	$415.70
	Total:	**4,436**	**$103,470.23**	**4,888**	**$184,333.89**

Top Specialty Therapeutic Classes by Fiscal Year

Hematological Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Hematological Agents		938	$19,137,313.34	719	$14,808,053.21
Anticoagulants		2,981	$3,289,982.22	2,782	$3,057,668.73
Hematopoietic Agents		703	$1,833,330.25	666	$1,997,832.24
	Total:	**4,622**	**$24,260,625.81**	**4,167**	**$19,863,554.18**

Biologicals		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Passive Immunizing Agents		3,815	$7,019,412.83	3,369	$6,640,258.05
Biological Agents		26	$792,741.72	18	$569,530.32
	Total:	**3,841**	**$7,812,154.55**	**3,387**	**$7,209,788.37**

Pain Products		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Analgesics - Anti-Inflammatory		2,489	$5,597,119.38	3,029	$7,848,963.14
	Total:	**2,489**	**$5,597,119.38**	**3,029**	**$7,848,963.14**

Endocrine Drugs		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Endocrine Drugs		2,010	$4,144,864.11	2,326	$5,467,368.15
Progestins				358	$1,294,693.10
	Total:	**2,010**	**$4,144,864.11**	**2,684**	**$6,762,061.25**

Psychotherapeutic/Neurologic Agents		2012		2013	
		Total Claims	Total Paid	Total Claims	Total Paid
Psychotherapeutic and Neurological Agents		1,299	$4,802,892.14	1,288	$5,616,477.40
	Total:	**1,299**	**$4,802,892.14**	**1,288**	**$5,616,477.40**
Cardiovascular Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Cardiovascular Agents		816	$1,615,907.71	937	$1,823,152.19
	Total:	**816**	**$1,615,907.71**	**937**	**$1,823,152.19**
Gastrointestinal Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Gastrointestinal Agents		149	$462,307.08	254	$886,903.27
	Total:	**149**	**$462,307.08**	**254**	**$886,903.27**
Specialized Respiratory Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Specialized Respiratory Agents		34	$253,375.64	31	$183,668.56
	Total:	**34**	**$253,375.64**	**31**	**$183,668.56**
Antiasthmatic and Bronchodilator Agents		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antiasthmatic and Bronchodilator Agents		92	$188,815.06	64	$147,436.95
	Total:	**92**	**$188,815.06**	**64**	**$147,436.95**
Anti-Infectives		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Antivirals		21	$59,131.33	9	$26,163.41
	Total:	**21**	**$59,131.33**	**9**	**$26,163.41**
Topical Products		**2012**		**2013**	
		Total Claims	**Total Paid**	**Total Claims**	**Total Paid**
Dermatological		4	$19,929.68		
	Total:	**4**	**$19,929.68**		

Grand Total	2012		2013	
	Total Claims	Total Paid	Total Claims	Total Paid
Both Traditional and Specialty Therapeutic Classes	6,325,588	$396,279,766.41	6,467,145	$405,724,771.42

Appendix D

30-Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications

Oklahoma Health Care Authority
April 2014

Introduction

This category was introduced for possible inclusion in the Product Based Prior Authorization program in February 2014. See the February and March 2014 DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations

The College of Pharmacy recommends establishing a Product Based Prior Authorization category for ophthalmic NSAIDs and ophthalmic corticosteroids to ensure appropriate cost-effective utilization in accordance with current treatment guidelines. The College of Pharmacy recommends the following tier list and criteria to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Health Care Authority.

In addition the College of Pharmacy will implement an educational initiative consisting of a targeted mailing to all prescribers of ophthalmic anti-inflammatory medications in the SoonerCare population in the previous 12 months. The mailing may include information regarding approval criteria of ophthalmic anti-inflammatory medications and a link to the OHCA web page which will contain the updated tier chart.

Ophthalmic Non-Steroidal Anti-Inflammatory Drug (NSAIDs) Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic NSAIDs (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier-1 anti-inflammatories lack.

Ophthalmic NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)	
Tier 1	**Tier 2**
Voltaren® (diclofenac) Solution 0.1%	Nevanac™ (nepafenac) 0.1% Suspension
Acular® (ketorolac) Solution 0.5%	Acuvail® (ketorolac) Solution 0.45%
Acular LS ® (ketorolac) Solution 0.4%	Ilevro™ (nepafenac) 0.3 % Suspension
Ocufen® (flurbiprofen) Solution 0.03%	Prolensa™ (bromfenac) 0.07% Solution
	Bromfenac 0.09% Solution

Ophthalmic Corticosteroid Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic corticosteroids (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier-1 anti-inflammatories lack.

Ophthalmic Corticosteroids	
Tier 1	**Tier 2**
Dexamethasone Sodium Phosphate Solution 0.1%	Lotemax® (loteprednol) Gel 0.5%
Maxidex™ (dexamethasone) Suspension 0.1%	Lotemax® (loteprednol) Ointment 0.5%
FML Liquifilm® (fluorometholone) Suspension 0.1%	Pred Forte® (prednisolone Acetate) Suspension 1%
Flarex® (fluorometholone) Suspension 0.1%	FML Forte® (fluorometholone) Suspension 0.25%
Lotemax® (loteprednol) Suspension 0.5%	FML S.O.P® (fluorometholone) Ointment 0.1%
Omnipred® (prednisolone Acetate) Suspension 1%	
Durezol® (difluprednate) Emulsion 0.05%	
Pred Mild® (prednisolone Acetate) Suspension 0.12%	
Prednisolone Sodium Phosphate Solution 1%	
Vexol® (rimexolone) Suspension 1%	

Appendix E

Annual Review of Anti-Diabetic Medications and 30-Day Notice to Prior Authorize Farxiga™ (Dapagliflozin) and Invokana™ (Canagliflozin)

Oklahoma Health Care Authority
April 2014

Current Prior Authorization Criteria

Tier-2 Approval Criteria:

1. A trial of a Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate
2. For initiation with dual or triple therapy, additional Tier-2 medications can be approved based on current AACE or ADA guidelines.

Tier-3 Approval Criteria:

1. Member must have tried a Tier-2 medication in the same category and have a documented clinical reason why the Tier-2 medication is not appropriate. (For Tier 3 medications that do not have a similar category in Tier-2, a medication from any category in Tier-2 may be used.)

Special Prior Authorization Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least 3 other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member.

Tier-1	Tier-2	Tier-3	Special PA
Biaguanides Metformin (Glucophage®) Metformin SR (Glucophage XR®) Metformin-Glyburide (Glucovance®) Metformin-Glipizide (Metaglip®) **Sulfonylureas** Glyburide (Diabeta®) Glyburide Micronized (Micronase®) Glipizide (Glucotrol®) Glipizide SR (Glucotrol XL®)	**DPP-4 Inhibitors** Linagliptin (Tradjenta®) Saxagliptin (Onglyza®) Saxagliptin-Metformin (Kombiglyze®) Sitagliptin (Januvia®) Sitagliptin-Metformin (Janumet®) Sitagliptin-Met ER (Janumet XR®) Sitagliptin-Simvastatin (Juvisync®) Alogliptin-Metformin (Kazano®) Alogliptin (Nesina®) Alogliptin-Pioglitazone (Oseni®)	**DPP-4 Inhibitors** Linagliptin-Metformin (Jentadueto™) **Thiazolidinediones** Pioglitazone-Metformin (Actoplus Met®, Actoplus Met XR®) Pioglitazone-Glimepiride (Duetact®) **Alpha-Glucosidase Inhibitors** Miglitol (Glyset®)	**Biaguanides** Metformin solution (Riomet®) Metformin Long-Acting (Fortamet®, Glumetza®) **Thiazolidinediones** Rosiglitazone (Avandia®) Rosiglitazone-Metformin (Avandamet®) Rosiglitazone-Glimepiride (Avandaryl®) **Amylinomimetic** Pramlintide (Symlin®)

Glimepiride (Amaryl®) **Miscellaneous** Chlorpropamide Tolbutamide	**Glinides** Repaglinide-Metformin (Prandimet®) Repaglinide (Prandin®) Nateglinide (Starlix®) **GLP-1 Agonists** Liraglutide (Victoza®) Exenatide (Byetta®) Exenatide Weekly (Bydureon®) **Alpha-Glucosidase Inhibitors** Acarbose (Precose®) **Thiazolidinediones** Pioglitazone (Actos®)		

*Tier structure based on supplemental rebate participation.

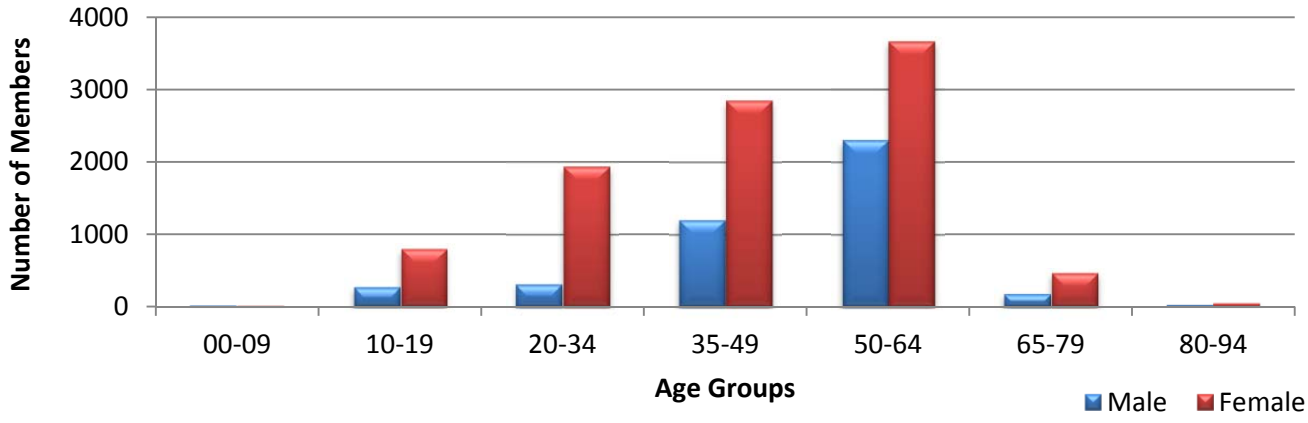
Utilization of Anti-Diabetic Medications

Comparison of Fiscal Years

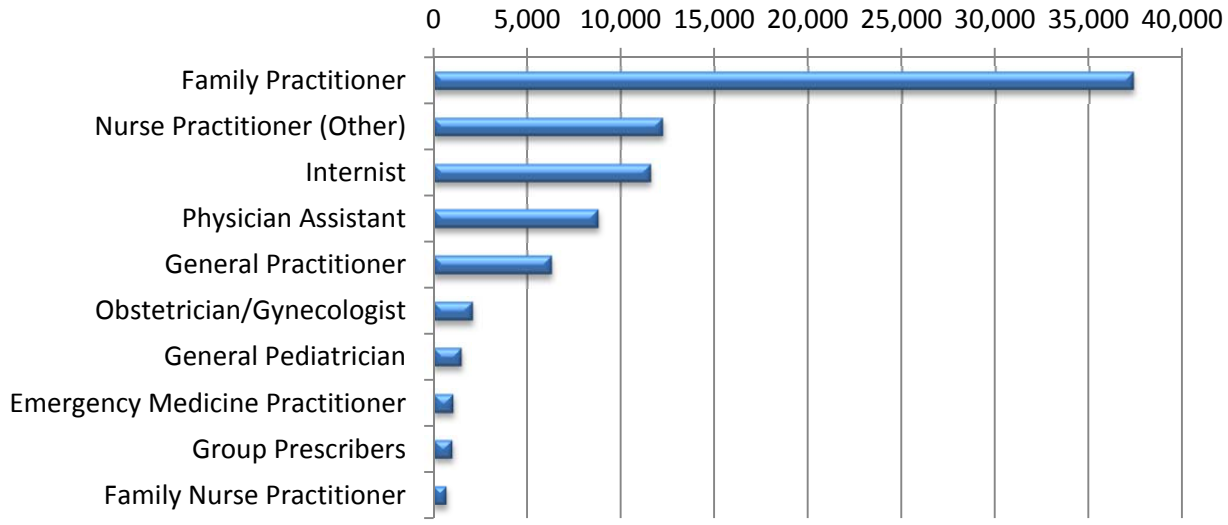
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	14,184	86,526	$5,442,894.21	$62.90	$1.88	5,338,285	2,902,864
2013	14,341	86,435	$4,833,191.10	$55.92	$1.67	5,347,132	2,887,250
%Change	**1.10%**	**-0.10%**	**-11.20%**	**-11.10%**	**-11.20%**	**0.20%**	**-0.50%**
Change	**157**	**-91**	**-$609,703.11**	**-$6.98**	**-$0.21**	**8,847**	**-15,614**

*Total number of unduplicated members

Demographics of Members Utilizing Anti-Diabetic Medications



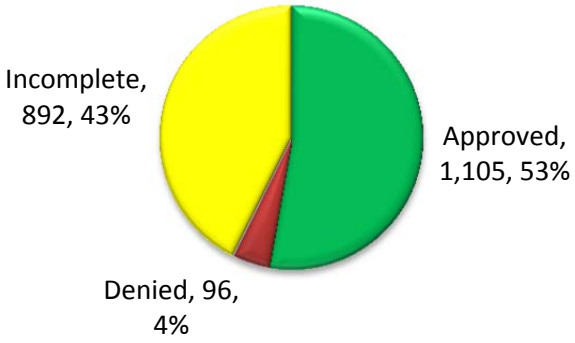
Top Prescriber Specialties of Anti-Diabetic Medications by Number of Claims



Prior Authorization of Anti-Diabetic Medications

There was a total of 2,093 petitions submitted for anti-diabetic medications during fiscal year 2013. 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

Anticipated Patent Expirations[1]

- Byetta® (exenatide), Bydureon® (exenatide) - 2016
- Januvia® (sitagliptin), Juvisync® (sitagliptin/simvastatin), Janumet® (sitagliptin/metformin) - 2017
- Tradjenta® (linagliptin), Jentadueto™ (linagliptin/metformin) - 2017
- Victoza® (liraglutide) - 2017
- Onglyza® (saxagliptin), Kombiglyze® (saxagliptin/metformin) - 2021
- Riomet® (metformin oral solution) – 2023

FDA Update[2]

- November 2013: The FDA announced it is removing certain restrictions on prescribing and use of Avandia® (rosiglitazone) to reflect new information regarding the cardiovascular risk of the medicine. Results from the Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycemia in Diabetes (RECORD) clinical trial showed no elevated risk of heart attack or death in patients being treated with Avandia® when compared to standard-of-care diabetes drugs. These data do not confirm the signal of increased risk of heart attacks that was found in a meta-analysis of clinical trials first reported in 2007.

Invokana™ (Canagliflozin) Medication Summary

- **FDA Approved:** March 2013
- **Indication:** Invokana™ is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- **Dosing:** The recommended dosing of Invokana™ is 100 to 300mg by mouth once daily, taken before the first meal of the day.
- **Mechanism of Action:** Invokana™ inhibits sodium-glucose co-transporter 2 (SGLT2), which are expressed in the proximal renal tubule and are responsible for the majority of reabsorption of filtered glucose from the tubular lumen. By inhibiting SGLT2, Invokana™ reduces reabsorption of filtered glucose and increases urinary glucose excretion.
- **Efficacy:** The efficacy of Invokana™ as monotherapy was evaluated in a 26-week, double-blind, placebo-controlled study in 584 patients with type 2 diabetes inadequately controlled on diet and exercise. Patients were randomized to Invokana™ 100 mg, Invokana™ 300 mg, or placebo, administered once daily for 26 weeks. Invokana™ 100 mg and 300 mg once daily resulted in a statistically significant improvement in HbA1C compared to placebo. Invokana™ 100 mg and 300 mg also resulted in a greater proportion of patients achieving an HbA1C less than 7%, significant reductions in fasting plasma glucose, improved postprandial glucose, and percent body weight reduction compared to placebo. Statistically significant mean changes from baseline in systolic blood pressure relative to placebo were -3.7 mmHg and -5.4 mmHg with Invokana™ 100 mg and 300 mg, respectively.
- **Utilization/Cost:** Invokana™ has been utilized by 34 members for a total of 109 claims since its approval in March 2013.

Medication	EAC Per Tablet or Capsule	EAC Per Day	EAC for 30 days of Therapy
Invokana™ 100mg and 300mg Tablets	$10.18	$10.18	$305.40
Metformin 1000mg Tablets	$0.08∞	$0.16	$4.80

EAC= estimated acquisition cost
∞ State maximum allowable cost (SMAC) pricing
Metformin daily dosing based on 2000mg per day.

Farxiga™ (Dapagliflozin) Medication Summary

- **FDA approved:** January 2014

- **Indication:** Farxiga™ is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

- **Dosing:** The recommended dosing of Farxiga™ is 5 to 10mg by mouth once daily, taken in the morning with or without food.

- **Mechanism of Action:** Farxiga™ is also a SGLT2 inhibitor that works similarly to Invokana™. By inhibiting SGLT2, Farxiga™ reduces reabsorption of filtered glucose and increases urinary glucose excretion.

- **Efficacy:** The efficacy of Farxiga™ as monotherapy was evaluated in a 24-week, double-blind, placebo-controlled study in 558 patients with type 2 diabetes inadequately controlled on diet and exercise. Following a 2-week diet and exercise placebo lead-in period, 485 patients with HbA1c ≥7% and ≤10% were randomized to Farxiga™ 5 mg or Farxiga™ 10 mg once daily in either the morning or evening, or placebo. At Week 24, treatment with Farxiga™ 10 mg every morning provided significant improvements in HbA1c and fasting plasma glucose compared with placebo. Farxiga™ has shown similar effects to Invokana™ on weight reduction and changes from baseline in systolic blood pressure.

- **Utilization/Cost:** Farxiga™ has been utilized by 1 member for 1 claim since its approval in January 2014.

Medication	EAC Per Tablet or Capsule	EAC Per Day	EAC for 30 days of Therapy
Farxiga™ 5mg and 10mg Tablets	$10.18	$10.18	$305.40
Metformin 1000mg Tablets	$0.08∞	$0.16	$4.80

EAC= estimated acquisition cost
∞ State maximum allowable cost (SMAC) pricing
Metformin daily dosing based on 2000mg per day.

Recommendations

The College of Pharmacy recommends the addition of Invokana™ and Farxiga™ to Tier-3 of the Anti-Diabetic Product Based Prior Authorization category. The existing criteria for this category will apply. In addition, the College of Pharmacy recommends moving Avandia®, Avandamet®, and Avandaryl® to Tier-3 in light of the FDA's recent removal of prescribing restrictions.

Tier-1	Tier-2	Tier-3	Special PA
Biaguanides Metformin (Glucophage®) Metformin SR (Glucophage XR®) Metformin-Glyburide (Glucovance®) Metformin-Glipizide (Metaglip®) **Sulfonylureas** Glyburide (Diabeta®) Glyburide Micronized (Micronase®) Glipizide (Glucotrol®) Glipizide SR (Glucotrol XL®) Glimepiride (Amaryl®) **Miscellaneous** Chlorpropamide Tolbutamide	**DPP-4 Inhibitors** Linagliptin (Tradjenta®) Saxagliptin (Onglyza®) Saxagliptin-Metformin (Kombiglyze®) Sitagliptin (Januvia®) Sitagliptin-Metformin (Janumet®) Sitagliptin-Met ER (Janumet XR®) Sitagliptin-Simvastatin (Juvisync®) Alogliptin-Metformin (Kazano®)1/1/14 Alogliptin (Nesina®) Alogliptin-Pioglitazone (Oseni®) **Glinides** Repaglinide-Metformin (Prandimet®) Repaglinide (Prandin®) Nateglinide (Starlix®) **GLP-1 Agonists** Liraglutide (Victoza®) Exenatide (Byetta®) Exenatide Qweek (Bydureon®) **Alpha-Glucosidase Inhibitors** Acarbose (Precose®) **Thiazolidinediones** Pioglitazone (Actos®)	**DPP-4 Inhibitors** Linagliptin-Metformin (Jentadueto™) **Thiazolidinediones** Pioglitazone-Metformin (Actoplus Met®, Actoplus Met XR®) Pioglitazone-Glimepiride (Duetact®) **Alpha-Glucosidase Inhibitors** Miglitol (Glyset®) **SGLT 2 Inhibitor** Canagliflozin (Invokana™) Dapagliflozin (Farxiga™) **Thiazolidinediones** Rosiglitazone (Avandia®) Rosiglitazone-Metformin (Avandamet®) Rosiglitazone-Glimepiride (Avandaryl®)	**Biaguanides** Metformin solution (Riomet®) Metformin Long-Acting (Fortamet®, Glumetza®) **Amylinomimetic** Pramlintide (Symlin®)

*Tier structure based on supplemental rebate participation.

Utilization Details of Anti-Diabetic Medications

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
METFORMIN PRODUCTS						
METFORMIN TAB 500MG	23,602	6,286	$175,573.52	3.75	3.63%	$7.44
METFORMIN TAB 850MG	1,915	448	$19,512.11	4.27	0.45%	$10.19
METFORMIN TAB 1000MG	18,897	4,302	$169,908.64	4.39	3.52%	$8.99
METFORMIN TAB 500MG ER	3,853	1,220	$37,378.47	3.16	0.77%	$9.70
METFORMIN TAB 750MG ER	400	124	$5,752.84	3.23	0.12%	$14.38
Subtotal	**48,667**	**11,214**	**$408,125.58**	**4.34**	**8.49%**	**$8.39**
GLIPIZIDE PRODUCTS						
GLIPIZIDE TAB 5MG	3,066	783	$18,681.09	3.92	0.39%	$6.09
GLUCOTROL TAB 5MG	1	1	$5.07	1	0.00%	$5.07
GLIPIZIDE TAB 10MG	3,399	801	$26,839.69	4.24	0.56%	$7.90
GLIPIZIDE ER TAB 2.5MG	378	105	$5,192.38	3.6	0.11%	$13.74
GLIPIZIDE XL TAB 2.5MG	77	26	$1,182.32	2.96	0.03%	$15.35
GLUCOTROL XL TAB 2.5MG	5	3	$58.00	1.67	0.00%	$11.60
GLIPIZIDE ER TAB 5MG	817	223	$11,828.64	3.66	0.25%	$14.48
GLIPIZIDE XL TAB 5MG	289	76	$4,166.57	3.8	0.09%	$14.42
GLIPIZIDE ER TAB 10MG	1,368	341	$28,261.72	4.01	0.58%	$20.66
GLIPIZIDE XL TAB 10MG	766	184	$16,824.98	4.16	0.36%	$21.96
Subtotal	**10,166**	**2,229**	**$113,040.46**	**4.56**	**2.41%**	**$11.12**
GLYBURIDE PRODUCTS						
GLYBURIDE TAB 1.25MG	120	43	$1,265.47	2.79	0.03%	$10.55
GLYBURIDE TAB 2.5MG	1,459	641	$16,706.97	2.28	0.36%	$11.45
GLYBURIDE TAB 5MG	6,046	1,435	$114,640.63	4.21	2.37%	$18.96
GLYBURIDE MCR TAB 1.5MG	5	3	$45.08	1.67	0.00%	$9.02
GLYBURIDE MCR TAB 3MG	85	18	$752.04	4.72	0.02%	$8.85
GLYBURIDE MCR TAB 6MG	81	18	$1,080.15	4.5	0.02%	$13.34
Subtotal	**7,796**	**2,012**	**$134,490.34**	**3.87**	**2.87%**	**$17.25**
GLIMEPIRIDE PRODUCTS						
GLIMEPIRIDE TAB 1MG	407	106	$2,948.17	3.84	0.06%	$7.24
GLIMEPIRIDE TAB 2MG	1,272	337	$10,759.65	3.77	0.23%	$8.46
GLIMEPIRIDE TAB 4MG	2,061	492	$19,312.36	4.19	0.40%	$9.37
Subtotal	**3,740**	**859**	**$33,020.18**	**4.35**	**0.70%**	**$8.83**
GLYBURIDE-METFORMIN PRODUCTS						
GLYB/MET TAB 5-500MG	1,139	196	$16,864.49	5.81	0.35%	$14.81
GLYB/MET TAB 2.5-500MG	374	67	$4,782.19	5.58	0.10%	$12.79
GLYB/MET TAB 1.25-250MG	18	5	$216.86	3.6	0.00%	$12.05
Subtotal	**1,531**	**263**	**$21,863.54**	**5.82**	**0.45%**	**$14.28**
GLIPIZIDE-METFORMIN PRODUCTS						
GLIP/MET TAB 5-500MG	217	39	$10,143.72	2.96	0.21%	$46.75
GLIP/MET TAB 2.5-500MG	62	17	$2,219.09	2.31	0.05%	$35.79
GLIP/MET TAB 2.5-250MG	4	2	$169.45	2.5	0.00%	$42.36

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
Subtotal	**283**	**57**	**$12,532.26**	**4.96**	**0.26%**	**$44.28**
TOLBUTAMIDE PRODUCTS						
TOLBUTAMIDE TAB 500MG	12	2	$1,118.43	6	0.02%	$93.20
Subtotal	**12**	**2**	**$1,118.43**	**6**	**0.02%**	**$93.20**
Tier-1 Subtotal	**72,195**	**16,636**	**$724,190.79**	**4.34**	**15.20%**	**$10.03**
SITAGLIPTIN PRODUCTS						
JANUVIA TAB 25MG	120	39	$38,363.35	3.08	0.79%	$319.69
JANUVIA TAB 50MG	1,019	250	$347,816.23	4.08	7.20%	$341.33
JANUVIA TAB 100MG	3,805	877	$1,235,661.24	4.34	25.57%	$324.75
Subtotal	**4,944**	**1,094**	**$1,621,840.82**	**4.52**	**33.56%**	**$328.04**
SITAGLIPTIN-METFORMIN PRODUCTS						
JANUMET TAB 50-500MG	479	95	$125,955.30	5.04	2.61%	$262.95
JANUMET TAB 50-1000MG	1,960	373	$481,495.55	5.25	9.96%	$245.66
JANUMET XR TAB 50-500MG	10	2	$1,177.00	5	0.02%	$117.70
JANUMET XR TAB 50-1000MG	130	30	$26,605.67	4.33	0.55%	$204.66
JANUMET XR TAB 100-1000MG	97	23	$24,042.95	4.22	0.50%	$247.87
Subtotal	**2,676**	**487**	**$659,276.47**	**5.49**	**13.64%**	**$246.37**
PIOGLITAZONE PRODUCTS						
PIOGLITAZONE TAB 15MG	378	92	$34,820.60	4.11	0.72%	$92.12
ACTOS TAB 15MG	101	61	$28,443.22	1.66	0.59%	$281.62
PIOGLITAZONE TAB 30MG	766	183	$91,863.30	4.19	1.90%	$119.93
ACTOS TAB 30MG	206	126	$76,755.42	1.63	1.59%	$372.60
PIOGLITAZONE TAB 45MG	435	121	$61,040.95	3.6	1.26%	$140.32
ACTOS TAB 45MG	159	84	$61,254.58	1.89	1.27%	$385.25
Subtotal	**2,045**	**421**	**$354,178.07**	**4.86**	**6.19%**	**$173.19**
LIRAGLUTIDE PRODUCTS						
VICTOZA INJ 18MG/3ML	1,479	356	$649,967.25	4.15	13.45%	$439.46
Subtotal	**1,479**	**356**	**$649,967.25**	**4.15**	**13.45%**	**$439.46**
LINAGLIPTIN PRODUCTS						
TRADJENTA TAB 5MG	991	216	$235,413.74	4.59	4.87%	$237.55
Subtotal	**991**	**216**	**$235,413.74**	**4.59**	**4.87%**	**$237.55**
SAXAGLIPTIN PRODUCTS						
ONGLYZA TAB 2.5MG	90	22	$23,719.45	4.09	0.49%	$263.55
ONGLYZA TAB 5MG	565	110	$168,867.27	5.14	3.49%	$298.88
Subtotal	**655**	**127**	**$192,586.72**	**5.16**	**3.98%**	**$294.03**
EXENATIDE PRODUCTS						
BYDUREON INJ	38	9	$13,880.74	4.22	0.30%	$365.28
BYETTA INJ 5MCG	73	18	$26,567.80	4.06	0.55%	$363.94
BYETTA INJ 10MCG	184	45	$78,328.83	4.09	1.62%	$425.70
Subtotal	**295**	**61**	**$118,777.37**	**4.84**	**2.54%**	**$402.64**
SAXAGLIPTIN-METFORMIN PRODUCTS						
KOMBIGLYZE TAB 2.5-1000	101	20	$21,109.94	5.05	0.44%	$209.01

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
KOMBIGLYZE TAB 5-500MG	13	4	$4,187.95	3.25	0.09%	$322.15
KOMBIGLYZE TAB 5-1000MG	137	25	$46,967.36	5.48	0.97%	$342.83
Subtotal	**251**	**47**	**$72,265.25**	**5.34**	**1.54%**	**$287.91**
NATEGLINIDE PRODUCTS						
NATEGLINIDE TAB 60MG	47	13	$3,292.26	3.62	0.07%	$70.05
STARLIX TAB 60MG	2	1	$133.02	2	0.00%	$66.51
NATEGLINIDE TAB 120MG	99	20	$7,601.81	4.95	0.16%	$76.79
STARLIX TAB 120MG	2	1	$177.50	2	0.00%	$88.75
Subtotal	**150**	**31**	**$11,204.59**	**4.84**	**0.23%**	**$74.70**
ACARBOSE PRODUCTS						
ACARBOSE TAB 25MG	82	24	$3,414.34	3.42	0.07%	$41.64
ACARBOSE TAB 50MG	42	11	$2,014.85	3.82	0.04%	$47.97
ACARBOSE TAB 100MG	15	2	$671.27	7.5	0.01%	$44.75
PRECOSE TAB 50MG	2	1	$87.08	2	0.00%	$43.54
Subtotal	**141**	**36**	**$6,187.54**	**3.92**	**0.12%**	**$43.88**
REPAGLINIDE PRODUCTS						
PRANDIN TAB 0.5MG	12	5	$2,235.91	2.4	0.05%	$186.33
PRANDIN TAB 1MG	60	12	$14,409.45	5	0.31%	$240.16
PRANDIN TAB 2MG	43	7	$15,505.93	6.14	0.33%	$360.60
Subtotal	**115**	**21**	**$32,151.29**	**5.48**	**0.69%**	**$279.58**
SITAGLIPTIN-SIMVASTATIN PRODUCTS						
SITAGLIP-SIMVAS TAB 100-20MG	3	2	$757.38	1.5	0.02%	$252.46
Subtotal	**3**	**2**	**$757.38**	**1.5**	**0.02%**	**$252.46**
Tier-2 Subtotal	**13,745**	**2,899**	**$3,954,606.49**	**4.74**	**80.83%**	**$287.71**
PIOGLITAZONE-METFORMIN PRODUCTS						
PIOGLIT/MET TAB 15-850MG	141	25	$36,608.13	5.64	0.76%	$259.63
PIOGLIT/MET TAB 15-500MG	99	15	$23,913.27	6.6	0.49%	$241.55
ACTOPLUS MET TAB 15-850MG	32	20	$10,821.48	1.6	0.22%	$338.17
ACTOPLUS MET TAB XR 15-1000MG	27	5	$7,848.38	5.4	0.16%	$290.68
ACTOPLUS MET TAB 15-500MG	25	12	$7,624.86	2.08	0.16%	$304.99
ACTOPLUS MET TAB XR 30-1000MG	5	2	$4,537.12	2.5	0.09%	$907.42
Subtotal	**329**	**49**	**$91,353.24**	**6.71**	**1.88%**	**$277.67**
MIGLITOL PRODUCTS						
GLYSET TAB 50MG	2	1	$244.74	2	0.01%	$122.37
Subtotal	**2**	**1**	**$244.74**	**2**	**0.01%**	**$122.37**
CANAGLIFLOZIN PRODUCTS						
INVOKANA TAB 300MG	2	1	$556.70	2	0.01%	$278.35
Subtotal	**2**	**1**	**$556.70**	**2**	**0.01%**	**$278.35**
LINAGLIPTIN-METFORMIN PRODUCTS						
JENTADUETO TAB 2.5-500	6	4	$1,555.56	1.5	0.03%	$259.26
JENTADUETO TAB 2.5-850	3	1	$748.38	3	0.02%	$249.46
JENTADUETO TAB 2.5-1000	63	26	$15,452.95	2.42	0.33%	$245.28

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
Subtotal	**72**	**31**	**$17,756.89**	**2.32**	**0.38%**	**$246.62**
Tier-3 Subtotal	**405**	**82**	**$109,911.57**	**4.94**	**2.28%**	**$271.39**
METFORMIN PRODUCTS						
METFORMIN TAB 500MG ER	2	1	$676.51	2	0.01%	$338.26
METFORMIN TAB 1000MG ER	27	6	$10,029.47	4.5	0.21%	$371.46
GLUMETZA TAB 500MG	4	1	$294.00	4	0.01%	$73.50
GLUMETZA TAB 1000MG	8	4	$4,445.88	2	0.09%	$555.74
RIOMET SOL	13	7	$1,307.44	1.86	0.03%	$100.57
Subtotal	**54**	**19**	**$16,753.30**	**2.84**	**0.35%**	**$310.25**
PRAMLINTIDE PRODUCTS						
SYMLIN PEN 60 INJ 1000MCG	6	2	$2,515.20	3	0.05%	$419.20
SYMLIN PEN 120 INJ 1000MCG	19	4	$21,212.00	4.75	0.44%	$1,116.42
Subtotal	**25**	**6**	**$23,727.20**	**4.17**	**0.50%**	**$949.09**
PIOGLITAZONE-GLIMEPIRIDE PRODUCTS						
DUETACT TAB 30-4MG	9	3	$3,434.77	3	0.07%	$381.64
PIOGLIT/GLIM 30-4MG	2	1	$566.98	2	0.01%	$283.49
Subtotal	**11**	**3**	**$4,001.75**	**3.67**	**0.08%**	**$363.80**
Special PA Subtotal	**90**	**28**	**$44,482.25**	**3.21**	**0.93%**	**$494.25**
Total	**86,435**	**14,341***	**$4,833,191.10**	**6.03**	**100%**	**$55.92**

*Total number of unduplicated members.

PRODUCT DETAILS OF INVOKANA™ (CANAGLIFLOZIN)[3]

INDICATIONS: Invokana™ is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

DOSAGE FORM: 100mg and 300mg tablets

ADMINISTRATION: Once daily by mouth before first meal of the day.

CONTRAINDICATIONS: Renal impairment, ESRD, dialysis, and hypersensitivity.

SPECIAL POPULATIONS:

- **Pregnancy Category C.** There are no adequate and well controlled studies in pregnant women.
- **Pediatric Use:** Safety and effectiveness in pediatric patients under 18 years of age have not been established.
- **Geriatric Use:** Higher incidence of adverse reactions related to reduced intravascular volume.
- **Renal Impairment:** Higher incidence of adverse reactions related to reduced intravascular volume. Do not initiate Invokana™ if eGFR is below 45mL/min/1.73 m^2.
- **Hepatic Impairment:** Not recommended with severe hepatic impairment.

WARNINGS & PRECAUTIONS:

- **Hypoglycemia:** A lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with Invokana™.
- **Hypotension:** Before initiation, assess status and correct hypovolemia in patients with renal impairment, the elderly, in patients with low systolic blood pressure, or if on diuretics, ACE inhibitor, or ARB.
- **Genital Mycotic Infections:** Monitor and treat if indicated.
- **Increased LDL-C**: Monitor LDL-C and treat per standard of care.
- **Hypersensitivity Reactions**: Discontinue and monitor until signs and symptoms resolve.
- **Hyperkalemia:** Monitor potassium levels in patients with impaired renal function and those predisposed to hyperkalemia.
- **Impairment in Renal function:** Monitor renal function during therapy. More frequent monitoring is recommended in patients with eGFR<60mL/min/1.73 m^2.

ADVERSE REACTIONS: (occurring >5%)

- Female genital mycotic infections, urinary tract infection, and increased urination.

PRODUCT DETAILS OF FARXIGA™ (DAPAGLIFLOZIN)[4]

INDICATIONS: Farxiga™ is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

DOSAGE FORM: 5mg and 10mg tablets

ADMINISTRATION: Once daily by mouth in the morning with or without food.

CONTRAINDICATIONS: Renal impairment, ESRD, dialysis, and hypersensitivity.

SPECIAL POPULATIONS:

- **Pregnancy Category C.** There are no adequate and well controlled studies in pregnant women.
- **Pediatric Use:** Safety and effectiveness in pediatric patients under 18 years of age have not been established.
- **Geriatric Use:** Higher incidence of adverse reactions related to reduced intravascular volume.
- **Renal Impairment:** Higher incidence of adverse reactions related to reduced intravascular volume.
- **Hepatic Impairment:** No dose adjustment recommended.

WARNINGS & PRECAUTIONS:

- **Hypoglycemia:** A lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with Farxiga™.
- **Hypotension:** Before initiation, assess status and correct hypovolemia in patients with renal impairment, the elderly, in patients with low systolic blood pressure, or if on diuretics, ACE inhibitor, or ARB.
- **Increased LDL-C**: Monitor LDL-C and treat per standard of care.
- **Bladder Cancer**: An imbalance in bladder cancers was observed in clinical trials. Farxiga™ should not be used in patients with active bladder cancer and should be used in caution in patients with a prior history of bladder cancer.
- **Genital mycotic infections:** Monitor and treat if indicated.
- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with any anti-diabetic drug.
- **Impairment in renal function:** Monitor renal function during therapy.

ADVERSE REACTIONS: (occurring >5%)

- Female genital mycotic infections, urinary tract infection, and nasopharyngitis.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalent Evaluations. Available online at: http://orange-book.findthebest.com/l/17767/. Last revised: 03/18/2014. Last accessed: 03/27/2014

[2] FDA News Release. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376516.htm. Last revised: 11/2013. Last accessed 03/27/2014.

[3] Ivokana™ Product Information. Janssen Pharmaceuticals Inc. Available online at: http://www.invokanahcp.com/prescribing-information.pdf. Last revised: 11/2013. Last accessed 03/27/2014.

[4] Farxiga™ Product Information. Bristol –Myers Squibb and AstraZeneca Pharmaceuticals. Available online at: http://packageinserts.bms.com/pi/pi_farxiga.pdf. Last revised: 01/2014. Last accessed 03/27/2014.

Appendix F

Calendar Year 2013 Annual Review of Topical Antifungal Medications and 30-Day Notice to Prior Authorize Luzu® (Luliconazole Topical Cream)

Oklahoma Health Care Authority
April 2014

Current Prior Authorization Criteria

Tier-2 Approval Criteria:

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

Topical Antifungal Medications	
Tier 1	**Tier 2**
ciclopirox 0.77% cream	ciclopirox solution, shampoo, & gel (Penlac® and Loprox®), and 0.77% Suspension
clotrimazole 1% Rx cream, solution	miconazole/zinc oxide/white petrolatum (Vusion®)
econazole 1% cream	oxiconazole (Oxistat®)
ketoconazole 2% cream, shampoo	sertaconazole nitrate (Ertaczo®)
nystatin cream, ointment	butenafine (Mentax®)
clotrimazole 1% cream (OTC)*	ketoconazole gel (Xolegel™)
terbinafine 1% cream (OTC)*	Naftifine 1% and 2% cream, 1% gel (Naftin®)
tolnaftate 1% cream (OTC)*	sulconazole (Exelderm®)
	ketoconazole foam 2% (Extina®)
	nystatin/triamcinolone cream, ointment
	clotrimazole/betamethasone 1% and 0.05% cream, lotion

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

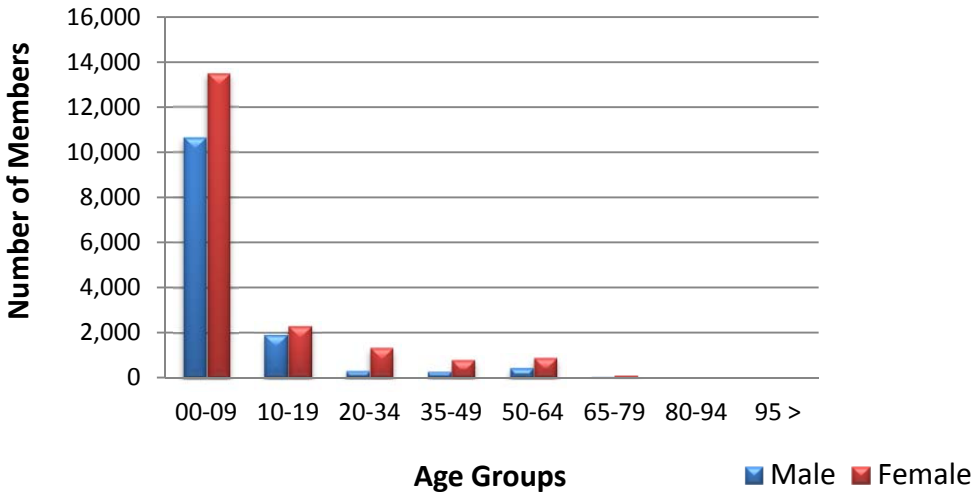
Utilization of Topical Antifungal Medications

Comparison of Calendar Years

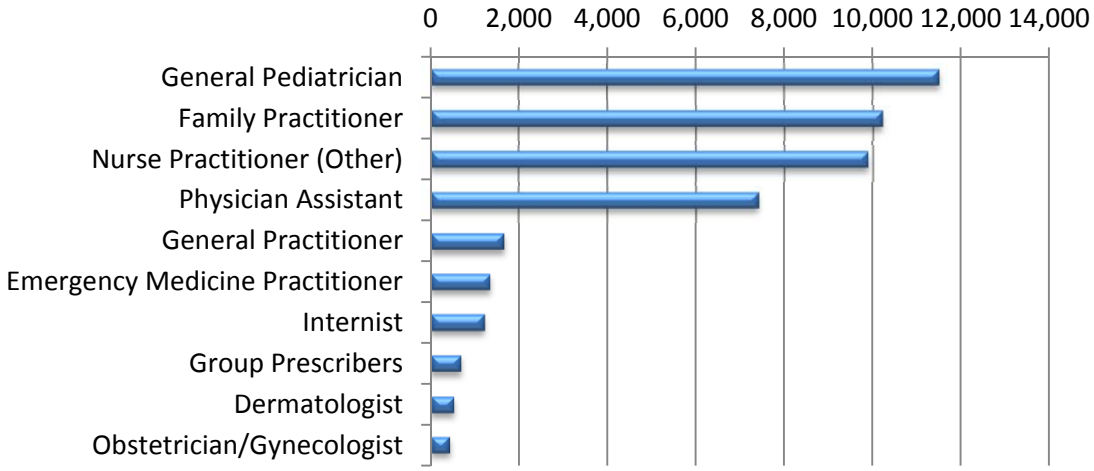
Calendar Year	Total Members*	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	35,905	51,046	$1,578,816.75	$30.93	$2.32	1,933,374	681,685
2013	32,678	46,383	$1,038,393.73	$22.39	$1.63	1,672,235	638,420
% Change	**-9.00%**	**-9.10%**	**-34.20%**	**-27.60%**	**-29.70%**	**-13.50%**	**-6.30%**
Change	**-3,227**	**-4,663**	**-$540,423.02**	**-$8.54**	**-$0.69**	**-261,139**	**-43,265**

*Total number of unduplicated members

Demographics of Members Utilizing Topical Antifungal Medications

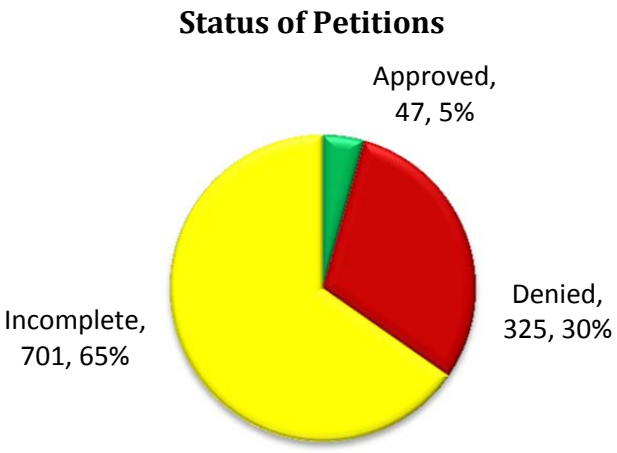


Top Prescriber Specialties of Topical Antifungal Medications by Number of Claims



Prior Authorization of Topical Antifungal Medications

There was a total of 1,073 petitions submitted for the topical antifungal medication PBPA category during calendar year 2013. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.



Market News and Updates

Anticipated Patent Expirations[1]

- Ertaczo® (sertaconazole nitrate)- May 2014
- Loprox® Gel (ciclopirox)- September 2018
- Extina® (ketoconazole foam 2%)- October 2018
- Xolegel™ (ketoconazole gel)- November 2020
- Vusion® (miconazole/zinc oxide/white petrolatum)- March 2028

FDA Drug Safety Communication[2]

- 07/26/2013- The FDA limited usage of Nizoral® (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems. The use of ketoconazole tablets in dermatophyte infections is no longer indicated. Ketoconazole oral tablets are not indicated for the treatment of fungal infections of the skin or nails.

New FDA Approved Medications

- In June of 2013, the FDA approved a new strength of Naftin® (naftifine) gel, which is manufactured by Merz Pharmaceuticals, LLC. The new strength, Naftin® 2% gel, is in addition to the already available Naftin® 1% gel.

Luzu® (luliconazole topical cream)[3]

FDA Approved: November 2013

Indication: Luzu® 1% cream is an azole antifungal indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older.

Dosing: Luzu ® is available as a 1% topical cream.

- Luzu® 1% cream is for topical use only. It is not for ophthalmic, oral, or intravaginal use.
- Interdigital Tinea Pedis: Apply to the affected and immediate surrounding area(s) once a day for two weeks.
- Tinea Cruris and Tinea Corporis: Apply to the affected and immediate surrounding area(s) once a day for one week.

Mechanism of Action: Luzu® 1% cream is an azole antifungal. The exact mechanism of action against dermatophytes is unknown, but Luzu® 1% cream appears to inhibit ergosterol synthesis by inhibiting the enzyme lanosterol demethylase. Inhibition of this enzyme's activity by azole antifungals results in decreased amounts of ergosterol, a constituent of fungal cell membranes, causing defects in the fungal cell membrane.

Contraindications: There are no contraindications for appropriate use of topical Luzu® 1% cream.

Efficacy:

Interdigital Tinea Pedis

- Luzu® 1 % cream safety and efficacy were evaluated in two randomized, double blind, vehicle-controlled, multi-center trials with a clinical and culture-confirmed diagnosis of interdigital tinea pedis in 423 subjects.
- Subjects were randomized to receive Luzu® 1% cream or vehicle applied to the entire area of the forefeet including all interdigital web spaces and approximately 1 inch of the surrounding area of the foot once a day for 14 days.

Efficacy Results at 4 Weeks Post-Treatment- Interdigital Tinea Pedis

	Study 1		**Study 2**	
	Luzu® 1% Cream N= 106 n (%)	Vehicle Cream N= 103 n (%)	Luzu® 1% Cream N= 107 n (%)	Vehicle Cream N= 107 n (%)
Complete Clearance*	28 (26%)	2 (2%)	15 (14%)	3 (3%)
Effective Treatment[+]	51 (48%)	10 (10%)	35 (33%)	16 (15%)
Clinical Cure**	31 (29%)	8 (8%)	16 (15%)	4 (4%)
Mycological Cure[++]	66 (62%)	18 (18%)	60 (56%)	29 (27%)

*Proportion of subjects who achieved both clinical cure and mycological cure

[+] Negative Potassium Hydroxide test (KOH) and culture and at most mild erythema and/or scaling and no pruritus

**Absence of erythema, scaling, and pruritus

[++] Negative KOH and negative fungal culture

Tinea Cruris

- Luzu® 1 % cream safety and efficacy were evaluated in a randomized, double blind, vehicle-controlled, multi-center trials in 256 subjects with a clinical and culture-confirmed diagnosis of tinea cruris.
- Subjects were randomized to receive Luzu® 1% cream or vehicle applied to the affected area and approximately 1 inch of the surrounding area once a day for 7 days.

Efficacy Results at 3 Weeks Post-Treatment- Tinea Cruris

	Luzu® 1% Cream N= 165 n (%)	Vehicle Cream N= 91 n (%)
Complete Clearance*	35 (21%)	4 (4%)
Effective Treatment[+]	71 (43%)	17 (19%)
Clinical Cure**	40 (24%)	6 (7%)
Mycological Cure[++]	129 (78%)	41 (4%)

*Proportion of subjects who achieved both clinical cure and mycological cure
[+] Negative KOH and culture and at most mild erythema and/or scaling and no pruritus
**Absence of erythema, scaling, and pruritus
[++] Negative KOH and negative fungal culture

Cost

Luzu® 1% cream is available as a 60 gram package size only. The current estimated acquisition cost (EAC) is $6.69 per gram or $401.40 per package. The following chart shows the cost comparison of available antifungal topical products with the FDA indication to treat tinea pedis, tinea cruris, and tinea corporis.

Medication Name	Package Size[+]	Cost per gram	Cost per package
Luzu® (luliconazole) 1% cream	**60 grams**	**$6.69 per gram[++]**	**$401.40**
clotrimazole 1% cream	45 grams	$0.98 per gram*	$44.10
econazole 1% cream	85 grams	$0.28 per gram*	$23.80
ketoconazole 2% cream	60 grams	$0.35 per gram*	$21.00

[+]Largest package size available
[++]Estimated Acquisition Cost
*State Maximum Allowable Cost

Discussion

In December of 2012, combination antifungal and corticosteroid products were placed in Tier-2 of the topical antifungal product based prior authorization category. At the same time, over the counter clotrimazole 1% cream, terbinafine 1% cream, and tolnaftate 1% cream became covered for members 0-20 years of age without prior authorization. These changes are reflected in utilization of this category with a 34.2% decrease in total cost which amounts to a cost savings of $540,423.02. These changes have resulted in an increase in prior authorizations submitted by an additional 851 prior authorizations compared to the previous calendar year. After evaluating the utilization data from the previous calendar year with the current criteria, it can be concluded that the changes made to this category are cost effective even after factoring in additional administrative costs related to prior authorization submissions.

Recommendations

The College of Pharmacy recommends the placement of Luzu® 1% cream (luliconazole) in Tier-2 of the Topical Antifungal Medications PBPA category. The existing criteria for this category will apply.

Topical Antifungal Medications	
Tier 1	**Tier 2**
ciclopirox 0.77% cream	ciclopirox solution, shampoo, & gel (Penlac® and Loprox®), and 0.77% Suspension
clotrimazole 1% Rx cream, solution	miconazole/zinc oxide/white petrolatum (Vusion®)
econazole 1% cream	oxiconazole (Oxistat®)
ketoconazole 2% cream, shampoo	sertaconazole nitrate (Ertaczo®)
nystatin cream, ointment	butenafine (Mentax®)
clotrimazole 1% cream (OTC)*	ketoconazole gel (Xolegel™)
terbinafine 1% cream (OTC)*	Naftifine 1% and 2% cream, 1% and 2% gel (Naftin®)
tolnaftate 1% cream (OTC)*	sulconazole (Exelderm®)
	ketoconazole foam 2% (Extina®)
	nystatin/triamcinolone cream, ointment
	clotrimazole/betamethasone 1% and 0.05% cream, lotion
	Luliconazole cream 1% (Luzu®)

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

Utilization Details for Topical Antifungal Medications

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/ CLAIM	COST/ DAY	% COST
Ciclopirox Products						
CICLOPIROX CREAM 0.77%	948	772	$18,564.23	$19.58	$1.40	1.79%
SUBTOTAL	**948**	**772**	**$18,564.23**	**$19.58**	**$1.40**	**1.79%**
Clotrimazole Products						
CLOTRIMAZOLE CREAM 1%	8,709	7,181	$182,485.19	$20.95	$1.46	17.57%
ATHLETE FOOT CREAM 1%	22	21	$171.92	$7.81	$0.55	0.02%
CLOTRIMAZOLE CRYSTALS	2	2	$13.20	$6.60	$0.26	0.00%
CLOTRIMAZOLE POWDER	19	9	$164.35	$8.65	$0.43	0.02%
CLOTRIMAZOLE SOLUTION 1%	197	173	$2,506.68	$12.72	$0.87	0.24%
SUBTOTAL	**8,949**	**7,386**	**$185,341.34**	**$11.35**	**$0.71**	**17.85%**
Econazole Cream						
ECONAZOLE CREAM 1%	1,251	1,042	$21,144.63	$16.90	$1.12	2.04%
SUBTOTAL	**1,251**	**1,042**	**$21,144.63**	**$16.90**	**$1.12**	**2.04%**
Ketoconazole Products						
KETOCONAZOLE CREAM 2%	4,111	3,494	$83,161.91	$20.23	$1.31	8.01%
KETOCONAZOLE SHAMPOO 2%	2,388	1,556	$42,389.53	$17.75	$0.59	4.08%
SUBTOTAL	**6,499**	**5,050**	**$125,551.44**	**$37.98**	**$0.95**	**12.09%**
Miconazole Products						
BAZA ANTIFUN CREAM 2%	1	1	$4.63	$4.63	$0.31	0.00%
MICONAZOLE CREAM 2%	1	1	$2.37	$2.37	$0.34	0.00%
MICONAZOLE POWDER	5	4	$130.82	$26.16	$0.93	0.01%
SUBTOTAL	**7**	**6**	**$137.82**	**$11.05**	**$0.53**	**0.01%**
Nystatin Products						
NYSTATIN CREAM 100000	17,862	13,781	$367,039.08	$20.55	$1.76	35.35%
NYSTATIN OINTMENT 100000	6,634	5,475	$174,946.00	$26.37	$2.33	16.85%
NYSTOP POWDER 100000	1,573	1,156	$58,566.76	$37.23	$2.70	5.64%
NYAMYC POWDER 100000	1,335	735	$50,066.34	$37.50	$2.69	4.82%
NYSTATIN POWDER 100000	886	478	$27,331.67	$30.85	$2.45	2.63%
SUBTOTAL	**28,290**	**21,625**	**$677,949.85**	**$30.50**	**$2.39**	**65.29%**
Terbinafine Products						
TERBINAFINE CREAM 1%	293	248	$3,916.47	$13.37	$0.93	0.38%
LAMISIL AT CREAM 1%	59	53	$899.65	$15.25	$1.24	0.09%
ATHLETE FOOT CREAM 1%	21	20	$314.66	$14.98	$1.13	0.03%
ATHLETE FOOT CREAM AF	4	4	$56.22	$14.06	$1.61	0.01%
SUBTOTAL	**377**	**325**	**$5,187.00**	**$14.41**	**$1.23**	**0.51%**
Tolnaftate Products						
TOLNAFTATE CREAM 1%	4	4	$34.28	$8.57	$0.42	0.00%
SM ANTIFUNGL CREAM 1%	1	1	$14.70	$14.70	$0.49	0.00%
SUBTOTAL	**5**	**5**	**$48.98**	**$11.64**	**$0.46**	**0.00%**
TIER-1 SUBTOTAL	**46,326**	**36,211**	**$1,033,925.29**	**$22.32**	**$1.10**	**99.57%**

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/ CLAIM	COST/ DAY	% COST
Ciclopirox Products						
CICLOPIROX SHAMPOO 1%	7	2	$632.94	$90.42	$3.23	0.06%
CICLOPIROX SOL UTION 8%	6	5	$89.59	$14.93	$0.49	0.01%
CICLODAN SOLUTION 8%	1	1	$9.34	$9.34	$0.67	0.00%
SUBTOTAL	**14**	**8**	**$731.87**	**$114.69**	**$1.46**	**0.07**
Clotrimazole/Betamethasone Products						
CLOTRIM/BETA CREAM DIPROP	19	15	$879.13	$46.27	$2.28	0.08%
CLOTRIM/BETA CREAM 1-0.05%	6	4	$367.46	$61.24	$3.22	0.04%
CLOTRIM/BETA LOTION DIPROP	3	2	$213.28	$71.09	$3.05	0.02%
SUBTOTAL	**28**	**21**	**$1,459.87**	**$59.54**	**$2.85**	**0.14%**
Ketoconazole Products						
KETOCONAZOLE FOAM2%	2	1	$273.56	$136.78	$5.47	0.03%
SUBTOTAL	**2**	**1**	**$273.56**	**$136.78**	**$5.47**	**0.03%**
Naftifine Products						
NAFTIN CREAM 2%	1	1	$602.40	$602.40	$20.08	0.06%
SUBTOTAL	**1**	**1**	**$602.40**	**$602.40**	**$20.08**	**0.06%**
Oxiconazole Products						
OXISTAT LOTION 1%	1	1	$187.08	$187.08	$6.24	0.02%
SUBTOTAL	**1**	**1**	**$187.08**	**$187.08**	**$6.24**	**0.02%**
Nystatin/Triamcinolone Products						
NYSTAT/TRIAM CREAM	5	5	$777.97	$155.59	$10.37	0.07%
NYSTAT/TRIAM OINTMENT	6	3	$435.69	$72.62	$5.45	0.04%
SUBTOTAL	**11**	**8**	**$1,213.66**	**$114.10**	**$7.91**	**0.11%**
TIER-2 SUBTOTAL	**57**	**40**	**$4,468.44**	**$78.39**	**$7.34**	**0.53%**
TOTAL:	**46,383**	**32,678***	**$1,038,393.73**	**$22.39**	**$1.63**	**100%**

*Total number of unduplicated members.

PRODUCT DETAILS OF LUZU® (LULICONAZOLE TOPICAL CREAM)[3]

INDICATIONS AND USE:

- Luzu® 1% cream is an azole antifungal indicated for the treatment of:
  - Interdigital Tinea Pedis
  - Tinea Cruris
  - Tinea Corporis

DOSAGE FORMS: Luzu® is a topical 1% cream available in a 60 gram package size.

ADMINSTRATION:

- **Interdigital Tinea Pedis:** Apply to affected and immediate surrounding area(s) once a day for 2 weeks.
- **Tinea Cruris and Tinea Corporis:** Apply to the affected and immediate surrounding area(s) once a day for one week.

CONTRAINDICATIONS: None.

SPECIAL POPULATIONS:

- **Pregnancy:** Category C.
- **Nursing Mothers:** It is not known whether Luzu® 1% cream is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Luzu® 1% cream is administered to women who are breastfeeding.
- **Pediatric Use:** The safety and effectiveness of Luzu® 1% cream in pediatric patients have not been established.
- **Geriatric Use:** Of the total number of subjects in clinical studies of Luzu® 1% cream, 8% were 65 and over, while 1.4% were 75 and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS:

- **Clinical Trials:** Application site reactions (<1%; occurred in both Luzu® 1% cream and vehicle arms of trial)
- **Post-Marketing:** Contact dermatitis, Cellulitis

DRUG INTERACTIONS:

- May inhibit the activity of CYP2C19 and CYP3A4 based on in vitro assessment. No in vivo drug interaction trials have been conducted.
- Based on in vitro assessment, Luzu® 1% cream is not expected to inhibit CYPs 1A2, 2C9, and 2D6.
- The induction potential of Luzu® 1% cream on CTP enzymes has not been evaluated.

PATIENT COUNSELING INFORMTION:

1. Luzu® 1% cream is used for a fungal infection on your skin.
2. Luzu® 1% cream is for topical use only. It should not be taken by mouth.
3. Luzu® 1% cream is not intended for intravaginal or ophthalmic use.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://orange-book.findthebest.com/. Last revised: 03/18/14. Last accessed 03/20/2014.

[2] FDA Limits Usage of Nizoral® (Ketoconazole) Oral Tablets Due to Potentially Fatal Liver Injury and Risk of Drug Interactions and Adrenal Gland Problems. Available online at: http://www.fda.gov/drugs/drugsafety/ucm362415.htm. Last revised:10/16/2013. Last accessed: 03/27/2014.

[3] Luzu® Product Information. Valeant Pharmaceuticals. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204153s000lbl.pdf. Last revised 11/2013. Last accessed 03/17/2014.

Appendix G

Fiscal Year 2013 Annual Review of Non-Steroidal Anti-Inflammatory Drugs and 30-Day Notice to Prior Authorize Zorvolex™ (Diclofenac) and Tivorbex™ (Indomethacin)

Oklahoma Health Care Authority
April 2014

Current Prior Authorization Criteria

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier 1	**Tier 2**	**Special PA**
Diclofenac potassium (Cataflam®) Diclofenac sodium (Voltaren®) Diclofenac sodium ER (Voltaren® XR) Etodolac (Lodine®) Etodolac ER (Lodine® XL) Flurbiprofen (Ansaid®) Ibuprofen (Motrin®) Ketoprofen (Orudis®) Meclofenamate (Meclomen®) Meloxicam (Mobic®) Nabumetone (Relafen®) Naproxen (Naprosyn®) Naproxen EC (EC-Naprosyn®) Naproxen sodium (Anaprox®) Oxaprozin (Daypro®) Sulindac (Clinoril®) Tolmetin (Tolectin®)	Celecoxib (Celebrex®) Diclofenac sodium/Misoprostol (Arthrotec®) Fenoprofen (Nalfon®)	Diclofenac epolamine patches (Flector®) Diclofenac potassium (Zipsor®) Diclofenac potassium powder packets for oral solution (Cambia®) Diclofenac sodium topical gel (Voltaren® Gel) Diclofenac sodium topical solution (Pennsaid®) Ibuprofen/Famotidine (Duexis®) Indomethacin (Indocin®) Ketoprofen ER (Oruvail®) Mefenamic acid (Ponstel®) Naproxen Sodium (Naprelan®) Naproxen/Esomeprazole (Vimovo®) Piroxicam (Feldene®)

Tier-2 Approval Criteria:

1. Previous use of at least two Tier-1 NSAID products (from different product lines) plus a PPI (proton pump inhibitor) within the last 120 days; or
2. For those with prior GI bleed who must have an NSAID, a Tier-2 product may be approved (Celebrex® should be taken with a PPI).

Special Prior Authorization Approval Criteria:

1. A unique indication for which a Tier-1 or Tier-2 medication is not appropriate, such as the diagnosis of gout for indomethacin; or
2. Previous use of at least two Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 product.

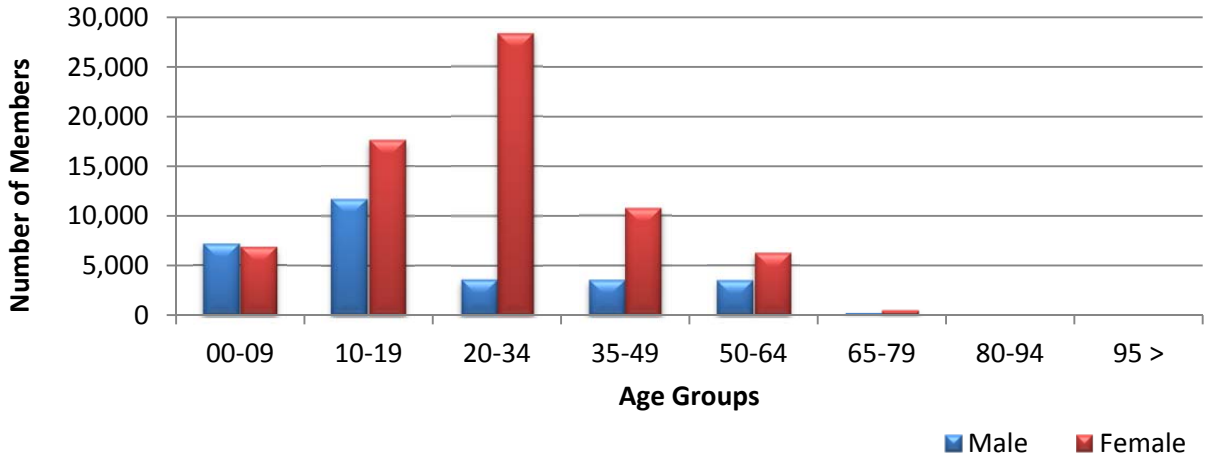
Utilization of NSAIDs

Comparison of Fiscal Years

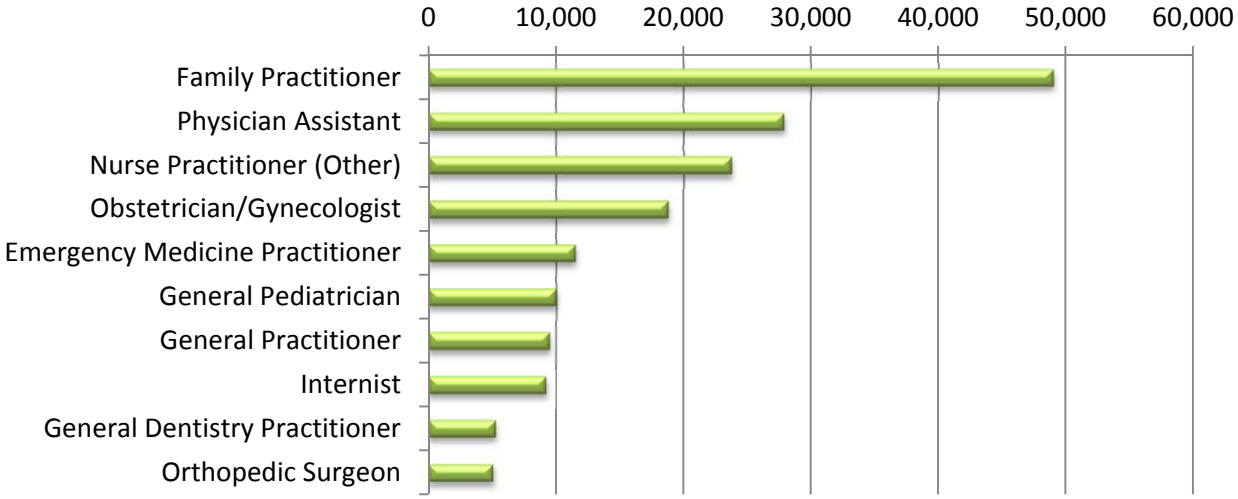
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Per-Diem Cost	Total Units	Total Days
2012	102,771	184,201	$2,068,135.77	$11.23	$0.52	12,031,539	3,942,892
2013	100,718	185,666	$2,227,392.67	$12.00	$0.55	12,601,471	4,035,295
% Change	**-2.00%**	**0.80%**	**7.70%**	**6.90%**	**5.80%**	**4.70%**	**2.30%**
Change	**-2,053**	**1,465**	**$159,256.90**	**$0.77**	**$0.03**	**569,932**	**92,403**

*Total number of unduplicated members.

Demographics of Members Utilizing NSAIDs



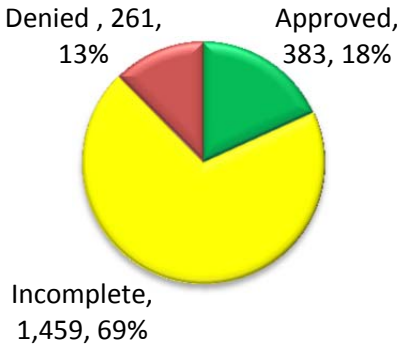
Top Prescriber Specialties of NSAIDs by Number of Claims



Prior Authorization of NSAIDs

There was a total of 2,103 petitions submitted for this category during fiscal year 2013. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expirations

- Naprelan® (naproxen sodium ER tablets)- 6/2014
- Celebrex® (celecoxib capsules)- 12/2015
- Flector® (diclofenac topical patches)- 4/2019
- Vimovo® (naproxen/esomeprazole tablets)- 2/2023
- Cambia® (diclofenac powder packets for oral solution)- 6/2026
- Duexis® (ibuprofen/famotidine tablets)- 7/2026
- Zipsor® (diclofenac potassium liquid capsules)- 2/2029
- Pennsaid® (diclofenac topical solution)- 8/2030

Iroko Pharmaceuticals, LLC, recently received FDA approval for two medications; both approvals were received through Supplemental New Drug Applications (sNDA). Zorvolex™ (diclofenac 18mg & 35mg capsules) was approved by the FDA in October 2013, and Tivorbex™ (indomethacin 20mg & 40mg capsules) was approved by the FDA in February 2014. Both products were approved as smaller doses than diclofenac and indomethacin products currently on the market, and were developed to address the FDA's public health advisory in 2005 that recommended NSAIDs be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Tivorbex™ is not yet available on the market.

In January 2014, the FDA approved a new strength of Pennsaid® (diclofenac topical solution), which is manufactured by Mallinckrodt Pharmaceuticals. The new strength, Pennsaid® 2%, is in addition to the already available Pennsaid® 1.5% topical solution. An Abbreviated New Drug Application (ANDA) was submitted by Paddock LLC in December 2013 to market a generic 1.5% diclofenac topical solution, and is pending approval from the FDA.

Zorvolex™ (Diclofenac) Capsules[6,7,8,9]

Indications: Zorvolex™ (diclofenac) is an NSAID that is indicated for the treatment of mild to moderate acute pain in adults. The manufacturer of Zorvolex™, Iroko Pharmaceuticals, LLC, is currently pursuing the additional indication for the treatment of osteoarthritis pain in adults. Zorvolex™ should be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Zorvolex™ is not indicated for long-term treatment.

Dosing: Zorvolex™ is available as 18mg and 35mg oral capsules. The recommended dosage is 18mg or 35mg by mouth three times daily. Zorvolex™ should be taken on an empty stomach. Zorvolex™ capsules do not result in an equivalent systemic exposure to diclofenac as other formulations of oral diclofenac. Other formulations contain a salt of diclofenac (i.e. diclofenac potassium or sodium) while Zorvolex™ contains the free acid; therefore, Zorvolex™ capsules are not interchangeable with other oral formulations of diclofenac, even if the milligram strength is the same. Patients with hepatic disease may require reduced doses of Zorvolex™ and should be started with a dose of 18mg three times daily, and if efficacy is not achieved, use of Zorvolex™ should be discontinued.

Mechanism of Action: Zorvolex™ is an NSAID with potent anti-inflammatory, analgesic, and antipyretic properties. The mechanism of action of Zorvolex™, like that of other NSAIDs, is not completely understood but may involve inhibition of cyclooxygenase (COX-1 and COX-2) pathways. Diclofenac's mechanism may also be related to prostaglandin synthetase inhibition.

Efficacy: The efficacy of Zorvolex™ in the treatment of acute pain was demonstrated in a multicenter, randomized, double-blind, placebo-controlled study comparing adult patients with pain following bunionectomy. The study enrolled 428 patients with a mean age of 40 years (range 18 to 65 years) and a minimal pain intensity rating of at least 40-mm on a 100-mm visual analog scale (VAS) during the 9-hour period after discontinuation of the anesthetic block following bunionectomy surgery. Patients were randomized equally across the treatment groups to Zorvolex™ 18mg, Zorvolex™ 35mg, or placebo taken three times daily. One tablet of hydrocodone/APAP 10mg/325mg was permitted every 4 to 6 hours as rescue medication. Approximately 82% of patients in the Zorvolex™ 35mg group, 85% of patients in the Zorvolex™ 18mg group, and 85% of the patients in the placebo group took rescue medication for pain management during the study. Both Zorvolex™ 18mg and 35mg demonstrated efficacy in pain intensity reduction compared with placebo, as measured by the sum of pain intensity difference over 0 to 48 hours after the first dose.

Cost: The estimated acquisition cost of Zorvolex™ is $2.64/capsule, regardless of strength. At recommended dosing (three times daily), a one month supply would cost $237.60, resulting in an annual cost of $2.851.20 (even though it is not indicated for long-term treatment). The following table compares Zorvolex™ with two generic oral formulations of diclofenac sodium.

MEDICATION NAME	STRENGTH	EAC*	DOSING REGIMEN	COST/ MONTH	COST/ YEAR
Zorvolex™ (diclofenac)	35 mg	$2.64	1 PO TID	$237.60	$2,851.20
Diclofenac sodium	75mg	$0.28	1 PO BID-TID	$16.80 - $25.20	$201.60 - $302.40
Diclofenac sodium	50mg	$0.19	1 PO BID-TID	$11.40 - $17.10	$136.80 - $205.20

Tivorbex™ (Indomethacin) Capsules[10,11,12]

Indications: Tivorbex™ (indomethacin) is an NSAID that is indicated for the treatment of mild to moderate acute pain in adults. Tivorbex™ should be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Tivorbex™ is not indicated for long-term treatment.

Dosing: Tivorbex™ is available as 20mg and 40mg oral capsules. The recommended dosage is 20mg by mouth three times daily or 40mg by mouth two to three times daily.

Mechanism of Action: Tivorbex™ is an NSAID with potent anti-inflammatory, analgesic, and antipyretic properties. The mechanism of action of Tivorbex™, like that of other NSAIDs, is not completely understood but may involve inhibition of cyclooxygenase (COX-1 and COX-2) pathways. Indomethacin's mechanism may also be related to prostaglandin synthetase inhibition.

Efficacy: The efficacy of Tivorbex™ in the treatment of acute pain was demonstrated in two multicenter, randomized, double-blind, placebo-controlled study comparing adult patients with pain following bunionectomy. The two studies enrolled a total of 835 patients with a mean age of 40 years (range 18 to 68 years) and a minimal pain intensity rating of at least 40-mm on a 100-mm visual analog scale (VAS) during the 9-hour period after discontinuation of the anesthetic block following bunionectomy surgery. Patients were randomized equally across the treatment groups to Tivorbex™ 20mg taken three times daily, Tivorbex™ 40mg taken twice daily, Tivorbex™ 40mg taken three times daily, or placebo. One tablet of hydrocodone/APAP 10mg/325mg was permitted every 4 to 6 hours as rescue medication. In Study 1, approximately 89% of patients in the Tivorbex™ 20mg three times daily group, 90% of patients in the Tivorbex™ 40mg twice daily group, 82% of patients in the Tivorbex™ 40mg three times daily group, and 97% of the patients in the placebo group took rescue medication for pain management during the study. Study 2 had similar results regarding rescue medication for pain management across the treatment groups. In both studies, Tivorbex™ 20mg taken three times daily, Tivorbex™ 40mg taken twice daily, and Tivorbex™ 40mg taken three times daily demonstrated efficacy in pain intensity reduction compared with placebo, as measured by the sum of pain intensity difference over 0 to 48 hours after the first dose.

Cost: The estimated acquisition cost of Tivorbex™ is not yet available.

Recommendations

The College of Pharmacy recommends the addition of Tivorbex™, based on the placement of other available indomethacin products, and Zorvolex™ to the Special PA category of the NSAIDs Product Based Prior Authorization category. The existing criteria for this category will apply.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)		
Tier 1	**Tier 2**	**Special PA**
Diclofenac potassium (Cataflam®)	Celecoxib (Celebrex®)	Diclofenac (Zorvolex™)
Diclofenac sodium (Voltaren®)	Diclofenac sodium/Misoprostol (Arthrotec®)	Diclofenac epolamine patches (Flector®)
Diclofenac sodium ER (Voltaren® XR)	Fenoprofen (Nalfon®)	Diclofenac potassium (Zipsor®)
Etodolac (Lodine®)		Diclofenac potassium powder packets for oral soln (Cambia®)
Etodolac ER (Lodine® XL)		Diclofenac sodium topical gel (Voltaren® Gel)
Flurbiprofen (Ansaid®)		Diclofenac sodium topical solution (Pennsaid®)
Ibuprofen (Motrin®)		Ibuprofen/Famotidine (Duexis®)
Ketoprofen (Orudis®)		Indomethacin (Indocin®)
Meclofenamate (Meclomen®)		Indomethacin (Tivorbex™)
Meloxicam (Mobic®)		Ketoprofen ER (Oruvail®)
Nabumetone (Relafen®)		Mefenamic acid (Ponstel®)
Naproxen (Naprosyn®)		Naproxen Sodium (Naprelan®)
Naproxen EC (EC-Naprosyn®)		Naproxen/Esomeprazole (Vimovo®)
Naproxen sodium (Anaprox®)		Piroxicam (Feldene®)
Oxaprozin (Daypro®)		
Sulindac (Clinoril®)		
Tolmetin (Tolectin®)		

Tier-2 Approval Criteria:

1. Previous use of at least two Tier-1 NSAID products (from different product lines) plus a PPI (proton pump inhibitor) within the last 120 days; or
2. For those with prior GI bleed who must have an NSAID, a Tier-2 product may be approved (Celebrex® should be taken with a PPI).

Special Prior Authorization Criteria:

1. A unique indication for which a Tier-1 or Tier-2 medication is not appropriate, such as the diagnosis of gout for indomethacin; or
2. Previous use of at least two Tier-1 NSAID products (from different product lines); and
3. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 product.
4. Additionally, use of Tivorbex™ will require a patient-specific, clinically significant reason why member cannot use other available generic indomethacin products.

Utilization Details of NSAIDs

Product Utilized	Total Claims	Total Members	Total Cost	Cost/Day	Cost/Claim	Percent COST
IBUPROFEN PRODUCTS						
IBUPROFEN TAB 800MG	51,847	34,844	$350,149.14	$0.38	$6.75	15.73%
IBUPROFEN SUS 100/5ML	17,544	14,181	$176,699.47	$0.88	$10.07	7.94%
IBUPROFEN TAB 600MG	14,365	11,305	$122,155.24	$0.60	$8.50	5.49%
IBUPROFEN TAB 400MG	7,071	5,174	$57,137.48	$0.56	$8.08	2.57%
ADVIL CHILD SUS 100/5ML	559	512	$3,650.79	$0.34	$6.53	0.16%
IBUPROFEN DRO 50/1.25	218	201	$2,095.42	$0.74	$9.61	0.09%
CHLD IBUPRFN DRO	51	46	$526.99	$0.87	$10.33	0.02%
CHILD ADVIL DRO 50/1.25	48	46	$339.14	$0.32	$7.07	0.02%
IBU-DROPS DRO 40MG/ML	19	18	$185.95	$0.54	$9.79	0.01%
IBU-DROPS DRO 50/1.25	12	10	$126.63	$0.65	$10.55	0.01%
IBUPROFEN SUS INFANTS	3	3	$31.86	$0.42	$10.62	0.00%
IBUPROFEN POW	1	1	$5.21	$0.17	$5.21	0.00%
SUBTOTAL	**91,738**	**64,131***	**$713,103.32**	**$0.49**	**$7.77**	**32.03%**
MELOXICAM PRODUCTS						
MELOXICAM TAB 15MG	24,204	11,003	$151,093.71	$0.17	$6.24	6.79%
MELOXICAM TAB 7.5MG	12,006	6,275	$101,969.66	$0.28	$8.49	4.58%
MELOXICAM SUS 7.5/5ML	206	55	$15,791.53	$2.34	$76.66	0.71%
MOBIC SUS 7.5/5ML	16	9	$2,178.27	$4.31	$136.14	0.10%
SUBTOTAL	**36,432**	**16,640***	**$271,033.17**	**$0.22**	**$7.44**	**12.18%**
NAPROXEN PRODUCTS						
NAPROXEN TAB 500MG	23,180	14,720	$152,307.11	$0.28	$6.57	6.84%
NAPROXEN TAB 375MG	3,136	2,152	$20,207.11	$0.30	$6.44	0.91%
NAPROXEN SOD TAB 550MG	3,122	2,450	$32,014.87	$0.59	$10.25	1.44%
NAPROXEN TAB 250MG	1,411	1,002	$11,576.11	$0.40	$8.20	0.52%
NAPROXEN DR TAB 500MG	985	531	$14,606.43	$0.56	$14.83	0.66%
NAPROXEN SUS 125/5ML	398	299	$7,992.62	$1.33	$20.08	0.36%
NAPROXEN SOD TAB 275MG	218	158	$2,327.52	$0.70	$10.68	0.10%
NAPROXEN DR TAB 375MG	136	95	$1,468.54	$0.48	$10.80	0.07%
SUBTOTAL	**32,586**	**20,654***	**$242,500.31**	**$0.33**	**$7.44**	**10.89%**
DICLOFENAC PRODUCTS						
DICLOFENAC TAB 75MG DR	5,881	3,204	$103,266.67	$0.63	$17.56	4.64%
DICLOFENAC TAB 50MG DR	1,278	780	$26,890.32	$0.84	$21.04	1.21%
DICLOFEN POT TAB 50MG	1,156	728	$14,992.57	$0.59	$12.97	0.67%
DICLOFENAC TAB 100MG ER	292	146	$5,804.66	$0.58	$19.88	0.26%
DICLOFENAC TAB 100MG XR	79	44	$1,740.14	$0.60	$22.03	0.08%
DICLOFENAC TAB 25MG DR	34	22	$2,289.41	$2.44	$67.34	0.10%
DICLOFENAC TAB 50MG EC	12	6	$282.28	$0.78	$23.52	0.01%
DICLOFENAC TAB 75MG EC	2	2	$40.62	$0.90	$20.31	0.00%
SUBTOTAL	**8,734**	**4,814***	**$155,306.67**	**$0.66**	**$17.78**	**6.98%**
KETOPROFEN PRODUCTS						
KETOPROFEN CAP 75MG	3,441	2,909	$52,858.30	$1.43	$15.36	2.37%

KETOPROFEN CAP 50MG	1,017	827	$8,781.54	$0.69	$8.63	0.39%
KETOPROFEN POW	164	97	$6,524.17	$1.75	$39.78	0.29%
SUBTOTAL	**4,622**	**3,767***	**$68,164.01**	**$1.27**	**$14.75**	**3.06%**
ETODOLAC PRODUCTS						
ETODOLAC TAB 400MG	2,317	1,269	$32,049.60	$0.56	$13.83	1.44%
ETODOLAC TAB 500MG	760	398	$12,028.55	$0.57	$15.83	0.54%
ETODOLAC CAP 300MG	523	415	$26,483.60	$2.83	$50.64	1.19%
ETODOLAC CAP 200MG	272	232	$10,245.07	$2.57	$37.67	0.46%
ETODOLAC ER TAB 400MG	222	95	$8,293.98	$1.17	$37.36	0.37%
ETODOLAC ER TAB 500MG	82	42	$3,508.24	$1.40	$42.78	0.16%
ETODOLAC ER TAB 600MG	56	30	$3,679.56	$1.71	$65.71	0.17%
SUBTOTAL	**4,232**	**2,402***	**$96,288.60**	**$0.93**	**$22.75**	**4.33%**
NABUMETONE PRODUCTS						
NABUMETONE TAB 750MG	2,093	960	$42,602.74	$0.71	$20.35	1.91%
NABUMETONE TAB 500MG	1,693	792	$33,142.80	$0.70	$19.58	1.49%
SUBTOTAL	**3,786**	**1,730***	**$75,745.54**	**$0.71**	**$20.01**	**3.40%**
SULINDAC PRODUCTS						
SULINDAC TAB 200MG	324	161	$6,435.15	$0.62	$19.86	0.29%
SULINDAC TAB 150MG	61	23	$924.44	$0.48	$15.15	0.04%
SUBTOTAL	**385**	**183***	**$7,359.59**	**$0.60**	**$19.12**	**0.33%**
OXAPROZIN PRODUCTS						
OXAPROZIN TAB 600MG	160	59	$20,522.37	$4.07	$128.26	0.92%
DAYPRO TAB 600MG	1	1	$208.97	$6.97	$208.97	0.01%
SUBTOTAL	**161**	**60***	**$20,731.34**	**$4.09**	**$128.77**	**0.93%**
FLURBIPROFEN PRODUCTS						
FLURBIPROFEN TAB 100MG	89	32	$1,222.64	$0.55	$13.74	0.05%
FLURBIPROFEN TAB 50MG	2	2	$27.04	$0.45	$13.52	0.00%
FLURBIPROFEN POW	1	1	$989.93	$33.00	$989.93	0.04%
SUBTOTAL	**92**	**35***	**$2,239.61**	**$0.96**	**$24.34**	**0.10%**
MECLOFENAMATE PRODUCTS						
MECLOFEN SOD CAP 100MG	21	17	$3,576.40	$13.97	$170.30	0.16%
MECLOFEN SOD CAP 50MG	19	2	$1,631.31	$2.86	$85.86	0.07%
SUBTOTAL	**40**	**19***	**$5,207.71**	**$6.30**	**$130.19**	**0.23%**
TOLMETIN PRODUCTS						
TOLMETIN SOD TAB 200MG	9	2	$1,017.08	$3.88	$113.01	0.05%
SUBTOTAL	**9**	**2***	**$1,017.08**	**$3.88**	**$113.01**	**0.05%**
TIER-1 SUBTOTAL	**182,817**	**100,324***	**$1,658,696.95**	**$0.42**	**$9.07**	**74.51%**
CELECOXIB PRODUCTS						
CELEBREX CAP 200MG	1,711	393	$394,472.86	$6.50	$230.55	17.72%
CELEBREX CAP 100MG	209	62	$35,066.21	$5.24	$167.78	1.58%
CELEBREX CAP 50MG	9	3	$610.86	$2.26	$67.87	0.03%
CELEBREX CAP 400MG	1	1	$249.20	$8.31	$249.20	0.01%
SUBTOTAL	**1,930**	**450***	**$430,399.13**	**$6.36**	**$223.00**	**19.33%**
DICLOFENAC/MISOPROSTOL PRODUCTS						

DICLO/MISOPR TAB 75-0.2MG	39	14	$6,435.41	$5.65	$165.01	0.29%
DICLO/MISOPR TAB 50-0.2MG	23	9	$4,560.59	$6.42	$198.29	0.20%
ARTHROTEC 75 TAB	21	9	$4,161.32	$6.03	$198.16	0.19%
ARTHROTEC 50 TAB	5	3	$1,084.45	$7.23	$216.89	0.05%
SUBTOTAL	**88**	**25***	**$16,241.77**	**$6.04**	**$184.57**	**0.73%**
FENOPROFEN PRODUCTS						
NALFON CAP 400MG	4	3	$779.91	$6.50	$194.98	0.04%
FENOPROFEN TAB 600MG	1	1	$99.49	$3.32	$99.49	0.00%
SUBTOTAL	**5**	**4***	**$879.40**	**$5.86**	**$175.88**	**0.04%**
TIER-2 SUBTOTAL	**2,023**	**479***	**$447,520.30**	**$6.35**	**$221.22**	**20.10%**
KETOPROFEN PRODUCTS						
KETOPROFEN CAP 200MG ER	271	118	$53,308.85	$6.19	$196.71	2.39%
SUBTOTAL	**271**	**118***	**$53,308.85**	**$6.19**	**$196.71**	**2.39%**
INDOMETHACIN PRODUCTS						
INDOMETHACIN CAP 50MG	135	53	$2,677.95	$0.73	$19.84	0.12%
INDOCIN SUS 25MG/5ML	41	7	$4,967.85	$4.68	$121.17	0.22%
INDOMETHACIN CAP 25MG	41	18	$746.93	$0.69	$18.22	0.03%
INDOMETHACIN CAP 75MG	28	10	$2,176.67	$2.64	$77.74	0.10%
SUBTOTAL	**245**	**86***	**$10,569.40**	**$1.59**	**$43.14**	**0.47%**
DICLOFENAC PRODUCTS						
VOLTAREN GEL 1%	117	56	$9,322.10	$3.51	$79.68	0.42%
CAMBIA POW 50MG	79	40	$19,812.50	$21.10	$250.79	0.89%
FLECTOR DIS 1.3%	13	11	$2,253.47	$7.15	$173.34	0.10%
PENNSAID SOL 1.5%	5	2	$996.40	$6.64	$199.28	0.04%
SUBTOTAL	**214**	**109***	**$32,384.47**	**$7.97**	**$151.33**	**1.45%**
NAPROXEN PRODUCTS						
NAPRELAN TAB 500MG CR	48	34	$16,270.08	$13.72	$338.96	0.73%
NAPRELAN TAB 375MG CR	18	11	$6,124.25	$11.89	$340.24	0.28%
SUBTOTAL	**66**	**45***	**$22,394.33**	**$13.17**	**$339.31**	**1.01%**
PIROXICAM PRODUCTS						
PIROXICAM CAP 20MG	19	4	$1,222.18	$1.63	$64.33	0.05%
PIROXICAM CAP 10MG	3	1	$18.12	$0.20	$6.04	0.00%
SUBTOTAL	**22**	**5***	**$1,240.30**	**$1.48**	**$56.38**	**0.06%**
SPECIAL PA SUBTOTAL	**818**	**361***	**$119,897.35**	**$5.48**	**$146.57**	**5.39%**
TOTAL	**185,658**	**100,718***	**$2,226,114.60**	**$0.55**	**$11.99**	**100.00%**

*Total number of unduplicated members

PRODUCT DETAILS OF ZORVOLEX™ (DICLOFENAC)

INDICATIONS AND USE: Zorvolex™ (diclofenac) is an NSAID indicated for the treatment of mild to moderate acute pain in adults.

DOSAGE FORMS: 18mg and 35mg capsules

ADMINISTRATION:

- The recommended dose of Zorvolex™ is 18mg or 35mg orally three times daily.
- The effectiveness of Zorvolex™ when taken with food has not been studied in clinical studies. Taking Zorvolex™ with food may cause a reduction in effectiveness compared to taking Zorvolex™ on an empty stomach.
- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.
- Zorvolex™ capsules are not interchangeable with other formulations of oral diclofenac even if the milligram strength is the same.

CONTRAINDICATIONS:

- Known hypersensitivity to diclofenac or any component of the drug product.
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-type reactions to NSAIDs have been reported in such patients.
- Perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate or well-controlled studies of Zorvolex™ in pregnant women. Starting at 30 weeks gestation, Zorvolex™, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Zorvolex™ can cause fetal harm when administered starting at 30 weeks gestation. If the drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to the fetus. Prior to 30 weeks gestation, Zorvolex™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In animals, no evidence of teratogenicity was observed in mouse, rat, or rabbit reproductive studies at doses of diclofenac equivalent to approximately 1 to 2 times the maximum recommended human dose (MRHD) of Zorvolex, 105 mg/day. In rats, maternally toxic doses were associated with dystocia, prolonged gestation, reduced fetal weights and growth, and reduced fetal survival. Diclofenac has been shown to cross the placental barrier in mice, rats, and humans. The effects of Zorvolex™ on labor and delivery in pregnant women are unknown. (Category C prior to 30 weeks gestation; Category D starting at 30 weeks gestation)
- **Nursing Mothers:** Based on the available data, diclofenac may be present in human milk. Caution should be exercised when Zorvolex™ is administered to a nursing woman.
- **Pediatrics:** The safety and effectiveness of Zorvolex™ in pediatric patients have not been established.
- **Geriatrics:** As with any NSAID, caution should be exercised in treating the elderly (65 years and older). In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and concomitant disease or other drug therapy. Diclofenac metabolites are known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more

likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. Older age increases the risk for GI bleeding. Most spontaneous reports of fatal GI events are in elderly or debilitated patients, and therefore special care should be taken in treating this population.

- **Renal Impairment:** Use with caution when initiating treatment with Zorvolex™ in patients with considerable dehydration. Long term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. No information is available from controlled clinical studies regarding the use of Zorvolex™ in patients with advanced renal disease. Therefore, treatment with Zorvolex™ is not recommended in patients with advanced renal disease. If Zorvolex™ therapy must be initiated, monitor the patient's renal function closely.
- **Hepatic Impairment:** Patients with hepatic disease may require reduced doses of Zorvolex™ compared to patients with normal hepatic function. As with other diclofenac products, treatment should be started at the lowest dose. Start treatment with a dose of Zorvolex™ 18mg three times daily and if efficacy is not achieved, discontinue use.

WARNINGS AND PRECAUTIONS:

Black Box Warning: Risk of Serious Cardiovascular and Gastrointestinal Events

Cardiovascular Risk

- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
- Zorvolex™ is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

- **Hepatic Effects:** Elevations of one or more liver tests may occur during therapy with Zorvolex™. These laboratory abnormalities may progress, remain unchanged, or be transient with continued therapy. Borderline elevations (greater than the upper limit of normal [ULN] to 3 times the ULN range) of transaminases have been observed in approximately 15% of diclofenac-treated patients. Of the markers of hepatic function, ALT (SGPT) is recommended for the monitoring of liver injury.
- **Hypertension:** NSAIDs, including Zorvolex™, can lead to new onset or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Use NSAIDs, including Zorvolex™, with caution in patients with hypertension. Monitor blood pressure closely during the initiation of NSAID treatment and throughout the course of therapy. Patients taking ACE inhibitors, thiazides, or loop diuretics may have impaired response to these therapies when taking NSAIDs.
- **Congestive Heart Failure and Edema:** Fluid retention and edema have been observed in some patients taking NSAIDs. Use Zorvolex™ with caution in patients with fluid retention or heart failure.
- **Renal Effects:** Use with caution when initiating treatment with Zorvolex™ in patients with considerable dehydration. Long term administration of NSAIDs has resulted in renal papillary

necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

- **Anaphylactoid Reactions:** As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to Zorvolex™. Zorvolex™ is contraindicated in patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.
- **Adverse Skin Reactions:** NSAIDs, including Zorvolex™, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations, and to discontinue Zorvolex™ at the first appearance of skin rash or any other sign of hypersensitivity.
- **Pregnancy:** Starting at 30 weeks gestation, Zorvolex™, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Zorvolex™ can cause fetal harm when administered starting at 30 weeks gestation. If the drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to the fetus.
- **Corticosteroid Treatment:** Zorvolex™ cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-responsive illness. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
- **Masking of Inflammation and Fever:** The pharmacological activity of Zorvolex™ in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infectious complications of presumed noninfectious, painful conditions.
- **Hematological Effects:** Anemia may occur in patients receiving NSAIDs, including Zorvolex™. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. In patients on long-term therapy with NSAIDs, including Zorvolex™, check hemoglobin or hematocrit if they exhibit signs or symptoms of anemia or blood loss. Zorvolex™ is not indicated for long-term treatment. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Carefully monitor patients treated with Zorvolex™ who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants.
- **Use in Patients with Preexisting Asthma:** Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, Zorvolex™ is contraindicated in patients with this form of aspirin sensitivity and should be used with caution in all patients with preexisting asthma.
- **Monitoring:** Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. For patients on

long-term treatment with NSAIDs, periodically check a CBC and a chemistry profile including liver function tests. Discontinue Zorvolex™ if abnormal liver tests or renal tests persist or worsen. Zorvolex™ is not indicated for long-term treatment.

ADVERSE REACTIONS:

- Serious adverse reactions (discussed elsewhere in the labeling):
  - Cardiovascular thrombotic events, gastrointestinal effects, hepatic effects, hypertension, congestive heart failure and edema, renal effects, anaphylactoid reactions, and serious skin reactions.
- Common adverse reactions (observed in clinical trials):
  - Edema, nausea, headache, dizziness, vomiting, constipation, pruritus, flatulence, pain in extremity, and dyspepsia.

DRUG INTERACTIONS:

- **Aspirin:** When administered with aspirin, the protein binding of Zorvolex™ is reduced. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of Zorvolex™ and aspirin is not generally recommended because of the potential of increased GI adverse reactions.
- **Anticoagulants:** The effects of anticoagulants, such as warfarin, and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than that with use of either drug alone.
- **ACE Inhibitors:** NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.
- **Diuretics:** Clinical studies, as well as post-marketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with Zorvolex™ and these diuretics, observe patients closely for signs of renal failure.
- **Lithium:** NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, observe patients carefully for signs of lithium toxicity.
- **Methotrexate:** NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This indicates that NSAIDs may enhance the toxicity of methotrexate. Use caution when NSAIDs are administered concomitantly with methotrexate.
- **Cyclosporine:** NSAIDs may affect renal prostaglandins and increase the toxicity of cyclosporine. Therefore, concomitant therapy with NSAIDs may increase cyclosporine's nephrotoxicity. Use caution when NSAIDs are administered concomitantly with cyclosporine.
- **Inhibitors or Substrates of Cytochrome P450 2C9 Other Considerations:** Diclofenac is metabolized predominately by cytochrome P450 2C9. Co-administration of diclofenac with another drug known to be metabolized by, or which inhibits, cytochrome P450 2C9 may unpredictably affect the pharmacokinetics of diclofenac or the co-administered drug. Caution should be used to evaluate each patient's medical history when consideration is given to prescribing diclofenac.

PATIENT COUNSELING INFORMATION:

1. Zorvolex™ (diclofenac) is a non-steroidal anti-inflammatory drug (NSAID) indicated for the treatment of mild to moderate acute pain in adults. Zorvolex™ is not indicated for use in children.
2. Take Zorvolex™ exactly as prescribed by your doctor. Zorvolex™ should be taken on an empty stomach. Zorvolex™ is not indicated for long-term treatment. Zorvolex™ should be taken at the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.
3. Before taking Zorvolex™, talk to your doctor or healthcare provider about other medications you are currently taking. Zorvolex™ has some possible drug-drug interactions that may result in adverse reactions.
4. Before taking Zorvolex™, talk to your doctor or healthcare provider if you are pregnant or plan to become pregnant, or are breastfeeding. Starting at 30 weeks gestation, Zorvolex™ and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Based on the available data, Zorvolex™ may be present in human milk; therefore, caution should be exercised when Zorvolex™ is taken by a woman who is breastfeeding.
5. Zorvolex™ should not be taken if you are allergic to diclofenac or any components of the drug product, or if you have a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Zorvolex™ should not be taken for perioperative pain following coronary artery bypass graft (CABG) surgery. Talk to your doctor or healthcare provider for more information.
6. NSAIDs, including Zorvolex™, may cause serious cardiovascular side effects, such as heart attack or stroke, which may result in hospitalization or even death. Be alert for the signs and symptoms of chest pain, shortness of breath, and slurring of speech. If these symptoms occur, stop taking Zorvolex™ and seek medical advice.
7. NSAIDs, including Zorvolex™, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization or even death. Be alert for the signs and symptoms of ulcerations and bleeding, such as upper abdominal pain, upset stomach/indigestion, black or dark tarry stools, or vomiting of blood. If these symptoms occur, stop taking Zorvolex™ and seek medical advice. The use of aspirin and an NSAID, including Zorvolex™, at the same time does increase the risk of serious GI events.
8. Be alert for the signs and symptoms of liver toxicity, such as nausea, fatigue, weakness, itching, yellowing of the eyes or skin, right upper quadrant tenderness, and “flu-like” symptoms. If these symptoms occur, stop taking Zorvolex™ and seek immediate medical therapy.
9. NSAIDs, including Zorvolex™, can cause serious skin side effects, such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which may result in hospitalization or even death, and may occur without warning. Be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching. If these symptoms develop or you develop any type of rash, stop taking Zorvolex™ and seek immediate medical therapy.
10. Anaphylactoid reactions may occur with Zorvolex™. Symptoms of anaphylactoid reactions include difficulty breathing and swelling of the face or throat. If these symptoms occur, stop taking Zorvolex™ and seek immediate emergency help.
11. Common adverse effects of Zorvolex™ include edema, nausea, headache, dizziness, vomiting, constipation, itching, gas, limb pain, and upset stomach/indigestion. Report any unexplained weight gain or edema (swelling caused by excess fluids in your body’s tissues) that occurs while taking Zorvolex™ to your doctor.

PRODUCT DETAILS OF TIVORBEX™ (INDOMETHACIN)[10,11]

INDICATIONS AND USE: Tivorbex™ (indomethacin) is an NSAID indicated for the treatment of mild to moderate acute pain in adults.

DOSAGE FORMS: 20mg and 40mg capsules

ADMINISTRATION:

- The recommended dose of Tivorbex™ is 20mg by mouth three times daily or 40mg by mouth two or three times daily.
- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.

CONTRAINDICATIONS:

- Known hypersensitivity to indomethacin or any component of the drug product.
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-type reactions to NSAIDs have been reported in such patients.
- Perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate or well-controlled studies of Tivorbex™ in pregnant women. Starting at 30 weeks gestation, Tivorbex™, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Tivorbex™ can cause fetal harm when administered starting at 30 weeks gestation. If the drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to the fetus. Prior to 30 weeks gestation, Tivorbex™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (Category C prior to 30 weeks gestation; Category D starting at 30 weeks gestation)
- **Nursing Mothers:** Based on the available data, indomethacin may be present in human milk. Caution should be exercised when Tivorbex™ is administered to a nursing woman.
- **Pediatrics:** The safety and effectiveness of Tivorbex™ in pediatric patients 17 years of age and younger have not been established.
- **Geriatrics:** As with any NSAID, caution should be exercised in treating the elderly (65 years and older) since advancing age appears to increase the possibility of adverse reactions. Indomethacin may cause confusion or rarely, psychosis; physicians should remain alert to the possibility of such adverse effects in the elderly. Indomethacin is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.
- **Renal Impairment:** Use with caution when initiating treatment with Tivorbex™ in patients with considerable dehydration. Long term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. No information is available from controlled clinical studies regarding the use of Tivorbex™ in patients with advanced renal disease. Therefore, treatment with Tivorbex™ is not recommended in patients with advanced renal disease. If Tivorbex™ therapy must be initiated, monitor the patient's renal function closely.
- **Hepatic Impairment:** The pharmacokinetics of Tivorbex™ has not been investigated in patients with hepatic impairment.

WARNINGS AND PRECAUTIONS:

Black Box Warning: Risk of Serious Cardiovascular and Gastrointestinal Events

Cardiovascular Risk

- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
- Tivorbex™ is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

- **Hepatic Effects:** Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs, including Tivorbex™. These laboratory abnormalities may progress, remain unchanged, or be transient with continued therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue Tivorbex™ immediately.
- **Hypertension:** NSAIDs, including Tivorbex™, can lead to new onset or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Use NSAIDs, including Tivorbex™, with caution in patients with hypertension. Monitor blood pressure closely during the initiation of NSAID treatment and throughout the course of therapy. Patients taking ACE inhibitors, thiazides, or loop diuretics may have impaired response to these therapies when taking NSAIDs.
- **Congestive Heart Failure and Edema:** Fluid retention and edema have been observed in some patients taking NSAIDs. Use Tivorbex™ with caution in patients with fluid retention or heart failure.
- **Renal Effects:** Use with caution when initiating treatment with Tivorbex™ in patients with considerable dehydration. Long term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state. No information is available from controlled clinical studies regarding the use of indomethacin in patients with advanced renal disease. Therefore, treatment with Tivorbex™ is not recommended in patients with advance renal disease. If Tivorbex™ therapy must be initiated, monitor patient function closely.

- **Anaphylactoid Reactions:** As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to Tivorbex™. Tivorbex™ is contraindicated in patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.
- **Central Nervous System Effects:** Tivorbex™ may aggravate depression or other psychiatric disturbances, epilepsy, and Parkinsonism, and should be used with caution in patients with these conditions. Discontinue Tivorbex™ if severe CNS adverse reactions develop. Tivorbex™ may cause drowsiness; therefore, caution patients about engaging in activities requiring mental alertness and motor coordination, such as driving a car. Indomethacin may also cause headache. Headache which persists despite dosage reduction requires cessation of therapy with Tivorbex™.
- **Skin Reactions:** NSAIDs, including Tivorbex™, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations, and to discontinue Tivorbex™ at the first appearance of skin rash or any other sign of hypersensitivity.
- **Fetal Toxicity:** Starting at 30 weeks gestation, Tivorbex™, and other NSAIDs, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Tivorbex™ can cause fetal harm when administered starting at 30 weeks gestation. If the drug is used during this time period in pregnancy, the patient should be apprised of the potential hazard to the fetus.
- **Corticosteroid Treatment:** Tivorbex™ cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-responsive illness. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
- **Masking of Inflammation and Fever:** The pharmacological activity of Tivorbex™ in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infectious complications of presumed noninfectious, painful conditions.
- **Hematological Effects:** Anemia may occur in patients receiving NSAIDs, including Tivorbex™. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. In patients on long-term therapy with NSAIDs, including Tivorbex™, check hemoglobin or hematocrit if they exhibit signs or symptoms of anemia or blood loss. Tivorbex™ is not indicated for long-term treatment. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Carefully monitor patients treated with Tivorbex™ who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants.
- **Use in Patients with Preexisting Asthma:** Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, Tivorbex™ is contraindicated in patients with this form of aspirin sensitivity and should be used with caution in all patients with preexisting asthma.
- **Monitoring:** Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. For patients on long-term treatment with NSAIDs, periodically check a CBC and a chemistry profile including

liver function tests. Discontinue Tivorbex™ if abnormal liver tests or renal tests persist or worsen. Tivorbex™ is not indicated for long-term treatment.

- **Ocular Effects:** Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients who had received prolonged therapy with Tivorbex™. Be alert to the possible association between the changes noted and Tivorbex™. It is advisable to discontinue therapy if such changes are observed. Blurred vision may be a significant symptom and warrants a thorough ophthalmological examination. Since these changes may be asymptomatic, ophthalmologic examination at periodic intervals is desirable in patients receiving prolonged therapy. Tivorbex™ is not indicated for long-term treatment.

ADVERSE REACTIONS:

- Serious adverse reactions (discussed elsewhere in the labeling):
  - Cardiovascular thrombotic events, gastrointestinal effects, hepatic effects, hypertension, congestive heart failure and edema, renal effects, anaphylactoid reactions, central nervous system effects, and serious skin reactions.
- Common adverse reactions (observed in clinical trials):
  - Nausea, post-procedural edema, headache, dizziness, vomiting, post-procedural hemorrhage, constipation, pruritus, diarrhea, dyspepsia, post-procedural swelling, pre-syncope, rash, upper abdominal pain, somnolence, generalized pruritus, hyperhidrosis, decreased appetite, hot flush, and syncope.

DRUG INTERACTIONS:

- Co-administration of antihypertensive agents with Tivorbex™ may reduce the effect of the antihypertensive agent. Concomitant use in patients with compromised renal function may result in further deterioration of renal function.
- Concomitant administration of Tivorbex™ and anticoagulants and platelet inhibitors (e.g., aspirin) is not generally recommended because of the potential of increased adverse effects including increased GI bleeding.

PATIENT COUNSELING INFORMATION:

1. Tivorbex™ is a non-steroidal anti-inflammatory drug (NSAID) used for the treatment of mild to moderate acute pain in adults.
2. Take Tivorbex™ exactly as prescribed by your doctor. Tivorbex™ should be taken at the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.
3. Before taking Tivorbex™, talk to your doctor or healthcare provider about other medications you are currently taking. Tivorbex™ has some possible drug-drug interactions that may result in adverse reactions.
4. Before taking Tivorbex™, talk to your doctor or healthcare provider if you are pregnant or plan to become pregnant, or are breastfeeding. Starting at 30 weeks gestation, Tivorbex ™ and other NSAIDs should be avoided by pregnant women. Based on the available data, Tivorbex ™ may be present in human milk; therefore, caution should be exercised when Tivorbex ™ is taken by a woman who is breastfeeding.
5. Tivorbex ™ should not be taken if you are allergic to indomethacin or any components of the drug product, or if you have a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Tivorbex ™ should not be taken for perioperative pain following coronary artery bypass graft (CABG) surgery. Talk to your doctor or healthcare provider for more information.

6. NSAIDs, including Tivorbex ™, may cause serious cardiovascular side effects, such as heart attack or stroke, which may result in hospitalization or even death. Be alert for the signs and symptoms of chest pain, shortness of breath, and slurring of speech. If these symptoms occur, stop taking Tivorbex ™ and seek medical advice.
7. NSAIDs, including Tivorbex ™, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization or even death. Be alert for the signs and symptoms of ulcerations and bleeding, such as upper abdominal pain, upset stomach/indigestion, black or dark tarry stools, or vomiting of blood. If these symptoms occur, stop taking Tivorbex ™ and seek medical advice. The use of aspirin and an NSAID, including Tivorbex ™, at the same time increases the risk of serious GI events.
8. Common adverse effects of Tivorbex ™ include edema, nausea, headache, dizziness, vomiting, constipation, itching, and upset stomach/indigestion.

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[2] Iroko Pharmaceuticals, LLC, Press Release: Iroko Pharmaceuticals Receives FDA Approval for Zorvolex™. Available online at: https://www.iroko.com/press-releases/iroko-pharmaceuticals-receives-fda-approval-for-zorvolex-2/. Last revised 10/18/13. Last accessed 3/19/14.

[3] Iroko Pharmaceuticals, LLC, Press Release: Iroko Pharmaceuticals Receives FDA Approval for Tivorbex™. Available online at: https://www.iroko.com/press-releases/iroko-pharmaceuticals-receives-fda-approval-for-tivorbex/. Last revised 2/24/14. Last accessed 3/19/14.

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[6] Zorvolex™ Full Prescribing Information. Iroko Pharmaceuticals, LLC. Available online at: https://www.zorvolex.com/wp-content/uploads/2013/12/Zorvolex_Approved_PI.pdf. Last revised 10/2013. Last accessed 3/19/14.

[7] Zorvolex™ Package Insert. Med Library.org. Available online at: http://medlibrary.org/lib/rx/meds/zorvolex-1/. Last revised 12/13/13. Last accessed 3/19/14.

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[9] Iroko Pharmaceuticals, LLC, Press Release: Iroko Pharmaceuticals Announces Acceptance for Filing of Zorvolex™ sNDA for the Treatment of Osteoarthritis Pain in Adults. Available online at: https://www.iroko.com/press-releases/iroko-pharmaceuticals-announces-acceptance-for-filing-of-zorvolex-snda-for-the-treatment-of-osteoarthritis-pain-in-adults/. Last revised 1/15/14. Last accessed 3/19/14.

[10] Tivorbex™ Full Prescribing Information. Iroko Pharmaceuticals, LLC. Available online at: https://www.iroko.com/wp-content/uploads/2014/02/tivorbexPI.pdf. Last revised 2/2014. Last accessed 4/1/14.

[11] Tivorbex™ Package Insert. Med Library.org. Available online at: http://medlibrary.org/lib/rx/meds/tivorbex/. Last revised 2/28/14. Last accessed 4/1/14.

[12] Indomethacin Drug Information. Micromedex 2.0. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 3/3/14. Last accessed 4/1/14.

Appendix H

Calendar Year 2013 Annual Review of Benign Prostatic Hyperplasia Medications

Oklahoma Health Care Authority
April 2014

Current Prior Authorization Criteria

Tier-2 Approval Criteria:

1. An FDA Approved Diagnosis; and
2. A 4-week trial of two Tier-1 medications from different pharmacological classes within the past 90 days; or
3. Documented adverse effect, drug interaction, or contraindication to all available Tier-1 products.

Tier-3 Approval Criteria:

1. An FDA Approved Diagnosis of Benign Prostatic Hyperplasia(BPH); and
2. A trial of at least two Tier-1 medications from different pharmacological classes; and
3. A 4-week trial of all Tier-2 medications within the past 5 months; or
4. Documented adverse effect, drug interaction, contraindication, or lack of efficacy to all available Tier-1 and Tier-2 products.
5. Authorizations for Cialis® (tadalafil) will be granted for 5mg tablets only.

Benign Prostatic Hyperplasia (BPH) Medications		
Tier 1	**Tier 2**	**Tier 3**
Alfuzosin (Uroxatral®) Doxazosin (Cardura®) Finasteride (Proscar®) Tamsulosin (Flomax®) Terazosin (Hytrin®)	Doxazosin ER (Cardura XL®) Dutasteride (Avodart®) Dutasteride/Tamsulosin (Jalyn®) Silodosin (Rapaflo®)	Tadalafil (Cialis®) 5mg

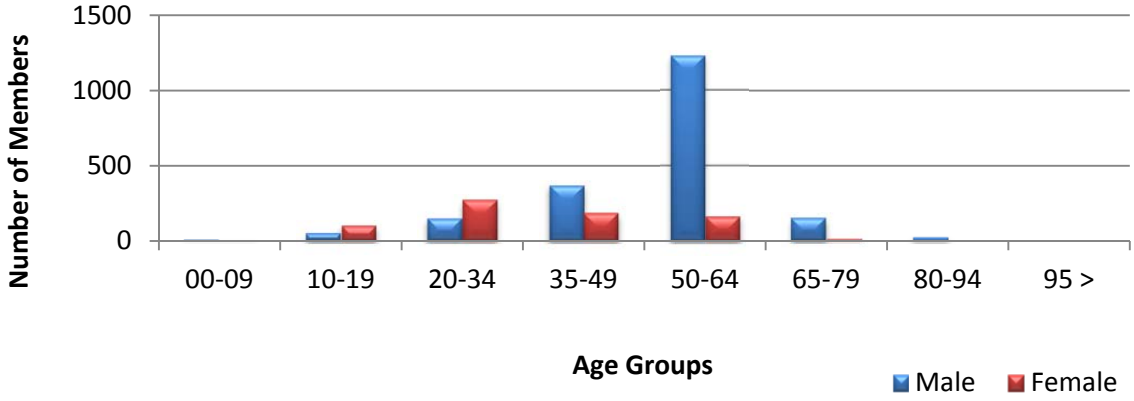
Utilization of BPH Medications

Comparison of Calendar Years

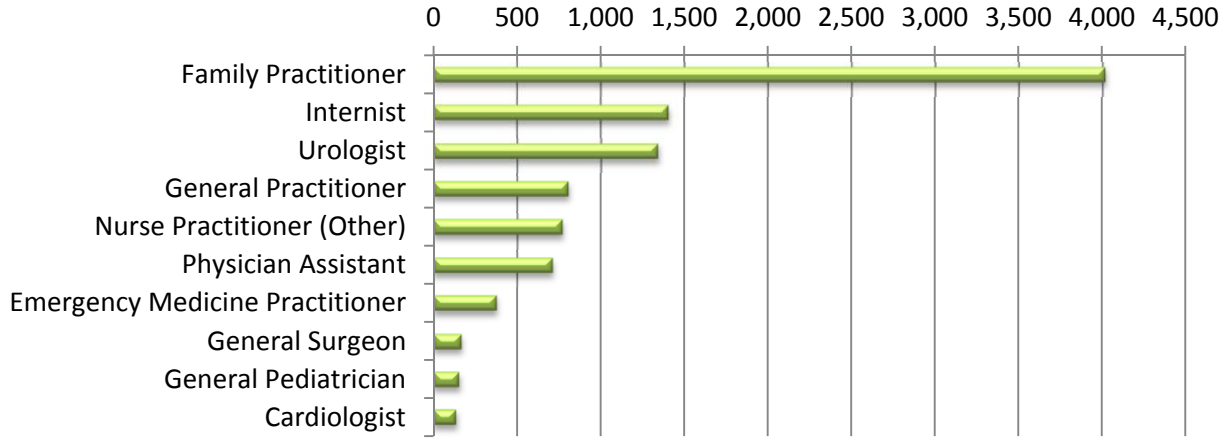
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Per-Diem Cost	Total Units	Total Days
2012	2,584	10,043	$198,085.73	$19.72	$0.54	404,134	369,665
2013	2,764	10,493	$205,853.84	$19.62	$0.54	415,783	380,602
% Change	**7.00%**	**4.50%**	**3.90%**	**-0.50%**	**0.00%**	**2.90%**	**3.00%**
Change	**180**	**450**	**$7,768.11**	**-$0.10**	**$0.00**	**11,649**	**10,937**

*Total number of unduplicated members.

Demographics of Members Utilizing BPH Medications



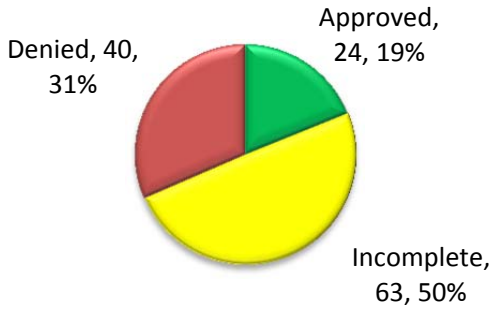
Top Prescriber Specialties of BPH Medications by Number of Claims



Prior Authorization of BPH Medications

There was a total of 127 petitions submitted for this category during calendar year 2013 Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expirations

- Avodart® (dutasteride)- 11/2015
- Jalyn® (dutasteride/tamsulosin)- 11/2015
- Rapaflo® (silodosin)- 12/2018
- Cialis® (tadalafil)- 11/2020

Sophiris Bio Inc. has one medication, PRX302, that has completed Phase 2 Clinical Trials and is currently recruiting for Phase 3 Clinical Trials. PRX302 is a localized injection that is non-systemic and highly targeted to prostate tissue, and is designed to be a single treatment for the long-term relief of BPH symptoms. PRX302 is a recombinant form of the native proaerolysin protein that has been engineered to be selectively activated by Prostate Specific Antigen (PSA), which is present only in prostate tissue. PRX302 works to relieve BPH symptoms by forming disruptive pores in the membranes of prostate cells resulting in selective cell death, thus creating a highly targeted, localized approach to killing prostate cells constricting the urethra. Phase 2 Clinical Trials showed a favorable safety profile and a clinically meaningful improvement in the International Prostate Symptom Score (IPSS) and urinary flow rate that was maintained for up to 12 months following a single, ultrasound-guided transperineal or transrectal intraprostatic injection.

Recommendations

The College of Pharmacy recommends no changes at this time.

Utilization Details of BPH Medications: Calendar Year 2013

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/DAY	COST/CLAIM	% COST
TAMSULOSIN PRODUCTS						
Tamsulosin 0.4mg caps	6,154	1,993	$83,906.71	$0.39	$13.63	40.76%
Flomax® 0.4mg caps	5	1	$2,083.69	$5.34	$416.74	1.01%
SUBTOTAL	**6,159**	**1,994***	**$85,990.40**	**$0.40**	**$13.96**	**41.77%**
DOXAZOSIN PRODUCTS						
Doxazosin 4mg tabs	948	217	$14,195.06	$0.41	$14.97	6.90%
Doxazosin 2mg tabs	612	166	$8,085.33	$0.36	$13.21	3.93%
Doxazosin 8mg tabs	292	67	$4,018.05	$0.35	$13.76	1.95%
Doxazosin 1mg tabs	227	87	$3,193.57	$0.38	$14.07	1.55%
Cardura® 8mg tabs	10	1	$90.97	$0.30	$9.10	0.04%
SUBTOTAL	**2,089**	**482***	**$29,582.98**	**$0.38**	**$14.16**	**14.37%**
FINASTERIDE PRODUCTS						
Finasteride 5mg tabs	787	177	$10,622.78	$0.34	$13.50	5.16%
SUBTOTAL	**787**	**177***	**$10,622.78**	**$0.34**	**$13.50**	**5.16%**
TERAZOSIN PRODUCTS						
Terazosin 2mg caps	327	81	$2,834.01	$0.22	$8.67	1.38%
Terazosin 5mg caps	310	72	$2,543.90	$0.19	$8.21	1.24%
Terazosin 1mg caps	213	62	$1,542.93	$0.20	$7.24	0.75%
Terazosin 10mg caps	80	26	$616.60	$0.16	$7.71	0.30%
SUBTOTAL	**930**	**225***	**$7,537.44**	**$0.20**	**$8.10**	**3.66%**
ALFUZOSIN PRODUCTS						
Alfuzosin 10mg tabs	150	31	$2,440.92	$0.40	$16.27	1.19%
SUBTOTAL	**150**	**31***	**$2,440.92**	**$0.40**	**$16.27**	**1.19%**
TIER-1 SUBTOTAL	**10,115**	**2,733***	**$136,174.52**	**$0.37**	**$13.46**	**66.15%**
DUTASTERIDE PRODUCTS						
Avodart® 0.5mg caps	237	48	$45,349.46	$4.45	$191.35	22.03%
SUBTOTAL	**237**	**48***	**$45,349.46**	**$4.45**	**$191.35**	**22.03%**
SILODOSIN PRODUCTS						
Rapaflo® 8mg caps	70	16	$11,782.53	$4.84	$168.32	5.72%
Rapaflo® 4mg caps	13	4	$2,919.26	$5.12	$224.56	1.42%
SUBTOTAL	**83**	**19***	**$14,701.79**	**$4.89**	**$177.13**	**7.14%**
DUTASTERIDE/TAMSULOSIN PRODUCTS						
Jalyn® 0.5/0.4mg caps	52	7	$7,914.16	$4.40	$152.20	3.84%
SUBTOTAL	**52**	**7***	**$7,914.16**	**$4.40**	**$152.20**	**3.84%**
TIER-2 SUBTOTAL	**372**	**70***	**$67,965.41**	**$4.54**	**$182.70**	**33.02%**
TADALAFIL PRODUCTS						
Cialis® 5mg tabs	6	1	$1,713.91	$9.52	$285.65	0.83%
SUBTOTAL	**6**	**1***	**$1,713.91**	**$9.52**	**$285.65**	**0.83%**
TIER-3 SUBTOTAL	**6**	**1***	**$1,713.91**	**$9.52**	**$285.65**	**0.83%**
TOTAL	**10,493**	**2,764***	**$205,853.84**	**$0.54**	**$19.62**	**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 2/4/14. Last accessed 2/5/14.
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Appendix I

Fiscal Year 2013 Annual Review of Muscle Relaxants and 30-Day Notice to Prior Authorize Lorzone™ (Chlorzoxazone)

Oklahoma Health Care Authority
April 2014

Current Prior Authorization Criteria

Skeletal Muscle Relaxants		
Tier 1	**Tier 2**	**Special PA**
Cyclobenzaprine (Flexeril®)	Metaxalone (Skelaxin®)	Carisoprodol (Soma®) 350mg
Baclofen (Lioresal®)		Carisoprodol w Aspirin
Tizanidine (Zanaflex®)		Carisoprodol, ASA, Codeine
Methocarbamol (Robaxin®)		Carisoprodol (Soma®) 250mg
Chlorzoxazone (Parafon Forte®)		Tizanidine Capsules (Zanaflex®)
Orphenadrine (Norflex®)		Cyclobenzaprine ER (Amrix®)
		Cyclobenzaprine 7.5mg (Fexmid®)

*Brand products are subject to the Brand Name Override where generic is available.

Tier-2 Approval Criteria:

1. Failure with at least two Tier-1 medications within the past 90 days defined as no beneficial response after at least two weeks of use during which time the drug has been titrated to the recommended dose.
2. Approvals will be for the duration of three months, except for members with chronic diseases such as multiple sclerosis, cerebral palsy, muscular dystrophy, paralysis, or other chronic musculoskeletal diagnosis confirmed with diagnostic results, in which case authorizations will be for the duration of one year.
3. For repeat authorizations, there must be documentation of failed withdrawal attempt within past three months defined as increase in pain and debilitating symptoms when medication was discontinued.

Soma® (Carisoprodol 350mg) or Carisoprodol 350mg Combination Products Approval Criteria:
A cumulative 90 day therapy window per 365 days will be in place for these products, further approval will be based on the following:

1. An additional approval for 1 month will be granted to allow titration or change to a Tier-1 muscle relaxant. This approval is one time only. Further authorizations will not be granted.
2. Clinical exceptions may be made for members with the following diagnosis and approvals will be granted for the duration of one year: multiple sclerosis, cerebral palsy, muscular dystrophy, or paralysis.
3. A quantity limit of 120 tablets per 30 days will apply.

Soma® (Carisoprodol 250mg) Approval Criteria:

1. An FDA approved diagnosis of acute musculoskeletal pain, in which case, the approval will be for 14 days per 365 day period. Conditions requiring chronic use will not be approved; and
2. Detailed documentation regarding member's inability to use other skeletal muscle relaxants including carisoprodol 350mg must be provided; and
3. A patient-specific, clinically significant reason why member cannot be drowsy for even a short period of time; and
4. Member must not have other current sedating medications in claims history.

Zanaflex® (Tizanidine Capsules) Approval Criteria:

1. Tizanidine tablets must be tried prior to consideration of the capsules; and
2. A patient-specific, clinically significant reason why the member cannot use the tablet formulation.

Amirix® (Cyclobenzaprine Extended-Release) and Fexmid® (Cyclobenzaprine 7.5mg) Approval Criteria:

1. Approval is based on clinical documentation of inability to take other generically available forms of cyclobenzaprine tablets; and
2. A quantity limit of 30 per 30 days will apply for Amirix® and 90 per 30 days for Fexmid®.

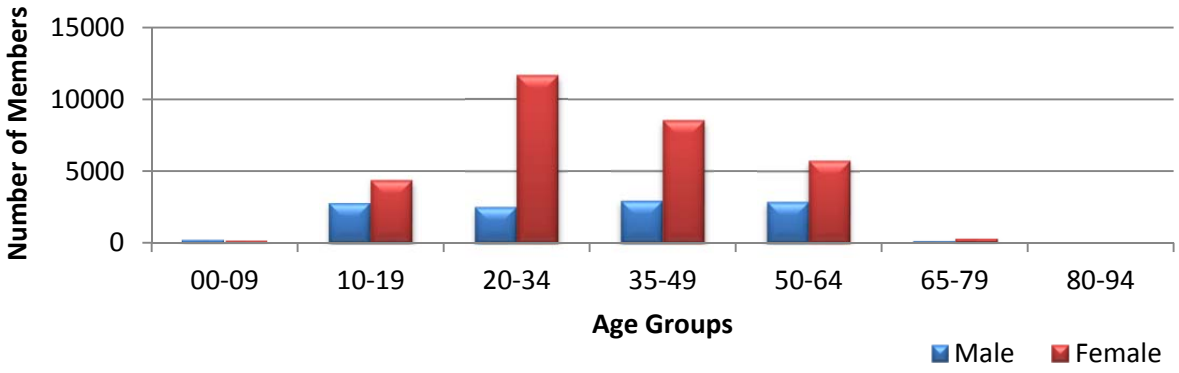
Utilization of Muscle Relaxants

Comparison of Fiscal Years

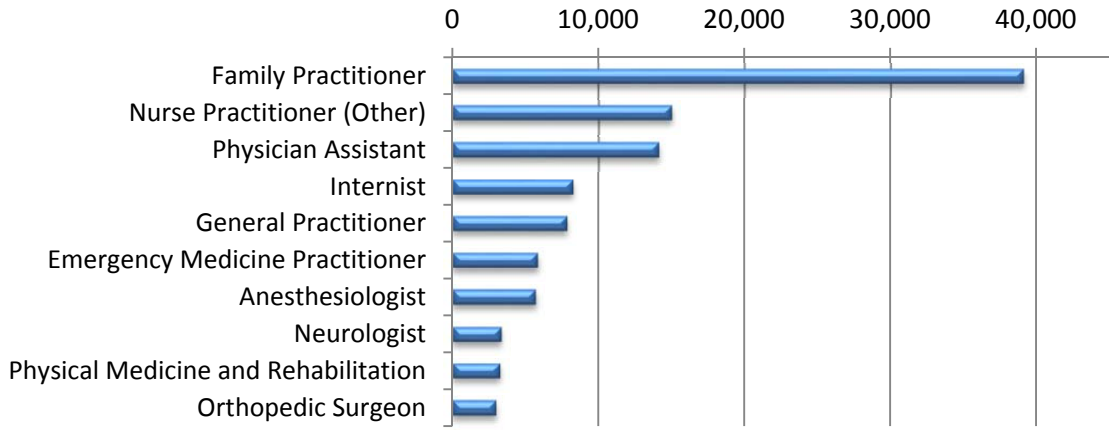
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	41,397	115,916	$1,275,817.39	$11.01	$0.47	7,586,211	2,714,174
2013	42,344	119,087	$1,459,910.99	$12.26	$0.52	7,785,369	2,825,471
% Change	**2.30%**	**2.70%**	**14.40%**	**11.40%**	**10.60%**	**2.60%**	**4.10%**
Change	**947**	**3,171**	**$184,093.60**	**$1.25**	**$0.05**	**199,158**	**111,297**

*Total number of unduplicated members

Demographics of Members Utilizing Muscle Relaxants



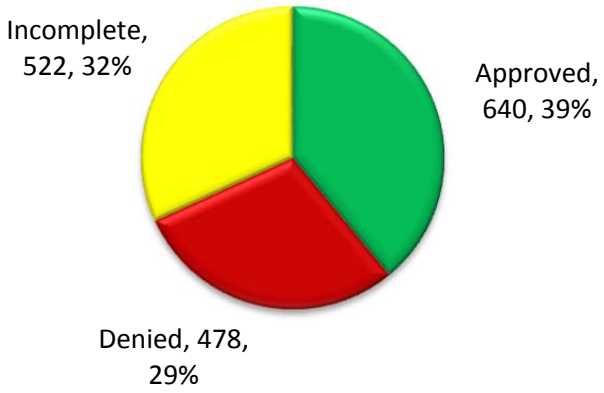
Top Prescriber Specialties of Muscle Relaxants by Number of Claims



Prior Authorization of Muscle Relaxants

There was a total of 1,640 petitions submitted for muscle relaxants during fiscal year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1, 2]

Patent Expirations

- Zanaflex® (tizanidine capsules)- 02/2012
- Amrix® (cyclobenzaprine extended-release)- 02/2025

FDA Update

- In January of 2014, the FDA advised consumers not to purchase or use Pro ArthMax®, a product promoted and sold as a dietary supplement for joint pain. FDA laboratory analysis confirmed that Pro ArthMax® contained the active drug ingredients diclofenac, ibuprofen, naproxen, indomethacin, nefopam, and chlorzoxazone.

Lorzone™ (Chlorzoxazone)[3,4]

- **Indication:** Lorzone™ (chlorzoxazone) is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute painful musculoskeletal conditions. Lorzone™ offers two new strengths (375mg and 750mg tablets) of chlorzoxazone. Chlorzoxazone is currently available generically in 500mg tablets.

- **Dosing:** The recommended dose is 375mg to 750mg by mouth three or four times daily.

- **Mechanism of Action:** Lorzone™ is a centrally-acting agent for painful musculoskeletal conditions. The mode of action of Lorzone™ has not been clearly identified, but may be related to its sedative properties. Data available from animal experiments as well as human study indicate that Lorzone™ acts primarily at the level of the spinal cord and subcortical areas of the brain where it inhibits multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm of varied etiology. The clinical result is a reduction of the skeletal muscle spasm with relief of pain and increased mobility of the involved muscles.

- **Efficacy:**
  - No clinical trials were performed for the approval of Lorzone™. The efficacy of Lorzone™ is based on previous approval of similar chlorzoxazone containing medications.
  - A published systematic review assessed the evidence for the comparative safety and efficacy of skeletal muscle relaxants for the treatment of spasticity and musculoskeletal conditions. This review found insufficient evidence to determine the relative efficacy or safety of chlorzoxazone for those specific conditions.

- **Utilization:**
  - There has been no utilization of Lorzone™ in the SoonerCare population in fiscal year 2013.
  - Generic chlorzoxazone 500mg tablets were utilized by approximately 820 members for a total of 1,590 claims during fiscal year 2013.

- **Cost:**

Lorzone™ or Chlorzoxaxone Dosage Form	EAC Per Tablet or Capsule	EAC Per Day	EAC for 30 days of Therapy
Lorzone™ 375mg and 750mg Tablets	$5.60	$22.40	$672.00
Chlorzoxazone 500mg Tablets	$0.25∞	$1.50	$45.00

EAC= estimated acquisition cost
∞ State maximum allowable cost (SMAC) pricing
Daily dosing based on an average daily dose of 750mg four times daily.

Recommendations

The College of Pharmacy recommends the addition of Lorzone™ (chlorzoxazone) to the special PA category of the Skeletal Muscle Relaxants Product Based Prior Authorization category. The following criteria will apply:

Lorzone ™ (Chlorzoxazone) Approval Criteria:

1. Generic chlorzoxazone 500mg tablets must be tried prior to consideration of Lorzone™.
2. A patient-specific, clinically significant reason why the member cannot use generic chlorzoxazone 500mg tablets.
3. The following quantity limits apply:
    a. Lorzone™ 375mg tablets: 120 tablets for 30 days
    b. Lorzone™ 750mg tablets: 120 tablets for 30 days

Skeletal Muscle Relaxants		
Tier 1	**Tier 2**	**Special PA**
Cyclobenzaprine (Flexeril®)	Metaxalone (Skelaxin®)	Carisoprodol (Soma®) 350mg
Baclofen (Lioresal®)		Carisoprodol w Aspirin
Tizanidine (Zanaflex®)		Carisoprodol, ASA, Codeine
Methocarbamol (Robaxin®)		Carisoprodol (Soma®) 250mg
Chlorzoxazone (Parafon Forte®)		Tizanidine Capsules (Zanaflex®)
Orphenadrine (Norflex®)		Cyclobenzaprine ER (Amrix®)
		Cyclobenzaprine 7.5mg (Fexmid®)
		Chlorzoxazone (Lorzone™)

Utilization Details of Muscle Relaxants

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim	Percent Cost
Cyclobenzaprine Products							
CYCLOBENZAPRINE TAB 10MG	50,351	23,613	$404,604.46	2.41	2.13	$8.04	27.71%
CYCLOBENZAPRINE TAB 5MG	7,491	4,905	$62,579.82	2.28	1.53	$8.35	4.29%
CYCLOBENZAPRINE POW HCL	10	8	$568.77	2.65	1.25	$56.88	0.04%
Subtotal	**57,852**	**27,606**	**$467,753.05**	**2.4**	**2.1**	**$8.09**	**32.04%**
Tizanidine Products							
TIZANIDINE TAB 4MG	17,555	5,775	$319,096.67	2.99	3.04	$18.18	21.86%
TIZANIDINE TAB 2MG	1,940	653	$27,413.02	2.7	2.97	$14.13	1.88%
Subtotal	**19,495**	**6,301**	**$346,509.69**	**2.96**	**3.09**	**$17.77**	**23.74%**
Baclofen Products							
BACLOFEN TAB 10MG	11,400	3,578	$90,268.99	3.16	3.19	$7.92	6.18%
BACLOFEN TAB 20MG	5,289	1,274	$84,716.27	3.76	4.15	$16.02	5.80%
BACLOFEN POW	218	49	$10,300.35	6.86	4.45	$47.25	0.71%
LIORESAL INT INJ 40MG/20	16	1	$30,927.76	1.95	16	$1,932.99	2.12%
Subtotal	**16,923**	**4,635**	**$216,213.37**	**3.4**	**3.65**	**$12.78**	**14.81%**
Methocarbamol Products							
METHOCARBAMOL TAB 750MG	5,016	2,484	$68,619.71	3.37	2.02	$13.68	4.70%
METHOCARBAMOL TAB 500MG	3,998	2,129	$48,435.33	3.19	1.88	$12.11	3.32%
Subtotal	**9,014**	**4,467**	**$117,055.04**	**3.29**	**2.02**	**$12.99**	**8.02%**
Orphenadrine Products							
ORPHENADRINE TAB 100MG ER	3,335	2,032	$67,854.09	1.96	1.64	$20.35	4.65%
ORPHEN/ASA/CAF 50-770-60MG	19	17	$985.22	2.52	1.12	$51.85	0.07%
ORPHEN/ASA/CAF 25-385-30MG	9	7	$607.12	3.69	1.29	$67.46	0.04%
Subtotal	**3,363**	**2,053**	**$69,446.43**	**1.96**	**1.64**	**$20.65**	**4.76%**
Chlorzoxazone Products							
CHLORZOXAZONE TAB 500MG	1,590	820	$14,137.05	2.94	1.94	$8.89	0.97%
Subtotal	**1,590**	**820**	**$14,137.05**	**2.94**	**1.94**	**$8.89**	**0.97%**
Tier-1 Subtotal	**108,237**	**39,691**	**$1,231,114.63**	**2.77**	**2.73**	**$11.37**	**84.34%**
Metaxalone Products							
METAXALONE TAB 800MG	469	163	$129,202.66	2.69	2.88	$275.49	8.85%
Subtotal	**469**	**163**	**$129,202.66**	**2.69**	**2.88**	**$275.49**	**8.85%**
Tier-2 Subtotal	**469**	**163**	**$129,202.66**	**2.69**	**2.88**	**$275.49**	**8.85%**
Carisoprodol Products							
CARISOPRODOL TAB 350MG	10,344	4,635	$89,275.83	2.66	2.23	$8.63	6.12%
CARISOPR/ASA TAB 200-325	12	8	$1,078.91	3.04	1.5	$89.91	0.07%
CARISOPRODOL TAB 250MG	6	6	$1,152.83	3.03	1	$192.14	0.08%
CARISOPR/ASA/COD 200-325-16MG	5	4	$457.35	3.94	1.25	$91.47	0.03%
Subtotal	**10,367**	**4,650**	**$91,964.92**	**2.66**	**2.23**	**$8.87**	**6.30%**
Cyclobenzaprine Products							
AMRIX CAP 15MG	13	2	$7,441.86	1	6.5	$572.45	0.51%
Subtotal	**13**	**2**	**$7,441.86**	**1**	**6.5**	**$572.45**	**0.51%**

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim	Percent Cost
Tizanidine Products							
TIZANIDINE CAP 6MG	1	1	$186.92	3	1	$186.92	0.01%
Subtotal	**1**	**1**	**$186.92**	**3**	**1**	**$186.92**	**0.01%**
Special PA Subtotal	**10,381**	**4,652**	**$99,593.70**	**2.66**	**2.23**	**$9.59**	**6.82%**
Total	**119,087**	**42,344***	**$1,459,910.99**	**2.76**	**2.81**	**$12.26**	**100%**

*Total number of unduplicated members

PRODUCT DETAILS OF LORZONE™ (CHLORZOXAZONE)[3]

INDICATIONS AND USE:

- Lorzone™ (chlorzoxazone) is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute painful musculoskeletal conditions.

DOSAGE FORMS:

- Lorzone™ is available as 375mg and 750mg tablets.

ADMISTRATION:

- The recommended dosing of Lorzone™ is 375mg to 750mg by mouth three or four times daily.
- If inadequate response is not obtained with a dose of 375mg or 500mg (2/3 of a 750mg tablet) three or four times daily, the dose may be increased to 750mg three or four times daily.
- As improvement occurs dosage can usually be reduced.
- Lorzone™ can be taken without regard to food.

CONTRAINDICATIONS:

- The use of Lorzone™ is contraindicated in patients with known intolerance to the drug.

SPECIAL POPULATIONS:

- **Pregnancy:** The safe use of Lorzone™ in pregnancy has not been established with respect to possible adverse effects upon fetal development. It should only be used in women of childbearing potential when the potential benefits outweigh the possible risks.
- **Breast feeding:** Infant risk cannot be ruled out.
- **Pediatric Patients:** The risks and benefits of treatment with Lorzone™ in children younger than 18 years of age are not established.

WARNINGS AND PRECAUTIONS:

- Serious (including fatal) hepatocellular toxicity has been reported in patients receiving Lorzone™. The mechanism is unknown but appears to be idiosyncratic and unpredictable. Factors predisposing patients to this rare event are not known.
    - Patients should be instructed to report early signs and/or symptoms of hepatoxicity such as fever, rash, anorexia, nausea, vomiting, fatigue, right upper quadrant pain, dark urine, or jaundice.
    - Lorzone™ use should be discontinued if a patient develops abnormal liver enzymes (e.g., AST, ALT, alkaline phosphates and bilirubin).
    - Lorzone™ should be discontinued immediately, and a physician consulted if any symptoms suggestive of liver dysfunction are observed.
- Lorzone™ should be used with caution in patients with known allergies or with a history of allergic reactions to drugs. If sensitivity reaction occurs such urticaria, redness, or itching of the skin, the drug should be stopped.

ADVERSE REACTIONS:

- Use of Lorzone™ has been associated with gastrointestinal bleeding, drowsiness, dizziness, light-headedness, malaise, or overstimulation.
- Rarely, allergic-type skin rashes, petechiae, or ecchymoses have developed during treatment.
- Angioneurotic edema or anaphylactic reactions have occurred but are extremely rare.
- There is no evidence that Lorzone™ will cause renal damage. Rarely, a patient may note discoloration of the urine resulting from a phenolic metabolite of Lorzone™. This finding is of no known clinical significance.

DRUG INTERACTIONS:

- The concomitant use of Lorzone™ and alcohol or other central nervous system depressants may have an additive effect.

PATIENT COUNSELING INFORMATION:

1. Take Lorzone™ by mouth as your doctor has prescribed.
2. Lorzone™ may cause light-headedness, dizziness, or somnolence. You should avoid activities requiring mental alertness or coordination until you know how Lorzone™ will affect you.
3. Lorzone™ may cause may cause malaise or overstimulation.
4. Lorzone™ may discolor your urine to an orange or red color.
5. Lorzone™ can cause liver complications. You should report signs/symptoms of hepatotoxicity to your doctor immediately. Signs of hepatotoxicity include fever, rash, anorexia, nausea, vomiting, fatigue, right upper quadrant pain, dark urine, or jaundice.
6. Avoid concomitant use of CNS depressants, including alcohol, while taking Lorzone™ as this may cause additive CNS depression.

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[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://orange-book.findthebest.com/. Last revised: 03/18/14. Last accessed 03/20/2014.

[2] FDA: Public Notification: Pro ArthMax® Contains Several Hidden Drug Ingredients. Available online at: http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/medicationhealthfraud/ucm381783.htm. Last revised 01/15/2014. Last accessed 03/20/2014.

[3] Lorzone™ Product Information. Vertical Pharmaceuticals Inc. Available online at: http://www.verticalpharma.com/sites/vertical/files/LorzonePrescribing%20Info.pdf. Last revised 10/2010. Last accessed 03/20/2014.

[4] Chou R, Peterson K, Helfand M. Comparative Efficacy and Safety of Skeletal Muscle Relaxants for Spasticity and Musculoskeletal Conditions: A Systematic Review. *J Pain Symptom Manage.* August 2004; 28 (2): 140-75.

Appendix J

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

FDA NEWS RELEASE

For Immediate Release: March 21, 2014

FDA approves Otezla to treat psoriatic arthritis

The U.S. Food and Drug Administration today approved Otezla (apremilast) to treat adults with active psoriatic arthritis (PsA).

PsA is a form of arthritis that affects some people with psoriasis. Most people develop psoriasis first and are later diagnosed with PsA. Joint pain, stiffness and swelling are the main signs and symptoms of PsA. Currently approved treatments for PsA include corticosteroids, tumor necrosis factor (TNF) blockers, and an interleukin-12/interleukin-23 inhibitor.

The safety and effectiveness of Otezla, an inhibitor of phosphodieasterase-4 (PDE-4), were evaluated in three clinical trials involving 1,493 patients with active PsA. Patients treated with Otezla showed improvement in signs and symptoms of PsA, including tender and swollen joints and physical function, compared to placebo.

Patients treated with Otezla should have their weight monitored regularly by a healthcare professional. If unexplained or clinically significant weight loss occurs, the weight loss should be evaluated and discontinuation of treatment should be considered. Treatment with Otezla was also associated with an increase in reports of depression compared to placebo.

The FDA is requiring a pregnancy exposure registry as a post-marketing requirement to assess the risks to pregnant women related to Otezla exposure.

In clinical trials, the most common side effects observed in patients treated with Otezla were diarrhea, nausea, and headache.

Otezla is manufactured for Celgene Corporation, Summit, N.J.

FDA NEWS RELEASE

For Immediate Release: March 28, 2014

FDA approves Topamax for migraine prevention in adolescents

First approved treatment for ages 12 to 17

The U.S. Food and Drug Administration approved Topamax (topiramate) for prevention (prophylaxis) of migraine headaches in adolescents ages 12 to 17. This is the first FDA approval of a drug for migraine prevention in this age group. The medication is taken on a daily basis to reduce the frequency of migraine headaches.

Topamax was first approved by the FDA in 1996 to prevent seizures. It was approved for migraine prevention in adults in 2004.

About 12 percent of the U.S. population experiences migraine headaches. Migraine headaches are characterized by episodes of throbbing and pulsating pain in the head, and may occur several times per month. Other common symptoms include increased sensitivity to light, noise, and odors, as well as nausea and vomiting. Many patients experience their first migraine attack before reaching adulthood, and migraine can be just as disabling in teens as it is in adults.

The safety and effectiveness of Topamax in preventing migraine headaches in adolescents ages 12 to 17 was established in a clinical trial that enrolled 103 participants. Those treated with Topamax experienced a decrease in the frequency of migraine of approximately 72 percent compared to 44 percent in participants that took an inactive drug (placebo).

The most common adverse reactions with the approved dose of Topamax (100 milligrams) were paresthesia (a burning or prickling sensation felt in the hands, arms, legs, or feet), upper respiratory infection, anorexia (loss of appetite), and abdominal pain.

Topamax must be dispensed with a Medication Guide that describes important safety information about the drug. Topamax and all anti-epileptic drugs may increase the risk of suicidal thoughts and behavior, and patients should be advised of the need to be alert for the emergence of, or worsening of, the signs and symptoms of depression, or unusual changes in mood or behavior.

Topamax increases the risk of the development of cleft lip and/or cleft palate (oral clefts) in infants born to women who take the drug during pregnancy. The benefits and risks of Topamax should be carefully weighed before using it in women of childbearing age. If the decision is made to use the medication by a woman of childbearing age, effective birth control should be used.
Topamax is manufactured by Janssen Pharmaceuticals, Inc. of Titusville, N.J.

FDA NEWS RELEASE

FDA clarifies Warning about Pediatric Use of Revatio (sildenafil) for Pulmonary Arterial Hypertension

This information is in follow-up to the FDA Drug Safety Communication issued on August 30, 2012.

[03-31-2014] The U.S. Food and Drug Administration (FDA) is clarifying its previous recommendation related to prescribing Revatio (sildenafil) for children with pulmonary arterial hypertension (PAH). Revatio is FDA-approved only to treat PAH in adults, not in children; however, health care professionals must consider whether the benefits of treatment with the drug are likely to outweigh its potential risks for each patient.
FDA revised the Revatio drug label in August 2012, adding a warning stating that "use of Revatio, particularly chronic use, is not recommended in children." This recommendation was based on an observation of increasing mortality with increasing Revatio doses in a long-term clinical trial in pediatric patients with PAH. FDA also issued a Drug Safety Communication at that time.
The purpose of the recommendation was to raise awareness of clinical trial results showing a higher risk of mortality in pediatric patients taking a high dose of Revatio when compared to pediatric patients taking a low dose. This recommendation was **not** intended to suggest that Revatio should *never* be used in children; however, some health care professionals have interpreted this information as a contraindication, and have refused to prescribe or administer the drug. We recognize there may be situations in which the benefit-risk profile of Revatio may be acceptable in individual children, for example, when other treatment options are limited and Revatio can be used with close monitoring.
The evidence behind our initial recommendation has not changed; we are simply clarifying the strength of the warning communicated in the Revatio drug label.

Safety Announcements

Effexor XR 150 Mg Extended-Release Capsules (Pfizer) and Venlafaxine HCl 150 Mg Extended-Release Capsules (Greenstone): Recall - Possible Presence of Tikosyn Capsules

[Posted 03/07/2014]
AUDIENCE: Pharmacy, Psychiatry, Family Practice
ISSUE: Pfizer Inc. issued a voluntary recall of one lot of 30-count Effexor XR (venlafaxine HCl) 150 mg extended-release capsules, one lot of 90-count Effexor XR (venlafaxine HCl) 150 mg extended-release capsules, and one lot of 90-count Greenstone LLC-branded Venlafaxine HC1 150 mg extended-release capsules. This action is being taken because of a pharmacist report that one bottle of Pfizer's Effexor XR contained one capsule of Tikosyn (dofetilide) 0.25mg in addition to the Effexor XR capsules.
The use of Tikosyn by an Effexor XR/Venlafaxine HCl patient, where the contraindications and drug-drug interactions with Tikosyn have not been considered by the prescribing physician, could cause serious adverse health consequences that could be fatal.
This recall is to the patient level and involves Pfizer lot numbers V130142 and V130140, which both expire in October 2015, and Greenstone lot number V130014, which expires in August 2015.
BACKGROUND: These products were distributed nationally to wholesalers, distributors, certain government agencies, patient assistance programs and retailers, such as pharmacies and hospitals. These direct customers are being notified by UPS next day mail, and Pfizer is arranging for the return of all recalled products.
RECOMMENDATION: Pharmacists should immediately quarantine, discontinue distribution of and return all recalled lots of these products, as well as notify any of their customers to whom they distributed the products. Patients with affected product should notify their physicians and/or return product to their pharmacies. Patients with questions regarding the return of product should contact Stericycle at 1-888-345-0481 (Monday to Friday 8am to 5pm ET). Patients with questions regarding this recall can contact Pfizer Medical Information at 1-800-438-1985 (Monday to Thursday 9am to 8pm ET or Friday, 9am to 5pm ET).

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Safety Announcements

FDA approves label changes for antibacterial Doribax (doripenem) describing increased risk of death for ventilator patients with pneumonia

This is an update to the January 5, 2012 FDA Statement on a recently terminated clinical trial with Doribax (doripenem).

[03-06-2014] The U.S. Food and Drug Administration (FDA) has concluded that Doribax (doripenem), an antibacterial drug that has been used to treat patients who develop pneumonia while on ventilators, carries an increased risk of death and lower clinical cure rates compared to use of imipenem and cilastatin for injection (marketed in the U.S. under the name Primaxin). Based on our analysis of data from a three-year clinical trial that was prematurely stopped in 2011 due to these safety concerns, we have approved changes to the Doribax drug label that describe these risks.

Doribax is not approved to treat any type of pneumonia, and the revised label also includes a new warning about this unapproved use. Health care professionals should consider whether the benefits of Doribax treatment are likely to exceed its potential risks in patients who develop pneumonia while on ventilators. Doribax is still considered safe and effective for its FDA-approved indications - treatment of adults with complicated intra-abdominal infections and complicated urinary tract infections, including kidney infections called pyelonephritis.

In the clinical trial that was stopped early, patients with ventilator-associated bacterial pneumonia received either 7-day Doribax treatment or 10-day treatment with imipenem and cilastatin, another antibacterial drug. In the intent-to-treat population, the 28-day all-cause mortality was higher in the Doribax arm (23.0 percent; n=31/135) than in the imipenem and cilastatin arm (16.7 percent; n=22/132) . Clinical cure rates were also lower in the Doribax arm.

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

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

Amikacin Injection
Ammonium Chloride Injection (initial posting date 3/8/2013) UPDATED 3/31/2014
Amytal Sodium Injection (initial posting date 1/31/2013)
Atropine Sulfate Injection UPDATED 3/31/2014
Barium Sulfate for Suspension (initial posting date 10/12/2012) UPDATED 3/25/2014
Bumetanide Injection (initial posting date 6/21/2012)
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection UPDATED 3/31/2014
Caffeine and Ergotamine Tartrate (Cafergot) Tablets (initial posting date 3/8/2012)
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection
Calcium Chloride Injection (initial posting date 12/13/2012)
Calcium Gluconate Injection (initial posting date 1/10/2013) UPDATED 3/26/2014
Chloramphenicol Sodium Succinate Injection (initial posting date 1/7/2014)
Chromic Chloride Injection UPDATED 3/31/2014
Cidofovir Injection (initial posting date 2/15/2013)
Clindamycin phosphate (Cleocin) Injection (initial posting date 10/2/2013) UPDATED 3/31/2014
Copper Injection (initial posting date 4/25/2013) UPDATED 3/31/2014
Cyanocobalamin Injection (initial posting date 1/25/2013)
Daunorubicin Hydrochloride Solution for Injection UPDATED 3/27/2014
Dexamethasone Sodium Phosphate Injection (initial posting date 1/15/2013) UPDATED 3/31/2014
Dexmethylphenidate Hydrochloride (Focalin) (initial posting date 2/13/2014) UPDATED 3/27/2014
Dobutamine Hydrochloride Injection (initial posting date 4/26/2013) UPDATED 3/31/2014
Doxorubicin (Adriamycin) Lyophilized Powder (initial posting date 12/2/2011)

Echothiophate Iodide (Phospholine Iodide) Ophthalmic Kit (initial posting date 3/20/2014)
Epinephrine Injection (initial posting date 4/27/2012) UPDATED 3/31/2014
Epinephrine 1mg/mL (Preservative Free) (initial posting date 6/21/2012)
Ethiodol (Ethiodized Oil) Ampules
Fentanyl Citrate (Sublimaze) Injection UPDATED 3/31/2014
Heparin Sodium Injection (initial posting date 7/5/2012) UPDATED 3/26/2014
Intravenous Fat Emulsion
Ketorolac Tromethamine Injection
Leucovorin Calcium Lyophilized Powder for Injection UPDATED 3/26/2014
Leuprolide Acetate Injection
Lidocaine Hydrochloride (Xylocaine) Injection (initial posting date - 2/22/2012) UPDATED 3/26/2014
Liotrix (Thyrolar) Tablets
Lorazepam (Ativan) Injection UPDATED 3/31/2014
Magnesium Sulfate Injection UPDATED 3/31/2014
Mannitol (Osmitrol, Resectisol) Injection (initial posting date - 12/21/2011)
Mecasermin [rDNA origin] (Increlex) Injection (initial posting date - 4/26/2013)
Methazolamide (Glauctabs, Neptazane) Tablets (initial posting date - 6/29/2012) 4
Methyldopate Hydrochloride Injection
Methylin Chewable Tablets (initial posting date 2/19/2013)
Methylphenidate Hydrochloride ER Tablets (initial posting date 2/19/2013) UPDATED 3/27/2014
Methylphenidate Hydrochloride Tablets (initial posting date 2/19/2013) UPDATED 3/27/2014
Methylprednisolone Sodium Succinate Injection (initial posting date 2/14/2014)
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free) UPDATED 3/31/2014
Multi-Vitamin Infusion (Adult and Pediatric)
Nalbuphine Hydrochloride (Nubain) Injection (initial posting date 5/15/2012) UPDATED 3/31/2014
Neostigmine Methylsulfate Injection (initial posting date 1/14/2013) UPDATED 3/31/2014
Nitroglycerin in 5% Dextrose Injection (initial posting date 12/20/2013) UPDATED 3/31/2014
Ondansetron (Zofran) Injection UPDATED 3/31/2014
Pancuronium Bromide Injection
Papaverine Hydrochloride Injection (initial posting date 12/17/2012)
Phosphate (Glycophos) Injection (initial posting date 5/29/2013)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting date 6/1/2012)
Potassium Acetate Injection, USP 2mEq/mL
Potassium Chloride Injection (initial posting date 5/15/2012) UPDATED 3/31/2014
Potassium Phosphate Injection UPDATED 3/24/2014
Procainamide HCL Injection UPDATED 3/31/2014
Prochlorperazine Injection (initial posting date 1/30/2012)
Reserpine Tablets (initial posting date 4/17/2013)
Rifampin for Injection (initial posting date 3/22/2013) UPDATED 3/31/2014
Secretin Synthetic Human (ChiRhoStim) Injection (ChiRhoStim) (initial posting date 6/15/2012) UPDATED 3/24/2014
Selenium Injection
Sincalide (Kinevac) Lyophilized Powder for Injection (initial posting date 6/21/2013)
Sodium Chloride 0.9% Injection Bags (initial posting date 1/15/2014) UPDATED 3/31/2014
Sodium Chloride 23.4%
Sodium Phosphate Injection
Succinylcholine (Anectine, Quelicin) Injection (initial posting date 8/17/2012)
Sufentanil Citrate (Sufenta) Injection UPDATED 3/31/2014
Telavancin (Vibativ) Injection
Tesamorelin (Egrifta) Injection Kit (initial posting date 3/26/2014) New!!
Thiotepa (Thioplex) for Injection
Ticarcillin Disodium/Clavulanic Potassium (Timentin) Injection (initial posting date 8/16/2012)

Tiopronin (Thiola) (initial posting date 10/31/2013)
Tobramycin Solution for Injection UPDATED 3/31/2014
Trace Elements (initial posting date 1/24/2013)
Verapamil Hydrochloride Injection, USP (initial posting date 4/17/2013) UPDATED 3/31/2014
Vitamin A Palmitate (Aquasol A)
Zinc Injection (initial posting date 2/15/2012) UPDATED 3/24/2014