Drug Utilization Review Board

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1A
Oklahoma City, Oklahoma 73107
Ponca Room

Wednesday
February 12, 2014
6:00 p.m.

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 – February 12, 2014**

DATE: February 3, 2014

NOTE: The DUR Board will meet at 6:00 p.m. The meeting will be held in the Ponca Room at the Oklahoma Health Care Authority Offices in Shepherd Mall. (North Entrance)

Enclosed are the following items related to the February 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 Unit, SoonerPsych Program Update – See Appendix B

Action Item – Vote to Prior Authorize Procysbi™ (Cysteamine Bitartrate) – See Appendix C

Action Item – Vote to Prior Authorize Ravicti® (Glycerol Phenylbutyrate) – See Appendix D

Action Item – Vote to Prior Authorize Sirturo™ (Bedaquiline Fumarate) – See Appendix E

Action Item – Vote to Prior Authorize Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa) – See Appendix F

Drug Utilization Review of Pulmonary Arterial Hypertension Medications and 30 Day Notice to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan)– See Appendix G

Drug Utilization Review of Cephalosporin Antibiotics and 30 Day Notice to Prior Authorize Select Cephalosporins – See Appendix H

Drug Utilization Review of Ophthalmic Anti-Inflammatory Medications– See Appendix I

FDA and DEA Updates – See Appendix J

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – February 12, 2014 @ 6:00 p.m.

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1-A
Oklahoma City, Oklahoma 73107
Ponca Room (North Entrance)

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. December 11, 2013 DUR Minutes – Vote
   B. December 11, 2013 DUR Recommendation Memorandum
   C. Correspondence

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

4. Update on DUR/ Medication Coverage Authorization Unit, SoonerPsych Program Update – See Appendix B
   A. Medication Coverage Activity for January 2014
   B. Pharmacy Help Desk Activity for January 2014
   C. SoonerPsych Program Update

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

5. Action Item – Vote to Prior Authorize Procysbi™ (Cysteamine Bitartrate) – See Appendix C
   A. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Ravicti® (Glycerol Phenylbutyrate) – See Appendix D
   A. COP Recommendations

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

7. Action Item – Vote to Prior Authorize Sirturo™ (Bedaquiline Fumarate) – See Appendix E
   A. COP Recommendations

Items to be presented by Dr. Le, Dr. Muchmore, Chairman

8. Action Item – Vote to Prior Authorize Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa) – See Appendix F
   A. COP Recommendations

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

9. Drug Utilization Review of Pulmonary Arterial Hypertension Medications and 30 Day Notice to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan) – Appendix G

A. Introduction
B. Current Authorization Criteria
C. Utilization Details
D. Prior Authorization
E. Market News and Updates
F. COP Recommendations
G. Utilization Details
H. Product Details of Adempas®
I. Product Details of Opsumit®

Items to be presented by Dr. Le, Dr. Muchmore, Chairman

10. Drug Utilization Review of Cephalosporin Antibiotics and 30 Day Notice to Prior Authorize Select Cephalosporins – See Appendix H

A. Introduction
B. Utilization
C. COP Recommendations
D. Utilization Details

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

11. Drug Utilization Review of Ophthalmic Anti-Inflammatory Medications – See Appendix I

A. Introduction
B. Utilization
C. Market News and Updates
D. COP Recommendations

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 JANUARY 8, 2014

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.		x
Anetta Harrell, Pharm.D.	x	
Evie Knisely, Pharm.D.	x	
Thomas Kuhls, M.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	
Jo'Nel Weber, Pharm.D.; Clinical Pharmacist		x
Graduate Students: Tim Pham		x
Visiting Pharmacy Student(s): Lakeisha Fisher, Jennifer Tieu	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	
Jill Ratterman, D.Ph.; Pharmacy Specialist		x
Garth Splinter, M.D., M.B.A.; Medicaid Director		x
Kerri Wade, Pharmacy Operations Manager	x	

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

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.		x
Anetta Harrell, Pharm.D.	x	
Evie Knisely, Pharm.D.	x	
Thomas Kuhls, M.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	
Jo'Nel Weber, Pharm.D.; Clinical Pharmacist		x
Graduate Students: Tim Pham		x
Visiting Pharmacy Student(s): Lakeisha Fisher, Jennifer Tieu	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	
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	Don Kempin, Novo Nordisk	Brian Maves, Pfizer
Eduardo Delugo, Novartis	Russell Wilson, J&J	Sharon Jackson, GSK
Phillip Lafferty, Celgene	Jim Fowler, Astra Zenca	
Jon A. Maguire, GSK	Roger Grotzinger, BMS	
Mark Livesay, PPOK	Kathy Phillips, Novo Nordisk	

PRESENT FOR PUBLIC COMMENT:	
Shawna Kittridge	Mercer
Barb Mart	Mercer
James Osborne	GSK
James Royall, MD	OUHSC
Mai Duong	Novartis
Heather Poole	Self

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**

Agenda Item: No 3 Speaker: Shawna Kittridge
Agenda Item: No 3 Speaker: Barb Mart
Agenda Item: No 6 Speaker: James Osborne
Agenda Item: No 10 Speaker: Dr. James Royall
Agenda Item: No 10 Speaker: Mai Duong
Agenda Item: No 10 Speaker: Heather Poole

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **INDEPENDENT REVIEW OF THE SOONERCARE PHARMACY BENEFIT AND MANAGEMENT**

AGENDA ITEM NO. 4: **APPROVAL OF DUR BOARD MINUTES**

4A: DECEMBER 11, 2013 DUR MINUTES

4B: DECEMBER 11, 2013 DUR RECOMMENDATION MEMORANDUM

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: **UPDATE ON DUR / MEDICATION COVERAGE AUTHORIZATION UNIT**

5A: MEDICATION COVERAGE ACTIVITY FOR DECEMBER 2013

5B: PHARMACY HELP DESK ACTIVITY FOR DECEMBER 2013

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 6:</u> **VOTE TO PRIOR AUTHORIZE BREO™ ELLIPTA™ (FLUTICASONE FUROATE AND VILANTEROL INHALATION POWDER)**

6A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 7:</u> **30 DAY NOTICE TO PRIOR AUTHORIZE PROCYSBI™ (CYSTEAMINE BITARTRATE)**

7A: INTRODUCTION

7B: MEDICATION SUMMARY

7C: COP RECOMMENDATIONS

7D: PRODUCT DETAILS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 8:</u> **30 DAY NOTICE TO PRIOR AUTHORIZE RAVICTI® (GLYCEROL PHENYLBUTYRATE)**

8A: INTRODUCTION

8B: MEDICATION SUMMARY

8C: COP RECOMMENDATIONS

8D: PRODUCT DETAILS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 9:</u> **30 DAY NOTICE TO PRIOR AUTHORIZE SIRTURO™ (BEDAQUILINE FUMARATE)**

9A: INTRODUCTION

9B: MEDICATION SUMMARY

9C: COP RECOMMENDATIONS

9D: PRODUCT DETAILS

Materials included in agenda packet; presented Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 10:</u> **30 DAY NOTICE TO PRIOR AUTHORIZE TOBI® (TOBRAMYCIN SOLUTION), TOBI® PODHALER™ (TOBRAMYCIN POWDER), AND PULMOZYME® (DORNASE ALFA)**

10A: INTRODUCTION

10B: UTILIZATION REVIEW

10C: UTILIZATION DETAILS

10D: COP RECOMMENDATIONS

Materials included in agenda packet; presented Dr. Le

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 11:</u> **FDA AND DEA UPDATES**

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

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 12:</u> **FUTURE BUSINESS**

Materials included in agenda packet; submitted by Dr. Cothran

12A: ANNUAL REVIEWS

12B: NEW PRODUCT REVIEWS

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 13:</u> **ADJOURNMENT**

The meeting was adjourned at 7:59 pm

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: January 09, 2014

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

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

Subject: DUR Board Recommendations from Meeting of January 08, 2014

Recommendation 1: Vote to Prior Authorize Breo™ Ellipta™ (Fluticasone Furoate/Vilanterol Inhalation Powder)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Breo™ Ellipta™ (fluticasone furoate/vilanterol inhalation powder) with the following criteria:

Consideration for approval requires the following:

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

Recommendation 2: 30 Day Notice to Prior Authorize Procysbi™ (Cysteamine Bitartrate)

NO ACTION REQUIRED.

Recommendation 3: 30 Day Notice to Prior Authorize Ravicti® (Glycerol Phenylbutyrate)

NO ACTION REQUIRED.

Recommendation 4: 30 Day Notice to Prior Authorize Sirturo™ (Bedaquiline)

NO ACTION REQUIRED.

Recommendation 5: 30 Day Notice to Prior Authorize Tobi® (Tobramycin Solution), Tobi® Podhaler™ (Tobramycin Powder), and Pulmozyme® (Dornase Alfa)

NO ACTION REQUIRED.

January 24th, 2014 The OU Child Study Center

Mr. Terry Cothran and members of the Drug Utilization Review Board,

We are writing from our Developmental and Behavioral Pediatrics practice at the OU Child Study Center expressing our concern about the current revision to the tier system of approved medications for Attention Deficit Hyperactivity Disorder (ADHD). In particular, we would like to see Concerta® and Adderall XR®, or their generic equivalents, returned to the tier 1 approved list. We also appreciate that our request is likely to conflict with what we presume to be OHCA's cost-containment goals that likely led to the changes in the tier system.

We feel compelled to request these changes given that we provide ADHD-related care to almost 300 SoonerCare members per year – in about 900 visits per year. We base our concerns on available scientific data, the pharmacologic differences between the listed medications, and our clinical expertise. The new list of tier one long-acting medications in the methylphenidate (MPH) category lacks a 12 hour preparation similar to that of OROS-MPH (Concerta®). The longest-acting tier 1 preparation, MPH CD (Metadate CD®), is designed to last 8 hours. Our patients' families taught us that 8 hours makes for inadequate coverage in a great many circumstances – particularly when children attend after school programs, have homework, or are cared for by adults other than their parents in the early afternoon. After the dose wears off, the child will need to take another dose of medication to provide afternoon coverage. This may ultimately lead to additional costs to OHCA. Adherence and symptom control with multiple doses are challenging for families, and in fact problems with adherence were the reasons for designing longer-acting medications. We feel that longer-acting formulations are commonly required for symptom improvements by reducing the burden of adherence. The current tier system does not provide a longer-acting methylphenidate until tier 3.

We express concern in the nonstimulant tier system as well because it may conflict with adjunctive use of alpha agonists. It is our practice to titrate the CNS stimulants to the maximum effect and occasionally treat with an adjuvant such as guanfacine ER (Intuniv®). Neither atomoxetine nor generic guanfacine are FDA approved as an adjuvant. However, the current tier system would likely generate an automatic prior authorization: adding time and further administrative effort for both clinics and your system.

Your former tier system is superior for its available long acting medications. Children who were formerly treated with these medications now have been generating prior authorizations during refilling procedures. We certainly are not alone in concern for the administrative time required to complete and return prior authorizations, and we imagine that the OHCA staff will be and are likely seeing a remarkable increase in PAs and administrative costs. The inconvenience is also felt by SoonerCare members, whose time is precious and adherence is at risk.

We have written you, respectfully, to ask for changes to the tier system of medications. The current system makes it more difficult for us to provide appropriate care for our patients. We have heard from other pediatricians in the state who are similarly concerned.

We will make ourselves available and welcome an opportunity to meet with you about these matters, if our input would be useful. We suggest the following as the state's sole referral center for Developmental and Behavioral Pediatrics:

1) Provide a methylphenidate preparation lasting > 8 hours
2) Allow for guanfacine ER automatic approval in patients also taking stimulants

January 24th, 2014 The OU Child Study Center

3) Allow for amphetamine/dextroamphetamine ER capsules in children <9 years of age, as we find lisdextroamphetamine to frequently cause insomnia
4) Re-label Ritalin SR®, Metadate ER®, and Methylin ER® and their generics as short acting, as they are twice daily dosing

Regards,

The Medical Staff of the Child Study Center

Mark Wolraich, MD; D. David O'Banion, MD; Laura McGuinn, MD; Ami Bax, MD; Neha Patel, DO; Don Hamilton, MD

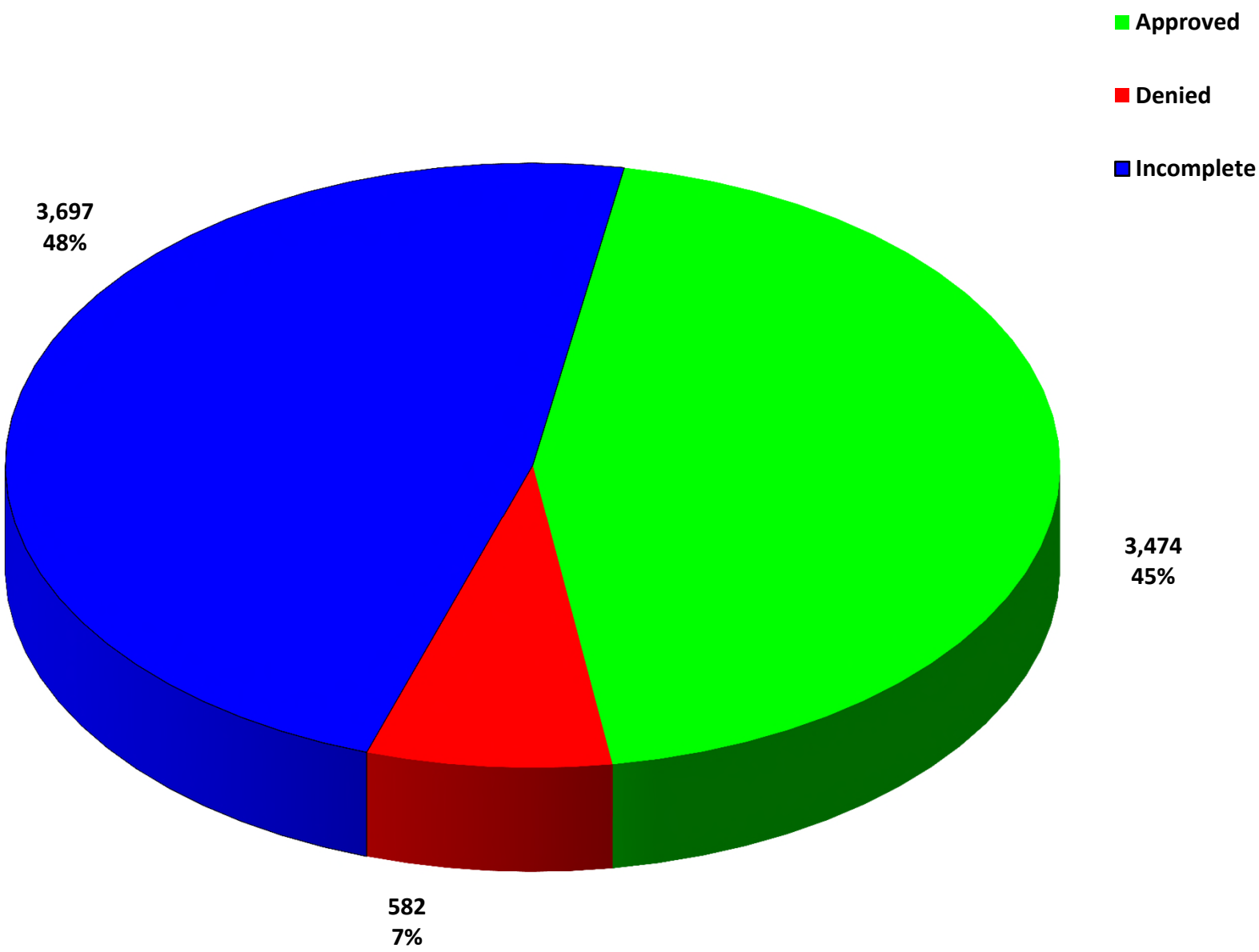
Please feel free to contact us directly though Dr. O'Banion at david-obanion@ouhsc.edu
or 405 271 5700 ext 45160 — please don't hesitate to contact me!
David O'Banion

We recommend the following comparison and review of recently-developed central nervous system stimulants.

Chavez, B et al. An Update on Central Nervous System Stimulant Formulations in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder. *Ann Pharmacother* 2009; 43: 1084-95

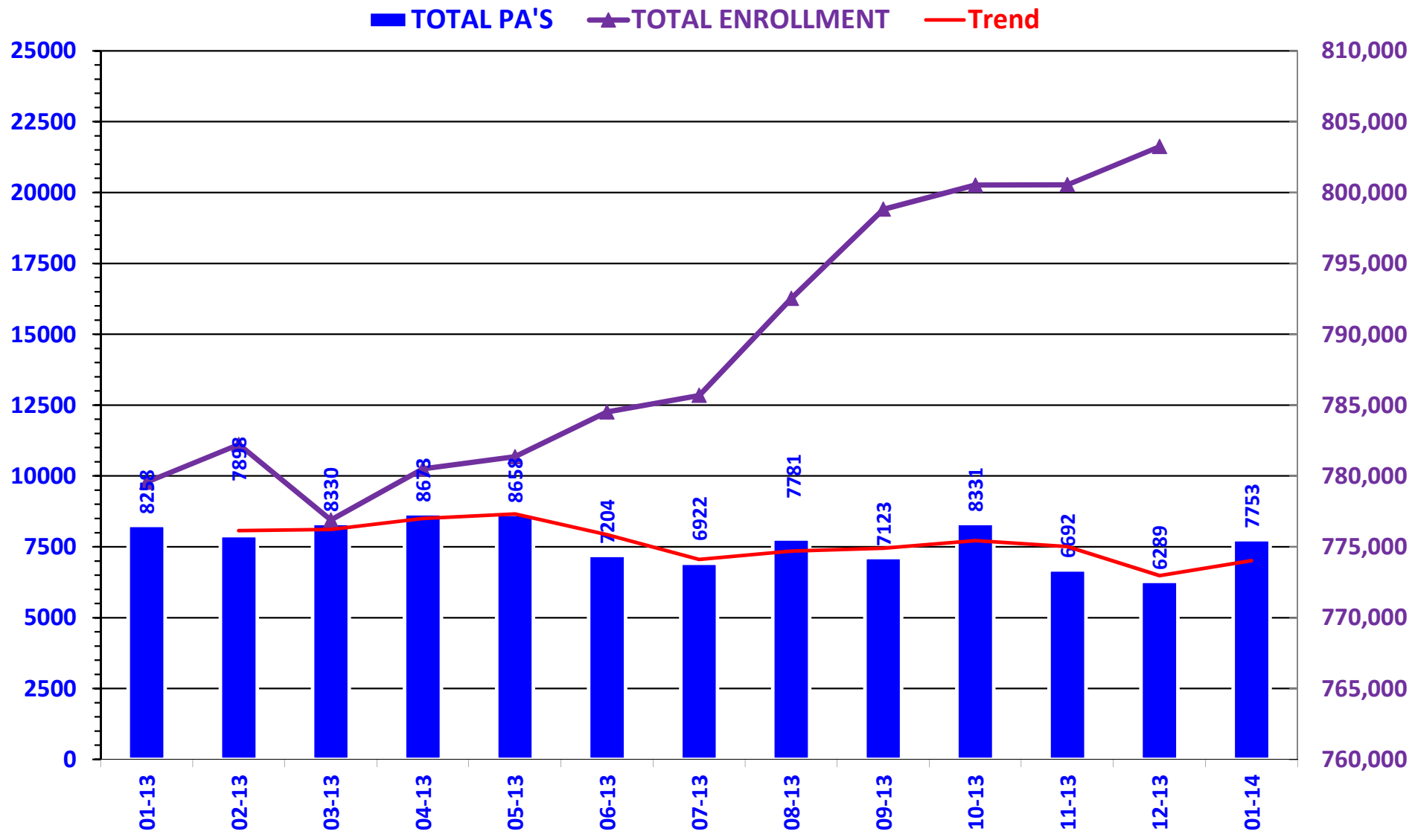
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY



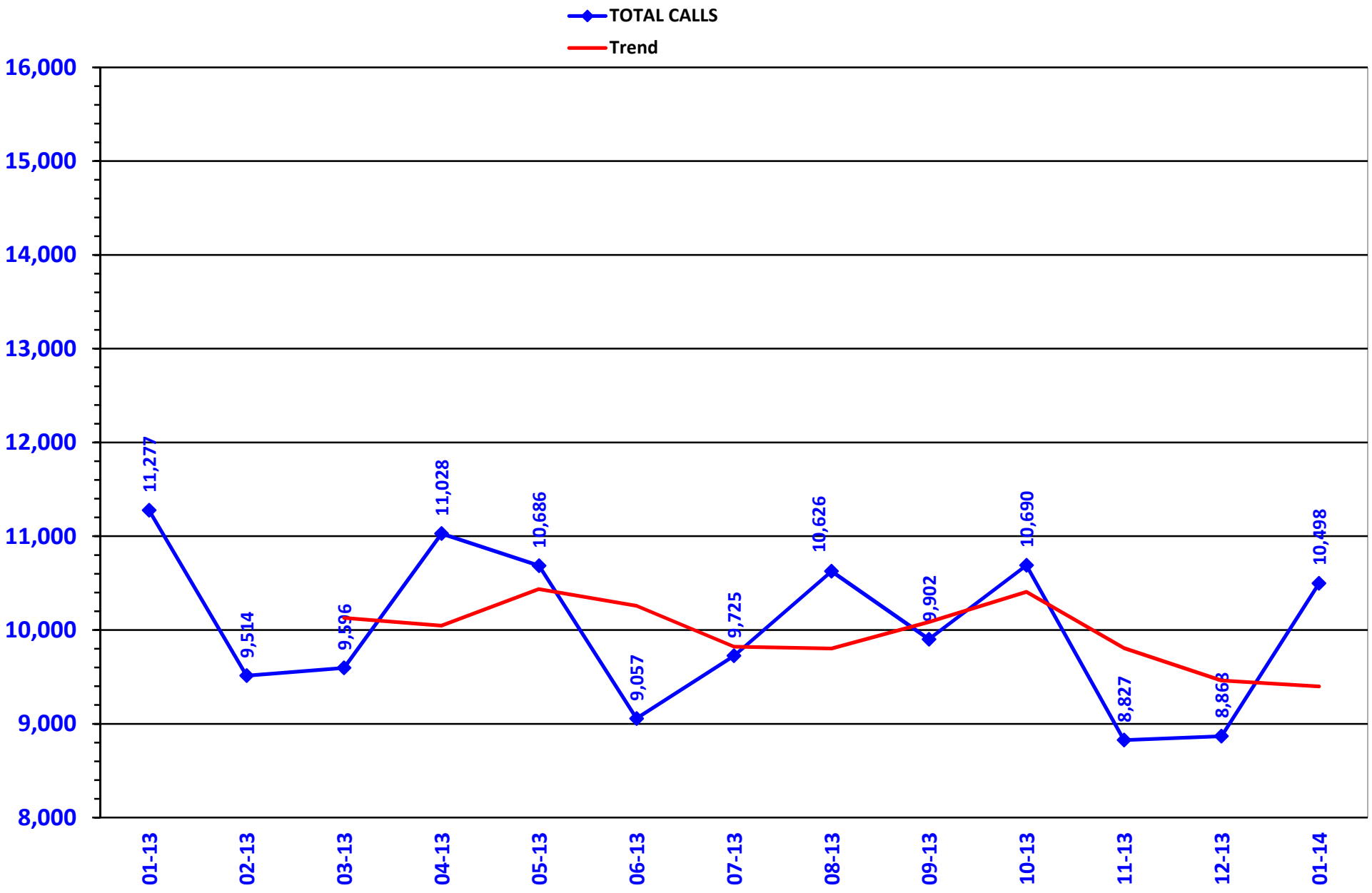
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2013– JANUARY 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JANUARY 2013- JANUARY 2014



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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	345	130	4	211	354
Analgesic, Narcotic	413	234	20	159	235
Angiotensin Receptor Antagonist	45	10	7	28	359
Antiasthma	272	140	11	121	326
Antibiotic	19	1	1	17	7
Anticoagulant	78	49	1	28	303
Anticonvulsant	87	37	1	49	318
Antidepressant	197	50	12	135	319
Antidiabetic	121	52	1	68	322
Antifungal	14	2	3	9	17
Antihistamine	107	79	3	25	349
Antihyperlipidemic	14	3	1	10	299
Antimigraine	78	25	7	46	303
Antiplatelet	17	9	0	8	326
Antiulcers	260	57	56	147	164
Anxiolytic	59	44	1	14	182
Atypical Antipsychotics	400	185	11	204	323
Benign Prostatic Hypertrophy	11	0	5	6	0
Biologics	53	30	1	22	326
Bladder Control	58	7	7	44	359
Botox	24	16	3	5	315
Calcium Channel Blockers	14	1	0	13	358
Cardiovascular	41	20	3	18	318
Chronic Obstructive Pulmonary Disease	15	2	2	11	360
Dermatological	127	29	51	47	83
Endocrine & Metabolic Drugs	81	46	9	26	140
Erythropoietin Stimulating Agents	33	14	0	19	112
Fibromyalgia	120	22	16	82	350
Gastrointestinal Agents	111	33	11	67	164
Genitourinary Agents	10	3	2	5	20
Glaucoma	10	3	0	7	264
Growth Hormones	67	50	7	10	166
HFA Rescue Inhalers	73	19	4	50	359
Insomnia	67	16	9	42	182
Multiple Sclerosis	45	22	1	22	196
Muscle Relaxant	129	37	37	55	61
Nasal Allergy	75	8	25	42	165
Neurological Agents	44	25	3	16	359
Nsaids	159	18	16	125	278
Ocular Allergy	32	10	1	21	194
Ophthalmic Anti-infectives	36	5	1	30	5
Osteoporosis	19	12	0	7	358
Other*	129	29	17	83	183
Otic Antibiotic	20	6	0	14	15
Pediculicide	92	31	8	53	17
Prenatal Vitamins	13	0	1	12	0
Statins	75	10	10	55	358
Stimulant	1,291	497	51	743	325
Suboxone/Subutex	215	163	5	47	78
Synagis	153	97	19	37	68
Testosterone	75	23	4	48	307
Topical Antibiotic	10	0	1	9	0
Topical Antifungal	54	2	9	43	103
Topical Corticosteroids	151	0	20	131	0
Vitamin	60	16	30	14	359
Pharmacotherapy	105	75	0	30	79
Emergency PAs	1	1	0	0	
Total	**6,424**	**2,505**	**529**	**3,390**	

* 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	83	64	1	18	120
Cumulative Early Refill	1	1	0	0	180
Dosage Change	310		1	31	7
High Dose	4	2	0	2	181
Ingredient Duplication	6	6	0	0	3
Lost/Broken Rx	73	62	4	7	4
NDC vs Age	2	2	0	0	110
Nursing Home Issue	71	66	0	5	4
Other	24	17	4	3	3
Quantity vs. Days Supply	671	419	32	220	272
Stolen	10	3	0	7	3
Temporary Unlock	43	30	10	3	19
Third Brand Request	32	20	1	11	22
Overrides Total	**1,329**	**969**	**53**	**307**	
Total Regular PAs + Overrides	**7,753**	**3,474**	**582**	**3,697**	

Denial Reasons	
Unable to verify required trials.	3,206
Does not meet established criteria.	579
Lack required information to process request.	471

Other PA Activity	
Duplicate Requests	523
Letters	4,169
No Process	62
Changes to existing PAs	579
Partials	803

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

SoonerPsych Program Update

Oklahoma Health Care Authority
February 2014

Physician Response to September Mailing: Poly-Pharmacy in Adult and Pediatric Members Receiving Atypical Antipsychotics

Approximately 2,071 prescribers for adults and children were listed on paid pharmacy claims for atypical antipsychotics in the 6 months prior to the report date. A total of 18,956 distinct members with atypical antipsychotic claims were reviewed for concomitant atypical antipsychotic use. Poly-pharmacy was determined by claims for two or more atypical antipsychotic medications concurrently for 90 days or more. The review period was for 6 months and was prevalent in nature (not based on a new start of an atypical antipsychotic). Members were eligible for inclusion in the mailing if their claims history indicated concurrent use of two or more atypical antipsychotic medications.

There were 10,543 members flagged for poly-pharmacy. 459 members were randomly chosen for inclusion in the mailing. Packets were mailed to 200 prescribers. The packets included information related to the use of concomitant atypical antipsychotic medications as well as patient specific prescription claim information with an optional individual member response page which allows the prescriber to provide feedback. Because some prescribers had multiple members, the maximum number of members included in a single packet was 10.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	200
Members	
Total Members Included	459
Total Responses Received	180

Prescriber Response Summary

Q#	Response	Total*
Q1	Possible billing error – Not my patient.	2
Q2	I am no longer seeing this patient.	12
Q3	Medication has been changed prior to date of review letter.	8
Q4	I was unaware of this situation and will consider making appropriate changes in therapy.	8
Q5	I am aware of this situation and will plan to continue monitoring this therapy.	105
Q6	I am continuing this medication from an original psychiatric prescription.	58
Q7	Other, comments.	62
	I am placing the Patient Detail Report in the patient's medical record	47

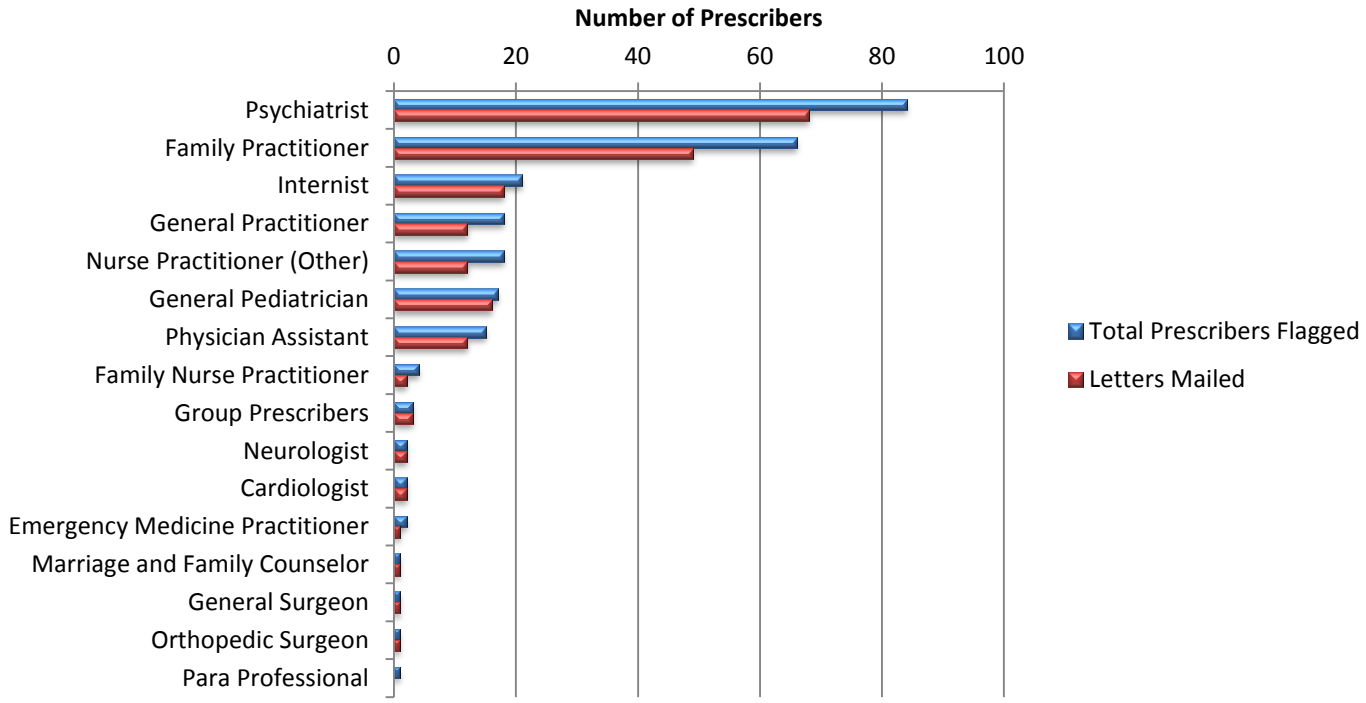
*Members can be included in multiple categories.

Summary of Additional Comments Provided

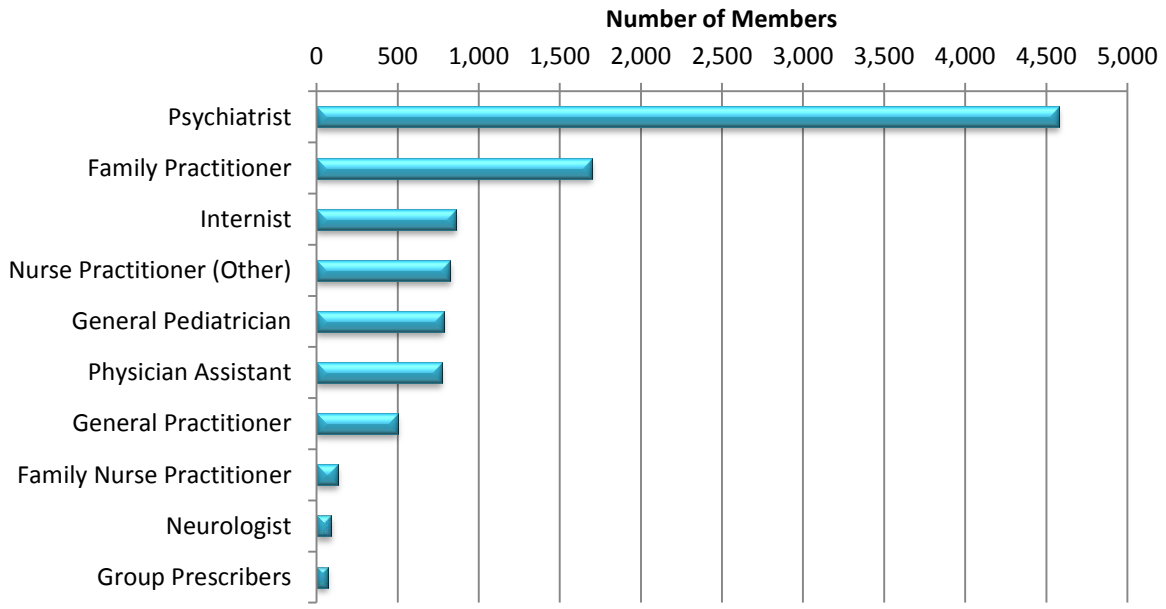
Comment Category	Total*
Patient specific information provided	27
Patient therapy is being followed by another prescriber	15
I am aware and will continue monitoring therapy	14
Continuing medications from previous prescriber	11
Medication has been discontinued	8
I plan to discontinue this medication gradually	8
No longer my patient	4
I plan to reevaluate current therapy	4
Not my patient	1
Patient has missed appointments/reports non-compliance/dropped out of treatment	1

*Members can be included in multiple categories, not all responses listed.

Prescribers Flagged Versus Prescribers Who Received a Letter By Prescriber Specialty



Top Ten Prescriber Specialties by Number of Members Included in Overall Review



Last Mailing –January 2014

The most recent mailing was processed in January and addressed Fazaclo™ and clozapine ODT prescribing for adult and pediatric members. For this project, pharmacy claims for clozapine products were reviewed, and prescribers linked to those claims were sent information regarding the pharmacokinetic properties of the different clozapine formulations as well as a prescriber summary report showing how their Fazaclo™ and clozapine ODT prescribing compared to other prescribers of clozapine products. The purpose of the mailing was to inform prescribers of the similarities of clozapine products despite significant cost differences, and to encourage prescribers to use the most cost-effective formulation. The review period was for twelve months, and total of 192 prescribers were included in the mailing.

Appendix C

Vote to Prior Authorize Procysbi™ (Cysteamine Bitartrate)

Oklahoma Health Care Authority
February 2014

Recommendations

The College of Pharmacy recommends the prior authorization of Procysbi™ (cysteamine bitartrate) with the following criteria:

Procysbi™ (Cysteamine Bitartrate) Approval Criteria:

1. An FDA approved diagnosis of nephropathic cystinosis; and
2. A patient specific, clinically significant reason why member cannot use the short-acting formulation Cystagon® (cysteamine bitartrate).

Appendix D

Vote to Prior Authorize Ravicti® (Glycerol Phenylbutyrate)

Oklahoma Health Care Authority
February 2014

Recommendations

The College of Pharmacy recommends prior authorization of Ravicti® (glycerol phenylbutyrate) with the following criteria:

Ravicti® (Glycerol Phenylbutyrate) Approval Criteria:

1. An FDA approved diagnosis of urea cycle disorder (UCD); and
2. Active management with protein restricted diet; and
3. A patient specific, clinically significant reason why member cannot use Buphenyl® (sodium phenylbutyrate).

Appendix E

Vote to Prior Authorize Sirturo™ (Bedaquiline Fumarate)

Oklahoma Health Care Authority
February 2014

Recommendations

The College of Pharmacy recommends the prior authorization of Sirturo™ (bedaquiline fumarate) with the following criteria:

Sirturo™ (Bedaquiline Fumarate) Approval Criteria:

1. An FDA approved diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB); and
2. Member must be 18 years of age or older; and
3. An alternative, effective treatment regimen cannot otherwise be provided; and
4. Medical supervision by an infectious disease specialist; and
5. Sirturo™ must be used in combination with at least three other drugs to which the patient's MDR-TB isolate has been shown to be susceptible; and
6. Sirturo™ must be administered under direct observation; and
7. Baseline ECG should be obtained and repeated 2, 12, and 24 weeks after starting treatment; and
8. Liver enzymes should be obtained at baseline and monitored monthly.
9. Sirturo™ will not be approved for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis. MDR-TB must be confirmed by sensitivity cultures indicating resistance to at least isoniazid and rifampin.
10. A maximum quantity of 188 tablets for the entire course of treatment will apply.
11. Approvals will be for the duration of 24 weeks.

Appendix F

Vote to Prior Authorize Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa)

Oklahoma Health Care Authority
February 2014

Recommendations

The College of Pharmacy recommends the following:

1. Reserve use of inhaled tobramycin products and Pulmozyme® (dornase alfa) for members who have a diagnosis of cystic fibrosis. These medications will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 24 months of claims history. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Restrict use of inhaled tobramycin products to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy. Use outside of this recommended regimen may be considered for coverage via a manual petition.
3. Access to Tobi® Podhaler™ will remain similar to Tobi® at this time. A study will be conducted over the course of the next year to evaluate and compare the impact of the two products on overall healthcare outcomes including hospitalizations and pharmacy costs. The results of this study may contribute to further recommendations regarding Tobi® Podhaler™.

Appendix G

Drug Utilization Review of Pulmonary Arterial Hypertension Medications and 30 Day Notice to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan)

Oklahoma Health Care Authority
February 2014

Introduction[1,2,3]

Pulmonary arterial hypertension (PAH) is a complex syndrome resulting from restricted blood flow through the pulmonary arterial circulation leading to increased pulmonary vascular resistance and ultimately right heart failure. By definition, PAH is characterized by an increase in mean pulmonary arterial pressure (PAP) of $\geq$25 mmHg at rest and an average primary capillary wedge pressure of $\leq$ 15 mmHg. As PAH progresses, the blood flow to the pulmonary arteries is restricted and the right side of the heart becomes enlarged due to the increased stress of pumping blood to the lungs. As a result of the excess strain on the heart and decreased oxygenated blood flow to the left side of the heart and systemic circulation, symptoms such as breathlessness, fatigue, syncope, weakness, and angina are common.

PAH is a rare disease with an estimated prevalence of 15-50[2,4] cases per million people. Idiopathic PAH (IPAH) has been estimated to have an annual incidence rate of 1-2 cases per million people in the US and Europe, and is estimated to be approximately 2-4 times more common in women than in men. The onset of PAH symptoms can occur at any age; however, the mean age of first diagnosis is approximately 45 years old. In pediatric patients diagnosed with PAH, the majority are diagnosed with IPAH or PAH associated with congenital heart disease (PAH-CHD). A recent epidemiological study revealed an annual incidence and point prevalence of 0.7 and 4.4 for IPAH and 2.2 and 15.6 for PAH-CHD cases per million children respectively.[3,5] While PAH is rare in infants and children, pediatric PAH is a challenge as current treatment decisions depend largely on results from evidence-based adult studies and clinical experience of pediatric experts.

Current Prior Authorization Criteria

Adcirca® (Tadalafil) and Revatio® (Sildenafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist.
3. Quantity limits:
    - Adcirca® (tadalafil) 20mg tablets: 60 tablets per 30 days.
    - Revatio® (sildenafil) 20mg tablets: 90 tablets per 30 days.

Tracleer® (bosentan) and Letairis® (ambrisentan) are available without prior authorization.

Treatment[1]

Current treatment guidelines recommend the use of edothelin receptor antagonists (ERAs) or phosphodiesterase-5 inhibitors (PDE-5) for first line treatment of PAH in low risk patients based on clinical assessment. Recently several new medications have been approved in this therapeutic class. Guidelines have not yet been developed as to their place in therapy. Intravenous (IV) prostacyclin (epoprostenol or treprostinil) is recommended as first line for high risk patients and more severe cases. If the high risk patient is not a candidate for IV therapy, other therapies should be considered. The following table reviews oral therapies only.

Generic	Trade	Indication	Dosage Form	Regimen	Mechanism of Action
TADALAFIL	ADCIRCA®	PAH to improve exercise ability	20 MG Tablets	(2) QD	PDE-5 Inhibitor
SILDENAFIL	*REVATIO®	PAH to improve exercise ability and delay clinical worsening	20 MG Tablets 10 MG/Ml Oral Suspension	TID	PDE-5 Inhibitor
AMBRISENTAN	LETAIRIS®	PAH to improve exercise ability and delay clinical worsening	5, 10 MG Tablets	QD	ERA
BOSENTAN	TRACLEER®	PAH to improve exercise ability and to decrease clinical worsening	62.5, 125 MG Tablets	BID	ERA
MACITENTAN	OPSUMIT ®	PAH to delay disease progression	10 MG Tablets	QD	ERA
RIOCIGUAT	ADEMPAS®	Chronic Thromboembolic Pulmonary Hypertension (CTEPH) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class PAH to improve exercise capacity, improve WHO functional class and to delay clinical worsening	0.5, 1, 1.5, 2, 2.5 MG Tablets	TID	Soluble guanylate cyclase stimulator
TREPROSTINIL	ORENITRAM™	PAH to improve exercise capacity	0.125, 0.25, 1 and 2.5 MG ER Tablets	BID	Prostacyclin vasodilator

*Available in generic formulation.

Utilization

Adcirca® and Revatio® Fiscal Year Comparison

Fiscal Year	Members*	Claims	Cost	Cost/Claim	Cost/Day	Units	Days
2012	137	617	$648,028.56	$1,050.29	$34.15	75,223	18,974
2013	134	666	$416,724.55	$625.71	$21.08	91,717	19,768
% Change	**-2.20%**	**7.90%**	**-35.70%**	**-40.40%**	**-38.30%**	**21.90%**	**4.20%**
Change	**-3**	**49**	**-$231,304.01**	**-$424.58**	**-$13.07**	**16,494**	**794**

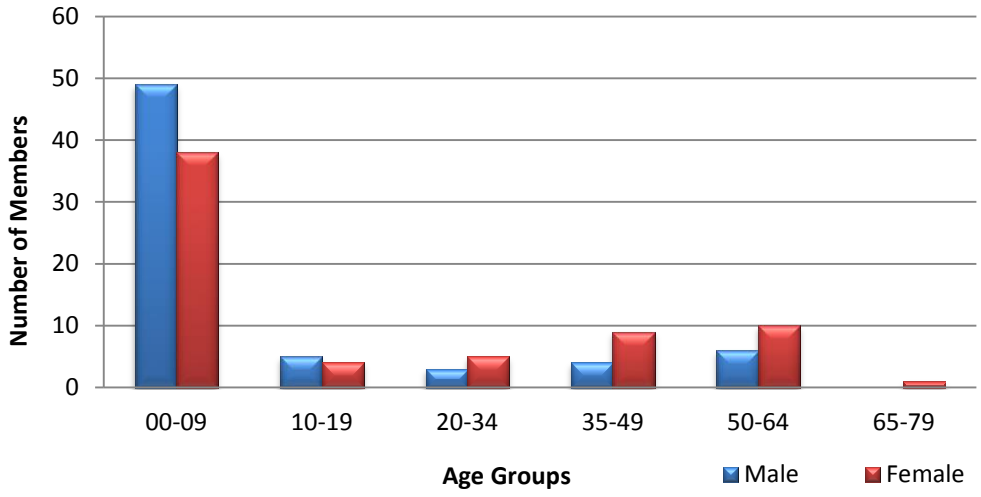
*Total number of unduplicated members

Tracleer® and Letairis® Fiscal Year Comparison

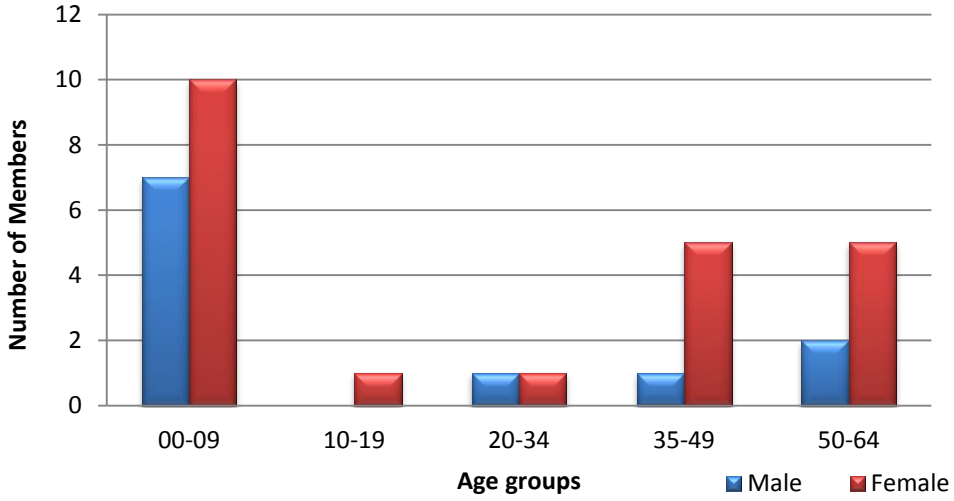
Fiscal Year	Members*	Claims	Cost	Cost/Claim	Cost/Day	Units	Days
2012	31	160	$566,195.75	$3,538.72	$119.30	5,266	4,746
2013	33	211	$703,539.36	$3,334.31	$114.68	5,517	6,135
% Change	6.50%	31.90%	24.30%	-5.80%	-3.90%	4.80%	29.30%
Change	2	51	$137,343.61	-$204.41	-$4.62	251	1,389

*Total number of unduplicated members

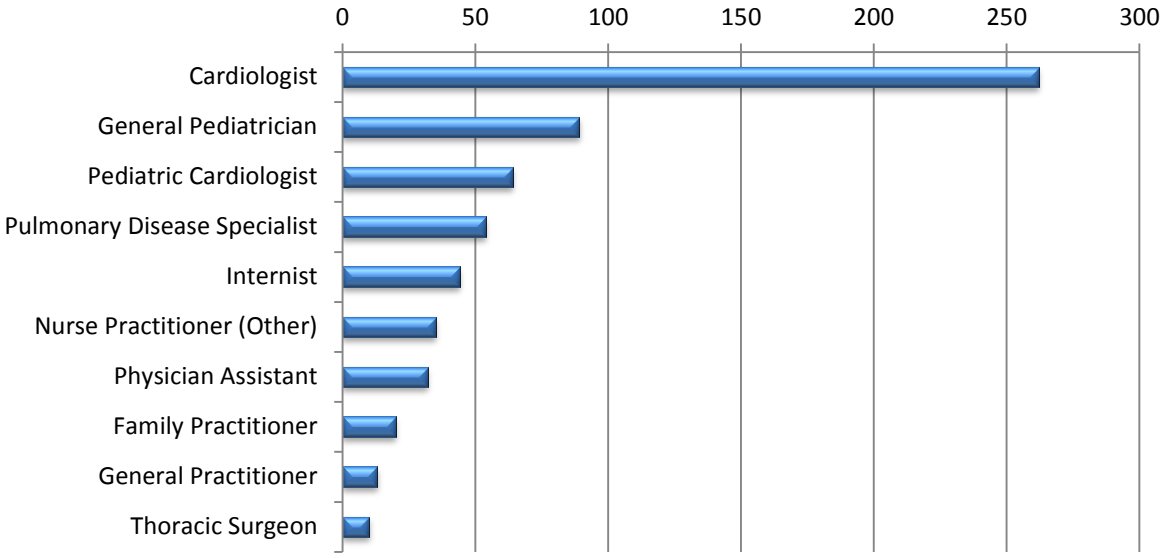
Demographics of Members Utilizing Adcirca® and Revatio®



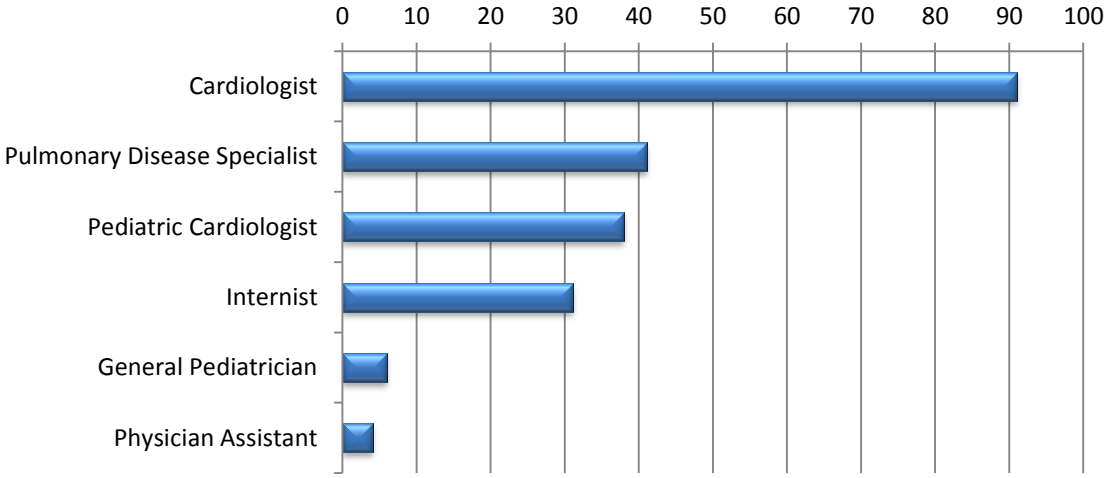
Demographics of Members Utilizing Tracleer® and Letairis®



Top Prescriber Specialties of Adcirca® and Revatio® by Number of Claims



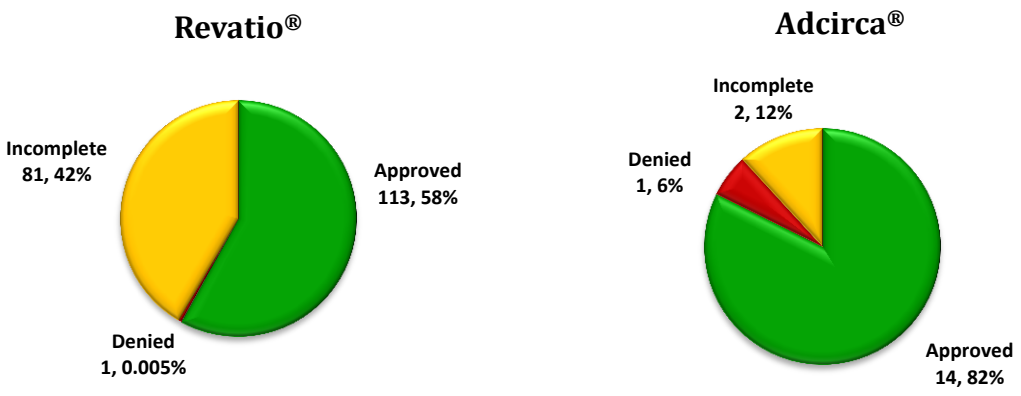
Top Prescriber Specialties of Tracleer® and Letairis® by Number of Claims



Prior Authorization

There were 17 petitions submitted for Adcirca® and 195 petitions submitted for Revatio® during fiscal year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates

Patent Expirations

1. Revatio® (sildenafil)- 09/2012
    a. Sildenafil generic oral tablets became available on the market November 2012.
2. Tracleer® (bosentan)- 11/2015
3. Adcirca® (tadalafil)- 11/2017
4. Letairis® (ambrisentan)- 07/2018

In 2013, Adempas®, Opsumit®, and Orenitram™ were FDA approved to treat PAH; each newly approved medication has a different mechanism of action. Adempas® is a first-in-class soluble guanylate cyclase stimulator, Opsumit® is an endothelin receptor antagonist, and Orenitram™ is a prostacyclin vasodilator. Adempas® and Opsumit® are contraindicated in pregnancy and therefore females are restricted use through Risk Evaluation and Mitigation Strategies (REMS) programs. The following section contains details of Adempas® and Opsumit®. Orenitram™ is not yet available.

Adempas® (Riociguat Oral Tablets)[6]

Indication: Adempas® is indicated for the treatment of:

- Adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (WHO Group 4), after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class.
- PAH (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening.

Dosing: Adempas® is available as an oral tablet in the following strengths: 0.5 mg, 1 mg, 1.5 mg, 2 mg, and 2.5 mg.

- The initial treatment is 1 mg by mouth three times daily.
- For patients who may not tolerate the hypotensive effect of Adempas®, consider a starting dose of 0.5 mg three times daily.
- Dose can be increased by 0.5 mg no sooner than 2-week intervals as tolerated to a maximum dose of 2.5 mg three times daily.

Mechanism of Action: Adempas® is a first-in-class soluble guanylate cyclase (sGC) stimulator with a dual mode of action. Adempas® sensitizes sGC to endogenous nitric oxide (NO) by stabilizing the NO-sGC binding and directly stimulating sGC via a different binding site, independently of NO. The NO-sGC complex catalyzes the synthesis of the signaling molecule cyclic guanosine monophosphate (cGMP). Adempas® stimulates the NO-sGC-cGMP pathway and leads to increased generation of cGMP with subsequent vasodilation.

Contraindications: Concomitant use of Adempas® with nitrates or nitric oxide, or with PDE inhibitors is contraindicated. Adempas® is contraindicated in pregnancy and is consequently only available through the Adempas® REMS program for all females.

Efficacy:

Chronic Thromboembolic Pulmonary Hypertension

- Treatment of CTEPH was evaluated in a double-blind, multi-center study (CHEST-1) conducted in 261 patients (range 18-80 years old) with CTEPH. The primary endpoint of the study was a change from baseline in six minute walking distance (6MWD) after 16 weeks. Improvements in walking distance were apparent from week 2 onward. At week 16, the placebo adjusted mean increase in 6MWD in the Adempas® treatment group was 46 meters. 83% of the Adempas® treatment group experienced improvement in 6MWD compared to 57% of the placebo group. 33% of the Adempas® treatment group had an improved change in their WHO functional class status compared to 15% in the placebo group.
- CHEST-2, an open-label extension study, included 237 patients who had completed CHEST-1 to evaluate Adempas® in long term treatment of CTEPH. The average treatment duration was 582 (+/- 317) days. The probabilities of survival were 97% at 1 year and 94% at 2 years, however without a control group the data must be interpreted cautiously.

Pulmonary Arterial Hypertension

- Treatment of PAH was evaluated in a double-blind, multi-center study (PATENT-1) conducted in 443 patients (mean age 51 years old) with PAH. Patients were randomized to three treatment groups: Adempas® titrated up to 1.5 mg, 2.5 mg, or placebo three times daily. 50% of patients were treatment-naïve with respect to PAH therapy, 44% were pre-treated with an endothelin receptor antagonist (ERA), and 6% were treated with a prostacyclin analogue. Adempas® was added in combination to these background therapies. The primary endpoint was change from baseline in 6MWD after 12 weeks which was designed to evaluate exercise capacity.

- The secondary endpoint was time to clinical worsening defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of PAH, start of new PAH-specific treatment, persistent decrease in 6MWD and persistent worsening of WHO Functional Class.
- Approximately 75% of patients were titrated up to the maximum dose of 2.5 mg three times a day by week 12. Improvements in walking distance were apparent from Week 2 onward. At Week 12, the placebo-adjusted mean increase in 6MWD in the Adempas® group was 36 meters. 76% of the Adempas® group experienced 6MWD improvement compared to 59% on placebo. Adempas® treated patients experienced a significant delay in time to clinical worsening compared to placebo-treated patients and had significantly fewer events of clinical worsening up to week 12.
- PATENT-2 is an open-label extension study that included 363 patients who previously completed PATENT-1. The average duration of treatment was 663 (+/- 319) days. The probabilities of survival were 97% at 1 year and 93% at 2 years, however without a control group this data must be interpreted cautiously.

Opsumit® (Macitentan Oral Tablets)[7]

Indication: Opsumit® is indicated for the treatment of adults with PAH (WHO Group 1) to delay disease progression. Disease progression is defined as death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH.

Dosing: Opsumit® is available as a 10 mg oral tablet. The FDA approved dose is 10 mg once daily. Doses greater than 10 mg once daily have not been studied and are not recommended.

Mechanism of Action: Opsumit® is an ERA that prevents the binding of endothelin (ET-1) at both its receptors (ET_A and ET_B) preventing vasoconstriction. Opsumit® displays high affinity and sustained occupancy at the ET receptors in human pulmonary arterial smooth muscle cells. One of the metabolites of Opsumit® is also pharmacologically active at the ET receptors and is estimated to be about 20% as potent as the parent drug.

Contraindications: Opsumit® is contraindicated in pregnancy and is consequently only available through the Opsumit® REMS program for all females.

Efficacy:

- The effect of Opsumit® on PAH progression was evaluated in a multi-center, long-term (average duration of exposure about 2 years), placebo-controlled study (SERAPHIN) in 742 patients (mean age of 46 years old) with symptomatic PAH. Participants were randomized to placebo, 3 mg Opsumit®, or 10 mg Opsumit® once daily.
- The primary endpoint was time to the first occurrence of death (from any cause), a significant morbidity event (defined as atrial septostomy, lung transplantation, initiation of IV or subcutaneous (SC) prostanoids), or “other worsening of PAH” during double-blind treatment plus 7 days.

Other worsening was defined as all of the following: a sustained ≥15% decrease from baseline in 6MWD, worsening of PAH symptoms (WHO functional class), and need for additional treatment for PAH. The secondary endpoint was time to PAH death or PAH hospitalization.

- At baseline, the majority of enrolled patients (64%) were being treated with a stable dose of specific PAH therapy, either oral PDE-inhibitors (61%) and/or inhaled/oral prostanoids (6%).
- Treatment with Opsumit® 10mg resulted in a 45% reduction in the occurrence of the primary endpoint compared to placebo up to the end of the double-blind treatment. The beneficial effect of Opsumit® 10mg was primarily attributable to a reduction in clinical worsening events (deterioration in 6MWD and worsening of PAH symptoms and need for additional PAH treatment). The risk of PAH related death or hospitalization for PAH was reduced by 50% in patients receiving Opsumit® 10 mg compared to placebo.
- Treatment with Opsumit® 10 mg resulted in a placebo-corrected mean increase in 6MWD of 22 meters at month 6 and with significant improvement in 6MWD by month 3. Treatment with Opsumit® 10 mg led to an improvement of at least one WHO functional class at month 6 in 22% of patients compared to 13% of placebo-treated patients.

Cost

The following chart is a cost comparison of available oral products. Orenitram™ (oral extended-release treprostinil tablets) cost and launch date information is currently unavailable. Please note, treprostinil is currently available as an oral inhalation, subcutaneous, and IV injection. These medications do not currently require a prior authorization and are not included in the following cost chart.

MEDICATION NAME	STRENGTH	DOSING	EACW∞	DAILY COST	MONTHLY COST
ADCIRCA®	20 MG	(2) QD	$33.42	$66.84	$2,005.20
*REVATIO®	20 MG	TID	$0.80¥	$2.40	$72.00
OPSUMIT ®	10 MG	QD	$240.77	$240.77	$7,223.10
TRACLEER®	62.5 MG, 125 MG	BID	$120.38	$240.76	$7,222.80
LETAIRIS®	5 MG, 10 MG	QD	$226.98	$226.98	$6,809.40
ADEMPAS®	0.5 MG, 1 MG, 1.5 MG, 2 MG, 2.5 MG	TID	$88.00	$264.00	$7,920.00

∞EACW does not reflect rebated prices
*Available in generic formulation
¥SMAC pricing

Discussion

Current treatment guidelines do not give preference to use of an ERA or PDE-5 inhibitor for first line treatment of PAH in low risk patients. The PDE-5 inhibitors (Adcirca® and Revatio®) currently require prior authorization due to the potential for inappropriate, off-label use for erectile dysfunction. Review of ERAs (Tracleer® and Letairis®) claims data does not show inappropriate utilization. All members on an ERA had an appropriate diagnosis and dosing was as indicated. Additionally, the ERAs do not possess the same risk of off-labeled use as the PDE-5 inhibitors.

Recommendations

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

Adempas® (Riociguat) Approval Criteria:

1. An 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 or cardiologist; and
3. Female members, prescribers, and dispensing pharmacies must be enrolled in the Adempas® REMS program.
4. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

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

Utilization Details for Pulmonary Arterial Hypertension Medications

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/ CLAIM	COST/ DAY	% COST
Phosphodiesterase-5 Inhibitors (PDE-5)						
SILDENAFIL TAB 20MG	339	91	$24,237.29	$71.50	$2.43	2.16%
REVATIO® TAB 20MG	223	83	$280,966.08	$1,259.94	$42.14	25.08%
SUBTOTAL	**562**	**174**	**$305,203.37**	**$543.07**	**$18.33**	**27.24%**
ADCIRCA® TAB 20MG	104	17	$111,521.18	$1,072.32	$35.78	9.95%
SUBTOTAL	**104**	**17**	**$111,521.18**	**$1,072.32**	**$35.78**	**9.95%**
Edothelin Receptor Antagonists (ERA)						
TRACLEER® TAB 62.5MG	135	22	$203,954.69	$1,510.78	$52.91	18.21%
TRACLEER® TAB 125MG	39	7	$258,241.76	$6,621.58	$220.72	23.05%
SUBTOTAL	**174**	**29**	**$462,196.45**	**$2,656.30**	**$91.98**	**41.26%**
LETAIRIS® TAB 10MG	24	5	$156,407.28	$6,516.97	$217.23	13.96%
LETAIRIS® TAB 5MG	13	2	$84,935.63	$6,533.51	$217.78	7.58%
SUBTOTAL	**37**	**7**	**$241,342.91**	**$6,522.78**	**$217.43**	**21.54%**
TOTAL	**877**	**147***	**$1,120,263.91**	**$3,369.51**	**$43.25**	**100%**

*Total number of unduplicated members.

PRODUCT DETAILS OF ADEMPAS® (RIOCIGUAT ORAL TABLET)[6]

INDICATIONS AND USE:

- Adempas® is a sGC stimulator indicated for the treatment of adults with:
    - Persistent/recurrent CTEPH, (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class.
    - PAH, (WHO Group 1), to improve exercise capacity, improve WHO functional class and to delay clinical worsening.

DOSAGE FORMS:

- Adempas® is an oral tablet available in the following strengths: 0.5 mg, 1 mg, 1.5 mg, 2 mg, and 2.5 mg.

ADMINSTRATION:

- Initiate treatment at 1 mg taken three times a day.
- For patients who may not tolerate the hypotensive effect of Adempas®, consider a starting dose of 0.5 mg three times a day.
- Increase dosage by 0.5 mg at intervals of no sooner than 2-weeks as tolerated to a maximum of 2.5 mg three times a day.

CONTRAINDICATIONS:

- Adempas® is contraindicated in pregnancy, concurrent use with nitrates or nitric oxide donors in any form, or PDE inhibitors.

SPECIAL POPULATIONS:

- Nursing mothers: Discontinue drug or breastfeeding depending on the importance of the medication to the mother.
- Renal impairment: Not recommended in patients with creatinine clearance <15 mL/min or in patients on dialysis.
- Hepatic impairment: Not recommended in patients with severe (Child Pugh C) hepatic impairment.
- Smoking: May require dosages higher than 2.5 mg three times a day if tolerated. Dose decrease may be required in patients who stop smoking.

WARNINGS AND PRECAUTIONS:

- Symptomatic hypotension
- Bleeding
- Pulmonary edema in patients with pulmonary veno-occlusive disease; if confirmed, discontinue treatment.

ADVERSE REACTIONS: (Incidence ≥3% and more common than placebo)

- Headache (27%)
- Dyspepsia/Gastritis (21%)
- Dizziness (20%)
- Nausea (14%)
- Diarrhea (12%)
- Hypotension (10%)
- Vomiting (7%)
- Anemia (7%)
- GERD (5%)
- Constipation (5%)

DRUG INTERACTIONS:

- Strong CYP and P-gp/BCRP inhibitors: For patients receiving strong CYP and P-gp/BCRP inhibitors, consider a starting dose of 0.5 mg three times a day. Monitor for hypotension.
- Antacids: Separate administration by at least 1 hour.

PATIENT COUNSELING INFORMATION:

1. Embryo-Fetal Toxicity: Instruct patients on the risk of fetal harm when Adempas® is used during pregnancy. Instruct females of reproductive potential to use effective contraception and to contact their physician immediately if they suspect they may be pregnant. Female patients must enroll in the Adempas® REMS program.
2. Adempas® REMS Program: For female patients, Adempas® is available only through a restricted program called the Adempas® REMS program. Male patients are not enrolled in the Adempas® REMS program. Inform female patients (and their guardians, if applicable) of the following important requirements:
    a. All female patients must sign an enrollment form.
    b. Advise female patients of reproductive potential that they must comply with the pregnancy testing and contraception requirements.
    c. Educate and counsel females of reproductive potential on the use of emergency contraception in the event of unprotected sex or contraceptive failure.
    d. Advise pre-pubertal females to report any changes in their reproductive status immediately to their prescriber.
    e. Review the medication guide and REMS educational materials with female patients.
3. Inform patients of the contraindication of Adempas® with nitrates or nitric oxide donors or PDE-5 inhibitors.
4. Advise patients about the potential risks/signs of hemoptysis and to report and potential signs of hemoptysis to their physicians.
5. Instruct patients on the dosing, titration, and maintenance of Adempas®.
6. Advise patients regarding activities that may impact the pharmacology of Adempas® (strong multi-pathway CYP inhibitors and P-gp/BCRP inhibitors and smoking). Patients should report all current medications and new medications to their physician.
7. Advise patients that antacids should not be taken within 1 hour of taking Adempas®.
8. Inform patients that Adempas® can cause dizziness, which can affect the ability to drive and use machines. They should be aware of how they react to Adempas®, before driving or operating machinery and if needed, consult their physician.

PRODUCT DETAILS OF OPSUMIT® (MACITENTAN ORAL TABLET)[7]

INDICATIONS AND USE:

- Opsumit® is an ERA indicated for the treatment of PAH, (WHO Group 1) to delay disease progression. Disease progression is defined as: death, initiation of IV or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms, and need for additional PAH treatment). Opsumit® also reduced hospitalization due to PAH.

DOSAGE FORMS:

- Opsumit® is available as an oral 10 mg strength tablet.

ADMINSTRATION:

- 10 mg once daily.
- Doses higher than 10 mg once daily have not been studied in patients with PAH and are not recommended.

CONTRAINDICATIONS:

- Opsumit® is contraindicated in pregnancy.

SPECIAL POPULATIONS:

- Nursing mothers: Discontinue drug or breastfeeding depending on the importance of the medication to the mother.

WARNINGS AND PRECAUTIONS:

- Other ERAs cause hepatotoxicity and liver failure. Obtain baseline liver enzymes and monitor as clinically indicated.
- Decreases in hemoglobin.
- Pulmonary edema in patients with pulmonary veno-occlusive disease; if confirmed, discontinue treatment.
- Decreases in sperm count have been observed in patients taking ERAs.

ADVERSE REACTIONS: (Incidence ≥3% and more common than placebo)

- Nasopharyngitis/pharyngitis (20%)
- Headache (14%)
- Anemia (13%)
- Bronchitis (12%)
- UTI (9%)
- Influenza (6%)

DRUG INTERACTIONS:

- Strong CYP3A4 inducers (rifampin) reduce exposure to Opsumit®. Avoid co-administration with Opsumit®.
- Strong CYP3A4 inhibitors (ketoconazole, ritonavir) increase exposure to Opsumit®. Avoid co-administration with Opsumit®.

PATIENT COUNSELING INFORMATION:

1. Embryo-Fetal Toxicity: Instruct patients on the risk of fetal harm when Opsumit® is used in pregnancy. Instruct females of reproductive potential to use effective contraception and to contact their physician immediately if they suspect they may be pregnant. Female patients must enroll in the Opsumit® REMS program.
2. Opsumit® REMS Program: For female patients, Opsumit® is available only through a restricted program called the Opsumit® REMS program. Male patients are not enrolled in the Opsumit® REMS program. Inform female patients (and their guardians, if applicable) of the following important requirements:
    a. Female patients must sign an enrollment form.
    b. Female patients of reproductive potential must comply with the pregnancy testing and contraception requirements.
    c. Educate and counsel females of reproductive potential on the use of emergency contraception in the event of unprotected sex or contraceptive failure.
    d. Advise pre-pubertal females to report any changes in their reproductive status immediately to their prescriber.
    e. Review the medication guide and REMS educational materials with female patients.
3. Decrease in Hemoglobin: Advise patients on the importance of hemoglobin testing.
4. Hepatotoxicity: Some products in this pharmacological class are hepatotoxic. Educate patients on signs of hepatotoxicity. Advise patients that they should contact their doctor if they have unexplained nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching.
5. Administration: Patients should be advised not to split, crush, or chew tablets.

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[1]McLaughlin, Vallerie V., Stephen L. Archer, David B. Badesch, Robyn J. Barst, Harrison W. Farber, Jonathan R. Lindner, Michael A. Mathier, Michael D. McGoon, Myung H. Park, Robert S. Rosenson, Lewis J. Rubin, Victor F. Tapson, and John Varga. "ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension." *Journal of the American College of Cardiology* 53.17 (2009): 1573-619.

[2] Pulmonary Arterial Hypertension. Available at: http://www.PAH-info.com Last revised 08/2013. Last accessed 01/23/2014.

[3] Vorhies, Erika E., and David Dunbar Ivy. "Drug Treatment of Pulmonary Hypertension in Children." *Pediatric Drugs* 16.1 (2014): 43-65.

[4] Peacock, A. J., N. F. Murphy, J. J. V. Mcmurray, L. Caballero, and S. Stewart. "An Epidemiological Study of Pulmonary Arterial Hypertension." European Respiratory Journal 30.1 (2007): 104-09.

[5] Loon, R. L. E. Van, M. T. R. Roofthooft, H. L. Hillege, A. D. J. Ten Harkel, M. Van Osch-Gevers, T. Delhaas, L. Kapusta, J. L. M. Strengers, L. Rammeloo, S.-A. B. Clur, B. J. M. Mulder, and R. M. F. Berger. "Pediatric Pulmonary Hypertension in the Netherlands: Epidemiology and Characterization During the Period 1991 to 2005." *Circulation* 124.16 (2011): 1755-764.

[6]Adempas® Product Information. Bayer. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Adempas_PI.pdf. Last revised 10/2013. Last accessed 01/16/2014.

[7]Opsumit® Product Information. Actelion. Available online at: http://opsumit.com/splash/pdf/OPSUMIT-Full-Prescribing-Information.pdf. Last revised 10/2013. Last accessed 01/16/2014.

Appendix H

Drug Utilization Review of Cephalosporin Antibiotics and 30 Day Notice to Prior Authorize Select Cephalosporins

Oklahoma Health Care Authority
February 2014

Introduction[1]

The cephalosporin family of antibiotics is one of the largest and most diversified families of antibiotics, consisting of five generations of compounds and broad spectrum bactericidal activity. Cephalosporin antibiotics disrupt the synthesis of the peptidoglycan layer of bacterial cell walls leading to the destruction of the bacteria.

The first cephalosporin antibiotic, cephalothin, was released by Elli Lilly & Company in 1964. Currently, the majority of the products in this class are no longer patent protected, and have become available in generic formulations. This review focuses on the utilization of the products currently available in this class of medication, and explores the possible strategies for cost effective use of these products in the SoonerCare population.

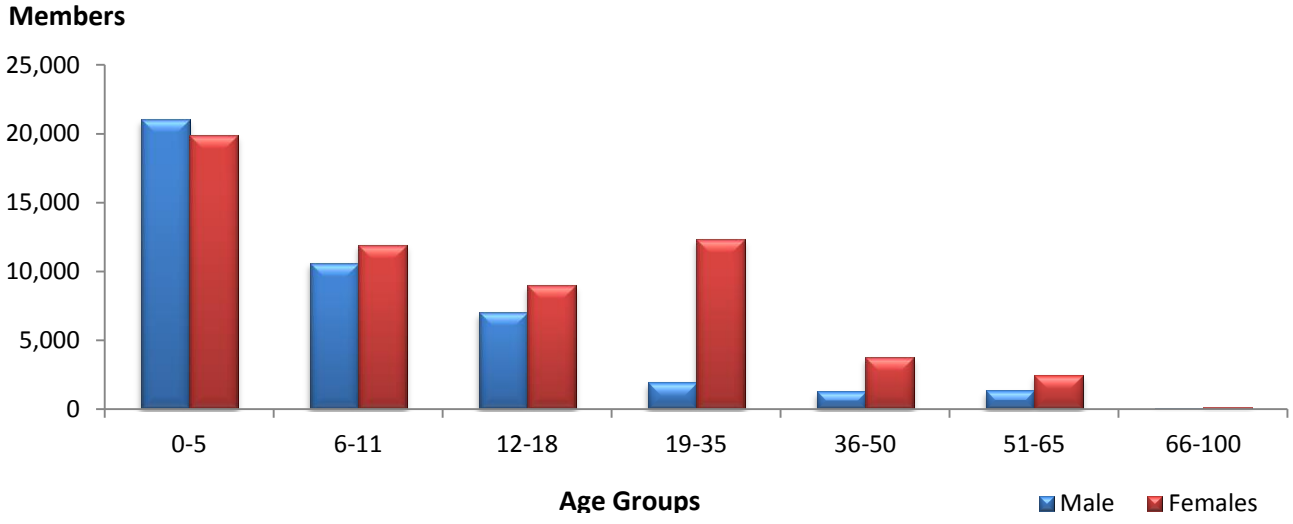
Utilization

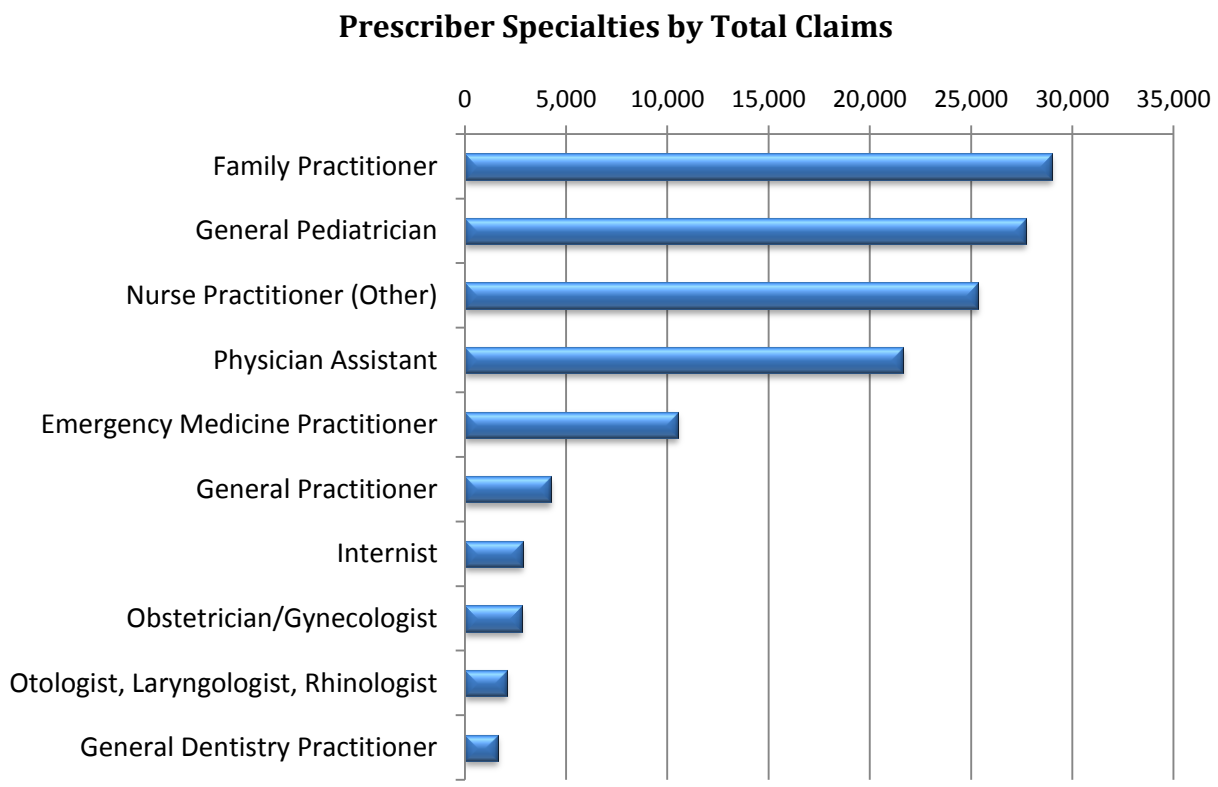
Cephalosporin Utilization Trends

Calendar Year	Total Members*	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	106,440	144,513	$7,812,565.88	$54.06	$5.64	10,407,457	1,385,515
2013	102,732	138,042	$9,941,869.98	$72.02	$7.52	9,910,251	1,321,307
% Change	-3.50%	-4.50%	27.30%	33.20%	33.30%	-4.80%	-4.60%
Change	-3,708	-6,471	$2,129,304.10	$17.96	$1.88	-497,206	-64,208

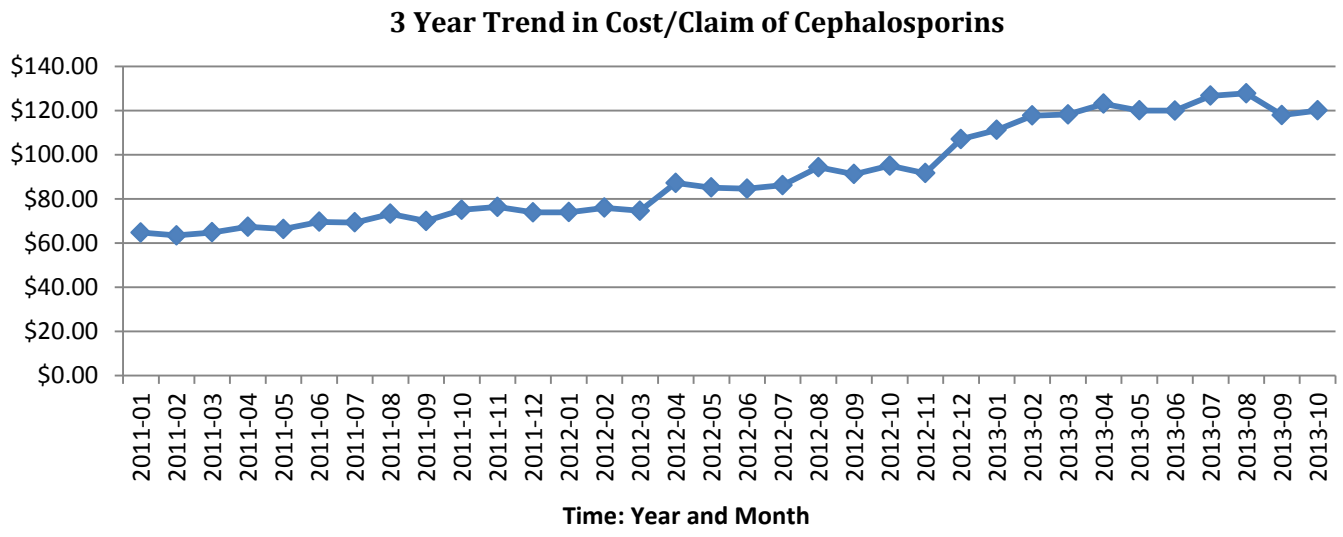
*Total number of unduplicated members.

Demographics



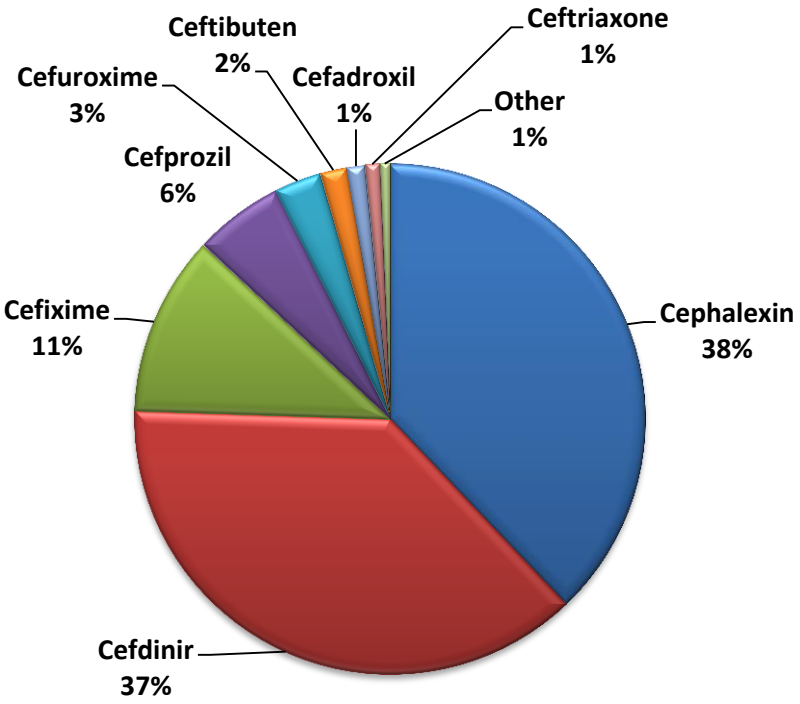


Utilization Evaluation



The trend shows the cost/claim for this category of medications has doubled over the past 3 years. The following charts show the products leading the market share as well as the cost drivers in this category.

Market Share by Total Claims



Market Share by Total Cost

Chemical Name	Products Utilized	Total Cost
Cefixime	Suprax®	$4,295,081
Cefdinir	Cefdinir	$3,407,723
Ceftibuten	Cedax®	$841,761
Cephalexin	Cephalexin	$600,546
Cefprozil	Cefprozil	$429,644
Cefuroxime	Cefuroxime/Ceftin®	$189,930
Other	Multiple Products	$100,523
Cefadroxil	Cefadroxil	$50,290
Ceftriaxone	Ceftriaxone/Rocephin®	$26,371

The most utilized products in this category are cephalexin and cefdinir, which hold 75% of the market share by total number of claims. Both of these products are available as generics and as a result, these two products only account for approximately $4 million dollars in calendar year 2013. The other major cost drivers for this category are cefixime and ceftibuten, both of which are not available in generic formulation, and account for over $5.1 million dollars, although they totaled only 13% of the claims. These products were evaluated to determine if clinical advantages exist.

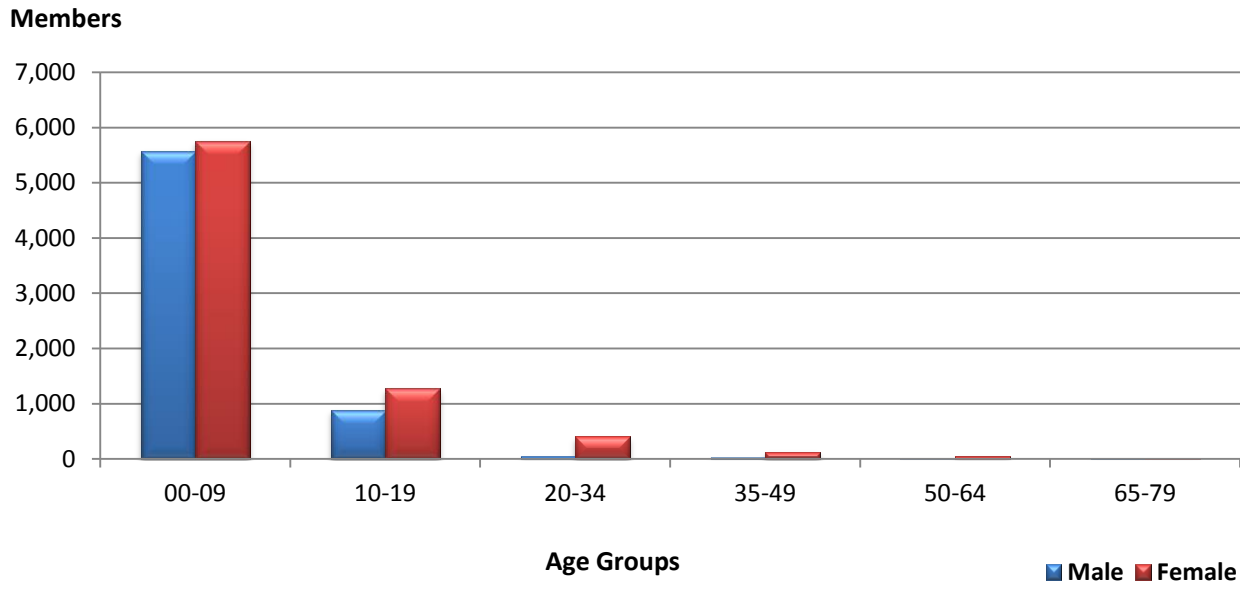
Clinical Evaluation

Medication and Frequency of Dosing	Pneumonia	Acute Exacerbation of Chronic Bronchitis	Acute Maxillary Sinusitis	Pharyngitis/ Tonsillitis/ Upper-RTIs	Lower-RTIs	Acute, Uncomplicated Urethral/Cervical Gonorrhea	Uncomplicated Urinary Tract Infections	Osteomyelitis/ Bone/Joint Infections	Acute Otitis Media	Skin & Skin Structure Infections
1st Generation										
Cefadroxil QD-BID				√			√			√
Cefazolin[6]	√			√	√		√	√		√
Cephalexin[1] BID-QID				√			√	√		√
2nd Generation										
Cefaclor BID-TID		√		√	√		√		√	√
Cefprozil QD-BID		√	√	√					√	√
Cefuroxime[2] BID				√	√	√	√	√		√
Cefotetan[9] QD-BID					√	√	√	√		√
Cefoxitin[10] TID-QID					√	√	√	√		√
3rd Generation										
Cefdinir QD-BID	√	√	√	√					√	√
Cefditoren BID	√	√		√						√
Cefixime QD		√	√	√	√	√	√		√	
Cefotaxime[8] QD-q4h					√	√	√	√		√
Cefpodoxime[4] QD-BID	√	√	√	√		√	√		√	√
Ceftibuten QD		√		√					√	
Ceftriaxone[3] QD-BID					√	√	√		√	√
Ceftazidime[5] BID-TID	√				√	√	√	√		√
4th/5th Generation										
Cefepime[7] BID-TID	√						√			√
Ceftaroline BID	√									√

Additional Indications:

1. Bacterial Endocarditis
2. Meningitis, Septicemia, Post-op Prophylaxis
3. Meningitis, Musculoskeletal Infections, Septicemia, Post-op Prophylaxis
4. Uncomplicated Ano-rectal Infections in Women
5. Meningitis, Septicemia, Abdominal Infections
6. Genital Infection, Infective Cholangitis, Infective Endocarditis, Post-Operative Infection Prophylaxis, Septicemia
7. Febrile Neutropenia, Complicated Abdominal Infections
8. Meningitis, Septicemia, Abdominal Infections, Post-Op Prophylaxis
9. Abdominal Infections, Post-Operative Infection Prophylaxis
10. Abdominal Infections, Post-Operative Infection Prophylaxis, Septicemia

Demographics of Members Utilizing Cefixime (Suprax®) and Ceftibuten (Cedax®)



Discussion

There is no evidence that one cephalosporin has a particular clinical advantage over the others regarding their general adverse effects profile. The efficacy is based on each agent's spectrum of activity, although frequency of dosing may offer an advantage in convenience.[2] SoonerCare utilization data shows the majority of the use of cefixime and ceftibuten are in children, most likely for common childhood infections such as upper respiratory tract infections or otitis media. Potential cost savings could be gained by using other low cost alternatives with similar microbial coverage.

If 90% of the claims for cefixime, ceftibuten, and cefditoren (average cost/claim of $283) were converted to either cephalexin, or cefdinir, (average cost/claim of $38), the potential cost savings would total approximately $4.5 million over the next year.

Recommendations

The College of Pharmacy recommends the prior authorization of cefixime (Suprax®), ceftibuten (Cedax®), and cefditoren (Spectracef®) with the criteria presented below. A pre-emptive educational initiative will be sent to prescribing and 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, cefdinir, or other cost effective therapeutic equivalent medication.

Utilization Details of Cephalosporins: Calendar Year 2013

Chemical Name	Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
Cephalexin	CEPHALEXIN CAP 250MG	3,348	3,037	$25,275.03	1.10	0.25%	$7.55
Cephalexin	CEPHALEXIN CAP 500MG	31,338	26,632	$233,340.71	1.18	2.35%	$7.45
Cephalexin	CEPHALEXIN TAB 250MG	1	1	$13.89	1.00	0.00%	$13.89
Cephalexin	CEPHALEXIN TAB 500MG	27	27	$572.75	1.00	0.01%	$21.21
Cephalexin	CEPHALEXIN SUS 125/5ML	1,911	1,780	$30,923.44	1.07	0.31%	$16.18
Cephalexin	CEPHALEXIN SUS 250/5ML	15,691	14,018	$310,420.23	1.12	3.12%	$19.78
	Subtotal	**52,316**		**$600,546.05**	**1.08**	**6.04%**	**$11.48**
Cefdinir	CEFDINIR CAP 300MG	9,592	8,525	$348,630.49	1.13	3.51%	$36.35
Cefdinir	CEFDINIR SUS 125/5ML	18,398	15,231	$1,039,824.09	1.21	10.46%	$56.52
Cefdinir	CEFDINIR SUS 250/5ML	23,939	20,125	$2,019,268.40	1.19	20.31%	$84.35
	Subtotal	**51,929**		**$3,407,722.98**	**1.18**	**34.28%**	**$65.62**
Cefixime	SUPRAX CAP 400MG	22	21	$3,809.04	1.05	0.04%	$173.14
Cefixime	SUPRAX TAB 400MG	2,298	2,081	$361,435.46	1.10	3.64%	$157.28
Cefixime	SUPRAX CHW 100MG	89	80	$21,943.67	1.11	0.22%	$246.56
Cefixime	SUPRAX CHW 200MG	532	475	$178,210.27	1.12	1.79%	$334.98
Cefixime	SUPRAX SUS 100/5ML	3,593	2,993	$632,305.06	1.20	6.36%	$175.98
Cefixime	SUPRAX SUS 200/5ML	9,192	7,427	$3,081,523.74	1.24	31.00%	$335.24
Cefixime	SUPRAX SUS 500/5ML	30	27	$15,853.69	1.11	0.16%	$528.46
	Subtotal	**15,756**		**$4,295,080.93**	**1.13**	**43.21%**	**$272.60**
Cefprozil	CEFPROZIL TAB 250MG	759	657	$24,462.27	1.16	0.25%	$32.23
Cefprozil	CEFPROZIL TAB 500MG	735	676	$37,230.91	1.09	0.37%	$50.65
Cefprozil	CEFPROZIL SUS 125/5ML	1,376	1,208	$51,487.53	1.14	0.52%	$37.42
Cefprozil	CEFPROZIL SUS 250/5ML	4,965	4,263	$316,463.58	1.16	3.18%	$63.74
	Subtotal	**7,835**		**$429,644.29**	**1.14**	**4.32%**	**$54.84**
Cefuroxime	CEFUROXIME TAB 250MG	1,423	1,274	$16,020.37	1.12	0.16%	$11.26
Cefuroxime	CEFUROXIME TAB 500MG	1,654	1,488	$26,139.51	1.11	0.26%	$15.80
Cefuroxime	CEFTIN SUS 125/5ML	205	196	$20,829.57	1.05	0.21%	$101.61
Cefuroxime	CEFTIN SUS 250/5ML	824	754	$126,813.56	1.09	1.28%	$153.90
Cefuroxime	CEFUROXIME INJ 1.5GM	3	2	$126.57	1.50	0.00%	$42.19
	Subtotal	**4,109**		**$189,929.58**	**1.17**	**1.91%**	**$46.22**
Ceftibuten	CEDAX CAP 400MG	264	246	$52,697.03	1.07	0.53%	$199.61
Ceftibuten	CEDAX SUS 180/5ML	2,096	1,707	$789,064.26	1.23	7.94%	$376.46
	Subtotal	**2,360**		**$841,761.29**	**1.17**	**8.47%**	**$356.68**
Cefadroxil	CEFADROXIL CAP 500MG	834	744	$10,240.40	1.12	0.10%	$12.28
Cefadroxil	CEFADROXIL TAB 1GM	6	6	$238.13	1.00	0.00%	$39.69
Cefadroxil	CEFADROXIL SUS 250/5ML	406	385	$21,344.45	1.05	0.21%	$52.57
Cefadroxil	CEFADROXIL SUS 500/5ML	348	327	$18,467.35	1.06	0.19%	$53.07
	Subtotal	**1,594**		**$50,290.33**	**1.06**	**0.50%**	**$31.55**
Ceftriaxone	CEFTRIAXONE INJ 250MG	71	69	$330.05	1.03	0.00%	$4.65
Ceftriaxone	CEFTRIAXONE INJ 500MG	88	73	$685.21	1.21	0.01%	$7.79
Ceftriaxone	CEFTRIAXONE INJ 1GM	939	670	$14,278.48	1.40	0.14%	$15.21
Ceftriaxone	ROCEPHIN INJ 1GM	6	6	$42.89	1.00	0.00%	$7.15
Ceftriaxone	CEFTRIAXONE INJ 1GM	2	1	$60.24	2.00	0.00%	$30.12
Ceftriaxone	CEFTRIAXONE INJ 2GM	59	39	$3,632.91	1.51	0.04%	$61.57
Ceftriaxone	CEFTRIAXONE INJ 10GM	97	52	$6,829.66	1.87	0.07%	$70.41

Chemical Name	Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
Ceftriaxone	CEFTRIAXONE/ INJ DEX 1GM	8	4	$96.56	2.00	0.00%	$12.07
Ceftriaxone	CEFTRIAX/DEX INJ 2GM	1	1	$415.16	1.00	0.00%	$415.16
	Subtotal	**1,271**		**$26,371.16**	**1.45**	**0.26%**	**$20.75**
Cefpodoxime	CEFPODOXIME TAB 100MG	80	62	$9,018.46	1.29	0.09%	$112.73
Cefpodoxime	CEFPODOXIME TAB 200MG	195	166	$24,807.48	1.17	0.25%	$127.22
Cefpodoxime	CEFPODO PROX SUS 100/5ML	17	15	$2,363.27	1.13	0.02%	$139.02
	Subtotal	**292**		**$36,189.21**	**1.20**	**0.36%**	**$123.94**
Ceftazidime	CEFTAZIDIME INJ 1GM	78	33	$7,271.05	2.36	0.07%	$93.22
Ceftazidime	TAZICEF INJ 1GM	7	6	$713.54	1.17	0.01%	$101.93
Ceftazidime	CEFTAZIDIME INJ 2GM	24	14	$6,021.95	1.71	0.06%	$250.91
Ceftazidime	TAZICEF INJ 2GM	3	2	$356.43	1.50	0.00%	$118.81
Ceftazidime	TAZICEF INJ 6GM	17	8	$2,333.32	2.13	0.02%	$137.25
Ceftazidime	CEFTAZIDIME INJ 6GM	17	9	$4,514.03	1.89	0.05%	$265.53
	Subtotal	**146**		**$21,210.32**	**1.79**	**0.21%**	**$145.28**
Cefazolin	CEFAZOLIN INJ 1GM	52	20	$1,206.03	2.60	0.01%	$23.19
Cefazolin	CEFAZOLIN INJ 10GM	84	43	$5,797.72	1.95	0.06%	$69.02
Cefazolin	CEFAZOLIN SOD 10G VIAL	3	1	$47.23	3.00	0.00%	$15.74
	Subtotal	**139**		**$7,050.98**	**2.52**	**0.07%**	**$50.73**
Cefaclor	CEFACLOR CAP 250MG	57	47	$2,741.19	1.21	0.03%	$48.09
Cefaclor	CEFACLOR CAP 500MG	35	25	$1,686.23	1.40	0.02%	$48.18
Cefaclor	CEFACLOR SUS 125/5ML	17	17	$824.45	1.00	0.01%	$48.50
Cefaclor	CEFACLOR SUS 250/5ML	14	13	$566.08	1.08	0.01%	$40.43
Cefaclor	CEFACLOR SUS 375/5ML	6	6	$631.65	1.00	0.01%	$105.28
	Subtotal	**129**		**$6,449.60**	**1.14**	**0.08%**	**$50.00**
Cefepime	CEFEPIME INJ 1GM	48	25	$4,784.95	1.92	0.05%	$99.69
Cefepime	CEFEPIME INJ 2GM	56	38	$10,079.65	1.47	0.10%	$179.99
	Subtotal	**104**		**$14,864.60**	**1.70**	**0.15%**	**$142.93**
Cefditoren	SPECTRACEF TAB 200MG	14	14	$1,517.08	1.00	0.02%	$108.36
Cefditoren	CEFDITOREN TAB 200MG	12	11	$1,193.21	1.09	0.01%	$99.43
Cefditoren	CEFDITOREN TAB 400MG	9	9	$1,631.16	1.00	0.02%	$181.24
Cefditoren	SPECTRACEF TAB 400MG	5	5	$1,395.74	1.00	0.01%	$279.15
	Subtotal	**40**		**$5,737.19**	**1.02**	**0.06%**	**$143.43**
Cefotaxime	CLAFORAN INJ 1GM	5	5	$74.52	1.00	0.00%	$14.90
Cefotaxime	CEFOTAXIME INJ 2GM	4	2	$70.04	2.00	0.00%	$17.51
Cefotaxime	CLAFORAN INJ 2GM	1	1	$77.77	1.00	0.00%	$77.77
Cefotaxime	CEFOTAXIME INJ 10GM	3	2	$140.24	1.50	0.00%	$46.75
	Subtotal	**13**		**$362.57**	**1.38**	**0.00%**	**$27.89**
Ceftarolin	TEFLARO INJ 400MG	1	1	$3,063.43	1.00	0.03%	$3,063.43
Ceftarolin	TEFLARO INJ 600MG	4	2	$4,038.05	2.00	0.04%	$1,009.51
	Subtotal	**5**		**$7,101.48**	**1.50**	**0.0007**	**$1,420.30**
Cefotetan	CEFOTETAN INJ 2GM/20ML	2	1	$611.46	2.00	0.01%	$305.73
	Subtotal	**2**		**$611.46**	**2.00**	**0.01%**	**$305.73**
Cefoxitin	CEFOXITIN INJ 2GM	2	2	$945.96	1.00	0.01%	$472.98
	Subtotal	**2**		**$945.96**	**1.00**	**0.01%**	**$472.98**
	Total	**138,042**	**102,732***	**$9,941,869.98**	**1.34**	**100.00%**	**$72.02**

***Total unduplicated members.**

[1] Ezequiel Perez-Inestrosa, Rafael Suau, Maria Isabel Montañez, Rebeca Rodriguez, Cristobalina Mayorga, Maria J Torres, Miguel Blanca. Cephalosporin Chemical Reactivity and Its Immunological Implications. Curr Opin Allergy Clin Immunol. 2005;5(4):323-330

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Appendix I

Drug Utilization Review of Ophthalmic Anti-Inflammatory Medications

Oklahoma Health Care Authority
February 2014

Introduction[1,2,3, 4]

Ocular inflammation can be caused by various etiologies such as surgery or trauma. Topical application to the eye with anti-inflammatory medications can reduce inflammation while minimizing systemic adverse effects. The following tables show the available ophthalmic anti-inflammatory medications in this category.

Ophthalmic Corticosteroids
*Dexamethasone Sodium Phosphate **(Decadron®)**
Dexamethasone **(Maxidex®)**
Difluprednate **(Durezol®)**
*Fluorometholone **(FML® Liquifilm®)**
Fluorometholone **(FML Forte®)**
Fluorometholone **(FML S.O.P.®)**
Fluorometholone **(Flarex®)**
Loteprednol **(Alrex®)**
Loteprednol **(Lotemax®)**
Prednisolone Acetate **(Pred Mild®)**
*Prednisolone Acetate **(Omnipred®)**
Prednisolone Acetate **(Pred Forte®)**
*Prednisolone Sodium Phosphate **(Prednisol®)**
Rimexolone **(Vexol®)**

*Available as a generic formulation.

Ophthalmic NSAIDs
Bromfenac **(Prolensa™)**
*Bromfenac **(Bromday™)**
*Diclofenac **(Voltaren®)**
*Flurbiprofen **(Ocufen®)**
*Ketorolac **(Acular®)**
*Ketorolac **(Acular LS®)**
Ketorolac **(Acuvail®)**
Nepafenac **(Nevanac®)**
Nepafenac **(Ilevro™)**

*Available as a generic formulation.

Ophthalmic non-steroidal anti-inflammatory drugs (NSAIDs) are effective at reducing pain and inflammation following surgery or injury. Additionally, ophthalmic NSAIDs prevent and treat cystoid macular edema (CME) following cataract surgery and help maintain papillary dilatation during the surgery. Ophthalmic NSAIDs are typically applied to the eye one day immediately prior to the ocular surgery and continued two weeks postoperatively.

Most agents in the ophthalmic corticosteroid class of medications are indicated to treat various steroid-responsive inflammatory ocular conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe. Ophthalmic corticosteroids are commonly used in managing postoperative inflammation following various ocular surgeries, anterior uveitis, ocular allergies, corneal injury from chemical or thermal burns, and penetration of foreign bodies. Ophthalmic corticosteroids are typically applied several times daily to the eye following surgery or other inflammatory causes. Once the inflammation has reduced, treatment should be tapered prior to discontinuation.

Treatment[1-28]

Guidelines for postoperative use of topical ophthalmic agents have not been established. Recommendations from the American Academy of Ophthalmology (AAO) state the operating surgeon is responsible for determining an appropriate regimen of postoperative medications. AAO guidelines state topical anti-inflammatory agents can be used postoperatively to reduce inflammation and to treat established cystoid macular edema in patients undergoing cataract surgery.

Ophthalmic NSAIDs have fewer approved indications, with most products being indicated only for post-operative inflammation. Ophthalmic corticosteroids are used for a wider variety of inflammatory conditions including uveitis, ocular allergies, and trauma.

Ophthalmic NSAIDs				
Generic	**Trade**	**Indication**	**Dosage Form**	**Regimen**
Bromfenac	Prolensa™	Cataract surgery, post-op inflammation, ocular pain	0.07% Solution 1.6mL & 3mL Bottles	1 drop in affected eye QD 1 day prior to surgery and continued 2 weeks postop
*Bromfenac	Bromday™	Cataract surgery, post-op inflammation, ocular pain	0.09% Solution **Brand:** 1.7mL Bottle (Discontinued) **Generic:** 2.5mL & 5mL Bottles	1 drop in affected eye QD 1 day prior to surgery and continued 2 weeks postop
*Diclofenac	Voltaren®	Cataract surgery post-op pain; Temporary relief of pain and photophobia in patients undergoing corneal refractive surgery	0.1% Solution¥ 2.5mL & 5mL Bottles	**Cataract Surgery:** 1 drop in affected eye QID 1 day prior to surgery and continued 2 weeks postop **Corneal Refractive Surgery:** 1-2 drops to the operative eye within 1 hour prior to surgery, 15 minutes after surgery, 1-2 drops continued QID for up to 3 days
*Flurbiprofen	Ocufen®	Intraoperative Miosis	0.03% Solution 2.5mL Bottle	1 drop every ½ hour beginning 2 hours prior to surgery (4 total drops)
*Ketorolac	Acular®	Inflammation post cataract surgery; ocular itching due to seasonal allergic conjunctivitis	0.5% Solution 5mL Bottle	**Postop Inflammation:** 1 drop in affected eye QID 1 day prior to surgery and continued 2 weeks postop **Ocular Itching:** 1 drop in affected eye QID
*Ketorolac	Acular LS®	Reduction of ocular pain following corneal refractive surgery	0.4% Solution 5mL Bottle	1 drop QID in affected eye for up to 4 days following surgery
Ketorolac	Acuvail®	Pain and inflammation post cataract surgery	0.45% Solution¥ 30 Single-Use Vials 0.4mL each	1 drop to affected eye BID 1 day prior to surgery and continued 2 weeks postop
Nepafenac	Nevanac®	Pain and inflammation post cataract surgery	0.1% Suspension 3mL Bottle	1 drop to affected eye TID 1 day prior to surgery and continued 2 weeks postop
Nepafenac	Ilevro™	Pain and inflammation post cataract surgery	0.3% Suspension 1.7mL Bottle	1 drop to affected eye QD 1 day prior to surgery and continued 2 weeks postop; 1 additional drop should be administered 30-120 minutes prior to surgery

*Available as a generic formulation.
¥ Preservative Free

Ophthalmic Corticosteroids				
Generic	**Trade**	**Indication**	**Dosage Form**	**Regimen**
*Dexamethasone Sodium Phosphate	Decadron®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.1% Solution 5mL Bottle	1-2 drops Q hour during the day and Q 2 hrs at night; reduce dose to every 4 hours when favorable response observed
Dexamethasone	Maxidex®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.1% Suspension 5mL Bottle	1 or 2 drops: Severe disease Q hour & tapered to discontinuation. Mild disease up to 4-6 times daily.
Difluprednate	Durezol®	Inflammation and pain associated with ocular surgery; endogenous anterior uveitis	0.05% Emulsion 5mL Bottle	**Surgery:** 1 drop eye QID 1 day prior to surgery and continued 2 weeks postop, followed by BID for a week then tapered based on response **Uveitis:** 1 drop QID for 14 days followed by taper as indicated
*Fluorometholone	FML® Liquifilm®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.1% Suspension 5mL Bottle	1-2 drops BID-QID for 24 to 48 hours; Can increase dose to 2 drops every hour
Fluorometholone	FML Forte®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.25% Suspension 5mL & 10mL Bottle	1 drop BID-QID; withdrawal gradually
Fluorometholone	FML S.O.P.®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.1% Ointment 3.5gm Tube	½ inch ribbon QD-TID (May be used Q 4 hrs during initial 48hrs)
Fluorometholone	Flarex®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	0.1% Suspension 5mL Bottle	1-2 drops QID (2 drops Q 2 hours may be used during initial 48 hours)
Loteprednol	Alrex®	Temporary relief of the symptoms of seasonal allergic conjunctivitis	0.2% Suspension 5mL & 10mL Bottle	1 drop in affected eye QID

Generic	Trade	Indication	Dosage Form	Regimen
Loteprednol	Lotemax®	**Gel & Ointment:** Post-op inflammation and pain of the eye **Suspension:** Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe; Post-op inflammation of the eye	0.5% **Suspension** 5mL, 10mL, & 15mL 0.5% **Gel** 5gm Tube 0.5% **Ointment** 3.5 gm Tube	**Suspension:** 1-2 drops QID 1 day prior to surgery and continued 2 weeks postop; can be given 1-2 drops QID for inflammation not associated with surgery **Gel:** 1-2 drops QID beginning day after surgery and continued 2 weeks post-op **Ointment:** ½ inch ribbon QID beginning day after surgery and continued 2 weeks post-op
Prednisolone Acetate	Pred Mild®	Mild to moderate noninfectious allergic and inflammatory disorders of the lid, conjunctiva, cornea, and sclera	0.12% Suspension 5mL Bottle	1-2 drops BID-QID
*Prednisolone Acetate	Omnipred®	Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	1% Suspension 5mL & 10mL Bottle	2 drops QID
Prednisolone Acetate	Pred Forte®	Steroid responsive inflammation of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe	1% Suspension 1mL, 5mL, 10mL, & 15mL	1-2 drops BID-QID
*Prednisolone Sodium Phosphate	Prednisol®	Steroid responsive inflammation of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe; recommended for moderate to severe inflammation, particularly when unusually rapid control is desired.	1% Solution 10mL Bottle	1-2 drops up to Q hour during the day and Q 2 hours during the night; reduce dosage to one drop Q 4 hours
Rimexolone	Vexol®	Post-op inflammation; anterior uveitis	1% Suspension 5mL & 10mL Bottle	**Surgery:** 1-2 drops QID beginning 24 hours after surgery and continued 2 weeks post-op **Uveitis:** 1-2 drops Q hour during waking hours for 1 week, 1 drop Q 2 hours during 2nd week & tapered

*Available as a generic formulation

Clinical Comparison[1-29]

Comparison of Efficacy

FDA approved indications of Ophthalmic NSAIDs are generally limited to post-surgical inflammation, while ophthalmic corticosteroids are indicated for multiple inflammatory conditions.

Several studies have found ophthalmic NSAIDs and corticosteroids offer equivalent anti-inflammatory efficacy for post-operative inflammation. There is evidence that topically applied NSAIDs alone or in combination with corticosteroids are more effective than topical corticosteroids alone in preventing and treating cystoid macular edema. AAO guidelines have not designated a preferred class of ophthalmic anti-inflammatories or a preferred medication within either class for post-surgical inflammation.

American Optometric Association (AOA) guidelines state ophthalmic corticosteroids are effective in anterior uveitis and in relieving allergy symptoms; however, their use should be limited to the acute suppression of symptoms due to the potential for adverse side effects with prolonged use. AOA guidelines specifically recommend the use of prednisolone acetate 1% in the treatment of anterior uveitis, a potentially sight threatening condition.

Comparison of Safety

Clinical trials comparing the adverse event profiles of ophthalmic steroids and ophthalmic NSAIDs have not offered significant clinical differences between the two classes when used short-term.

Most side effects of the ophthalmic corticosteroids are related to potency, duration of action, and ability to penetrate the cornea. Ophthalmic corticosteroids have the potential for long-term adverse events such as elevated intraocular pressure (IOP) and cataract formation. The risk for developing increased IOP and cataracts may be minimized by using a site-specific ophthalmic corticosteroid such as loteprednol and ophthalmic corticosteroids with limited ocular penetration, such as fluorometholone.

Ophthalmic corticosteroids are contraindicated in patients with viral and fungal infections of the eye. Prolonged use of ophthalmic corticosteroids may cause ocular hypertension, defects in visual acuity and fields of vision, cataract formation, and secondary ocular infections. Perforations have occurred in patients with thinning of the cornea or sclera.

Ophthalmic NSAIDs may cause keratitis. Long term use may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration, or corneal perforation. Using ophthalmic NSAIDs beyond 14 days can increase a patient's risk of severe corneal adverse events. The risk of corneal complications does not appear to be higher with one agent in the class than another.

Special Populations

All products in both classes of ophthalmic anti-inflammatories are Pregnancy Category C. Use of ophthalmic NSAIDs during late pregnancy should be avoided due to the known effects of systemic NSAIDs on the fetal ductus arteriosus.

Ophthalmic steroids are frequently used to treat pediatric ocular allergies. Fluorometholone (FML®, FML Forte®, FML S.O.P.®) has been studied in children ages two years and older. The safety and efficacy of other products in the ophthalmic corticosteroid class have not been studied, but dexamethasone and prednisolone are used frequently in children.

The establishment of the safety and effectiveness of ophthalmic NSAIDs in pediatric patients is limited. Nepafenac (Ilevro™, Nevanac®) is FDA approved in children ten years of age and older. Ketorolac products (Acular®, Acular LS®) have been approved for use in children; Acular® is indicated in age two years and older and Acular LS® is indicated in age three years and older.

Utilization Trends Among SoonerCare Members

Comparison of Fiscal Years: Ophthalmic NSAIDs

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	664	882	$70,377.89	$79.79	$4.17	3,874	16,872
2013	710	1,008	$88,913.95	$88.21	$4.62	4,454	19,266
% Change	**6.90%**	**14.30%**	**26.30%**	**10.60%**	**10.80%**	**15.00%**	**14.20%**
Change	**46**	**126**	**$18,536.06**	**$8.42**	**$0.45**	**580**	**2,394**

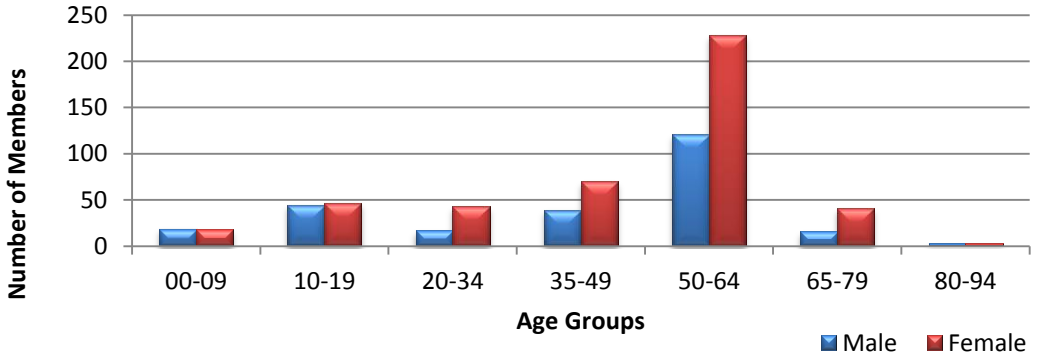
*Total number of unduplicated members

Comparison of Fiscal Years: Ophthalmic Corticosteroids

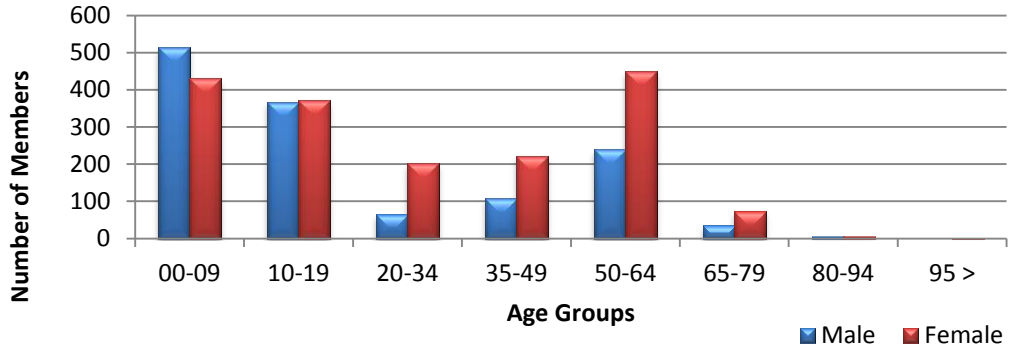
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	2,647	3,661	$156,704.18	$42.80	$2.29	26,955	68,319
2013	3,086	4,318	$175,056.93	$40.54	$2.23	29,816	78,497
%Change	**16.60%**	**17.90%**	**11.70%**	**-5.30%**	**-2.60%**	**10.60%**	**14.90%**
Change	**439**	**657**	**$18,352.75**	**-$2.26**	**-$0.06**	**2,861**	**10,178**

*Total number of unduplicated members.

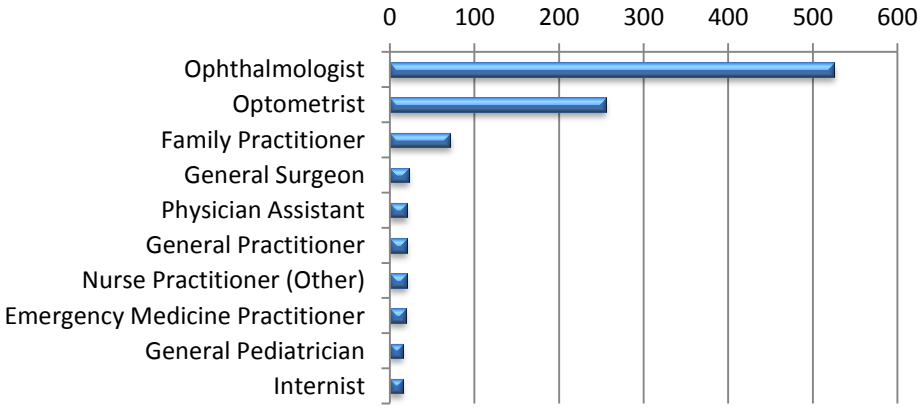
Demographics of Members Utilizing Ophthalmic NSAIDs



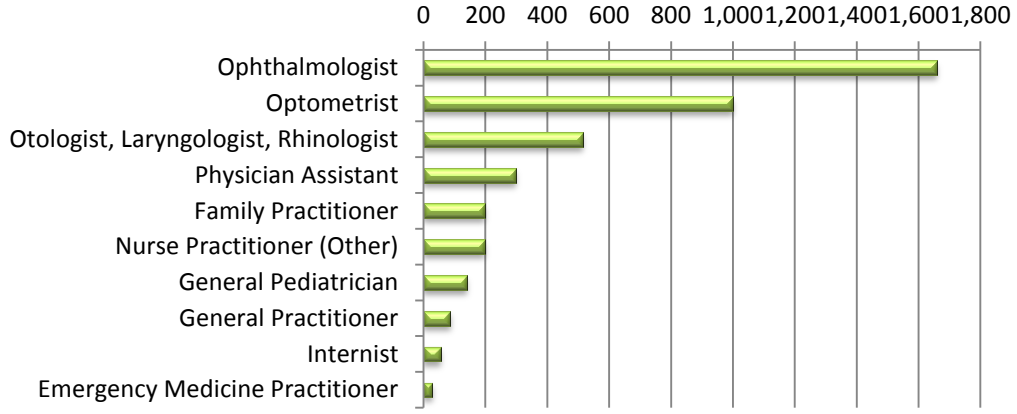
Demographics of Members Utilizing Ophthalmic Corticosteroids



Top Prescriber Specialties of Ophthalmic NSAIDs by Number of Claims



Top Prescriber Specialties of Ophthalmic Corticosteroids by Number of Claims



Utilization Details of Ophthalmic NSAIDs

Chemical Name	Product Utilized	Claims	Members	Cost	% Cost	Cost/ Claim
Proposed Tier 1 Products						
Diclofenac	Diclofenac Sol 0.1%	149	115	$1,675.76	1.88%	$11.25
Subtotal		**149**	**115**	**$1,675.76**	**1.88%**	**$11.25**
Ketorolac	Ketorolac Sol 0.5%	224	170	$4,158.57	4.68%	$18.57
Ketorolac	Ketorolac Sol 0.4%	144	115	$2,166.58	2.44%	$15.05
Subtotal		**368**	**285**	**$6,325.15**	**7.12%**	**$17.19**
Flurbiprofen	Flurbiprofen Sol 0.03%	2	2	$21.00	0.02%	$10.50
Subtotal		**2**	**2**	**$21.00**	**0.02%**	**$10.50**
Proposed Tier 2 Products						
Bromfenac	Bromday® Sol 0.09%	114	87	$22,905.14	25.76%	$200.92
Bromfenac	Bromfenac Sol 0.09%	18	12	$2,133.12	2.40%	$118.51
Bromfenac	Prolensa™ Sol 0.07%	7	7	$1,113.48	1.25%	$159.07
Subtotal		**139**	**102**	**$26,151.74**	**29.41%**	**$188.14**
Nepafenac	Nevanac ® Sus 0.1%	340	226	$52,464.78	59.01%	$154.31
Nepafenac	Ilevro™ Sus 0.3%	2	2	$306.22	0.34%	$153.11
Subtotal		**342**	**228**	**$52,771.00**	**59.35%**	**$154.30**
Ketorolac	Acuvail® Sol 0.45%	8	5	$1,969.30	2.21%	$246.16
Subtotal		**8**	**5**	**$1,969.30**	**2.21%**	**$246.16**
Total		**1,008**	***710**	**$88,913.95**	**100%**	**$88.21**

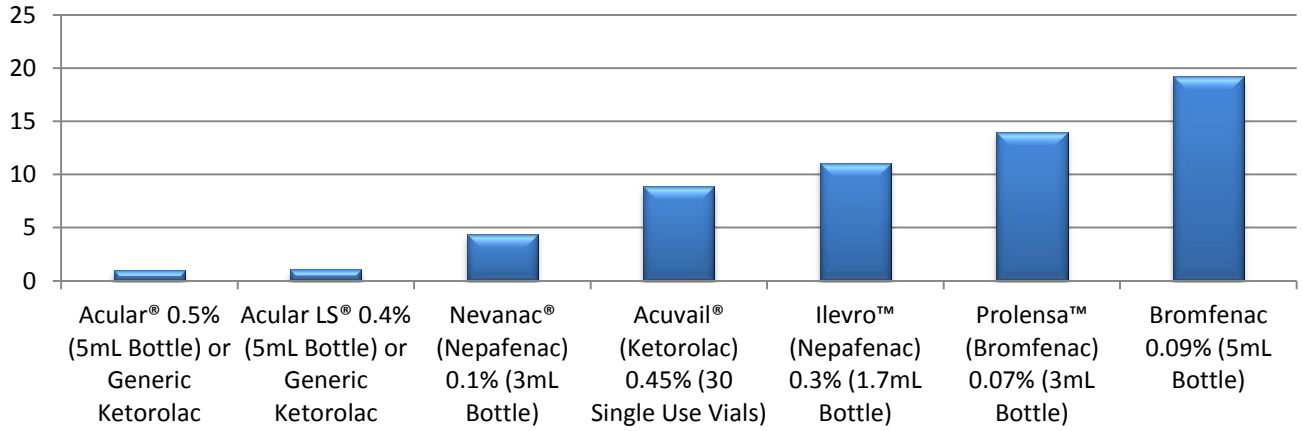
*Total number of unduplicated members

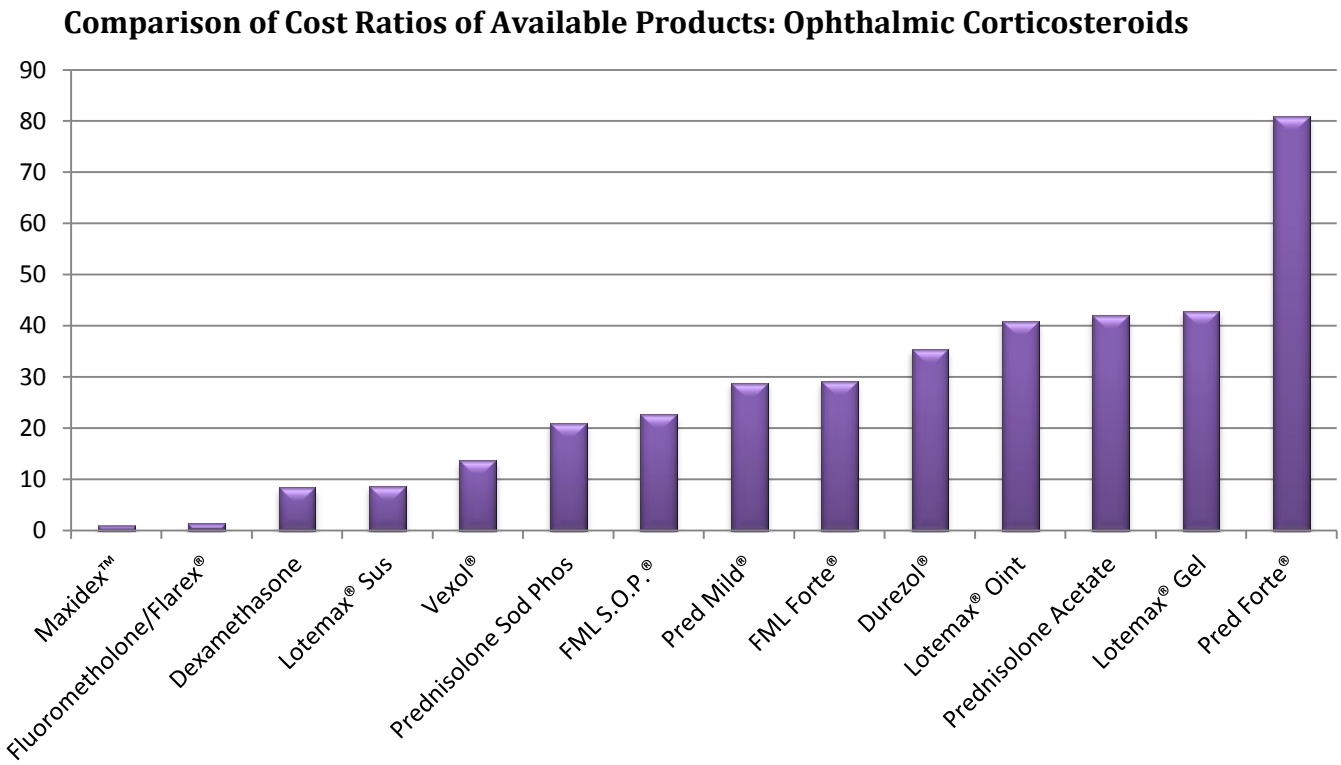
Utilization Details of Ophthalmic Corticosteroids

Chemical Name	Product Utilized	Claims	Members	Cost	% Cost	Cost/ Claim
Proposed Tier 1 Products						
Dexamethasone	Dexameth Sod Phos 0.1%	1,196	1,022	$29,216.11	16.69%	$24.43
Dexamethasone	Maxidex® Sus 0.1%	12	12	$889.31	0.51%	$74.11
Subtotal		**1,208**	**1,032**	**$30,105.42**	**17.20%**	**$24.92**
Prednisolone	Prednisolone Sus 1%	1,961	1,382	$29,047.15	16.59%	$14.81
Subtotal		**1,961**	**1,382**	**$29,047.15**	**16.59%**	**$14.81**
Loteprednol	Lotemax® Sus 0.5%	272	209	$47,385.99	27.07%	$174.21
Subtotal		**272**	**209**	**$47,385.99**	**27.07%**	**$174.21**
Fluorometholone	Fluorometh Sus 0.1%	214	167	$2,926.75	1.67%	$13.68
Fluorometholone	Flarex® Sus 0.1%	10	8	$510.85	0.29%	$51.09
Subtotal		**224**	**175**	**$3,437.60**	**1.96%**	**$15.35**
Proposed Tier 2 Products						
Prednisolone	Pred Forte® Sus 1%	75	54	$4,912.63	2.81%	$65.50
Prednisolone	Pred Mild® Sus 0.12%	40	31	$1,395.42	0.80%	$34.89
Prednisolone	Prednisol Sod Phos 1%	14	9	$696.60	0.40%	$49.76
Subtotal		**129**	**94**	**$7,004.65**	**4.01%**	**$54.30**
Difluprednate	Durezol ® 0.05%	363	210	$42,786.61	24.44%	$117.87
Subtotal		**363**	**210**	**$42,786.61**	**24.44%**	**$117.87**
Loteprednol	Lotemax ® Gel 0.5%	61	51	$7,889.40	4.51%	$129.33
Loteprednol	Lotemax® Oint 0.5%	24	17	$3,639.05	2.08%	$151.63
Loteprednol	Alrex® Sus 0.2%	1	1	$277.06	0.16%	$277.06
Subtotal		**86**	**69**	**$11,805.51**	**6.75%**	**$137.27**
Fluorometholone	FML Forte® Sus 0.25%	28	26	$1,125.07	0.64%	$40.18
Fluorometholone	FML® Oint 0.1%	25	22	$1,211.80	0.69%	$48.47
Subtotal		**53**	**48**	**$2,336.87**	**1.33%**	**$44.09**
Rimexolone	Vexol ®Sus 1%	22	14	$1,147.13	0.66%	$52.14
Subtotal		**22**	**14**	**$1,147.13**	**0.66%**	**$52.14**
Total		**4,318**	***3,086**	**$175,056.93**	**100%**	**$40.54**

*Total number of unduplicated members

Comparison of Cost Ratios of Available Products: Ophthalmic NSAIDs





Market News and Updates

Anticipated Patent Expirations

- Lotemax® ointment (loteprednol) - 2014
- Durezol® (difluprednate) - 2019
- Nevanac® (nepafenac) - 2027
- Acuvail® (ketorolac) - 2029

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 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 last 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%	Durezol® (Difluprednate) Emulsion 0.05%
Flarex® (Fluorometholone) Suspension 0.1%	Pred Mild® (Prednisolone Acetate) Suspension 0.12%
Lotemax® (Loteprednol) Suspension 0.5%	Pred Forte® (Prednisolone Acetate) Suspension 1%
Omnipred® (Prednisolone Acetate) Suspension 1%	Prednisolone Sodium Phosphate Solution 1%
	FML Forte® (Fluorometholone) Suspension 0.25%
	FML S.O.P® (Fluorometholone) Ointment 0.1%
	Vexol® (Rimexolone) Suspension 1%

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[6] Bromday® Product Information. Bausch & Lomb, Inc. Available online at http://www.bausch.com/ecp/-/m/BL/United%20States/Files/Package%20Inserts/Pharma/Bromday-prescribing-info.pdf. Last revised 10/2012. Last accessed 01/24/14.
[7] Voltarten Ophthalmic® Product Information. Novartis Pharmaceuticals. Available online at: http://www.pharma.us.novartis.com/product/pi/pdf/voltaren_ophthalmic.pdf. Last revised 04/2011. Last accessed 01/24/14.
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Appendix J

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

FDA NEWS RELEASE

For Immediate Release: Jan. 8, 2014
FDA approves Farxiga to treat type 2 diabetes

The U.S. Food and Drug Administration today approved Farxiga (dapaglifozin) tablets to improve glycemic control, along with diet and exercise, in adults with type 2 diabetes.
Type 2 diabetes affects about 24 million people and accounts for more than 90 percent of diabetes cases diagnosed in the United States. Over time, high blood sugar levels can increase the risk for serious complications, including heart disease, blindness, and nerve and kidney damage.
Farxiga is a sodium-glucose co-transporter 2 (SGLT2) inhibitor that blocks the reabsorption of glucose by the kidney, increases glucose excretion, and lowers blood glucose levels. The drug's safety and effectiveness were evaluated in 16 clinical trials involving more than 9,400 patients with type 2 diabetes. The trials showed improvement in HbA1c (hemoglogin A1c or glycosylated hemoglobin, a measure of blood sugar control).
Farxiga has been studied as a stand-alone therapy and in combination with other type 2 diabetes therapies including metformin, pioglitazone, glimepiride, sitagliptin, and insulin. Farxiga should not be used to treat people with type 1 diabetes; those who have increased ketones in their blood or urine (diabetic ketoacidosis); or those with moderate or severe renal impairment, end stage renal disease, or patients on dialysis.

An increased number of bladder cancers were diagnosed among Farxiga users in clinical trials so Farxiga is not recommended for patients with active bladder cancer. Patients with a history of bladder cancer should talk to their physician before using Farxiga. Farxiga can cause dehydration, leading to a drop in blood pressure (hypotension) that can result in dizziness and/or fainting and a decline in renal function. The elderly, patients with impaired renal function, and patients on diuretics to treat other conditions appeared to be more susceptible to this risk.
The FDA is requiring six post-marketing studies for Farxiga:

- a cardiovascular outcomes trial (CVOT) to evaluate the cardiovascular risk of Farxiga in patients with high baseline risk of cardiovascular disease;
- a double-blind, randomized, controlled assessment of bladder cancer risk in patients enrolled in the CVOT;
- an animal study evaluating the role of Farxiga-induced urinary flow/rate and composition changes on bladder tumor promotion in rodents;
- two clinical trials to assess the pharmacokinetics, efficacy, and safety in pediatric patients; and
- an enhanced pharmacovigilance program to monitor reports of liver abnormalities and pregnancy outcomes.

In clinical trials the most common side effects observed in patients treated with Farxiga were genital mycotic (fungal) infections and urinary tract infections.
Farxiga is marketed by Bristol-Meyers Squibb Company, Princeton, N.J. and AstraZeneca Pharmaceuticals L.P., Wilmington, Del.

FDA NEWS RELEASE

For Immediate Release: Jan. 23, 2014
FDA prohibits Ranbaxy's Toansa, India facility from producing and distributing drugs for the U.S. market
Another Ranbaxy facility added to existing consent decree

The U.S. Food and Drug Administration today notified Ranbaxy Laboratories, Ltd., that it is prohibited from manufacturing and distributing active pharmaceutical ingredients (APIs) from its facility in Toansa, India, for

FDA-regulated drug products. The Toansa facility is now subject to certain terms of a consent decree of permanent injunction entered against Ranbaxy in January 2012.

The decree contains, among other things, provisions to ensure compliance with current good manufacturing practice (CGMP) requirements at Ranbaxy facilities in Paonta Sahib and Dewas, India, as well as provisions to address data integrity issues at those facilities. In September 2013, the FDA added Ranbaxy's Mohali facility to the CGMP provisions of the decree.

Under the decree, the FDA has issued an order prohibiting Ranbaxy from:

- distributing in the United States drugs manufactured using API from Toansa, including drugs made by Ranbaxy's Ohm Laboratories facility in New Jersey;
- manufacturing API at its Toansa facility for FDA-regulated drug products;
- exporting API from Toansa to the United States for any purpose; and
- providing API from Toansa to other companies, including other Ranbaxy facilities, making products for American consumers.

The FDA exercised its authority under a provision in the consent decree which permits the agency to extend the decree's terms to any Ranbaxy-owned or operated facility if an FDA inspection finds the facility in violation of the Federal Food, Drug, and Cosmetic Act or FDA regulations, including CGMP requirements. CGMP requirements serve as the primary regulatory safeguard over drug manufacturing and must be followed by companies to ensure manufacturing quality. The FDA also acted under a separate provision in the decree which permits the agency to order additional corrective actions that FDA determines are necessary to achieve compliance with the law or the decree.

The FDA's inspection of the Toansa facility, which concluded on Jan. 11, 2014, identified significant CGMP violations. These included Toansa staff retesting raw materials, intermediate drug products, and finished API after those items failed analytical testing and specifications, in order to produce acceptable findings, and subsequently not reporting or investigating these failures.

The agency is evaluating potential drug shortage issues that may result from this action. If the FDA determines that a medically necessary drug is in shortage or at risk of shortage, the FDA may modify this order to preserve patient access to drugs manufactured under controls that are sufficient to assure quality, safety and effectiveness.

As a result of this action, Ranbaxy is now prohibited from manufacturing API for FDA-regulated drugs at the Toansa facility and from introducing API from that facility into interstate commerce, including into the United States, until the firm's methods and controls used to manufacture drugs at the Toansa facility are established, operated and administered in compliance with CGMP.

Ranbaxy is required to hire a third-party expert to thoroughly inspect the Toansa facility and certify to the FDA that the facility and its methods and controls are adequate to ensure continuous compliance with CGMP. Ranbaxy will not be permitted to resume manufacturing and distributing API for FDA-regulated drugs from the Toansa facility until the agency is satisfied that Ranbaxy has addressed its manufacturing quality issues at that facility.

The FDA recommends that patients not disrupt their drug therapy because this could jeopardize their health. Patients who are concerned about their medications should talk with their health care professional before discontinuing treatment.

Safety Announcements

FDA warns of possible harm from exceeding recommended dose of over-the-counter sodium phosphate products to treat constipation

[1-8-2014] The U.S. Food and Drug Administration (FDA) is warning that using more than one dose in 24 hours of over-the-counter (OTC) sodium phosphate drugs to treat constipation can cause rare but serious harm to the kidneys and heart, and even death. OTC sodium phosphate drug products include oral solutions taken by mouth and enemas used rectally. Consumers and health care professionals should always read the Drug Facts label for OTC sodium phosphate drugs and use these products as recommended on the label, and not exceed the labeled dose. Caregivers should not give the oral products to children 5 years and younger without first discussing with a health care professional. Health care professionals should use caution when recommending an oral dose of these products for children 5 years and younger. The rectal form of these products should never be given to children younger than 2 years.

FDA has become aware of reports of severe dehydration and changes in the levels of serum electrolytes from taking more than the recommended dose of OTC sodium phosphate products, resulting in serious adverse effects on organs, such as the kidneys and heart, and in some cases resulting in death. These serum electrolytes include calcium, sodium, and phosphate. According to the reports, most cases of serious harm occurred with a single dose of sodium phosphate that was larger than recommended or with more than one dose in a day.
Some individuals may be at higher risk for potential adverse events when the recommended dose of OTC sodium phosphate is exceeded. These individuals include young children; individuals older than 55 years; patients who are dehydrated; patients with kidney disease, bowel obstruction, or inflammation of the bowel; and patients who are using medications that may affect kidney function. These medications include diuretics or water pills; angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) used to treat high blood pressure; and nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and naproxen.

Safety Announcements

FDA recommends health care professionals discontinue prescribing and dispensing prescription combination drug products with more than 325 mg of acetaminophen to protect consumers

[1/14/2014] FDA is recommending health care professionals discontinue prescribing and dispensing prescription combination drug products that contain more than 325 milligrams (mg) of acetaminophen per tablet, capsule, or other dosage unit. There are no available data to show that taking more than 325 mg of acetaminophen per dosage unit provides additional benefit that outweighs the added risks for liver injury. Further, limiting the amount of acetaminophen per dosage unit will reduce the risk of severe liver injury from inadvertent acetaminophen overdose, which can lead to liver failure, liver transplant, and death.
We recommend that health care providers consider prescribing combination drug products that contain 325 mg or less of acetaminophen. We also recommend that when a pharmacist receives a prescription for a combination product with more than 325 mg of acetaminophen per dosage unit that they contact the prescriber to discuss a product with a lower dose of acetaminophen. A two tablet or two capsule dose may still be prescribed, if appropriate. In that case, the total dose of acetaminophen would be 650 mg (the amount in two 325 mg dosage units). When making individual dosing determinations, health care providers should always consider the amounts of both the acetaminophen and the opioid components in the prescription combination drug product.
In January 2011 we asked manufacturers of prescription combination drug products containing acetaminophen to limit the amount of acetaminophen to no more than 325 mg in each tablet or capsule by January 14, 2014. We requested this action to protect consumers from the risk of severe liver damage which can result from taking too much acetaminophen. This category of prescription drugs combines acetaminophen with another ingredient intended to treat pain (most often an opioid), and these products are commonly prescribed to consumers for pain, such as pain from acute injuries, post-operative pain, or pain following dental procedures.
More than half of manufacturers have voluntarily complied with our request. However, some prescription combination drug products containing more than 325 mg of acetaminophen per dosage unit remain available.
In the near future we intend to institute proceedings to withdraw approval of prescription combination drug products containing more than 325 mg of acetaminophen per dosage unit that remain on the market.
Cases of severe liver injury with acetaminophen have occurred in patients who:

- took more than the prescribed dose of an acetaminophen-containing product in a 24-hour period;
- took more than one acetaminophen-containing product at the same time; or
- drank alcohol while taking acetaminophen products.

Inadvertent overdose from prescription combination drugs containing acetaminophen accounts for nearly half of all cases of acetaminophen-related liver failure in the United States, some of which result in liver transplant or death.
Acetaminophen is also widely used as an over-the-counter (OTC) pain and fever medication, and is often combined with other ingredients, such as cough and cold ingredients. We will address OTC acetaminophen

products in another regulatory action. Many consumers are often unaware that many products (both prescription and OTC) contain acetaminophen, making it easy to accidentally take too much.

Current Drug Shortages Index (as of January 24, 2014):

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

Acetylcysteine Inhalation Solution
Amikacin Injection
Aminocaproic Acid Injection (initial posting date 3/8/2013)
Aminophylline (initial posting date 12/10/2012)
Ammonium Chloride Injection (initial posting date 3/8/2013) UPDATED 1/27/2014
Amytal Sodium Injection (initial posting date 1/31/2013)
Atracurium Besylate (initial posting date 2/27/2012)
Atropine Sulfate Injection UPDATED 1/23/2014
Barium Sulfate for Suspension (initial posting date 10/12/2012)
Bismuth Subsalicylate; Metronidazole; Tetracycline Hydrochloride (Helidac) (initial posting date 3/8/2012)
Bumetanide Injection (initial posting date 6/21/2012) 1/27/2014
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection UPDATED 1/27/2014
Buprenorphine Hydrochloride (Buprenex) Injection
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)
Chloramphenicol Sodium Succinate Injection (initial posting date 1/7/2014)
Chromic Chloride Injection
Cidofovir Injection (initial posting date 2/15/2013)
Citric Acid; Gluconolactone; Magnesium Carbonate (Renacidin) Solution for Irrigation (initial posting date 6/30/2012)
Clindamycin phosphate (Cleocin) Injection (initial posting date 10/2/2013) UPDATED 1/28/2014
Copper Injection (initial posting date 4/25/2013)
Cyanocobalamin Injection (initial posting date 1/25/2013)
Daunorubicin Hydrochloride Solution for Injection
Denileukin Diftitox (Ontak) (initial posting date 9/22/2012)
Desmopressin Acetate (DDAVP) Injection (initial posting date 5/7/2013)
Dexamethasone Sodium Phosphate Injection (initial posting date 1/15/2013) UPDATED 1/23/2014
Dextrose Injection (initial posting date 5/23/2012) UPDATED 1/27/2014
Dipyridamole Injection (initial posting date 7/24/2012) UPDATED 1/23/2014
Dobutamine Hydrochloride Injection (initial posting date 4/26/2013)
Doxorubicin (Adriamycin) Lyophilized Powder (initial posting date 12/2/2011) UPDATED 1/22/2014
Epinephrine Injection (initial posting date 4/27/2012) UPDATED 1/27/2014
Epinephrine 1mg/mL (Preservative Free) (initial posting date 6/21/2012)
Ethiodol (Ethiodized Oil) Ampules
Etomidate (Amidate) Injection (initial posting date 2/9/2012) UPDATED 1/21/2014
Fentanyl Citrate (Sublimaze) Injection UPDATED 1/27/2014
Furosemide Injection (initial posting date 6/20/2012)
Heparin Sodium Injection (initial posting date 7/5/2012) UPDATED 1/27/2014
Hydromorphone Hydrochloride (Dilaudid) Injection (initial posting date 3/7/2012) UPDATED 1/27/2014
Hydromorphone Hydrochloride Tablets (initial posting date 2/19/2013)
Intravenous Fat Emulsion
Isoniazid; Rifampin (Rifamate) Capsules (initial posting date 3/15/2013)

Ketorolac Tromethamine Injection
Leucovorin Calcium Lyophilized Powder for Injection
Leuprolide Acetate Injection
Levothyroxine Sodium (Levoxyl) Tablets (initial posting date - 3/15/2013)
Lidocaine Hydrochloride (Xylocaine) Injection (initial posting date - 2/22/2012) UPDATED 1/27/2014
Liotrix (Thyrolar) Tablets
Lorazepam (Ativan) Injection
Magnesium Sulfate Injection UPDATED 1/27/2014
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)
Methyldopate Hydrochloride Injection
Methylin Chewable Tablets (initial posting date 2/19/2013)
Methylphenidate Hydrochloride ER Tablets (initial posting date 2/19/2013) UPDATED 1/28/2014
Methylphenidate Hydrochloride Tablets (initial posting date 2/19/2013) UPDATED 1/28/2014
Metoclopramide (Reglan) Injection
Morphine Sulfate Injection
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)
Multi-Vitamin Infusion (Adult and Pediatric)
Nalbuphine Hydrochloride (Nubain) Injection (initial posting date 5/15/2012)
Neostigmine Methylsulfate Injection (initial posting date 1/14/2013)
Nitroglycerin in 5% Dextrose Injection (initial posting date 12/20/2013)
Ondansetron (Zofran) 2mg/mL Injection UPDATED 1/27/2014
Pancuronium Bromide Injection UPDATED 1/27/2014
Papaverine Hydrochloride Injection (initial posting date 12/17/2012)
Pegvisomant (Somavert) Injection (initial posting date 10/21/2013)
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 1/27/2014
Potassium Phosphate Injection
Procainamide HCL Injection UPDATED 1/27/2014
Prochlorperazine Injection (initial posting date 1/30/2012)
Promethazine Injection (initial posting date 2/10/2012)
Reserpine Tablets (initial posting date 4/17/2013)
Rifampin for Injection (initial posting date 3/22/2013) UPDATED 1/22/2014
Secretin Synthetic Human (ChiRhoStim) Injection (ChiRhoStim) (initial posting date 6/15/2012)
Selenium Injection
Sincalide (Kinevac) Lyophilized Powder for Injection (initial posting date 6/21/2013) UPDATED 1/27/2014
Sodium Chloride 0.9% Injection Bags (initial posting date 1/15/2014) UPDATED 1/27/2014
Sodium Chloride 23.4%
Sodium Phosphate Injection UPDATED 1/27/2014
Succinylcholine (Anectine, Quelicin) Injection (initial posting date 8/17/2012)
Sufentanil Citrate (Sufenta) Injection UPDATED 1/27/2014
Sulfamethoxazole 80mg/ml;Trimethoprim 16mg/ml (SMX/TMP) (Bactrim) Injection
Telavancin (Vibativ) Injection
Tetracycline Capsules
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 1/27/2014

Trace Elements (initial posting date 1/24/2013)
Tromethamine (Tham) Injection (initial posting date 5/2/2012)
Verapamil Hydrochloride Injection, USP (initial posting date 4/17/2013) UPDATED 1/27/2014
Vitamin A Palmitate (Aquasol A)
Zinc Injection (initial posting date 2/15/2012)