Drug Utilization Review Board

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

Wednesday
November 14, 2012
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: Chris Le, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – November 14, 2012

DATE: November 8, 2012

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 November meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

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

Update on DUR / MCAU Program – See Appendix B.

Action Item – Vote on 2013 Meeting Dates – See Appendix C.

Action Item – Vote to Update Bladder Control PBPA Category and Prior Authorize Myrbetriq™ – See Appendix D.

Action Item – Vote to Update Antidepressants PBPA Category and Prior Authorize Forfivo XL® and Fluoxetine 60mg Tablets – See Appendix E.

Action Item – Vote to Prior Authorize Miscellaneous Butalbital-Acetaminophen-Caffeine Products – See Appendix F.

Action Item – Annual Review of Daliresp® – See Appendix G.

Action Item – Annual Review of Topical Antifungal Medications – See Appendix H.

30 Day Notice to Prior Authorize Relistor® – See Appendix I.

30 Day Notice to Prior Authorize Rayos® – See Appendix J.

FDA and DEA Updates – See Appendix K.

Future Business

Adjournment

ORI-4403 • P.O. BOX 26901 • OKLAHOMA CITY, OKLAHOMA 73126-0901 • (405) 271-9039 • FAX: (405) 271-2615

Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – November 14, 2012 @ 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. October 10, 2012 DUR Minutes – Vote
- B. October 11, 2012 DUR Recommendation Memorandum

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

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.
- A. Medication Coverage Activity for October 2012
- B. Pharmacy Help Desk Activity for October 2012
- C. Retrospective Drug Evaluation: Focusing on Duplication of Narcotic Therapy

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

5. Action Item – Vote on 2013 Meeting Dates – See Appendix C.

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

6. Action Item – Vote to Update Bladder Control PBPA Category and Prior Authorize Myrbetriq™ – See Appendix D.
- A. COP Recommendations

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

7. Action Item – Vote to Update Antidepressants PBPA Category and Prior Authorize Forfivo XL® and Fluoxetine 60mg Tablets – See Appendix E.
- A. COP Recommendations

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

8. Action Item – Vote to Prior Authorize Miscellaneous Butalbital-Acetaminophen-Caffeine Products – See Appendix F.

A. COP Recommendations

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

9. Action Item – Annual Review of Daliresp® – See Appendix G.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. COP Recommendations

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

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

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details

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

11. 30 Day notice to Prior Authorize Relistor® – See Appendix I.

A. Overview
B. Product Summary
C. COP Recommendations
D. Product Information

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

12. 30 Day notice to Prior Authorize Rayos® – See Appendix J.

A. Product Summary
B. COP Recommendations
C. Product Information

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

13. FDA and DEA Updates – See Appendix K.

14. Future Business

A. Utilization Review of COPD Medications
B. Annual Reviews
C. New Product Reviews

15. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of OCTOBER 10, 2012

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.: Vice-Chairman	X	
Mark Feightner, Pharm.D.		X
Anetta Harrell, Pharm.D.	X	
Evelyn 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	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Shellie Keast, Pharm.D, M.S.; DUR Manager	X	
Chris Le, Pharm.D.; Clinical Coordinator	X	
Mark Livesay, Operations Manager	X	
Carol Moore, Pharm.D.; Clinical Pharmacist		X
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist		X
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research	X	
Leslie Robinson, D.Ph.; PA Coordinator	X	
Jennifer Sipols, Pharm.D.; Clinical Pharmacist		X
Jo Nel Weber, Pharm.D.; Clinical Pharmacist	X	
Graduate Students: Amany Hussein, Manish Mittal	X	
Visiting Pharmacy Student(s): n/a		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Garth Splinter, M.D., M.B.A.; Director of Medicaid/Medical Services		X
Rebecca Pasternik-Ikard, Deputy State Medicaid Director	X	
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	X	
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Carter Kimble, M.Ph.; Public Affairs- Information Representative		X
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	
Stacey Hale, Pharmacy Research Analyst	X	

OTHERS PRESENT:		
Sam Smothers, Medimmune	Toby Thompson, Pfizer	Don Kempin, Novo Nordisk
Gary Karg, Novartis	Mark DeClerk, Lilly	Jim Fowler, AstraZeneca
Bill Clark, BMS	Warren Tayes, Merck	Michael Hathaway, Otsuka
Ed Overholt	Roger Grotzinger, BMS	Jim Chapman, Abbott
Anthony DeLeon, Shire	Vanessa Papion, UCB	Jody Jensen, UCB
Brian Maves, Pfizer	Tone Jones, Sunovion	Kathy Phillips, Novo Nordisk
Ron Schnare, Shire	Bob G., Lundback	

PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 6	Jody Jensen
Agenda Item No. 4	Ed Overholt

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. 6 Jody Jensen

Agenda Item No. 4 Ed Overholt

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: September 12, 2012 DUR Minutes

Dr. Winegardener moved to approve as submitted; seconded by Dr. Preslar.

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review Response: April 2012

4B: Medication Coverage Activity: September 2012

4C: Pharmacy Help Desk Activity: September 2012

4D: Retrospective Drug Evaluation: Focusing on Safety

Reports included in agenda packet; presented by Dr. Keast.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE CIALIS®

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

Dr. Kuhls moved to approve with the addition to the Tier 3 PA Criteria, " . . . contraindication to all available Tier 1 and Tier 2 products, or lack of efficacy of all Tier 1's"; seconded by Dr. Rhymer.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE NEUPRO®

For Public Comment: Jody Jensen

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

Dr. Bell moved to approve with the change to Parkinson's Disease criteria, no. 3 "Failed treatment or intolerance of …. "; seconded by Dr. Harrell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: ANNUAL REVIEW OF BLADDER CONTROL MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MYRBETRIQ™

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE FORFIVO XL™ AND FLUOXETINE 60 MG

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF ALZHEIMER'S MEDICATIONS

Materials included in agenda packet; presented by Drs. Sipols and Le.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE MISCELLANEOUS BUTALBITAL PRODUCTS
Materials included in agenda packet; presented by Dr. Moore.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: FDA & DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: FUTURE BUSINESS
Materials included in agenda packet; submitted by Dr. Cothran.
A: Annual Reviews
B: New Product Reviews
C: Utilization Review of COPD Medications
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ADJOURNMENT
The meeting was adjourned at 7:24 p.m.

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

Memorandum

Date: October 11, 2012

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

From: Chris Le, Pharm.D.
Assistant Director
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of October 10, 2012

Recommendation 1: Vote to Prior Authorize Cialis® (tadalafil)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of a Tier 3 and placement of Cialis® (tadalafil) into Tier 3 of the Benign Prostatic Hyperplasia PBPA category with the following criteria:

Tier 2 Prior Authorization Criteria:

1. FDA approved diagnosis.
2. A 4-week trial of two Tier 1 medications from different pharmacological classes within 90 days.
3. Documented adverse effect, drug interaction, or contraindication to all available Tier 1 products.

Tier 3 Prior Authorization Criteria:

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

Tier 1	Tier 2	Tier 3
Uroxatral® (Alfuzosin)	Rapaflo® (Silodosin)	Cialis® (tadalafil) 5mg
Hytrin® (Terazosin)	Cardura XL® (Doxazosin)	
Cardura® (Doxazosin)	Avodart® (Dutasteride)	
Flomax® (Tamsulosin)	Jalyn® (Dutasteride/Tamsulosin)	
Proscar® (Finasteride)		

Recommendation 2: Vote to Prior Authorize of Neupro® (rotigotine transdermal system)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Neupro® (rotigotine transdermal system) with the following criteria:

Parkinson's Disease

1. FDA approved indication for the treatment of signs and symptoms of Parkinson's Disease
2. Must be 18 years old or older
3. ~~Prior use of or~~ Failed treatment, intolerance, or clinically significant reason why member cannot use oral dopamine agonists

Restless Leg Syndrome

1. FDA approved indication of Restless Leg Syndrome.
2. Must be 18 years or older.
3. Must provide documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
    a. carbidopo/levodopa
    b. pramipexole
    c. ropinirole

Recommendation 3: Annual Review of Bladder Control Medications

No Action Required

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

Recommendation 4: Annual Review of Antidepressants PBPA Category

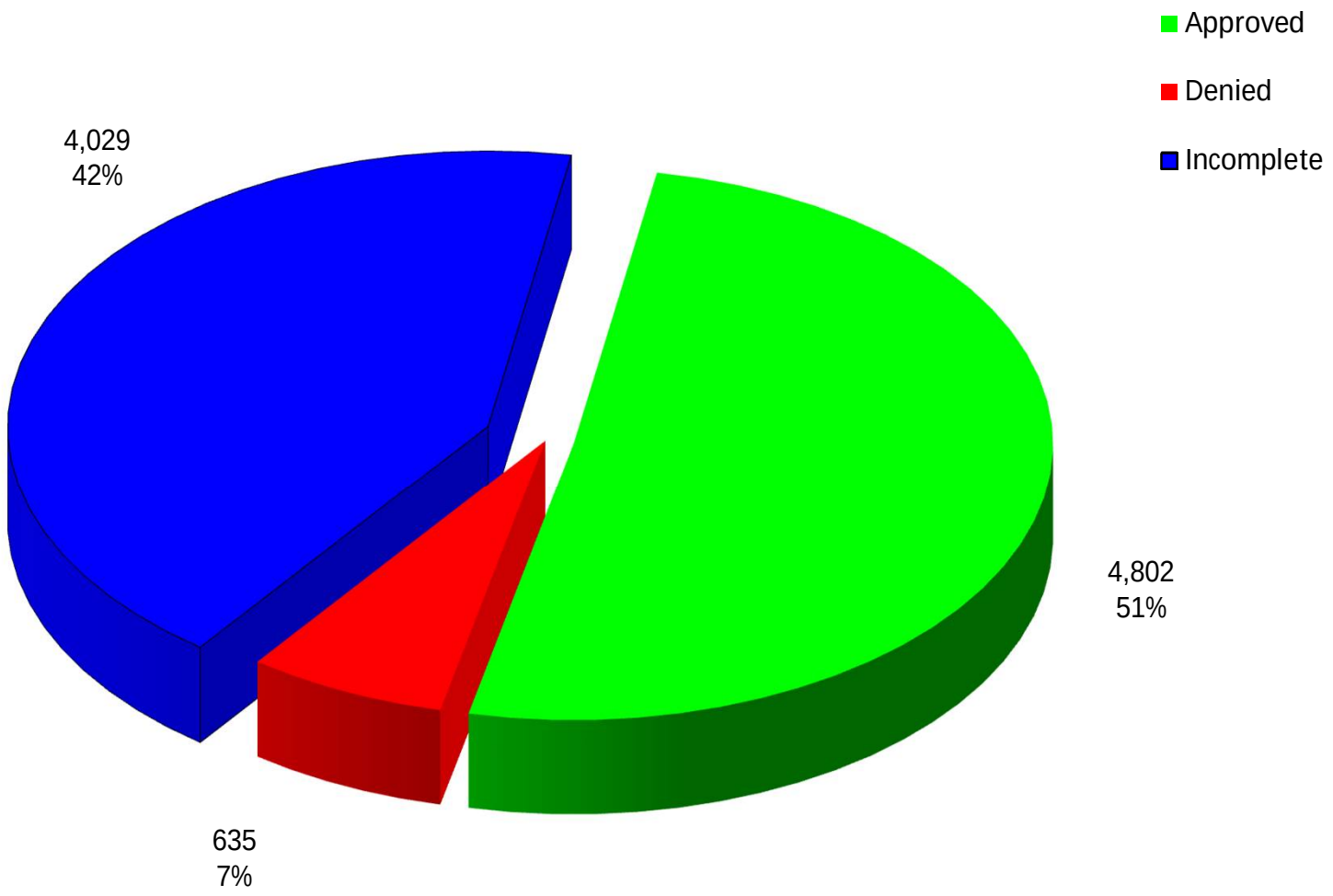
No Action Required

Recommendation 5: Annual Review of Alzheimer's Medications

No Action Required

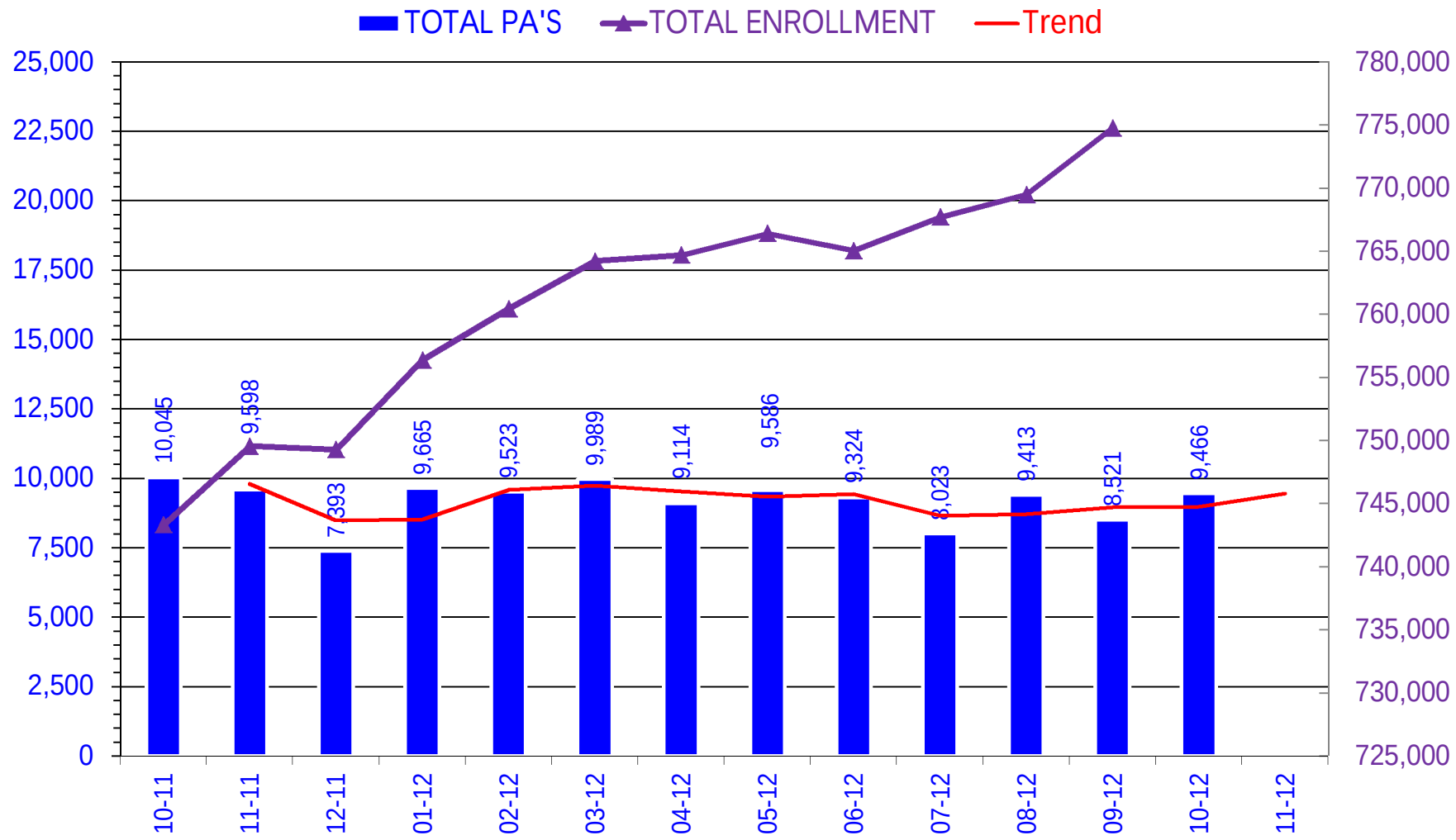
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: October 2012



PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: October 2011 – October 2012



PA totals include approved/denied/incomplete/overrides

Prior Authorization Activity

10/1/2012 Through 10/31/2012

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	420	171	6	243	358
Analgesic, Narcotic	400	182	17	201	284
Angiotensin Receptor Antagonist	53	16	5	32	360
Antiasthma	1,084	547	21	516	246
Antibiotic	18	3	2	13	123
Anticoagulant	16	13	0	3	321
Anticonvulsant	114	70	1	43	325
Antidepressant	274	100	16	158	322
Antidiabetic	140	65	5	70	350
Antihistamine	200	160	5	35	356
Antihyperlipidemic	10	2	2	6	360
Antimigraine	78	23	10	45	343
Antiplatelet	25	16	0	9	333
Antiulcers	338	97	51	190	100
Anxiolytic	110	78	3	29	250
Atypical Antipsychotics	464	287	5	172	350
Biologics	44	25	0	19	347
Bladder Control	79	18	6	55	357
Cardiovascular	33	12	6	15	262
Dermatological	122	30	37	55	98
Endocrine & Metabolic Drugs	131	46	13	72	266
Erythropoietin Stimulating Agents	59	24	8	27	109
Fibromyalgia	167	42	27	98	358
Gastrointestinal Agents	73	38	4	31	111
Glaucoma	20	5	0	15	305
Growth Hormones	62	46	0	16	165
HFA Rescue Inhalers	125	26	12	87	344
Insomnia	100	26	4	70	185
Multiple Sclerosis	30	15	0	15	178
Muscle Relaxant	125	39	40	46	79
Nasal Allergy	169	18	35	116	195
Neurological Agents	45	33	0	12	330
Nsaids	176	34	15	127	262
Ocular Allergy	71	25	6	40	112
Ophthalmic	47	13	0	34	17
Osteoporosis	29	14	3	12	358
Other*	172	34	13	125	203
Otic Antibiotic	38	9	2	27	7
Pediculicide	135	37	2	96	11
Prenatal Vitamins	26	3	2	21	113
Smoking Cess.	36	11	2	23	33
Statins	58	32	2	24	359
Stimulant	800	428	31	341	340
Suboxone/Subutex	153	113	3	37	80
Synagis	522	214	120	188	141
Topical Antibiotic	10	0	0	10	0
Topical Antifungal	16	2	0	14	16
Topical Corticosteroids	45	0	10	35	0
Vitamin	51	13	30	8	293

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

Pharmacotherapy	89	71	1	17	238
Emergency PAs	3	3	0	0	
Total	**7,605**	**3,329**	**583**	**3,693**	
Overrides					
Brand	90	56	4	30	330
Dosage Change	653	598	6	49	6
High Dose	4	4	0	0	297
Ingredient Duplication	14	12	0	2	4
Lost/Broken Rx	106	100	4	2	5
NDC vs Age	10	8	1	1	281
Nursing Home Issue	127	124	0	3	8
Other	47	43	2	2	30
Quantity vs. Days Supply	805	523	35	247	289
Stolen	5	5	0	0	5
Overrides Total	**1,861**	**1,473**	**52**	**336**	
Total Regular PAs + Overrides	**9,466**	**4,802**	**635**	**4,029**	

Denial Reasons	
Unable to verify required trials.	3,471
Does not meet established criteria.	614
Lack required information to process request.	547

Other PA Activity

Duplicate Requests: 671

Letters: 3,062

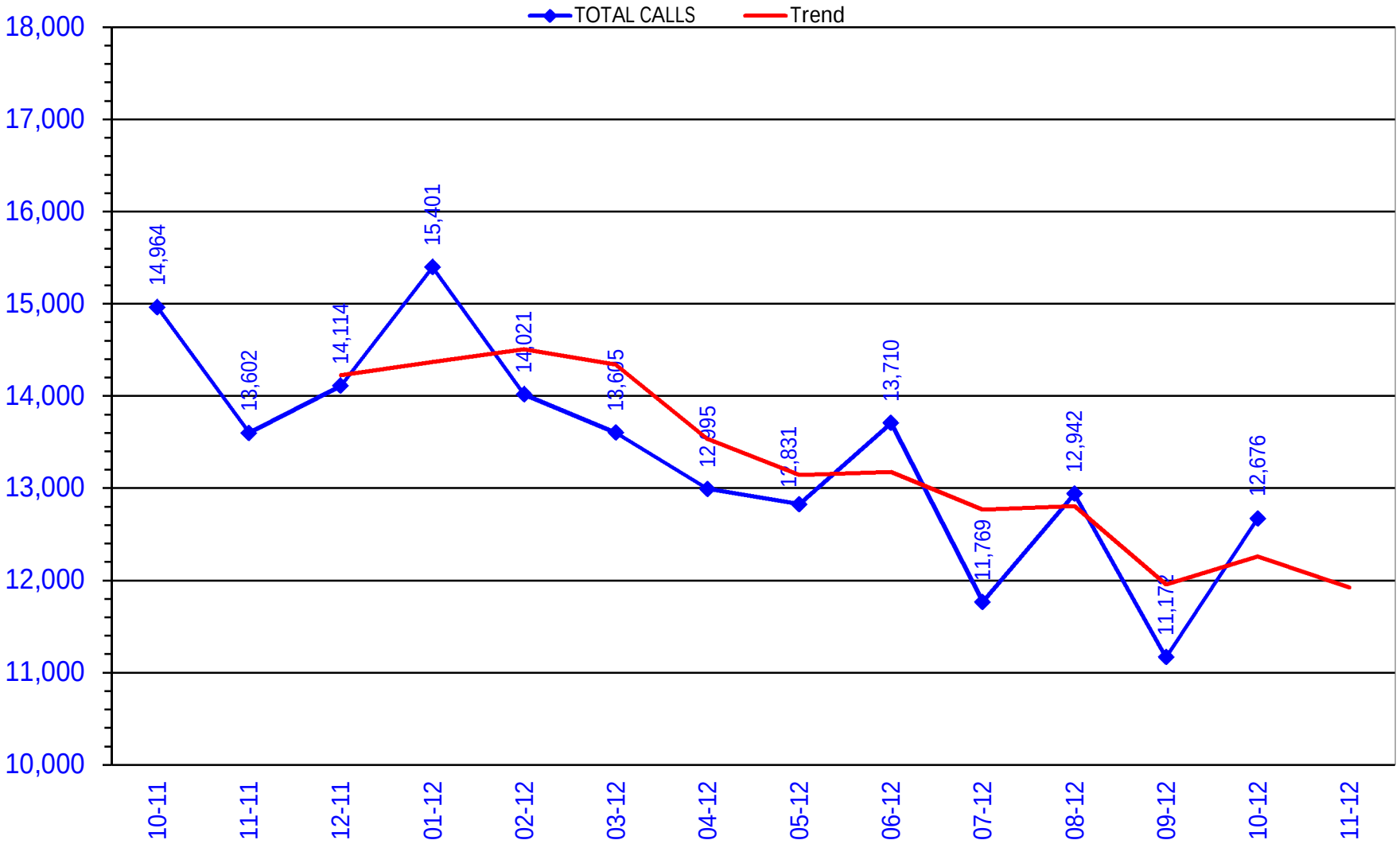
No Process: 577

Changes to existing PAs: 445

Partials: 1,046

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

CALL VOLUME MONTHLY REPORT:
October 2011 – October 2012



RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

Duplication of Narcotic Therapy

July and August 2012

Parameters	Total Messages	Messages Reviewed	Members Reviewed	Members Intervened
Males and Females Age 0-31	21,042	1,319	1,262	279

Letters		
Prescribers: 548	Pharmacies: 283	Total Letters: 831

	Top 25 Narcotic Combination Messages Arranged by Total Messages Reviewed	Messages Flagged	Messages Reviewed	Members Reviewed	Members Intervened
1	Tramadol HCl Tab and Hydrocodone-APAP Tab	5,246	347	332	87
2	Oxycodone-APAP Tab and Hydrocodone-APAP Tab	3,714	240	230	68
3	Hydrocodone-APAP Tab and Hydrocodone-APAP Tab	1,320	97	96	4
4	APAP-Codeine Tab and Hydrocodone-APAP Tab	702	67	63	12
5	Tramadol HCl Tab and Oxycodone-APAP Tab	652	60	57	17
6	Oxycodone HCl Tab and Hydrocodone-APAP Tab	1,138	42	40	10
7	Tramadol HCl Tab and APAP-Codeine Tab	314	33	33	7
8	Morphine Sulfate Tab E.R. and Hydrocodone-APAP Tab	668	23	23	1
9	Fentanyl Transdermal Patch and Hydrocodone-APAP Tab	534	23	19	4
10	Oxycodone-APAP Tab and Oxycodone-APAP Tab	330	22	22	5
11	APAP-Codeine Solution and Hydrocodone-APAP Solution	138	22	22	8
12	Meperidine HCl Tab and Hydrocodone-APAP Tab	118	21	19	3
13	Oxycodone HCl Tab and Oxycodone-APAP Tab	274	14	12	8
14	Morphine Sulfate Tab and Morphine Sulfate Tab E.R.	344	12	12	0
15	Oxycodone HCl Tab and Oxycodone HCl Tab E.R.	402	11	9	0
16	Morphine Sulfate Tab E.R. and Oxycodone-APAP Tab	259	11	11	2
17	Tramadol HCl Tab and Hydrocodone-Ibuprofen Tab	150	11	11	1
18	Oxycodone HCl Tab E.R. and Hydrocodone-APAP Tab	412	9	8	2
19	Morphine Sulfate Tab E.R. and Oxycodone HCl Tab	232	8	8	1
20	Fentanyl Transdermal Patch and Oxycodone-APAP Tab	211	8	7	1
21	Fentanyl Transdermal Patch and Oxycodone HCl Tab	215	8	7	0
22	Oxymorphone HCl Tab E.R. and Hydrocodone-APAP Tab	73	8	7	1
23	Tramadol HCl Tab and Pentazocine-Naloxone Tab	76	8	8	1
24	Oxycodone-APAP Tab and Hydrocodone-Ibuprofen Tab	44	8	8	2
25	Hydrocodone-APAP Tab and Hydrocodone-APAP Solution	30	8	8	0

Appendix C

2013 DUR MEETING DATES

Oklahoma Health Care Authority Drug Utilization Review Board
November 2012

Meetings are held the second Wednesday of each month:

January 9, 2013

February 13, 2013

March 13, 2013

April 10, 2013

May 8, 2013

June 12, 2013

July 10, 2013

August 14, 2013

September 11, 2013

October 9, 2013

November 13, 2013

December 11, 2013

Appendix D

Vote to Update Bladder Control PBPA Category and Prior Authorize Myrbetriq (Mirabegron)

Oklahoma Health Care Authority
November 2012

Recommendations:

The College of Pharmacy recommends the following:

1. Placement of Myrbetriq™ (mirabegron), Urispas® (flavoxate), and Detrol® (tolterodine) into Tier 3.
2. Placement of Sanctura XR™ (trospium ER) into Tier 2.

The existing criteria will apply:

Tier 2 Authorization Criteria:

1. Trial of one Tier 1 medication that yielded inadequate clinical response or adverse effects, or
2. A unique FDA approved indication not covered by Tier 1 products.

Tier 3 Authorization Criteria:

1. Trial of all Tier 2 medications that yielded inadequate clinical response or adverse effects, or
2. A unique FDA approved indication not covered by lower tiered products.

This category will be grandfathered.

Bladder Control Medications		
Tier 1	Tier 2	Tier 3
Oxybutynin (Ditropan®)	Oxybutynin ER Tabs (Ditropan XL®) Trospium ER (Sanctura XR™)	Oxybutynin Patch (Oxytrol®) Oxybutynin Gel (Gelnique™) Tolterodine ER Tabs (Detrol LA®) Fesoterodine (Toviaz™) Solifenacin (VESIcare®) Darifenacin (Enablex®) Trospium (Sanctura™) Mirabegron (Myrbetriq™) Flavoxate (Urispas®) Tolterodine (Detrol®)

Appendix E

Vote to Update Antidepressants PBPA Category and Prior Authorize Forfivo XL® (Bupropion Extended Release) and Fluoxetine 60mg Tablets

Oklahoma Health Care Authority
November 2012

Recommendations

The College of Pharmacy recommends the following changes to the Antidepressant PBPA category:

1. Add Forfivo XL™ (bupropion extended release) to Tier 3
2. Revise the antidepressants PBPA category prior authorization criteria as shown below:

Tier 2 Authorization Criteria

1. A documented, recent (within 6 months) trial of two Tier 1 medications at least 4 weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier 1 selection must include at least one medication from the SSRI category and one medication from the dual acting category.
2. Prior stabilization on the Tier 2 medication documented within the last 100 days. A past history of success on the Tier 2 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by Tier 1 products or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Tier 3 Authorization Criteria

1. A documented, recent (within 6 months) trial with two Tier 1 medications (one from each category) and a Tier 2 medication at least 4 weeks in duration and titrated to recommended dose, that did not provide an adequate response.
2. Prior stabilization on the Tier 3 medication documented within the last 100 days. A past history of success on the Tier 3 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Special Criteria:

1. Use of fluoxetine 60mg tablets requires a patient specific, clinically significant reason why member cannot take three fluoxetine 20mg capsules.

STATE OF OKLAHOMA

OKLAHOMA HEALTH CARE AUTHORITY

Statement of Medical Necessity for Brand-Name Drug Override

Pharmacy Management Consultants
Prior Authorization Unit

Phone: 405-522-6205 Opt 4 or 1-800-522-0114 Opt 4
Fax: 405-271-4014 or 800-224-4014

After completing this form, please **fax** this form and any requested documentation to Pharmacy Management Consultants. Please make sure that the member's ID Number is on every page faxed.

THIS SECTION IS TO BE COMPLETED BY THE PHARMACY:

Member Name:	Member ID Number:
Member Date of Birth:	Dispensing Pharmacy Phone Number:
Dispensing Pharmacy Name:	Dispensing Pharmacy Fax Number:
Dispensing Pharmacy NPI:	Requested Drug Name & Strength:
Requested Drug NDC Number:	Requested Drug Monthly Quantity:
Requested Drug Dosing Regimen:	Requested Drug Fill Date:
Prescriber Name:	Prescriber NPI:
Prescriber Phone Number:	Prescriber Fax Number:

THIS SECTION MUST BE COMPLETED AND SIGNED BY THE PRESCRIBER:

Patient needs the requested brand-name drug rather than its FDA approved generic equivalent because:

- ❑ **Patient experienced an adverse event while using the generic medication.**
- ❑ **The generic medication was not effective for the patient.**
- ❑ **Other (Please explain):** _____

Please answer the following questions about what happened when the patient took the generic medication:

1. **Generic medication taken** (Give labeled strength, mfr/labeler, lot #, & exp. date, if known)**:**

   _____

   _____

2. **Dose, frequency, & route used:**

   _____

3. **Date(s) patient took the generic medication** (give from/to or best estimate)**:**

   _____

   _____

4. **Diagnosis for use:**

   _____

Member ID Number (REQUIRED) :

5. Description of adverse event or problem:

_____

_____

_____

_____

6. How long after beginning use of drug did the event occur?

_____

7. Outcomes attributed to adverse event caused by generic medication:

❑ **Life-threatening** ❑ **Hospitalization – initial or prolonged** ❑ **Disability**

❑ **Intervention was required to prevent permanent impairment/damage**

❑ **Other:** _____

8. Event abated after use stopped or dose reduced? ❑ **Yes** ❑ **No** ❑ **Doesn't apply**

If yes, how long after stopping or reducing dose of drug did event abate?

_____

9. Event reappeared after reintroduction? ❑ **Yes** ❑ **No** ❑ **Doesn't apply**

10. Concomitant medical products & therapy dates:_____

_____

_____

11. Relevant Tests/Laboratory Data, Including Dates:_____

_____

12. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)**:**

_____

_____

_____

13. Patient's drug/excipient allergies:

_____

14. Patient's Weight: _____

15. Patient's Height: _____

**** OHCA may request additional supporting documentation.****

Prescriber Signature: _____ **Date:** _____

(With this signature, the prescriber confirms that the information above is accurate and verifiable in patient records.) http://www.okhca.org

Appendix F

Vote to Prior Authorize Miscellaneous Butalbital-Acetaminophen-Caffeine Products

Oklahoma Health Care Authority
November 2012

Products

Dolgic Plus® (butalbital-acetaminophen-caffeine, 50-750-40 mg)
Phrenilin Forte® (butalbital-acetaminophen 50-650 mg)
Orbivan® (butalbital-acetaminophen-caffeine 50-300-40 mg)
Orbivan® CF (butalbital-acetaminophen 50-300 mg)
Esgic-Plus® (butalbital-acetaminophen-caffeine 50-500-40 mg)

Recommendations

The College of Pharmacy recommends the prior authorization of these products with the following criteria:

1. FDA approved indication for the treatment of tension-type headache, and
2. Must be 12 years of age or older, and
3. Failure within the previous 60 days of the following:
    a. All available formulations of butalbital/acetaminophen products available in generic
    b. At least two NSAIDs, unless contraindicated

Appendix G

Fiscal Year 2012 Annual Review of Daliresp® (Roflumilast)

Oklahoma HealthCare Authority
November 2012

Current Prior Authorization of Daliresp® (roflumilast)

Daliresp® was FDA approved on February 28, 2011 and the prior authorization was initiated July 27, 2011. The following is the approval criteria:

1. Diagnosis is COPD with history of chronic bronchitis; and
2. FEV </= 50% of predicted; and
3. Inadequately controlled on long acting bronchodilator therapy (must have 3 or more claims for long acting bronchodilators in the previous 6 months.)

Utilization of Daliresp® (roflumilast) tablets

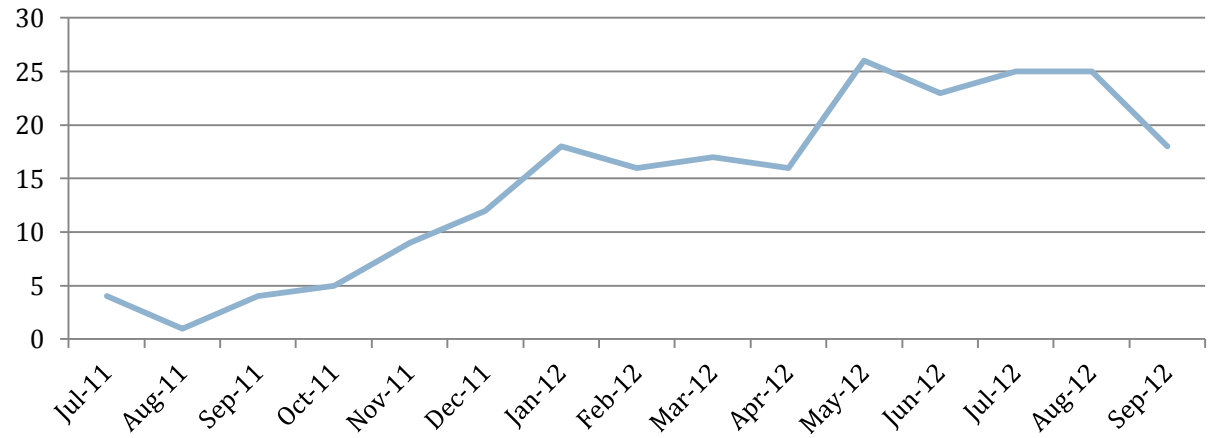
Utilization Trends

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2011	1	1	$182.68	$182.68	$6.09	30	30
2012	44	165	$30,049.76	$182.12	$6.10	4,923	4,923
% Change	4,300.0%	16,400.0%	16,349.4%	-0.3%	0.2%	16,310.0%	16,310.0%
Change	43	164	$29,867.08	$0.56	$0.01	4,893	4,893

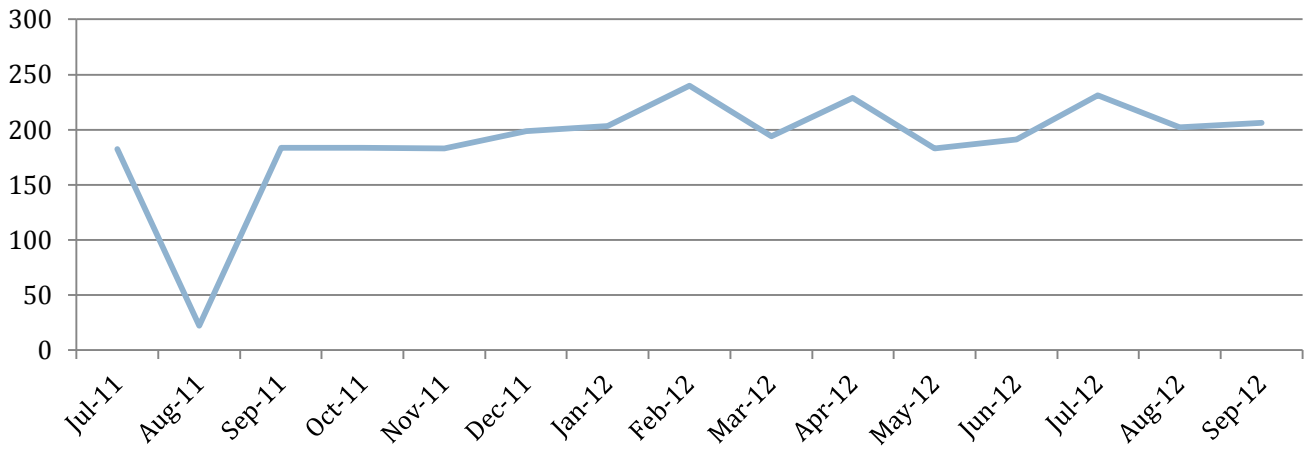
Utilization Details

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY
Daliresp 500mcg	165	4,923	4,923	44	$30,049.76	1	3.75	$6.10

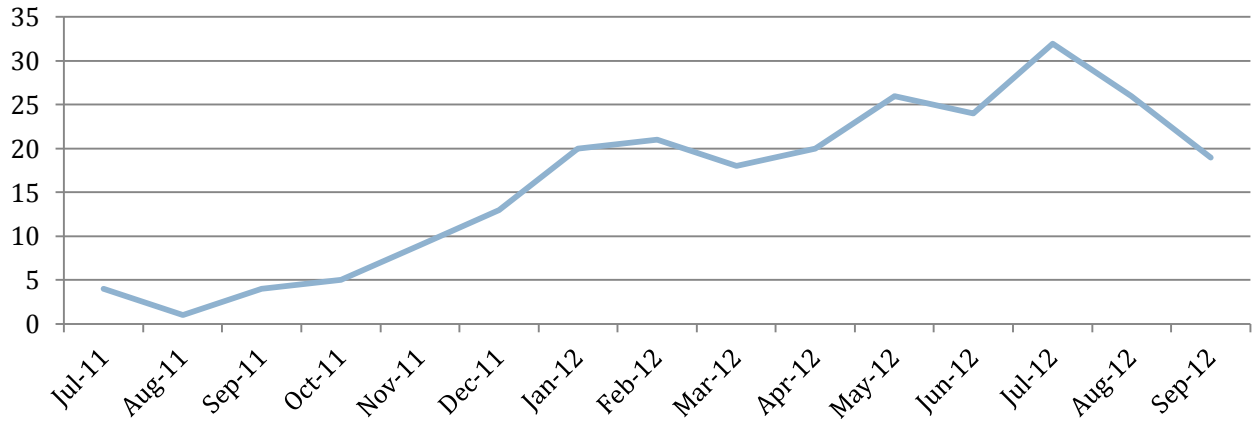
Total Utilizers by Month



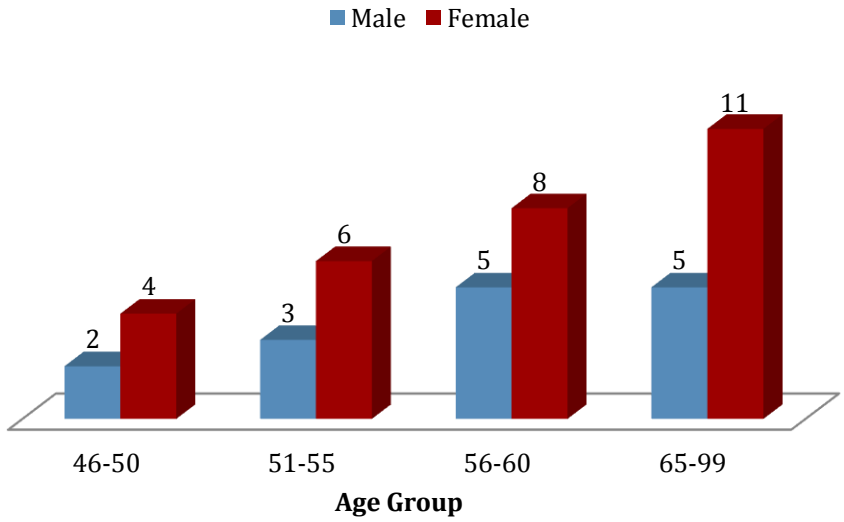
Cost/Member by Month



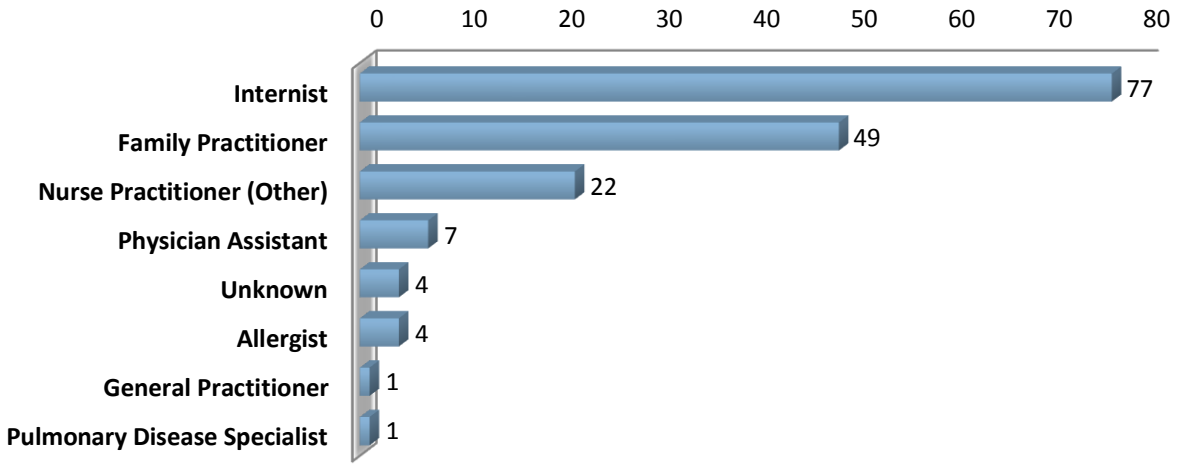
Total Claims by Month



Demographics for FY 2012

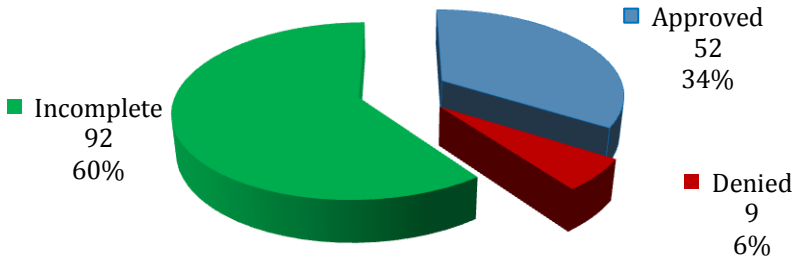


Top Prescriber Specialties by Number of Claims for FY 2012



Prior Authorization of Daliresp® (roflumilast) tablets

There were a total of 153 petitions submitted for this medication during fiscal year 2012. The following chart shows the status of the submitted petitions:



Conclusions

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

Appendix H

Annual Review of Topical Antifungal Medications- Fiscal Year 2012

Oklahoma HealthCare Authority
November 2012

Current Prior Authorization Criteria

Tier 2 Approval Criteria:

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

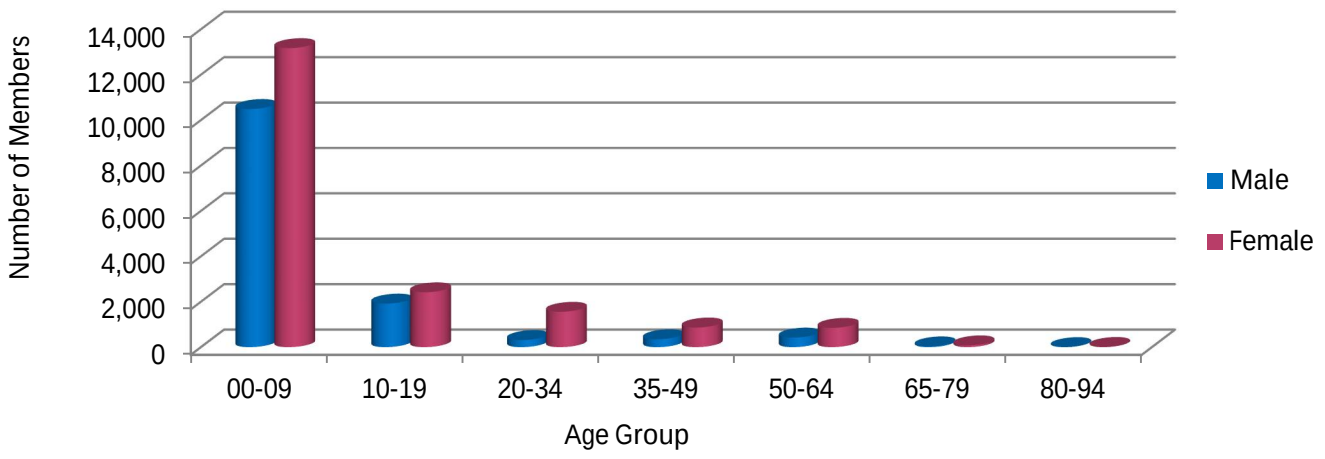
Tier 1	Tier 2
clotrimazole/betamethasone-1% & 0.05% cream & lotion	ciclopirox solution, shampoo, & gel (Penlac® and Loprox®), includes 0.77% Suspension
clotrimazole -cream, solution	miconazole/zinc oxide/white petrolatum (Vusion®)
ciclopirox -0.77% Cream	oxiconazole (Oxistat®)
econazole - 1% cream	sertaconazole nitrate (Ertaczo®)
ketoconazole -2% cream, shampoo	butenafine (Mentax®)
nystatin- cream, ointment	ketoconazole gel (Xolegel™)
nystatin/triamcinolone - cream, ointment	ketoconazole foam 2% (Extina®)
	naftifine (Naftin®)
	sulconazole (Exelderm®)

Utilization of Topical Antifungal Medications

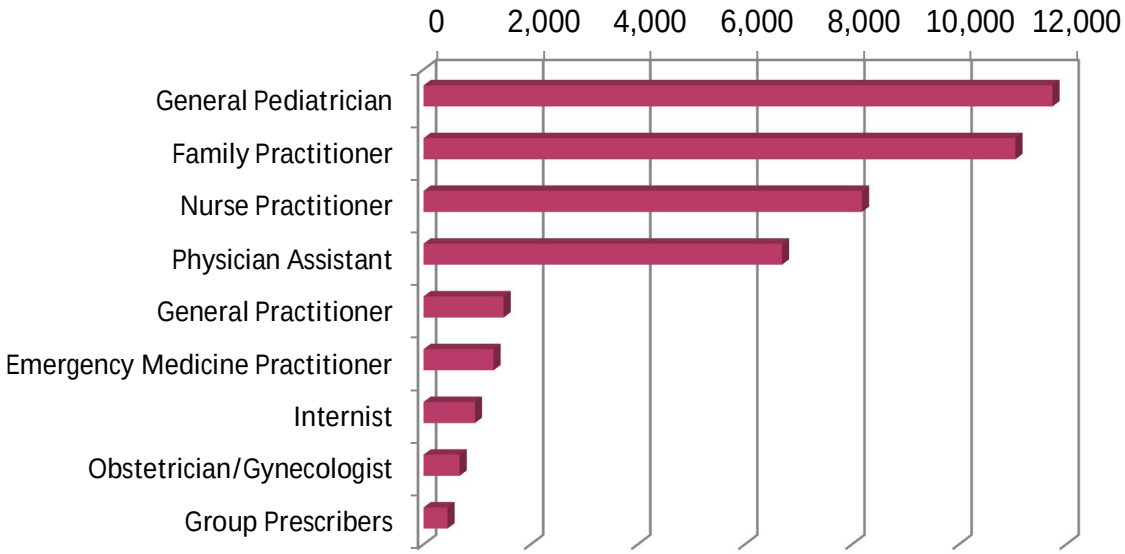
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost / Claim	Cost/Day	Units	Days
2011	30,974	44,050	$557,837.54	$12.66	$1.02	1,516,552	545,739
2012	32,463	44,459	$1,223,372.18	$27.52	$2.15	1,514,996	570,232
% Change	4.8%	0.9%	119.3%	117.4%	110.8%	-0.1%	4.5%
Change	1,489	409	$665,534.64	$14.86	$1.13	-1,556	24,493

Demographics of Members Utilizing Topical Antifungal Medications: FY 2012



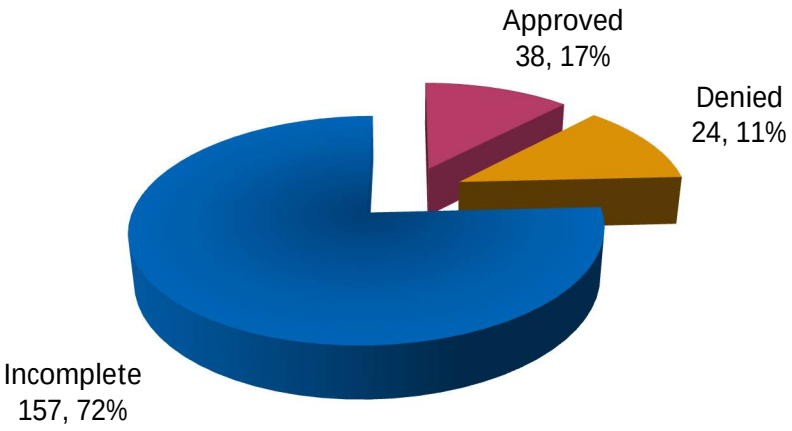
Prescribers of Topical Antifungal Medications by Number of Claims: FY 2012



Prior Authorization of Topical Antifungal Medications

There were a total of 219 petitions submitted for this PBPA category during fiscal year 2012. The following chart shows the status of the submitted petitions.

Status of Petitions for Topical Antifungal Medications: FY 2012



Market News and Update

Patent Expirations :

- Vusion® (miconazole/zinc oxide/ white petrolatum)- Patent expired in March 2009. However, no generic products are available.
- Ertaczo® (sertaconazole nitrate)- November 2014
- Xolegel™ (ketoconazole gel)- December 2018
- Extina® (ketoconazole foam 2%)- October 2018

Cost Increases of Antifungal Products

Between fiscal years 2011 and 2012 the total cost for this category increased by 119%. This is due to price increases of certain products whose manufacturer is the sole supplier of the product. The following chart shows the top 10 products utilized in this category which were the same products during both fiscal years; however there were significant changes in costs.

MEDICATION	2012 CLAIMS	2011 CLAIMS	2012 COST	2011 COST	2012 COST/ CLAIM*	2011 COST/ CLAIM
Nystatin Cr 100000 Unit/GM	13,949	13,937	$286,289.69	$89,677.53	$20.90	$6.43
Clotrim w/ Betam Cr 1-0.05%	7,311	7,643	$359,939.24	$128,972.53	$52.68	$16.87
Clotrimazole Cream 1%	5,829	5,051	$153,904.54	$132,825.60	$26.49	$26.30
Nystat-Triam Cr 100000-0.1	5,356	5,433	$147,387.60	$40,649.99	$76.40	$7.48
Nystatin Oint 100000 U/GM	5,105	4,618	$115,826.91	$33,620.62	$26.52	$7.28
Ketoconazole Cream 2%	3,609	3,873	$70,058.48	$60,615.00	$24.18	$15.65
Econazole Nitrate Cream 1%	1,302	1,307	$22,467.98	$19,971.90	$16.40	$15.28
Nystat-Triam Oint 100000-0.1	929	1,056	$27,563.81	$7,061.60	$78.58	$6.69
Ciclopirox Cream 0.77%	604	615	$13,403.03	$11,694.42	$18.44	$19.02
Clotrim w/ Beta Lot 1-0.05%	278	301	$15,782.72	$8,719.05	$52.07	$28.97

*2012 Cost/Claim utilizes most current cost/claim data from September 2012 utilization data

Conclusion and Recommendations

The College of Pharmacy recommends the following changes to the Topical Antifungal Medications PBPA category:

Placement of the following medications into Tier-2:

- Nystatin/Triamcinolone Cream 100,000-0.1 Unit/Gram %
- Nystatin/Triamcinolone Ointment 100,000-0.1 Unit/Gram %
- Clotrimazole/Betamethasone Cream 1-0.05%
- Clotrimazole/Betamethasone Lotion 1-0.05%

Coverage of the following OTC medications and placement into Tier-1:

- Clotrimazole 1% Cream
- Terbinafine 1% Cream
- Tolnaftate 1% Cream

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

Utilization Details of Topical Antifungal Medications: Fiscal Year 2012

MEDICATION	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	%COST
Nystatin Cream 100000 Unit/GM	13,949	11,040	$286,289.69	2.7	1.26	$1.78	23.40%
Clotrimw/ Betameth Cr 1-0.05%	7,311	5,532	$359,939.24	2.74	1.32	$3.61	29.42%
Clotrimazole Cream 1%	5,829	4,919	$153,904.54	2.42	1.18	$1.94	12.58%
Nystatin-Triam Cr 100000-0.1 Unit/GM-%	5,356	4,348	$147,387.60	2.86	1.23	$2.15	12.05%
Nystatin Oint 100000 Unit/GM	5,105	4,150	$115,826.91	2.67	1.23	$1.99	9.47%
Ketoconazole Cream 2%	3,609	2,968	$70,058.48	2.48	1.22	$1.26	5.73%
Econazole Nitrate Cream 1%	1,302	1,046	$22,467.98	2.89	1.24	$1.15	1.84%
Nyst-Triam Oint 100000-0.1 Unit/GM-%	929	778	$27,563.81	2.48	1.19	$2.31	2.25%
Ciclopirox Cr0.77%	604	480	$13,403.03	2.77	1.26	$1.58	1.10%
Clotrimazole w/ Betameth Lot 1-0.05%	278	243	$15,782.72	1.94	1.14	$3.43	1.29%
Clotrimazole Soln 1%	130	111	$1,951.09	1.93	1.17	$0.98	0.16%
Ketoconazole Foam 2%	30	19	$6,702.08	3.07	1.58	$9.36	0.55%
Ciclopirox Solution 8%	11	7	$120.11	0.35	1.57	$0.46	0.01%
Ciclopirox Shampoo 1%	4	1	$365.14	4	4	$3.04	0.03%
Ertaczo® (Sertaconazole Nitr Cr2%)	4	2	$329.58	2	2	$4.39	0.03%
Extina® (Ketoconazole Foam 2%)	3	3	$710.30	2.5	1	$8.88	0.06%
Exelderm® (Sulconazole Nitr Sol 1%)	2	2	$151.06	2.4	1	$6.04	0.01%
Oxistat® (Oxiconazole Nitr Cr 1%)	1	1	$91.81	2	1	$6.12	0.01%
Mentax® (Butenafine HCl Cr1%)	1	1	$72.78	1	1	$4.85	0.01%
Vusion® (Miconazole-Zc Ox- Petrol Oint)	1	1	$254.23	5	1	$25.42	0.02%
TOTALS:	44,459	32,576*	$1,223,372.18	2.66	1.36	$2.15	100%

*Total number of unduplicated members

Current Prices of Topical Antifungals of Utilized Products as of September 2012

MEDICATION	CLAIMS	MEMBERS	CLAIMS/ MEMBER	COST/ UNITS	COST/ CLAIM	COST
Nystatin Cr 100000 Unit/GM	1,098	1,032	1.06	$0.67	$20.90	$22,953.24
Clotrim/Beta Cr 1-0.05% (DIPROP)	572	545	1.05	$1.41	$52.68	$30,132.75
Clotrim Cr 1%	487	469	1.04	$0.79	$26.49	$12,898.30
Nystatin Oint 100000 Unit/GM	452	412	1.1	$0.81	$26.52	$11,986.59
Nystatin-Triam Cr 100000-0.1 Unit/GM%	430	402	1.07	$2.18	$76.40	$32,850.60
Ketoconazole Cr 2%	309	287	1.08	$0.59	$24.18	$7,471.03
Ketocon Shampoo 2%	167	158	1.06	$0.20	$23.69	$3,956.19
Nystatin-Triam Oint 100000-0.1 Unit/GM%	91	87	1.05	$2.54	$78.58	$7,150.66
Econazole Nitrate Cr 1%	75	68	1.1	$0.38	$16.40	$1,229.88
Ciclopirox Olamine Cr 0.77%	43	42	1.02	$0.42	$18.44	$793.00
Clotrim w/ Beta Lotion 1-0.05%	29	24	1.21	$1.57	$52.07	$1,509.99
Clotrim Soln 1%	11	9	1.22	$0.57	$11.89	$130.79
Clotrim w/ Beta Cr 1-0.05%	3	3	1	$0.88	$48.49	$145.46
Ketocon Foam 2%	3	3	1	$2.98	$248.40	$745.20
Sertaconazole Nitrate Cr 2% (Ertaczo)	1	1	1	$4.36	$261.87	$261.87
TOTALS:	4,080	3,654	1.12	$1.36	$65.80	$146,772.44

Current Prices of Topical Antifungals Not Utilized in September 2012

MEDICATION	PRICE/ UNIT	MAX PACKAGE SIZE	COST/ PACKAGE
Ciclopirox Topical 8% Solution	$0.99/ ML	6.6	$6.53
Ciclopirox Olamine Topical 0.77% Suspension	$0.69/ ML	60	$41.40
Ciclopirox Topical 1% Shampoo	$0.74/ ML	120	$88.80
Exelderm (Sulconazole Nitrate Topical 1% Solution)	$2.99/ ML	30	$89.70
Ciclopirox Topical 0.77% Gel	$0.93/ GRAM	100	$93.00
Exelderm (Sulconazole Nitrate Topical 1% Cream)	$2.48/ GRAM	60	$148.80
Mentax (Butenafine HCL Topical 1% Cream)	$5.04/ GRAM	30	$151.20
Ertaczo (Sertaconazole Nitrate Topical 2% Cream)	$4.30/ GRAM	60	$258.00
Vusion (Miconazole Nitrate/Zinc Ox/Pet Topical 0.25%-15%)	$5.41/ GRAM	50	$270.50
Oxistat (Oxiconazole Nitrate Topical 1% Lotion)	$4.69/ ML	60	$281.40
Naftin (Naftifine HCL Topical 1% Gel)	$3.24/ GRAM	90	$291.60
Naftin (Naftifine HCL Topical 1% Cream)	$3.24/ GRAM	90	$291.60
Naftin (Naftifine HCL Topical 2% Cream)	$6.48/ GRAM	45	$291.60
Xolegel (Ketoconazole Topical 2% Gel)	$7.63/ GRAM	45	$343.35
Extina (Ketoconazole Topical 2% Foam)	$3.64/ GRAM	100	$364.00
Oxistat (Oxiconazole Nitrate Topical 1% Cream)	$4.69/ GRAM	90	$422.10

OTC Topical Antifungal Products for Coverage Consideration

Name	Cost/Package	Pack size(gm)	Current EAC/Unit
Tolnaftate 1% Cream	$1.04	30	$0.0346
Tolnaftate 1% Cream	$1.85	30	$0.0616
Tolnaftate 1% Cream	$2.19	30	$0.0730
Tolnaftate 1% Cream	$2.25	30	$0.0751
Tolnaftate 1% Cream	$1.48	15	$0.0986
Tolnaftate 1% Cream	$3.04	30	$0.1012
Tolnaftate 1% Cream	$3.08	30	$0.1027
Tolnaftate 1% Cream	$1.54	14	$0.1103
Tolnaftate 1% Cream	$2.11	15	$0.1408
Tolnaftate 1% Cream	$2.42	15	$0.1613
Tolnaftate 1% Cream	$5.27	30	$0.1757
Tolnaftate 1% Cream	$2.77	15	$0.1848
Tolnaftate 1% Cream	$7.66	30	$0.2552
Tolnaftate 1% Cream	$4.49	15	$0.2992
Terbinafine 1% Cream	$8.29	30	$0.2763
Terbinafine 1% Cream	$9.23	30	$0.3077
Terbinafine 1% Cream	$7.53	24	$0.3139
Terbinafine 1% Cream	$8.79	24	$0.3663
Terbinafine 1% Cream	$5.53	15	$0.3684
Terbinafine 1% Cream	$5.02	12	$0.4187
Terbinafine 1% Cream	$7.03	15	$0.4688
Terbinafine 1% Cream	$7.12	15	$0.4746
Terbinafine 1% Cream	$7.03	12	$0.5859
Terbinafine 1% Cream	$7.03	12	$0.5859
Clotrimazole 1% Cream	$3.17	30	$0.1056
Clotrimazole 1% Cream	$6.15	30	$0.2050
Clotrimazole 1% Cream	$3.38	15	$0.2253
Clotrimazole 1% Cream	$7.05	30	$0.2351
Clotrimazole 1% Cream	$7.56	30	$0.2520
Clotrimazole 1% Cream	$3.96	15	$0.2640
Clotrimazole 1% Cream	$8.10	30	$0.2700
Clotrimazole 1% Cream	$14.30	45	$0.3178
Clotrimazole 1% Cream	$4.83	15	$0.3221
Clotrimazole 1% Cream	$9.68	30	$0.3227
Clotrimazole 1% Cream	$5.27	15	$0.3514
Clotrimazole 1% Cream	$5.27	15	$0.3514
Clotrimazole 1% Cream	$5.27	15	$0.3514
Clotrimazole 1% Cream	$5.98	15	$0.3983
Clotrimazole 1% Cream	$13.99	30	$0.4664
Clotrimazole 1% Cream	$7.48	15	$0.4987
Clotrimazole 1% Cream	$11.62	15	$0.7744

Appendix I

30 Day Notice to Prior Authorize Relistor® (Methylnaltrexone Bromide)

Oklahoma Health Care Authority
November 2012

Relistor® (methylnaltrexone bromide)
Salix Pharmaceuticals, Inc
FDA approved: April 2008

Introduction [1, 2, 3]

Opioid-induced bowel dysfunction (OBD), often described as constipation, is the result of several opioid effects on the gastrointestinal tract, including delayed gastric emptying, slow bowel motility, incomplete evacuation, bloating, abdominal distention, and gastric reflux. OBD occurs whether opioids are administered acutely or chronically, is found in 90% of patients treated with opioids, and is a significant problem in 50% to 60% of adult patients with advanced cancer.

Along with non-pharmaceutical treatments, such as increased fluid and fiber intake, physical activity, and a toileting routine, laxatives should be given routinely as a preventative measure, not on an as-needed (PRN) basis, to patients treated with opioids. A common therapy for patients on chronic opioids is the combination of a stool softener and stimulant laxative. Commonly used stool softeners and stimulants include docusate sodium, senna, lactulose, and polyethylene glycol. Osmotic stimulants are another alternative if the combination of stool softener/stimulant is ineffective. Promotility agents most directly counter the mechanism of opioid-induced constipation. Continuous subcutaneous or intravenous infusion of metoclopramide (to 60 mg/day) reverses the "opioid bowel syndrome," enabling patients to continue with oral opioids. Bulk-forming laxatives such as psyllium and methylcellulose should be avoided as they increase stool volume without promoting peristaltic action.

Relistor (methylnaltrexone bromide) Summary[4]

Relistor® (methylnaltrexone bromide) is a peripherally-acting mu-opioid receptor antagonist. As a quaternary amine, the ability of methylnaltrexone bromide to cross the blood-brain barrier is restricted. This allows methylnaltrexone bromide to function as a peripherally-acting mu-opioid receptor antagonist in tissues such as the gastrointestinal tract, thereby decreasing the constipating effects of opioids without impacting opioid-mediated analgesic effects on the central nervous system.

Indications and Dosing Recommendations

Relistor® (methylnaltrexone bromide) is FDA approved for opioid-induced constipation (OIC) in patients with advanced illness, who are receiving palliative care, when response to laxative therapy has not been sufficient.

It is administered as a subcutaneous injection, to be given every other day, as needed, but no more frequently than one injection every 24 hours. The recommended dose of Relistor® is 8 mg for patients who weigh 38 to 61 kg (84 to 135 lbs) or 12 mg for patients weighing 62 to 114 kg (136 to 251 lb). Patients whose weight falls outside of these ranges should be dosed at 0.15 mg/kg.

Cost

Unit size	Estimated Acquisition Cost per Unit (EAC)	Monthly Cost (QOD Dosing)*
8 mg/0.4 ml pre-filled syringes	$60.64	$913.62
12 mg/0.6 ml pre-filled syringes, vials, and kits	$51.98	$783.72

*QOD = every other day, $4.02 dispensing fee included

Recommendations

The College of Pharmacy recommends prior authorization of Relistor® (methylnaltrexone bromide) with the following criteria:

1. FDA approved indication for the treatment of opioid-induced constipation in patients with severe disease (defined as terminal disease such as incurable cancer or other end-stage disease) who are receiving palliative care (life expectancy less than 6 months), and
2. Current use of opioid medications, and
3. Treatment attempts with a minimum of three alternate products, excluding bulk forming laxatives, must be documented, and
4. Mechanical gastrointestinal obstruction has been ruled out

Relistor® (Methylnaltrexone Bromide) Product Information[4]

INDICATIONS: These products are indicated for the treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. Use of Relistor® beyond four months has not been studied.

DOSAGE FORMS: Pre-filled syringe (8 mg/0.4 ml and 12 mg/0.6 ml) or single-use vial (12 mg/0.6 ml) for subcutaneous injection in upper arm, abdomen or thigh

ADMINISTRATION: The usual schedule is one dose every other day, as needed, but no more frequently than one dose in a 24-hour period. The recommended dose of Relistor® is 8 mg for patients weighing 38 to less than 62 kg (84 to less than 136 lb) or 12 mg for patients weighing 62 to 114 kg (136 to 251 lb). Patients whose weight falls outside of these ranges should be dosed at 0.15 mg/kg.

CONTRAINDICATIONS:

- Known or suspected mechanical gastrointestinal obstruction.

SPECIAL POPULATIONS:

- Pregnancy Category B: Teratogenic Effects: There are no adequate and well-controlled studies in pregnant women. Reproduction studies have been performed in pregnant rats at intravenous doses up to about 14 times the recommended maximum human subcutaneous dose of 0.3 mg/kg based on the body surface area and in pregnant rabbits at intravenous doses up to about 17 times the recommended maximum human subcutaneous dose based on the body surface area and have revealed no evidence of impaired fertility or harm to the fetus due to methylnaltrexone bromide.
- Labor and Delivery: Effects of Relistor® on mother, fetus, duration of labor, and delivery are unknown. There were no effects on the mother, labor, delivery, or on offspring survival and growth in rats following subcutaneous injection of methylnaltrexone bromide at dosages up to 25 mg/kg/day.
- Nursing Mothers: It is not known whether this drug is excreted in human milk. Results from an animal study using [^{3} H]-labeled methylnaltrexone bromide indicate that methylnaltrexone bromide is excreted via the milk of lactating rats
- Pediatric Use: Safety and efficacy of Relistor® have not been established in pediatric patients.
- Geriatric Use: In the phase 2 and 3 double-blind studies, a total of 77 (24%) patients aged 65-74 years (54 methylnaltrexone bromide, 23 placebo) and a total of 100 (31.2%) patients aged 75 years or older (61 methylnaltrexone bromide, 39 placebo) were enrolled. There was no difference in the efficacy or safety profile of these elderly patients when compared to younger patients. Therefore, no dose adjustment is recommended based on age.
- Renal Impairment: No dose adjustment is required in patients with mild or moderate renal impairment. Dose-reduction by one half is recommended in patients with severe renal impairment (creatinine clearance less than 30 mL/min). In a study of volunteers with varying degrees of renal impairment receiving a single dose of 0.30 mg/kg methylnaltrexone bromide, renal impairment had a marked effect on the renal excretion of methylnaltrexone bromide. Severe renal impairment decreased the renal clearance of methylnaltrexone bromide by 8 to 9 - fold and resulted in a 2-fold increase in total methylnaltrexone bromide exposure (AUC). C_{max}

was not significantly changed. No studies were performed in patients with end-stage renal impairment requiring dialysis.

- Hepatic Impairment: No dose adjustment is required for patients with mild or moderate hepatic impairment. The effect of mild and moderate hepatic impairment on the systemic exposure to methylnaltrexone bromide has been studied in 8 subjects each, with Child-Pugh Class A and B, compared to healthy subjects. Results showed no meaningful effect of hepatic impairment on the AUC or C_{max} of methylnaltrexone bromide. The effect of severe hepatic impairment on the pharmacokinetics of methylnaltrexone bromide has not been studied.

WARNINGS & PRECAUTIONS:

- Severe or Persistent Diarrhea: If severe or persistent diarrhea occurs during treatment, advise patients to discontinue therapy with Relistor® and consult their physician.
- Intestinal Perforation: Rare cases of gastrointestinal (GI) perforation have been reported in advanced illness patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the GI tract (i.e., cancer, peptic ulcer, Ogilvie's syndrome). Perforations have involved varying regions of the GI tract: (e.g., stomach, duodenum, and colon). Use Relistor® with caution in patients with known or suspected lesions of the GI tract. Advise patients to discontinue therapy with Relistor® and promptly notify their physician if they develop severe, persistent, and/or worsening abdominal symptoms.
- Peritoneal Catheters: Use of Relistor® has not been studied in patients with peritoneal catheters.

ADVERSE REACTIONS:

Frequently Observed:

- abdominal pain
- flatulence
- nausea
- dizziness
- hyperhidrosis
- diarrhea

Infrequently observed:

- abdominal cramps
- fever
- GI perforation
- syncope
- muscle spasm
- vomiting
- diaphoresis
- flushing
- malaise
- injection site pain

DRUG INTERACTIONS:

- Drugs Metabolized by Cytochrome P450 Isozymes: weak inhibitor of CYP2D6. In a clinical drug interaction study in healthy adult male subjects, a subcutaneous dose of 0.30 mg/kg of methylnaltrexone bromide did not significantly affect the metabolism of dextromethorphan, a CYP2D6 substrate.

PATIENT INFORMATION:

- Dosing is every other day, as needed, but no more frequently than one dose in a 24-hour period.

- Elimination can occur within 30 minutes of administration of the medication, so patient should be close to a bathroom once dose is given.
- Do not take Relistor® if severe or persistent diarrhea occurs.
- Patients should not continue taking Relistor® and should notify their physician promptly if they experience severe, persistent, and/or worsening abdominal symptoms because these could be symptoms of intestinal perforation.
- Relistor® should be discontinued if opioid pain medications are stopped.

References

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3. Hoffman: Hematology: Basic Principles and Practice, 5th ed. Bookmark URL: /books/linkTo?type=bookPage&isbn=978-0-443-06715-0&eid=4-u1.0-B978-0-443-06715-0..50096-0--cesec33
4. Relistor® Label Information. Salix Pharmaceuticals, Inc. Available online at: http://www.salix.com/products/Relistor.aspx . Last revised 2012.

Appendix J

30 Day Notice to Prior Authorize Rayos® (Prednisone, Delayed Release)

Oklahoma Health Care Authority
November, 2012

Rayos® (prednisone, delayed release)
Horizon Pharma, Inc
FDA approved: September 2012

Summary[1]

Rayos® is a delayed-release formulation of prednisone indicated as follows:

- an anti-inflammatory or immunosuppressive agent for certain allergic, dermatologic, gastrointestinal, hematologic, ophthalmologic, nervous system, renal, respiratory, rheumatologic, specific infectious disease, or conditions and organ transplantation
- for the treatment of certain endocrine conditions
- for palliation of certain neoplastic conditions

Rayos® is available in 1 mg, 2 mg, and 5 mg tablets. Dosing is based on disease severity and patient response. Patients stable on immediate release prednisone, prednisolone, or methylprednisolone should be switched to an equivalent dose of Rayos®. The initial dosage ranges from 5 to 60 mg, once daily, depending on the indication and is adjusted to adequate response. Maintenance dose should be the lowest dose that will maintain an adequate clinical response. Rayos® should be withdrawn gradually if discontinuing long-term or high-dose therapy.

The safety of Rayos® was evaluated in 375 rheumatoid arthritis patients in two randomized double-blind placebo-controlled trials. Patients treated with Rayos® ranged in age from 20 to 80 years (median age 56 years), with 85% female, 99% Caucasian, 1% African-American, and <1% Asian. Patients received Rayos® 3 mg to 10 mg once daily at 10 pm; the majority (84%) received ≤5 mg. The clinical trial experience did not raise new safety concerns beyond those already established for immediate-release prednisone.

Dose Equivalent Cost Comparison

Drug	Strength	Cost/unit	Drug	Strength	Cost/unit
Rayos®	5 mg	$7.39	Prednisone	5 mg	EAC - $0.02
Cortisone	25 mg	SMAC - $0.29	Hydrocortisone	20 mg	SMAC - $0.41
Prednisolone	5 mg	EAC - $0.50	Methylprednisolone	4 mg	SMAC - $1.21
Dexamethasone	0.75 mg	EAC - $0.10			

SMAC – State Maximum Allowable Cost, EAC – Estimated Acquisition Cost

Recommendations

The College of Pharmacy recommends the prior authorization of Rayos® (prednisone, delayed release).

Approval Criteria:
Approval requires a patient specific, clinically significant reason why the member cannot use immediate release corticosteroid products.

PRODUCT INFORMATION

DOSAGE FORMS AND STRENGTHS

Delayed-release Tablets, 1 mg, 2 mg, 5 mg

INDICATIONS:

Rayos® is a delayed-release corticosteroid indicated as follows:

- an anti-inflammatory or immunosuppressive agent for certain allergic, dermatologic, gastrointestinal, hematologic, ophthalmologic, nervous system, renal, respiratory, rheumatologic, specific infectious disease, or conditions and organ transplantation
- for the treatment of certain endocrine conditions
- for palliation of certain neoplastic conditions

CONTRAINDICATIONS

Hypersensitivity to prednisone or to any of the excipients.

WARNINGS AND PRECAUTIONS

- **Alterations in Endocrine Function**: Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia. Monitor patients for these conditions with chronic use.
- **Increased Risks Related to Infection**: May increase the risks related to infections with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic infections.
- **Alterations in Cardiovascular/Renal Function:** Can cause elevation of blood pressure, salt, and water retention, and increased excretion of potassium and calcium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. These agents should be used with caution in patients with congestive heart failure, hypertension, or renal insufficiency.
- **Use in Patients with Gastrointestinal Disorders:** Increased risk of gastrointestinal perforation in patients with certain GI disorders. Signs of GI perforation, such as peritoneal irritation may be masked in patients receiving corticosteroids.
- **Behavioral and Mood Disturbances:** May be associated with central nervous system effects ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.
- **Decrease in Bone Density:** Decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e., decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy and bone density should be monitored in patients on long term corticosteroid therapy.

- **Ophthalmic Effects:** Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.
- **Vaccination**: Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered; however, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.
- **Effect on Growth and Development**: Long-term use of corticosteroids can have negative effects on growth and development in children.
- **Use in Pregnancy**: Prednisone can cause fetal harm when administered to a pregnant woman. Human and animal studies suggest that use of corticosteroids during the first trimester of pregnancy is associated with an increased risk of orofacial clefts, intrauterine growth restriction, and decreased birth weight. If this drug is used during pregnancy, or if the patient becomes pregnant while using this drug, the patient should be apprised of the potential hazard to the fetus.
- **Neuromuscular Effects**: Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect.
- **Kaposi's Sarcoma**: Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

ADVERSE REACTIONS

Common adverse reactions for corticosteroids include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.

- **Allergic Reactions:** Anaphylaxis, angioedema
- **Cardiovascular:** Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis
- **Dermatologic:** Acne, allergic dermatitis, cutaneous and subcutaneous atrophy, dry scalp, edema, facial erythema, hyper or hypopigmentation, impaired wound healing, increased sweating, petechiae and ecchymoses, rash, sterile abscess, striae, suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria
- **Endocrine:** Abnormal fat deposits, decreased carbohydrate tolerance, development of Cushingoid state, hirsutism, manifestations of latent diabetes mellitus and increased requirements for insulin or oral hypoglycemic agents in diabetics, menstrual irregularities, moon facies, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery or illness), suppression of growth in children
- **Fluid and Electrolyte Disturbances:** Fluid retention, potassium loss, hypertension, hypokalemic alkalosis, sodium retention

- **Gastrointestinal:** Abdominal distention, elevation in serum liver enzymes levels (usually reversible upon discontinuation), hepatomegaly, hiccups, malaise, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, ulcerative esophagitis
- **General:** Increased appetite and weight gain
- **Metabolic:** Negative nitrogen balance due to protein catabolism
- **Musculoskeletal:** Osteonecrosis of femoral and humeral heads, charcot-like arthropathy, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, steroid myopathy, tendon rupture, vertebral compression fractures
- **Neurological:** Arachnoiditis, convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudo-tumor cerebri) usually following discontinuation of treatment, insomnia, meningitis, mood swings, neuritis, neuropathy, paraparesis/paraplegia, paresthesia, personality changes, sensory disturbances, vertigo
- **Ophthalmic:** Exophthalmos, glaucoma, increased intraocular pressure, posterior subcapsular cataracts, and central serous chorioretinopathy
- **Reproductive:** Alteration in motility and number of spermatozoa

- **DRUG INTERACTIONS**
- **Aminoglutehimide:** may lead to loss of corticosteroid-induced adrenal suppression.
- **Amphotericin B Injection**: There have been cases reported in which concomitant use of Amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart
- **Anticholinesterase Agents**: May produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.
- **Anticoagulant Agents**: Co-administration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.
- **Antidiabetic Agents**: Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
- **Antitubercular Drugs**: Serum concentrations of isoniazid may be decreased.
- CYP 3A4 Inducers (e.g., Barbiturates, Phenytoin, Carbamazepine, and Rifampin): Drugs such as barbiturates, phenytoin, ephedrine, and rifampin, which induce hepatic microsomal drug metabolizing enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
- **CYP 3A4 Inhibitors (e.g., Ketoconazole, Macrolide Antibiotics)**: Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60% leading to increased risk of corticosteroid side effects.
- **Cholestyramine:** May increase the clearance of corticosteroids.
- **Cyclosporine:** Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.
- **Digitalis:** may be at increased risk of arrhythmias due to hypokalemia.
- **Estrogens, Including Oral Contraceptives:** May decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.

- **Nonsteroidal Anti-Inflammatory Drugs (NSAIDS) Including Aspirin and Salicylates**: Increased risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids; this could lead to decreased salicylate serum levels or increase the risk of salicylate toxicity when corticosteroid is withdrawn.
- **Potassium-Depleting Agents (e.g., Diuretics, Amphotericin B):** When corticosteroids are administered concomitantly with potassium-depleting agents, patients should be observed closely for development of hypokalemia.
- **Skin Tests:** May suppress reactions to skin tests.
- **Toxoids and Live or Attenuated Vaccines:** Diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible

USE IN SPECIFIC POPULATIONS

- **Pregnancy: Category D**
  Multiple cohort and case controlled studies in humans suggest that maternal corticosteroid use during the first trimester increases the rate of cleft lip with or without cleft palate from about 1/1000 infants to 3-5/1000 infants. Two prospective case control studies showed decreased birth weight in infants exposed to maternal corticosteroids in utero.
- **Nursing Mothers**
  Prednisolone, the active metabolite of prednisone, is secreted in human milk. Reports suggest that prednisolone concentrations in human milk are 5 to 25% of maternal serum levels, and that total infant daily doses are small, about 0.14% of the maternal daily dose. The risk of infant exposure to prednisolone through breast milk should be weighed against the known benefits of breastfeeding for both the mother and baby.
- **Pediatric Use**
  The efficacy and safety of prednisone in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (>2 years of age), and aggressive lymphomas and leukemias (>1 month of age). However, some of these conclusions and other indications for pediatric use of corticosteroid, e.g., severe asthma and wheezing, are based on adequate and well-controlled trials conducted in adults, on the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations. The adverse effects of prednisone in pediatric patients are similar to those in adults. Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Children who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in children than some commonly used tests of HPA axis function. The linear growth of

children treated with corticosteroids by any route should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of other treatment alternatives. In order to minimize the potential growth effects of corticosteroids, children should be titrated to the lowest effective dose

- **Geriatric Use**
  No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects, and other reported clinical experience with prednisone has not identified differences in responses between the elderly and younger patients. However, the incidence of corticosteroid-induced side effects may be increased in geriatric patients and are dose-related. Osteoporosis is the most frequently encountered complication, which occurs at a higher incidence rate in corticosteroid-treated geriatric patients as compared to younger populations and in age-matched controls. Routine screening is recommended.
  It has been reported that equivalent weight-based doses yield higher total and unbound prednisolone plasma concentrations and reduced renal and non-renal clearance in elderly patients compared to younger populations. Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

PATIENT COUNSELING INFORMATION

Patients should be informed of the following information before initiating therapy with Rayos® and periodically during the course of ongoing therapy.

- Patients should be warned not to discontinue the use of Rayos® abruptly or without medical supervision, to advise any medical attendants that they are taking it, and to seek medical advice at once should they develop fever or other signs of infection.
- Patients should discuss with their physician if they have had recent or ongoing infections or if they have recently received a vaccine.
- Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.
- There are a number of medicines that can interact with Rayos®. Patients should inform their healthcare provider of all the medicines they are taking, including over-the-counter and prescription medicines (such as phenytoin, diuretics, digitalis or digoxin, rifampin, amphotericin B, cyclosporine, insulin or diabetes medicines, ketoconazole, estrogens including birth control pills and hormone replacement therapy, blood thinners such as warfarin, aspirin or other NSAIDS, barbiturates), dietary supplements, and herbal products. If patients are taking any of these drugs, alternate therapy, dosage adjustment, and/or special test may be needed during the treatment.
- Patients should be told to take Rayos® with food. Patients should be advised not to break, divide, or chew Rayos®.
- Patients should be advised of common adverse reactions that could occur with Rayos® use to include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.

References

1. Rayos® Label Information. Horizon Pharma, Inc. Available online at: http://www.rayosrx.com Last revised 2012.

Appendix K

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

FDA NEWS RELEASE

For Immediate Release: Nov. 2, 2012
FDA expands use of Xarelto to treat, reduce recurrence of blood clots

The U.S. Food and Drug Administration today expanded the approved use of Xarelto (rivaroxaban) to include treating deep vein thrombosis (DVT) or pulmonary embolism (PE), and to reduce the risk of recurrent DVT and PE following initial treatment.

Blood clots occur when blood thickens and clumps together. DVT is a blood clot that forms in a vein deep in the body. Most deep vein blood clots occur in the lower leg or thigh. When a blood clot in a deep vein breaks off and travels to an artery in the lungs and blocks blood flow, it results in a potentially deadly condition called PE.

Xarelto is already FDA-approved to reduce the risk of DVTs and PEs from occurring after knee or hip replacement surgery (July 2011), and to reduce the risk of stroke in people who have a type of abnormal heart rhythm called non-valvular atrial fibrillation (November 2011).

The FDA reviewed Xarelto's new indication under the agency's priority review program, which provides an expedited six-month review for drugs that offer major advances in treatment or that provide treatment when no adequate therapy exists.

"Xarelto is the first oral anti-clotting drug approved to treat and reduce the recurrence of blood clots since the approval of warfarin nearly 60 years ago," said Richard Pazdur, M.D., director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research.

Other drugs approved by FDA to treat or reduce the risk of blood clots include Lovenox (enoxaparin), generic versions of enoxaparin, Arixtra (fondaparinux), Fragmin (dalteparin), Coumadin (warfarin), and heparin.

The safety and effectiveness of Xarelto for the new indications were evaluated in three clinical studies. A total of 9,478 patients with DVT or PE were randomly assigned to receive Xarelto, a combination of enoxaparin and a vitamin K antagonist (VKA), or a placebo. The studies were designed to measure the number of patients who experienced recurrent symptoms of DVT, PE or death after receiving treatment.

Results showed Xarelto was as effective as the enoxaparin and VKA combination for treating DVT and PE. About 2.1 percent of patients treated with Xarelto compared with 1.8 percent to 3 percent of patients treated with the enoxaparin and VKA combination experienced a recurrent DVT or PE. Additionally, results from a third study showed extended Xarelto treatment reduced the risk of recurrent DVT and PE in patients. About 1.3 percent of patients treated with Xarelto compared with 7.1 percent of patients receiving placebo experienced a recurrent DVT or PE.

The major side effect observed with Xarelto is bleeding, similar to other anti-clotting drugs.

Xarelto is marketed by Raritan, N.J.-based Janssen Pharmaceuticals Inc.

FDA NEWS RELEASE

For Immediate Release: Nov. 6, 2012
FDA approves Xeljanz for rheumatoid arthritis

The U.S. Food and Drug Administration today approved Xeljanz (tofacitinib) to treat adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to, or who are intolerant of, methotrexate.

RA is an autoimmune disease, in which the body's immune system mistakenly attacks healthy tissue leading to inflammation of the joints and surrounding tissues. According to the Centers for Disease Control and Prevention, RA affects an estimated 1.5 million Americans. Xeljanz, a pill taken twice daily, works by blocking molecules called "Janus kinases," which are important in the joint inflammation of RA.

Xeljanz is being approved ahead of the product's prescription drug user fee goal date of Nov. 21, 2012, the date the agency was scheduled to complete review of the drug application.

The safety and effectiveness of Xeljanz were evaluated in seven clinical trials in adult patients with moderately to severely active RA. In all of the trials, patients treated with Xeljanz experienced improvement in clinical response and physical functioning compared to patients treated with placebo.

The use of Xeljanz was associated with an increased risk of serious infections, including opportunistic infections (infections that occur primarily when the immune system is suppressed), tuberculosis, cancers and lymphoma. Xeljanz carries a Boxed Warning regarding these safety risks. Xeljanz treatment is also associated with increases in cholesterol and liver enzyme tests and decreases in blood counts.

The FDA approved Xeljanz with a Risk Evaluation and Mitigation Strategy (REMS), which consists of a Medication Guide advising patients about important safety information and a communication plan to inform health care providers about the serious risks associated with Xeljanz.

To study the long-term effects of Xeljanz on heart disease, cancer, and serious infections, the FDA is requiring a postmarketing study that will evaluate two doses of Xeljanz and include a group of patients on another approved treatment to serve as a comparison.

The most common adverse reactions in clinical trials were upper respiratory tract infections, headache, diarrhea, and inflammation of the nasal passage and the upper part of the pharynx.

Xeljanz is marketed by New York-based Pfizer Inc.

Safety Announcements

FDA Drug Safety Communication: Update on the risk for serious bleeding events with the anticoagulant Pradaxa

This update is a follow-up to the FDA Drug Safety Communication of 12/7/2011[1]: Safety review of post-market reports of serious bleeding events with the anticoagulant Pradaxa (dabigatran etexilate mesylate)

Safety Announcement

[11-02-2012] The U.S. Food and Drug Administration (FDA) has evaluated new information about the risk of serious bleeding associated with use of the anticoagulants (blood thinners) dabigatran (Pradaxa) and warfarin (Coumadin, Jantoven, and generics). Following the approval of Pradaxa, FDA received a large number of post-marketing reports of bleeding among Pradaxa users. As a result, FDA investigated the actual rates of gastrointestinal bleeding (occurring in the stomach and intestines) and intracranial hemorrhage (a type of bleeding in the brain) for new users of Pradaxa compared to new users of warfarin. This assessment was done using insurance claims and administrative data from FDA's Mini-Sentinel pilot of the Sentinel Initiative[2]. The

results of this Mini-Sentinel assessment indicate that bleeding rates associated with new use of Pradaxa do not appear to be higher than bleeding rates associated with new use of warfarin, which is consistent with observations from the large clinical trial used to approve Pradaxa (the RE-LY trial).[1] (see Data Summary). FDA is continuing to evaluate multiple sources of data in the ongoing safety review of this issue.

Pradaxa and warfarin are important medications used to reduce the risk of stroke and blood clots in patients with non-valvular atrial fibrillation (AF), the most common heart rhythm abnormality, which causes the heart (upper chambers or atria) to beat rapidly and irregularly. Although these drugs reduce the number of strokes in patients with non-valvular AF, they can cause bleeding, potentially leading to serious or even fatal outcomes. The risk of bleeding is a well-recognized risk of anticoagulant drugs.

FDA has not changed its recommendations regarding Pradaxa. Pradaxa provides an important health benefit when used as directed. Healthcare professionals who prescribe Pradaxa should carefully follow the dosing recommendations in the drug label, especially for patients with renal impairment (when kidneys don't function normally) to reduce the risk of bleeding. Patients with atrial fibrillation should not stop taking Pradaxa without first talking to their healthcare professional. Stopping use of anticoagulant medications such as Pradaxa can increase the risk of stroke. Strokes can lead to permanent disability and death.

Facts on Pradaxa

Pradaxa is an anticoagulant medication used to reduce the risk of stroke and blood clots in patients with non-valvular atrial fibrillation (AF), the most common type of heart rhythm abnormality.

The safety and efficacy of Pradaxa were studied in a clinical trial comparing Pradaxa with the anticoagulant warfarin. In the trial, patients taking Pradaxa had fewer strokes than those who took warfarin.[1]

From approval in October 2010 through August 2012, a total of approximately 3.7 million Pradaxa prescriptions were dispensed, and approximately 725,000 patients received a dispensed prescription for Pradaxa from U.S. outpatient retail pharmacies.[2]

Mini-Sentinel is a pilot project of the Sentinel Initiative. The Sentinel Initiative is sponsored by FDA to create an active surveillance system using pre-existing electronic healthcare data from multiple sources to assess the safety of approved drugs and other medical products. See the Data Summary section for additional information on the findings, strengths and limitations of the Mini-Sentinel assessment.

As part of an ongoing safety review of Pradaxa, FDA is also conducting two planned, protocol-based observational assessments which will assess patients taking Pradaxa and evaluate bleeding events. The agency will continue to communicate to health professionals and the public any relevant information that becomes available on the risk of bleeding and Pradaxa.

Additional Information for Healthcare Professionals (updated from 12/7/2011)

- Results from the FDA assessment of bleeding rates using data from the Mini-Sentinel project indicate that intracranial and gastrointestinal hemorrhage incidence rates for new users of Pradaxa do not appear to be higher than the rates for the same types of bleeding for new users of warfarin.
- Make sure your patients know the signs and symptoms of bleeding and when to seek care.
- Pradaxa is approved to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.
- Pradaxa is eliminated by the kidneys, therefore:
  - Renal function should be assessed prior to treatment with Pradaxa to determine the appropriate dose.
  - Renal function should be reassessed during treatment with Pradaxa if clinically indicated (e.g., fluctuating renal function, diuretic use, hypovolemia), and the dose should be adjusted following the recommendations in the drug label.
- For patients with creatinine clearance (CrCl) > 30 mL/min, the recommended dose of Pradaxa is 150 mg given orally twice daily.
- For patients with severe renal impairment, follow the recommended doses:
  - For patients with CrCl 15-30 mL/min, the recommended dose is 75 mg orally twice daily.

- Dosing recommendations for patients with a CrCl <15 mL/min or on dialysis cannot be provided.
- Report adverse events involving Pradaxa to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Data Summary

Pradaxa (dabigatran) and warfarin are important medications used to reduce the risk of stroke and blood clots in patients with non-valvular atrial fibrillation. Bleeding that may lead to serious or even fatal outcomes is a well-recognized complication of all anticoagulant therapies. In the large clinical trial with 18,000 patients that compared the efficacy and safety of Pradaxa and warfarin (RE-LY, 2010), the rate of serious bleeding was similar between the two drugs.[1] However, after Pradaxa's approval, a large number of reports of bleeding were submitted to FDA's Adverse Events Reporting System (AERS) database.

FDA believes that a simple comparison between Pradaxa and warfarin with respect to the numbers of post-marketing reports of bleeding in the AERS database is misleading because bleeding events associated with warfarin (a well-recognized consequence of warfarin use, which has been available for many years) are likely underreported compared to events occurring with the more recently available Pradaxa. [See DSC from 12/7/11[3] for further discussion] FDA continues to evaluate multiple sources of data in the ongoing safety review of this issue.

References

1. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-1151.
2. IMS, Vector One®: National (VONA) and Total Patient Tracker (TPT) Database. October 2010 to August 2012. Extracted September 2012.

Safety Announcements

FDA Drug Safety Communication: Serious adverse events from accidental ingestion by children of over-the counter eye drops and nasal sprays

Safety Announcement

[10-25-2012] The U.S. Food and Drug Administration (FDA) is warning the public that accidental ingestion (swallowing) by children of over-the-counter (OTC; available without a prescription) eye drops used to relieve redness and nasal decongestant sprays can result in serious harm. The eye drops and nasal sprays that have been involved in the cases of accidental ingestion contain the active ingredients tetrahydrozoline, oxymetazoline, or naphazoline.

The cases of accidental ingestion reviewed by FDA occurred in children 5 years of age and younger. No deaths were reported; however, serious events requiring hospitalization such as coma, decreased heart rate, decreased breathing, and sedation have occurred. Ingestion of only a small amount (1-2 mL) of the eye drops or nasal spray can lead to serious adverse events in young children. Most of these redness-relief eye drops and nasal decongestant sprays currently do not come packaged with child-resistant closures, so children can accidentally ingest the drug if the bottles are within easy reach.

Additional Information for Health Care Professionals

- Cases of accidental ingestion of over-the-counter redness-relief eye drops or nasal decongestant sprays containing the active ingredients tetrahydrozoline, oxymetazoline, or naphazoline have resulted in serious adverse events in young children 5 years of age and younger.
- Advise parents and caregivers to call the toll-free Poison Help Line (1-800-222-1222) and to seek emergency medical care immediately if their child accidentally swallows these eye drops or nasal decongestant spray.
- Advise consumers to store these products out of reach of children at all times.

- Report adverse events or medication errors involving these eye drops or nasal decongestant sprays to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

FDA identified 96 cases of accidental ingestion of products containing tetrahydrozoline, oxymetazoline, or naphazoline by young children, reported between 1985 and October 2012 to the Agency's Adverse Event Reporting System (AERS and FAERS) databases and to the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES) database. The children ranged in age from 1 month to 5 years. Fifty-three cases reported hospitalization due to symptoms including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypotension, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, drooling, and coma.

References

1. Spiller HA, Rogers J, Sawyer TS. Drug facilitated sexual assault using an over-the-counter ocular solution containing tetrahydrozoline (Visine®). Legal Medicine 2007;9:192-5.
2. Katar S, Taskesen M, Okur N. Naloxone use in a newborn with apnea due to tetrahydrozoline intoxication. Pediatr Int 2010;52:488-9.
3. Tobias JD. Central nervous system depression following accidental ingestion of Visine eye drops. Clin Pediatr (Phila). 1996;35:539-40.

Current Drug Shortages Index (as of November 7, 2012):

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

Acetylcysteine Inhalation Solution
Alfentanil Injection (initial posting 1/23/2012)
Amikacin Injection
Amino Acid Products UPDATED 10/31/2012
Ammonium Chloride Injection[5]
Ammonul (sodium phenylacetate and sodium benzoate) Injection 10%/10% (initial posting 9/18/2008)
Amphetamine Mixed Salts, ER Capsules (initial posting 10/31/2011)
Amphetamine Mixed Salts Immediate-Release Tablets (initial posting 1/12/2012)
Aquasol A
Atracurium besylate (initial posting 2/27/2012)
Atropine Sulfate Injection UPDATED 10/31/2012
Bacteriostatic 0.9% Sodium Chloride (initial posting 9/10/2012)
Barium Sulfate for Suspension (initial posting 10/12/2012)
Boniva (ibandronate sodium) Injection (initial posting 6/6/2012)
Bumetanide Injection (initial posting 6/21/2012) UPDATED 10/31/2012
Bupivacaine Hydrochloride Injection UPDATED 10/31/2012
Buprenorphine Injection
Butorphanol Injection UPDATED 10/31/2012
Caffeine, anhydrous (125 mg/mL) and Sodium benzoate (125 mg/mL)
Caffeine and Ergotamine Tartrate Tablet (initial posting 3/8/2012)
Cardiolite, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection (initial posting 2/14/2012)
Cetrorelix Acetate for Injection (initial posting 9/20/2012)
Chloroprocaine (Nesacaine) Injection (initial posting 3/28/2012)
Chromic Chloride Injection
Citric Acid; Gluconolactone; Magnesium Carbonate Solution (Renacidin); Irrigation (initial posting 6/30/2012)
Corticorelin Ovine Triflutate

Daunorubicin Hydrochloride Solution for Injection
Desmopressin Injection
Dexrazoxane Injection
Dextroamphetamine Tablets (initial posting 1/12/2012)
Dextrose Injection (initial posting 5/23/2012)
Diazepam Injection
Dipyridamole Injection (initial posting 7/24/2012)
Doxorubicin (adriamycin) lyophilized powder (initial posting 12/2/2011)
Doxorubicin Liposomal (Doxil) Injection
Edetate Calcium Disodium (Calcium Disodium Versenate) Injection (initial posting 10/12/2012)
Epinephrine Injection (initial posting 4/27/2012) UPDATED 11/5/2012
Epinephrine 1mg/mL (Preservative Free) (initial posting 6/21/2012)
Erythromycin Lactobionate Injection (initial posting 6/12/2012) UPDATED 10/31/2012
Esomeprazole (Nexium) For Delayed-Release Oral Suspension (initial posting 4/10/2012)
Ethiodol (ETHIODIZED OIL) ampules
Etomidate Injection (initial posting 2/9/2012) UPDATED 11/1/2012
Fentanyl Citrate Injection UPDATED 10/31/2012
Fluticasone Propionate and Salmeterol (Advair HFA) Inhalation Powder
Foscarnet Sodium Injection
Fosphenytoin Sodium Injection (initial posting 3/30/2012)
Fospropofol disodium (Lusedra) Injection (initial posting 6/18/2012)
Furosemide Injection (initial posting 6/20/2012) UPDATED 10/31/2012
Ganite (gallium nitrate injection) (initial posting 4/4/2012)
Helidac (bismuth subsalicylate/tetracycline hydrochloride/metronidazole) Therapy (initial posting 3/8/2012)
Heparin Sodium Premixes (initial posting 7/5/2012)
Hydromorphone Hydrochloride Injection (initial posting 3/7/2012) UPDATED 10/31/2012
Intravenous Fat Emulsion
Isoniazid Tablets
Ketorolac Injection UPDATED 10/31/2012
Leucovorin Calcium Lyophilized Powder for Injection
Leuprolide Acetate Injection
Lidocaine Hydrochloride Injection UPDATED 10/31/2012
Lidocaine HCL, 4% Topical Solution UPDATED 10/31/2012
Lorazepam Injection UPDATED 10/31/2012
Magnesium Sulfate Injection
Mannitol Injection
Methazolamide Tablets
Methotrexate Injection UPDATED 11/1/2012
Methyldopate Injection
Metoclopramide Injection
Midazolam Injection UPDATED 10/31/2012
Mitomycin Powder for Injection
Morphine Sulfate Injection UPDATED 10/31/2012
Morphine Sulfate Injection (Preservative Free) UPDATED 10/31/2012
Multi-Vitamin Infusion (Adult and pediatric) 9/18/2012
Nalbuphine HCl Injection (initial posting 5/15/2012) UPDATED 10/31/2012
Naloxone Injection (initial posting 2/22/2012) UPDATED 10/31/2012
Naltrexone Oral Tablets (initial posting 2/22/2012)
Nefazodone Tablets (initial posting 4/16/2012)
Neurolite, Kit for the Preparation of Technetium Tc99m Bicisate for Injection (initial posting 5/4/2012)
Nitroglycerin Ointment USP, 2% (Nitro-Bid) (Initial posting 10/23/2012)

Norethindrone and Ethinyl Estradiol Tablets, USP (Ovcon 50 Tablets) (initial posting 4/16/2012)
Ondansetron Injection 2 mg/mL UPDATED 10/31/2012
Ondansetron Injection 32 mg/50 mL premixed bags
Ontak injection (initial posting 9/22/2011)
Oxsoralen (methoxsalen) 1% topical lotion (initial posting 7/6/2010)
Oxymorphone Hydrochloride Oral Tablet (initial posting 3/19/2012) UPDATED 10/31/2012
Pancuronium Bromide Injection UPDATED 10/31/2012
Pegasys (peginterferon alfa-2a) Injection - Prefilled Syringes (initial posting 3/26/2012)
Pentamidine isethionate inhalant (NebuPent) (initial posting 8/27/2012)
Pentamidine isethionate for injection (Pentam 300) (initial posting 8/27/2012)
Pentostatin for Injection (Nipent) (initial posting 3/21/2012)
Perflutren Lipid Microsphere (DEFINITY) Injection
Phentolamine Mesylate (initial posting 6/4/2012)
Phytonadione Injectable Emulsion (Vitamin K)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting 6/1/2012)
Potassium Chloride Injection 2 mEq/mL (initial posting 5/15/2012) UPDATED 10/31/2012
Potassium Phosphate Injection UPDATED 10/31/2012
Procainamide HCL Injection
Prochlorperazine Injection (initial posting 1/30/2012)
Promethazine Injection (initial posting 2/10/2012)
Propofol Injection (initial posting 4/5/2012) UPDATED 11/7/2012
Protonix (pantoprazole) Injection (initial posting 2/23/2012)
Secretin Injection (ChiRhoStim) (initial posting 6/15/2012)
Selenium Injection
Sodium Acetate Injection (initial posting 3/20/2012) UPDATED 10/31/2012
Sodium Bicarbonate Injection (initial posting 4/4/2012)
Sodium Chloride 0.9% (5.8mL and 20mL) (initial posting 5/4/2012)
Sodium Chloride 23.4%
Sodium Lactate Injection (initial posting 5/17/2012)
Succinylcholine Injection (initial posting 8/17/2012)
Sufentanil Citrate Injection UPDATED 10/31/2012
Sulfamethoxazole 80mg/trimethoprim 16mg/ml injection (SMX/TMP)
Telavancin (Vibativ) Injection (initial posting 1/6/2012)
Tetracycline Capsules
Thiotepa for Injection (initial posting 12/2/2011)
Thyrogen (thyrotropin alfa) injection 1.1mg/vial (initial posting 11/22/2011)
Thyrolar Tablets (initial posting 12/31/2009
Ticarcillin disodium/Clavulanic Potassium Injection (Timentin) (initial posting 8/16/12)
Ticlopidine Tablets
Tobramycin Solution for Injection UPDATED 10/31/2012
Tromethamine Injection (initial posting 5/2/2012)
Viaspan Cold Storage Solution 1000 mL Bag (initial posting 4/16/2012)
Vinblastine Sulfate Injection (initial posting 1/31/2012)
Zinc Injection (initial posting 2/15/2012) UPDATED 10/31/2012