Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

Wednesday

October 10, 2007

@ 6:00 p.m.

THE UNIVERSITY OF OKLAHOMA

THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Gorman, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – October 10, 2007**

DATE: October 4, 2007

NOTE: **THE DUR BOARD WILL MEET AT 6:00 P.M.**

Enclosed are the following items related to the October 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 to Prior Authorize Lidoderm® – **See Appendix C.**

Action Item – Cough and Cold Utilization Review – **See Appendix D.**

Action Item – Annual Review of Antihypertensives – **See Appendix E.**

Action Item – Annual Review of Ultram® ER and ODT – **See Appendix F.**

30 Day Notice to Prior Authorize Xyzal® – **See Appendix G.**

30 Day Notice to Prior Authorize Nuvigil™ – **See Appendix H.**

60 Day Notice to Prior Authorize Topical Antifungals – **See Appendix I.**

FDA and DEA Updates **– See Appendix J.**

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – October 10, 2007 @ 6:00 p.m.

Oklahoma Health Care Authority
4545 N. Lincoln Suite 124
Oklahoma City, Oklahoma 73105
Oklahoma Health Care Authority Board Room

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. McNeill, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. McNeill, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. McNeill, Chairman:

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

A. September 12, 2007 DUR Minutes – Vote
B. September 13, 2007 DUR Recommendations Memorandum

Items to be presented by Dr. Flannigan, Dr. McNeill, Chairman:

4. Update on DUR/MCAU Program – See Appendix B.

A. Retrospective Drug Utilization Review for June 2007
B. Retrospective Drug Utilization Review Response for March 2007
C. Medication Coverage Activity Audit for September 2007
D. Help Desk Activity Audit for September 2007

Items to be presented by Dr. Chonlahan, Dr. McNeill, Chairman:

5. Action Item – Vote to Prior Authorize Lidoderm® – See Appendix C.

A. COP Recommendations
B. PA Criteria

Items to be presented by Dr. Gorman, Dr. McNeill, Chairman

6. Action Item – Cough and Cold Utilization Review – See Appendix D.

A. Current Policy
B. Utilization Review
C. COP Recommendations

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

7. Action Item – Annual Review of Antihypertensives – See Appendix E.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Chonlahan, Dr. McNeill, Chairman

8. Action Item – Annual Review of Ultram® ER and ODT – See Appendix F

A. Product Summary
B. Current PA Criteria
C. Utilization Review
D. COP Recommendations

Items to be presented by Dr. Flannigan, Dr. McNeill, Chairman

9. 30 Day Notice to Prior Authorize Xyzal® – See Appendix G.

A. Product Summary
B. Cost Comparison
C. PA Criteria
D. COP Recommendations

Items to be presented by Dr. Browning, Dr. McNeill, Chairman

10. 30 Day Notice to Prior Authorize Nuvigil™ – See Appendix H.

A. Product Summary
B. COP Recommendations

Items to be presented by Dr. Patel, Dr. McNeill, Chairman

11. 60 Day Notice to Prior Authorize Topical Antifungals – See Appendix I.

A. Product Summary
B. Utilization Review
C. COP Recommendations

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Narcotic Utilization Follow-Up
B. Erythropoiesis-Stimulating Agents Follow-Up
C. Osteoporosis Utilization Review
D. Carisoprodol Annual Review
E. Amitiza® Annual Review
F. New Product Reviews
G. Annual Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of SEPTEMBER 12, 2007

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Jay D. Cunningham, D.O.	X	
Mark Feightner, D.Ph.	X	
Dorothy Gourley, D.Ph.		X
Evelyn Knisely, Pharm.D.	X	
Thomas Kuhls, M.D.	X	
Dan McNeill, Ph.D., PA-C; Chairman	X	
Cliff Meece, D.Ph.; Vice-Chairman	X	
John Muchmore, M.D., Ph.D.	X	
James Rhymer, D.Ph	X	

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph.; PA Coordinator	X	
Metha Chonlahan, D.Ph.; Clinical Pharmacist	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Kelly Flannigan, Pharm.D.; Operations Manager	X	
Shellie Gorman, Pharm.D.; DUR Manager	X	
Ronald Graham, D.Ph.; Pharmacy Director	X	
Chris Le, Pharm.D.; Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Principal Investigator		X
Visiting Pharmacy Students: Brian Meadows, Thuy Tran	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A.; Pharmacy Operations Manager		X
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Nico Gomez; Director of Gov't and Public Affairs		X
Lynn Mitchell, M.D., M.P.H,; Director of Medical Services		X
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director		X
Howard Pallotta, J.D.; Director of Legal Services		X
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Rodney Ramsey; Drug Reference Coordinator	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist		X

OTHERS PRESENT:

Jim Delatte, Takeda	Vince Morrison, Forest Pharm.	Aaron Walker, Schering
Joseph Medina, Sepracor	Lana Stewart, Merck	Aliza Tomlinson, OMJPS
Richard Ponder, J&J	Jim Dunlap, Eli Lilly	Paul Sparks, Allergen
Michael Mason, Alcon	Laura Mitchell, Purdue	Justin Springfield, Sepracor
A.C. Depaz, Shire	Jerry Gomez, King Pharm.	

PRESENT FOR PUBLIC COMMENT:

Patrick Harvey, Sepracor — Agenda Item No. 8

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: Roll Call

Dr. McNeill called the meeting to order. Roll call by Dr. Graham established the presence of a quorum.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

Dr. McNeill acknowledged speakers for Public Comment.

ACTION: NONE REQUIRED.

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

3A: July 11, 2007 DUR Minutes

Dr. Meece moved to approve minutes as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 4: **UPDATE ON DUR/MCAU PROGRAM**

4A: Retrospective Drug Utilization Review Report: April 2007
4B: Retrospective Drug Utilization Review Report: May 2007
4C: Retrospective Drug Utilization Review Response: January 2006
4D: Retrospective Drug Utilization Review Response: February 2006
4E: Medication Coverage Activity Report: July 2007
4F: Medication Coverage Activity Report: August 2007
4G: Help Desk Activity Report: July 2007
4H: Help Desk Activity Report: August 2007
4I: Pharmacotherapy Management Annual Report FY2007

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE OPHTHALMIC ANTI-INFECTIVE PRODUCTS**

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

Dr. Kuhls moved to approve*; seconded by Dr. Feightner.

* With noted changes to COP Recommendations/Approval Criteria:

(1) " . . . not known to be covered by any tier one antibiotics." (2) " . . . to ~~indicated~~ all tier one medications."

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE OMNARIS™ AND VERAMYST™**

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

Dr. Meece moved to approve; seconded by Dr. Kuhls.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE EXFORGE®**

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

Dr. Muchmore moved to approve; seconded by Dr. Bell.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE BROVANA™**

For Public Comment: Patrick Harvey: Thanks for having me here and I appreciate the time that everybody took to prepare the materials and as I stated once before, you know, we're on board with all these recommendations. It's a very well done job with the exception of the number two where it says a member must have a previous trial of Advair, Serevent or Foradil in the past

45 days. I think, you know, from a standpoint of cost, I can understand why that would be, you know, imperative, and coming from a managed care background, I agree with it, but I think the issue here we have are these people that are moderate to severe, very severe COPD'ers are going to be coming from the nebulized short acting beta agonist and due to, you know, compliance, are going from a four time a day to a twice a day drug, it would be beneficial for them to go to Brovana. And quite frankly, my research showed that most people, given the choice of a handheld metered dose inhaler that's going to be convenient to carry, and a short amount of time to administer the dose, is going to choose that overwhelmingly over a ten to fifteen minute nebulized treatment that they're going to take at home. Now there are some portable devices that I've heard of but I don't think they're too widely accepted now. So for somebody to be on a short acting nebulized treatment and then have to go to a Advair, Serevent or Foradil that is a, you know, metered dose inhaler, they're going to be in that group that won't be able to effectively use a handheld device. Now, you know, to make a physician go through a PA process and a pharmacist to review that, 99.9% of them are going to be approved due to that, or that fact alone. So if you have a way I guess of doing it electronically, that would be one thing. That way you wouldn't be taking up the pharmacist's review time and the doctor's time to fill out a PA. But I think it would be unnecessary to have it as it is now. According to the, you know, the national COPD treatment guidelines, and what CMS has also adopted, is the fact that Brovana is to be used only in those that have progressed to the point where regular use of a short acting beta agonist or overuse of one is a criteria before they go to the Brovana. So that's the only comments I have at this time. If there's any questions I'd be glad to try to entertain them.
Materials included in agenda packet; presented by Dr. Flannigan.
Dr. Muchmore moved to approve*; seconded by Dr. Kuhls.
* With noted changes to COP Recommendations/Approval Criteria:
(2) " . . . are unable to effectively use hand-actuated devices or ~~are~~ who have become ~~stable~~ unstable on nebulized short-acting β2-agonist therapy."
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **VOTE TO APPROVE UPDATED MAINTENANCE DRUG LIST**
Materials included in agenda packet; presented by Dr. Flannigan.
Dr. Meece moved to approve*; seconded by Dr. Muchmore.
* With noted changes to COP Recommendations/Approval Criteria: Delete "vildagliptin" until approved by FDA.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 10: **NARCOTIC UTILIZATION REVIEW**
Materials included in agenda packet; presented by Dr. Gorman.
Dr. Meece moved to approve; seconded by Dr. Muchmore.
Add drugs/quantity limits on page 43 of packet to drugs/quantity limits on page 42 of packet.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE LIDODERM®**
Materials included in agenda packet; presented by Dr. Chonlahan.
ACTION: NONE REQUIRED.

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

AGENDA ITEM NO. 13: **FUTURE BUSINESS**
13A: Utilization Review of Antifungals
13B: Utilization Review of Osteoporosis Products
13C: Annual Reviews
13D: New Product Reviews
Materials included in agenda packet; submitted by Dr. Graham.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 14: **ADJOURNMENT**
The meeting was declared adjourned.

The University of Oklahoma College of Pharmacy

Pharmacy Management Consultants
ORI W-4403; PO Box 26901
Oklahoma City, OK 73190
(405)-271-9039

Memorandum

Date: September 13, 2007

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

From: Shellie Gorman, Pharm.D.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of September 12, 2007.

Recommendation 1: Vote to Prior Authorization Ophthalmic Anti-Infective and Anti-Infective/Steroid Products

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Ophthalmic Anti-Infective Products to the PBPA program with the following approval criteria:

Approval Criteria for Anti-Infectives:

1. Approved indication/suspected infection by organism not known to be covered by any tier one antibiotics.
2. Known contraindication to all indicated tier one medications.
3. Prescription by optometrists/ophthalmologists or
4. When used for pre/post-operative prophylaxis.

Ophthalmic Anti-infectives: Liquids	
Tier 1	**Tier 2**
Ciloxan Solution (Ciprofloxacin)	Vigamox (Moxifloxacin)
Quixin (Levofloxacin)	Zymar (Gatifloxacin)
Gentak (Gentamicin)	Azasite (Azithromycin)
Ocuflox (Ofloxacin)	
AK-Tob (Tobramycin)	
Bleph-10, Sodium Sulamyd (Sodium Sulfacetamide)	
Viroptic (Trifluridine)	
Natacyn (Natamycin)	
Polytrim (PolymyxinB/Trimethoprim)	
AK-Spore (Neomycin/PolymyxinB/Gramacidin)	
Ophthalmic Anti-infectives: Ointments	
Tier 1	**Tier 2**
AK-Tracin (Bacitracin)	
AK-Poly-Bac (Bacitracin/PolymyxinB)	
Ciloxan Ointment (Ciprofloxacin)	
Tobrex (Tobramycin)	
Neosporin (Neomycin/Polymyxin B/Bacitracin)	
A/T/S, Ilotycin, Roymicin (Erythromycin)	
Gentak (Gentamicin)	
Bleph-10, Sodium Sulamyd (Sodium Sulfacetamide)	

Approval Criteria for Anti-Infective/Steroids:

1. Prescription by optometrists/ophthalmologists or
2. When used for pre/post-operative prophylaxis.

Ophthalmic Anti-Infective/Steroid Combination Products	
Tier 1	**Tier 2**
	Tobradex (Tobramycin/Dexamethasone) Susp & Oint
	Zylet (Tobramycin/Loteprednol) Suspension
	Blephamide (Sulf/Prednisolone) Susp & Oint
	Pred-G (Gentamicin/Prednisolone) Susp & Oint
	Poly-Pred (Neo/Poly/Prednisolone) Susp
	Cortisporin (Neo/Poly/Hydrocortisone) Susp
	Maxitrol (Neo/Poly/Dexamethasone) Susp & Oint
	Bac/Poly/Neo/Hydrocortisone Ointment
	Neo/Poly/Bac/Hydrocortisone Ointment

Recommendation 2: Vote to Prior Authorize Veramyst™ and Omnaris™ Nasal Sprays

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends inclusion of Veramyst™ and Omnaris™ with the Tier 2 Nasal Allergy Products.

Nasal Allergy Products	
Tier 1*	***Tier 2***
Corticosteroids	Veramyst™
Fluticasone (Flonase®)	Omnaris™
flunisolide	
Nasonex®	
Beconase® AQ	
Nasacort® AQ	
Rhinocort® AQ	
Other	
Astelin®	
Ipratropium bromide	

*Brand products are subject to the Brand Name Override where generic is available.
Blue color indicated supplemental rebate participation.

Criteria for approval of a Tier 2 product:

1. Documented adverse effect or contraindication to the preferred products.
2. Failure with at least two Tier 1 medications defined as no beneficial response after at least two weeks each of use during which time the drug has been titrated to the recommended dose (at least one trial must be a corticosteroid).
3. Approvals will be for the duration of three months, except for clients with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.

Recommendation 3: Vote to Prior Authorize Exforge®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing Exforge® in the PBPA program as a Tier 2 ARB. A quantity limit of one unit per day would be applied.

Existing ARB criteria (as follows) would apply.
In order to get a Tier 2 ARB, client must meet **one** of the following criteria:

- Tier 1 ACEI drug failure (i.e. inadequate clinical response or adverse effect), or
- contraindication to the Tier 1 ACEI drugs , or
- already stabilized on the Tier 2 drug, or
- using the Tier 2 drug for a unique indication which the Tier 1 ACEI drug lacks.

Recommendation 4: Vote to Prior Authorize Brovana™

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization and the following restrictions of Brovana™:

1. Member must be over 18 years of age and have one of the following diagnoses: COPD, chronic bronchitis, or emphysema.
2. ~~2.~~ Member must have previous trial with Advair®, Serevent® or Foradil® in the past 45 days. A clinical exception will be given for those members who are unable to effectively use hand-actuated devices or ~~are stable on nebulized therapy~~ who have become unstable on nebulized short-acting β_2-agonist therapy.
3. Quantity limit of 120ml for a 30 day supply.

Recommendation 5: Vote to Approve Updated Maintenance Drug List

MOTION CARRIED by unanimous approval.

The Oklahoma Health Care Authority has selected drugs from certain disease states that are considered maintenance medications because they are taken on a regular schedule to treat chronic conditions. Daily dosage quantity limits still apply. Items in red are additions to the original list approved at the July 2004 DUR Board Meeting. (NOTE: Only changes listed below.)

Antidepressants:
- bupropion
- citalopram
- duloxetine
- escitalopram
- fluoxetine
- fluvoxamine
- mirtazapine
- paroxetine
- sertraline
- trazodone
- venlafaxine

Cardiovascular:
- aliskiren
- bosentan
- clofibrate
- diltiazem
- eplerenone
- ezetimibe
- ezetimibe/simvastatin
- fenofibrate
- gemfibrozil
- niacin/lovastatin
- nimodipine
- pindolol
- amlodipine/valsartan

Anticoagulation:
- anagrelide
- aspirin/dipyridamole

Diabetic:
- sitagliptin
- sitagliptin/metformin
- vildagliptin*

Others:
- felbamate
- folic acid
- oxcarbazepine
- pregabalin
- tiagabine
- topiramate
- zonisamide

*When approved by the FDA.

Recommendation 6: Vote to Update Narcotic Quantity Limits

MOTION CARRIED by unanimous approval.

The college of pharmacy recommends adding quantity limits to the following products:

Drug	Restriction
Fentanyl buccal (**Fentora**) 100, 200, 400, 600, 800 mcg buccal tablets	120 tablets per 30 days
Oxymorphone (**Opana IR**) 5 & 10 mg tablets	5 mg – 120 per 30 days 10 mg – 240 per 30 days
Oxymorphone (**Opana ER**) 5, 10, 20, & 40 mg tablets	5, 10 & 20 mg – 60 per 30 days 40 mg – 120 per 30 days
Pentazocine (**Talwin Cpd, Talwin NX, Talacen**) tablets	12.5 mg / Aspirin 325 mg – 240 tablets per 30 days 50 mg / Naloxone 0.5 mg – 360 tablets per 30 days 25 mg / APAP 650 mg – 180 tablets per 30 days
All product combinations containing acetaminophen (**Lortab, Percocet, Tylenol w/Codeine**, **Darvocet**, etc)	Maximum of 4 gms of APAP per day for 30 days (or as product labeling indicates)
All product combinations containing aspirin (**Percodan, Fiorinal**, etc)	Maximum of 4 gms of ASA per day for 30 days (or as product labeling indicates)
All product combinations containing ibuprofen (**Vicoprofen, Reprexain**)	150 tablets per 30 days

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for June 2007

Module	**Drug Interaction**	**Duplication of Therapy**	**Drug-Disease Precautions**	**Dosing & Duration**
Total # of messages returned by system when no limits were applied	38,463	57,628	926,144	29,947
Limits which were applied	Established, Major, Males and Females, Age 0-18	Amphetamines/ Stimulants,Males and Females, age 16-21 years old,	Contraindicated, Males and Females 19 years, Pregnant	High dose and Duration, Males and Females, Oxazolidinones (Zyvox), 0-150 years old
Total # of messages after limits were applied	11	142	581	8
Total # of members reviewed after limits were applied	11	130	283	8

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
124		121	

Retrospective Drug Utilization Review Report

Claims Reviewed for March 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 46-55	Anti-anxiety Agents, Males and Females, Age 66-150	Contraindicated, Diabetes, Males and Females, Age 0-35	High dose, Strattera, Males and Females, Age 11-150

Response Summary (Prescriber)
Letters Sent: 36
Response Forms Returned: 17

The response forms returned yielded the following results:

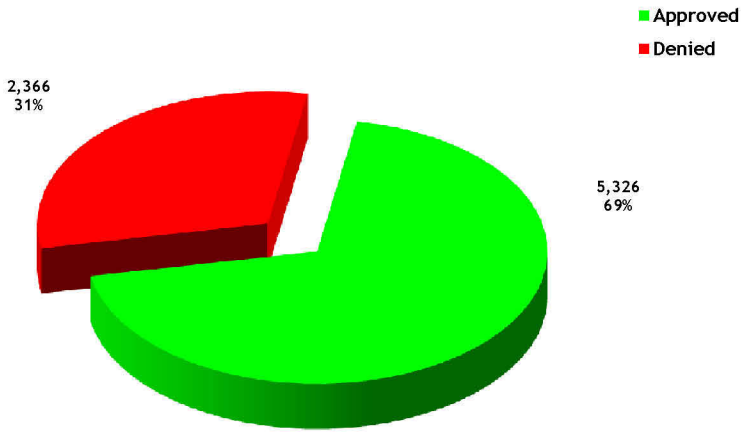
4 (24%)	*Record Error—Not my patient.*
3 (18%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
2 (12%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
6 (35%)	*I am aware of this situation and will plan to continue monitoring therapy.*
2 (12%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 30
Response Forms Returned: 22

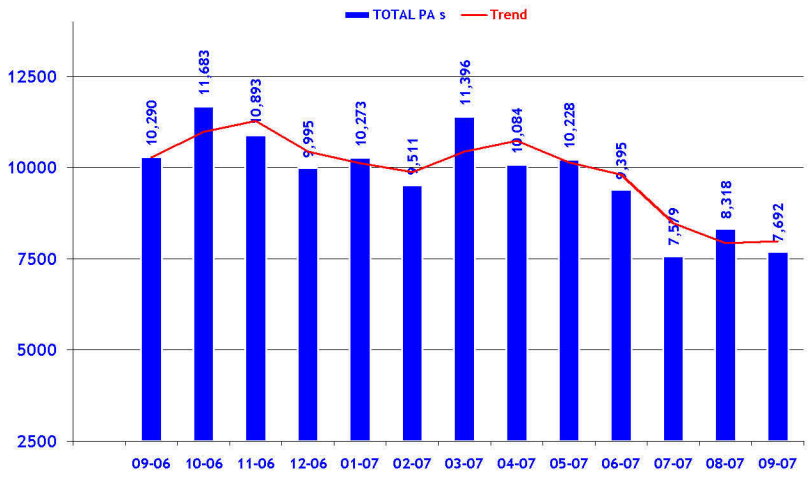
The response forms returned yielded the following results:

0 (0%)	*Record Error—Not my patient.*
3 (14%)	*No longer my patient.*
2 (9%)	*Medication has been changed prior to date of review letter.*
1 (5%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
12 (55%)	*I am aware of this situation and will plan to continue monitoring therapy.*
4 (18%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT
September 2007



PRIOR AUTHORIZATION REPORT
September 2006 – September 2007



Activity Audit for

September 01, 2007 Through September 30, 2007

	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	213	9	10	19
Angiotensin Receptor Antagonist	365	21	41	62
Antidepressant	277	201	401	602
Antihistamine	108	506	506	1,012
Antiulcers	27	15	5	20
Anxiolytic	101	2,601	389	2,990
Calcium Channel Blockers	198	8	4	12
Growth Hormones	178	34	3	37
HTN Combos	277	8	15	23
Insomnia	97	51	39	90
Nsaids	297	28	74	102
Plavix	233	148	16	164
Stimulant	237	876	212	1,088
Others	109	820	651	1,471
Emergency PAs		0	0	0
Total		**5,326**	**2,366**	**7,692**
Overrides				
Brand	217	19	5	24
Dosage Change	16	325	19	344
Lost/Broken Rx	12	95	8	103
Nursing Home Issue	15	43	1	44
Other	16	21	6	27
Quantity vs. Days Supply	220	202	134	336
Stolen	11	7	0	7
Wrong D.S. on Previous Rx	0	0	1	1
Overrides Total		**712**	**174**	**886**

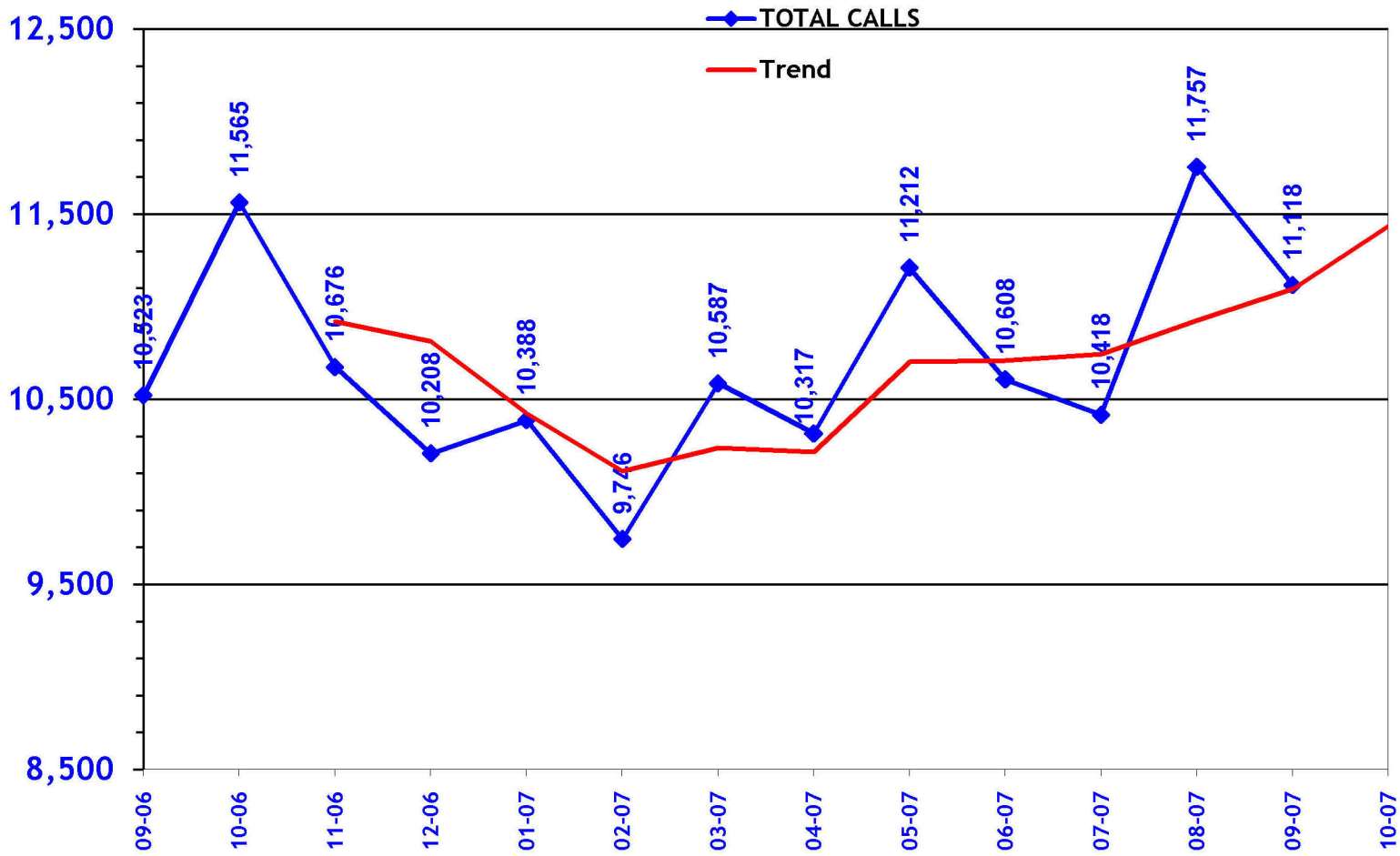
Denial Reasons

Lack required information to process request.	2,029
Unable to verify required trials.	989
Not an FDA approved indication/diagnosis.	117
Does not meet established criteria.	99
Considered duplicate therapy. Member has a prior authorization for similar medication.	99
Requested dose exceeds maximum recommended FDA dose.	73
Member has active PA for requested medication.	36
Medication not covered as pharmacy benefit.	12
Member not approved for TB coverage and/or medication requested not associated with TB symptoms.	2

Duplicate Requests	391
* Changes to existing	661

** Changes to existing PA's: Backdates, changing units, end dates, etc.*

CALL VOLUME MONTHLY REPORT
September 2006 – September 2007



04-06 thru 03-07: corrected totals

Appendix C

Vote to Prior Authorize Lidoderm® Patches

Oklahoma Health Care Authority

October 2007

Recommendations

The College of Pharmacy recommends prior authorization of Lidoderm® (lidocaine) patches to ensure safe and appropriate use of this medication for FDA approved indications as advised by the FDA and as supported by current treatment guidelines.

PA Criteria

1. FDA approved diagnosis.

2. Provide documented treatment attempts at recommended dosing or contraindication to at least one agent from two of the following drug classes:

    a. Tricyclic antidepressants
    b. Anticonvulsants
    c. Topical or Oral Analgesics

3. Quantity limit of no more than 3 patches per day with a maximum of 90 patches in a month.

Public Health Advisory – February 2007

Topical application can result in high systemic levels and lead to toxic effects (e.g. irregular heart rates, seizures, coma, respiratory depression, death). At risk are consumers, particularly those without the supervision of trained professionals, who apply large amounts of anesthetics (or cover large areas of the skin), leave these products on for long periods of time, or use materials, wraps, or dressings to cover the skin after anesthetic application. Application to areas of skin irritation, rash, and broken skin may also increase the risk of systemic absorption. The degree of systemic exposure following topical application is highly variable between patients; however, all of these practices listed may increase the degree of systemic absorption and should be avoided. The FDA is aware of two fatalities (presenting initially as seizures and then coma) following use of highly concentrated compounded topical anesthetics applied to legs and subsequently wrapped with plastic wrap to lessen pain of

Appendix D

Cough and Cold Coverage Update

Oklahoma Health Care Authority *October 10, 2007*

Current Policy

Selected non-prescription cough and cold products are covered for children less than 21 years of age.

Generally, products covered

- Are liquid formulations
- Do not contain antihistamines
- May contain APAP, cough suppressants, expectorants, and/or decongestants
- Must have a federal drug rebate contract on file.

Since these products are covered only for children, ***there is no copay and they do not count against the monthly prescription limit.***

There is no requirement for a prescription from a prescribing practitioner. Pharmacist recommendation and approval are all that is necessary to submit the claim.

The prescriber name "OTC" and prescriber number 1000001 should be submitted on the claim for payment.

Utilization

From November 28, 2006 through September 18, 2007 a total of 13,802 SoonerCare members under 21 years of age received OTC Cough and Cold medications. The following table is a summary of usage based on the first product ingredient listed. Forty-two percent of all claims were for children 2 years of age or less. A complete table is included at the end of this report.

GCN Description	Total Paid	Total Claims	Total Quantity	Total Days	Mean Paid	Mean Qty	Mean Days	Mean Age
ACETAMINOPHEN	$ 80,401.21	10,493	983,448	107,936	7.66	93.72	10.29	3.97
DEXTROMETHORPHAN	$ 43,161.22	4,476	431,794	47,728	9.64	96.47	10.66	5.87
GUAIFENESIN	$ 66,033.27	8,191	1,144,781	83,454	8.06	139.76	10.19	5.52
IBUPROFEN	$ 2,659.59	310	41,876	3,715	8.58	135.08	11.98	3.25
PSEUDOEPHEDRINE	$ 9,437.64	1,383	107,905	13,759	6.82	78.02	9.95	3.55
	$ 201,692.93	**24,853**	**2,709,804**	**256,592**	**8.12**	**109.03**	**10.32**	**4.43**

Delsym Utilization

According to the DEA Office of Diversion Control, dextromethorphan is often abused by adolescents. Abusers report a heightened sense of perceptual awareness, altered time perception and visual hallucinations. Because of concerns raised during both RetroDUR and In-House reviews over excessive use of this product, Delsym was removed from the covered products in August 2007. It has the third highest number of claims and second highest cost.

Delsym (2,603 Claims)	Sum	Mean	Min	Max
Total Paid	$ 29,000.75	11.14	2.14	25.57
Quantity	272,632	104.74	15	355
Day Supply	28,650	11.01	1	180
Claims / Member	-	1.24	1	12
Age	-	6.72	0	20

Other Overutilization Issues

Because these products can be purchased without a prescription, further review was conducted of all products. There appears to be issues of overutilization by some members across more than one drug category. All members with 10 or more claims have been referred to OHCA for review. Several of the 107 members with 10 or more claims belong to the same family unit.

Number of Claims	Number of Members
10 or More	107
5 to 9	728
Less than 5	8,619

Other Concerns

FDA issued a public health advisory regarding the use of cough and cold products on August 15, 2007. Some of the items mentioned are:

- Do ***not*** use cough and cold products in children under 2 years of age UNLESS given specific directions to do so by a healthcare provider.
- If other medicines (over-the-counter or prescription) are being given to a child, the child's healthcare provider should review and approve their combined use.

Recommendations

The College of Pharmacy has the following recommendations for the Cough and Cold products:

1. Either discontinue OTC coverage for children less than 2 years of age ***or*** require a prior authorization.
2. Only allow a maximum of 5 claims per year for this category.

Utilization by GCN Description

GCN Description	Total Paid	Total Claims	Total Quantity	Total Days	Mean Paid	Mean Qty	Mean Days	Mean Age
ACETAMINOPHEN ORAL 100MG/ML DROPS	$3,763.15	544	10,203	4,801	6.92	18.76	8.83	0.34
ACETAMINOPHEN ORAL 100MG/ML DROPS SUSP	$2,711.98	470	9,508	5,444	5.77	20.23	11.58	0.74
ACETAMINOPHEN ORAL 160MG/5ML ELIXIR	$9,803.33	1,332	161,215	12,008	7.36	121.03	9.02	4.46
ACETAMINOPHEN ORAL 160MG/5ML GEL	$8.43	1	120	10	8.43	120.00	10.00	1.00
ACETAMINOPHEN ORAL 160MG/5ML LIQUID	$625.85	94	13,645	715	6.66	145.16	7.61	5.17
ACETAMINOPHEN ORAL 160MG/5ML ORAL SUSP	$43,949.03	5,704	712,978	62,110	7.70	125.00	10.89	5.03
ACETAMINOPHEN ORAL 160MG/5ML SOLUTION	$134.10	24	2,952	322	5.59	123.00	13.42	5.25
ACETAMINOPHEN ORAL 167MG/5ML LIQUID	$780.90	96	24,378	894	8.13	253.94	9.31	13.27
ACETAMINOPHEN ORAL 80MG/0.8ML DROPS SUSP	$18,624.44	2,228	48,449	21,632	8.36	21.75	9.71	0.51
DEXTROMETHORPHAN HBR ORAL 10MG/5ML LIQUID	$13.22	2	238	16	6.61	119.00	8.00	5.50
DEXTROMETHORPHAN HBR ORAL 15MG/5ML SYRUP	$525.59	76	8,996	755	6.92	118.37	9.93	7.46
DEXTROMETHORPHAN HBR ORAL 30MG/5ML LIQUID	$29,000.75	2,603	272,632	28,650	11.14	104.74	11.01	6.72
DEXTROMETHORPHAN HBR ORAL 5MG/5ML SYRUP	$11.81	2	240	25	5.91	120.00	12.50	1.50
DEXTROMETHORPHAN HBR ORAL 7.5MG/5ML GEL	$8.43	1	120	6	8.43	120.00	6.00	18.00
DEXTROMETHORPHAN HBR ORAL 7.5MG/5ML SYRUP	$1,823.53	259	30,467	2,621	7.04	117.63	10.12	4.46
DEXTROMETHORPHN/ACETAMINOPH/CP ORAL 5-160-1/5 ORAL SUSP	$63.25	8	960	57	7.91	120.00	7.13	3.38
D-METHORPHAN HB/ACETAMINOPHEN ORAL 5-160MG/5 ORAL SUSP	$2,801.97	389	46,584	4,218	7.20	119.75	10.84	5.37
D-METHORPHAN HB/P-EPHED HCL ORAL 10-20MG/5 ELIXIR	$44.42	7	896	70	6.35	128.00	10.00	8.00
D-METHORPHAN HB/P-EPHED HCL ORAL 15-30MG/5 LIQUID	$190.49	24	3,341	184	7.94	139.21	7.67	6.21
D-METHORPHAN HB/P-EPHED HCL ORAL 2.5-7.5/.8 DROPS	$5,211.64	661	11,246	5,791	7.88	17.01	8.76	0.86
D-METHORPHAN HB/P-EPHED HCL ORAL 7.5-15MG/5 SYRUP	$2,890.39	368	47,436	4,488	7.85	128.90	12.20	4.65
D-METHORPHAN/PE/ACETAMINOPHEN ORAL 5-325MG/15 LIQUID	$105.91	14	2,925	129	7.57	208.93	9.21	11.21
D-METHORPHAN/P-EPHED/ACETAMINP ORAL 20-60-650 SOLUTION	$13.10	2	297	30	6.55	148.50	15.00	1.00
D-METHORPHAN/P-EPHED/ACETAMINP ORAL 30-60-1000 LIQUID	$60.72	9	1,560	102	6.75	173.33	11.33	7.11
D-METHORPHAN/P-EPHED/ACETAMINP ORAL 30-60-650 SOLUTION	$20.97	4	592	82	5.24	148.00	20.50	8.00
D-METHORPHAN/P-EPHED/ACETAMINP ORAL 5-15-160MG DROPS	$206.09	25	420	294	8.24	16.80	11.76	0.56
D-METHORPHAN/P-EPHED/ACETAMINP ORAL 7.5-15-160 LIQUID	$168.94	22	2,844	210	7.68	129.27	9.55	5.59
GUAIFEN/D-METHORPHAN HB/PE ORAL 100-10-5MG LIQUID	$4,009.04	527	82,627	5,583	7.61	156.79	10.59	5.81
GUAIFEN/DM HB/P-EPHEDRINE ORAL 100-10-30 SYRUP	$3,604.47	526	78,253	5,505	6.85	148.77	10.47	6.18
GUAIFEN/DM HB/P-EPHEDRINE ORAL 40-6-2/ML DROPS	$29.60	5	150	60	5.92	30.00	12.00	0.80
GUAIFEN/DM HB/P-EPHEDRINE ORAL 5-15MG/2.5 DROPS	$431.51	46	1,545	744	9.38	33.59	16.17	1.39
GUAIFEN/DM/P-EPHED/ACETAMINOPH ORAL 10-30-324 EXPECT.	$13.56	2	360	20	6.78	180.00	10.00	4.00

GUAIFENESIN/ACETAMINOPHEN ORAL 200-500/15 SOLUTION	$387.56	50	11,880	448	7.75	237.60	8.96	10.82
GUAIFENESIN/D-METHORPHAN HB ORAL 100-10MG/5 LIQUID	$520.49	62	8,764	565	8.40	141.35	9.11	6.39
GUAIFENESIN/D-METHORPHAN HB ORAL 100-10MG/5 SYRUP	$21,899.43	2,998	474,967	31,952	7.30	158.43	10.66	6.40
GUAIFENESIN/D-METHORPHAN HB ORAL 100-5/2.5 DROPS	$2,047.71	259	8,038	2,455	7.91	31.03	9.48	0.78
GUAIFENESIN/D-METHORPHAN HB ORAL 100-5MG/5 LIQUID	$11,906.81	1,221	146,491	12,003	9.75	119.98	9.83	5.39
GUAIFENESIN/D-METHORPHAN HB ORAL 200-10MG/5 LIQUID	$18.87	3	356	30	6.29	118.67	10.00	0.33
GUAIFENESIN/D-METHORPHAN HB ORAL 200-10MG/5 SYRUP	$575.96	81	9,400	877	7.11	116.05	10.83	5.70
GUAIFENESIN/D-METHORPHAN HB ORAL 200-30MG/5 LIQUID	$22.24	3	358	24	7.41	119.33	8.00	14.00
GUAIFENESIN/D-METHORPHAN HB ORAL 66.7-6.7/5 ELIXIR	$46.56	8	960	42	5.82	120.00	5.25	6.88
GUAIFENESIN ORAL 100MG/5ML LIQUID	$9,152.27	981	117,232	8,594	9.33	119.50	8.76	5.82
GUAIFENESIN ORAL 100MG/5ML SYRUP	$3,935.15	569	99,180	6,078	6.92	174.31	10.68	6.57
GUAIFENESIN/P-EPHED HCL ORAL 100-30MG/5 SYRUP	$734.30	118	15,341	1,491	6.22	130.01	12.64	5.80
GUAIFENESIN/P-EPHED HCL ORAL 50-15MG/5 SYRUP	$525.67	66	7,932	666	7.96	120.18	10.09	5.14
GUAIFENESIN/PHENYLEPHRINE HCL ORAL 100-5MG/5 LIQUID	$6,112.07	657	79,873	6,227	9.30	121.57	9.48	6.76
GUAIFN/DM/PHENYLEPH/ACETAMINOP ORAL 10-5-325/5 LIQUID	$60.00	9	1,074	90	6.67	119.33	10.00	5.44
IBUPROFEN ORAL 100MG/5ML GEL	$8.43	1	120	10	8.43	120.00	10.00	2.00
IBUPROFEN/PSEUDOEPHEDRINE HCL ORAL 100-15MG/5 ORAL SUSP	$2,651.16	309	41,756	3,705	8.58	135.13	11.99	4.50
PSEUDOEPHEDRINE HCL ORAL 15MG/5ML LIQUID	$2,662.10	347	42,920	3,235	7.67	123.69	9.32	5.67
PSEUDOEPHEDRINE HCL ORAL 15MG/5ML SYRUP	$9.86	2	236	37	4.93	118.00	18.50	3.00
PSEUDOEPHEDRINE HCL ORAL 30MG/5ML SYRUP	$3,347.83	583	54,890	5,649	5.74	94.15	9.69	4.61
PSEUDOEPHEDRINE HCL ORAL 9.4MG/ML DROPS	$3,417.85	451	9,859	4,838	7.58	21.86	10.73	0.93
TOTALS	**$201,692.93**	**24,853**	**2,709,805**	**256,592**				

Members with More than 10 Claims

Number	Claims	Gender	Age	Comments
1	88	M	3	Multiple Family Members on List
2	84	M	8	Multiple Family Members on List
3	40	M	1	
4	32	M	6	Multiple Family Members on List
5	29	F	5	
6	25	M	3	
7	24	F	7	
8	20	M	5	Multiple Family Members on List
9	19	M	6	
10	19	M	5	Multiple Family Members on List
11	19	M	4	Multiple Family Members on List
12	19	F	3	
13	19	M	3	
14	19	M	1	Multiple Family Members on List
15	18	M	1	
16	17	F	8	
17	17	F	3	
18	17	F	3	
19	17	F	2	Multiple Family Members on List
20	17	M	1	
21	16	M	15	
22	16	M	8	
23	16	M	13	Multiple Family Members on List
24	16	M	7	Multiple Family Members on List
25	16	M	7	
26	16	F	7	Multiple Family Members on List
27	16	M	13	
28	16	F	1	
29	16	F	1	Multiple Family Members on List
30	15	F	6	Multiple Family Members on List
31	15	M	2	
32	15	M	2	
33	15	F	1	
34	15	M	1	
35	14	M	7	
36	14	M	1	
37	14	M	1	
38	14	M	1	
39	14	M	1	
40	14	F	1	
41	13	M	19	Multiple Family Members on List
42	13	F	7	Multiple Family Members on List
43	13	M	5	
44	13	M	5	
45	13	M	6	
46	13	F	19	
47	13	M	7	Multiple Family Members on List
48	13	F	8	Multiple Family Members on List
49	12	F	8	Multiple Family Members on List
50	12	M	3	
51	12	F	1	Multiple Family Members on List
52	12	M	1	Multiple Family Members on List
53	12	M	3	

54	12	M	1	
55	12	F	0	
56	11	M	15	Multiple Family Members on List
57	11	M	15	
58	11	M	12	
59	11	M	9	
60	11	F	7	
61	11	F	12	
62	11	M	7	
63	11	M	6	
64	11	F	5	
65	11	F	3	
66	11	M	3	
67	11	M	12	
68	11	M	3	
69	11	F	2	
70	11	M	2	
71	11	M	2	
72	11	M	2	
73	11	M	1	
74	11	M	5	
75	11	M	1	
76	11	M	3	Multiple Family Members on List
77	11	F	1	Multiple Family Members on List
78	10	M	15	
79	10	M	12	
80	10	F	18	
81	10	F	11	Multiple Family Members on List
82	10	F	11	
83	10	F	9	
84	10	M	8	Multiple Family Members on List
85	10	M	8	
86	10	M	7	
87	10	M	6	Multiple Family Members on List
88	10	M	6	
89	10	M	6	
90	10	M	5	Multiple Family Members on List
91	10	M	4	Multiple Family Members on List
92	10	F	3	
93	10	M	3	Multiple Family Members on List
94	10	F	3	
95	10	F	2	
96	10	M	2	
97	10	M	1	
98	10	M	1	
99	10	F	1	
100	10	F	1	
101	10	M	1	Multiple Family Members on List
102	10	F	2	
103	10	F	1	
104	10	M	1	
105	10	F	1	
106	10	F	1	
107	10	F	4	

Appendix E

Required Annual Review of Antihypertensives PBPA Category: FY 2007

Oklahoma HealthCare Authority

October 2007

Overview

There are 7 categories of antihypertensive medications currently included in the Product Based Prior Authorization program:

1. Calcium Channel Blockers (**CCBs**)
2. Angiotensin I Converting Enzyme Inhibitors (**ACEIs**)
3. **ACE/CCBs** Combination Products
4. ACE inhibitor and hydrochlorathiazide combination products (**ACEI/HCTZs**)
5. Angiotensin II Receptor Blockers (**ARBs**)
6. ARB and hydrochlorathiazide combination products (**ARB/HCTZs**)
7. Direct Renin Inhibitors (**DRIs**)

The following are the criteria for authorization. If specific drugs or drug classes were approved with special criteria they are also listed. However, most of the antihypertensives are under the general criteria for authorization.

General Criteria for Authorization

To qualify for a Tier-2 medication, there must be one of the following:

- documented inadequate response to a Tier-1 drug of the same class (exception applies to the ARB categories, in which case the tier one class is the ACEIs)
- contraindication to the Tier-1 drugs
- previous stabilization on the Tier-2 drug
- a unique indication for the Tier-2 drug which the Tier-1 drugs lack

Criteria for DRIs Authorization (Tekturna)

- FDA approved indication.
- Recent trial, within the previous 6 months and at least 4 weeks in duration, of an ACE Inhibitor (or an ARB if previous trial of an ACEI) and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control.
- Aliskiren may be used in either monotherapy or combination therapy.

Criteria for Amlodipine/Atorvastatin (Caduet)

Approval of Caduet requires the following:

- an FDA approved diagnosis from each drug category (CCBs and HMG-CoA Reductase Inhibitor.)
- documented inadequate response to a tier-1 CCB.
- current use of an HMG-CoA Reductase Inhibitor.

CCB MEDICATIONS	
Tier 1	**Tier 2**
amlodipine (Norvasc)	bepridil (Vascor)
amlodipine/atorvastatin (Caduet)*	diltiazem (Cardizem LA)
diltiazem (Cardizem)	isradipine (Dynacirc)
diltiazem (Tiazac, Taztia XT)	nicardipine (Cardene SR)
diltiazem CD (Cardizem CD)	nimodipine (Nimotop)
diltiazem ER (Cartia XT, Diltia XT)	nisoldipine (Sular)
diltiazem SR (Cardizem SR)	verapamil (Covera HS)
diltiazem XR (Dilacor XR)	verapamil (Verelan PM)
felodipine (Plendil)	
isradipine (Dynacirc CR)	
nicardipine (Cardene)	
nifedipine (Adalat, Procardia)	
nifedipine CC (Adalat CC)	
nifedipine XL (Nifedical XL, Procardia XL)	
verapamil (Calan, Isoptin, Verelan)	
verapamil SR (Calan SR, Isoptin SR)	
ACE INHIBITORS	
benazepril (Lotensin)	perindopril erbumine (Aceon)
captopril (Capoten)	ramipril (Altace)
enalapril (Vasotec)	trandolapril (Mavik)
enalaprilat (Vasotec IV)	
fosinopril (Monopril)	
lisinopril (Prinivil, Zestril)	
moexipril (Univasc)	
quinapril (Accupril)	
ACE/CCB COMBINATIONS	
trandolapril/verapamil (Tarka)*	enalapril/felodipine (Lexxel)
	benazepril/amlodipine (Lotrel)
ACEI/HCTZ COMBINATIONS	
benazepril/HCTZ (Lotensin HCT)	quinapril/HCTZ (Accuretic)
captopril/HCTZ (Capozide)	moexipril/HCTZ (Uniretic)
enalapril/HCTZ (Vasoretic)	
fosinopril/HCTZ (Monopril HCT)	
lisinopril/HCTZ (Prinzide, Zestoretic)	
ARB AND ARB/HCTZ COMBINATION	
Avalide*	All other ARBs and ARB combos
DIRECT RENIN INHIBITORS	
Tier-1 ACE inhibitor + diuretic	Aliskiren (Tekturna)

Blue highlight indicates tier changes from last fiscal year.

*Tier one due to supplemental rebate participation.

Utilization Trends of Antihypertensives

	Fiscal Year 2006 (all members)	Fiscal Year 2007	Percent Change	
Total Members	51,581	19,621	Decreased	62.0 %
Total Claims	231,165	102,890	Decreased	55.5 %
Total Cost	$9,983,536.52	$4,083,733.59	Decreased	59.1 %
Total Days	9,497,063	4,111,579	Decreased	56.7 %
Per Diem	1.05	$0.99	Decreased	5.71 %

	Fiscal Year 2006 (Nonduals)	Fiscal Year 2007	Percent Change	
Total Members	16,852	19,621	Increased	16.4 %
Total Claims	86,550	102,890	Increased	18.9 %
Total Cost	$3,570,230.23	$4,083,733.59	Increased	14.4 %
Total Days	3,596,901	4,111,579	Increased	14.3 %
Per Diem	$0.99	$0.99	Unchanged	0.00 %

Utilization Summary of Antihypertensives: FY 2007

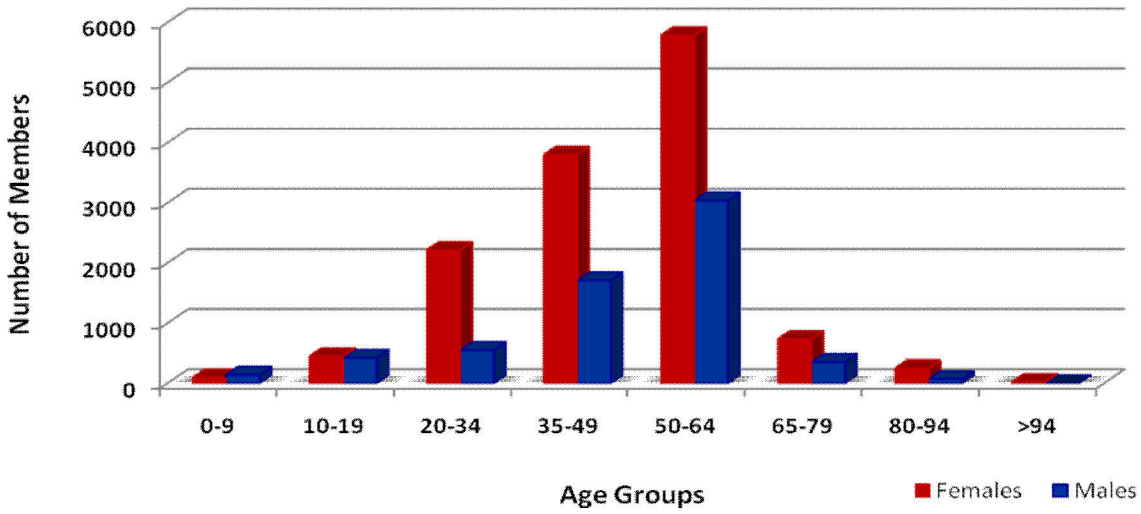
	Claims	Units	Days	Members	Cost	Cost/Claim	Perdiem
CCBs	25,413	1,203,497	985,604	6,190	$1,503,365.75	$59.16	$1.53
ACEIs	50,620	2,401,815	2,001,881	11,453	$600,941.37	$11.87	$0.30
ARBs	8,069	358,204	337,115	1,754	$681,123.28	$84.41	$2.02
CCB/ACE	3,994	183,688	169,034	789	$504,745.78	$126.38	$2.99
ACE/HCTZ	7,562	367,092	312,701	1,897	$99,250.74	$13.12	$0.32
ARB/HCTZ	7,232	319,871	305,244	1,556	$694,306.47	$96.00	$2.27
TOTALS	102,890	4,834,167	4,111,579	19,621*	$4,083,733.39	$39.69	$0.99

*Total number of unduplicated members.

Comparison of Cost vs. Claims between Antihypertensive Classes

	Claims	% of Claims	Cost	% of Cost
CCBs	25,413	24.7	$1,503,365.75	36.8
ACEIs	50,620	49.2	$600,941.37	14.7
ARBs	8,069	7.8	$681,123.28	16.7
CCB/ACE	3,994	3.9	$504,745.78	12.4
ACE/HCTZ	7,562	7.3	$99,250.74	2.4
ARB/HCTZ	7,232	7.0	$694,306.47	17.0
Totals	102,890	100.0	$4,083,733.39	100.0

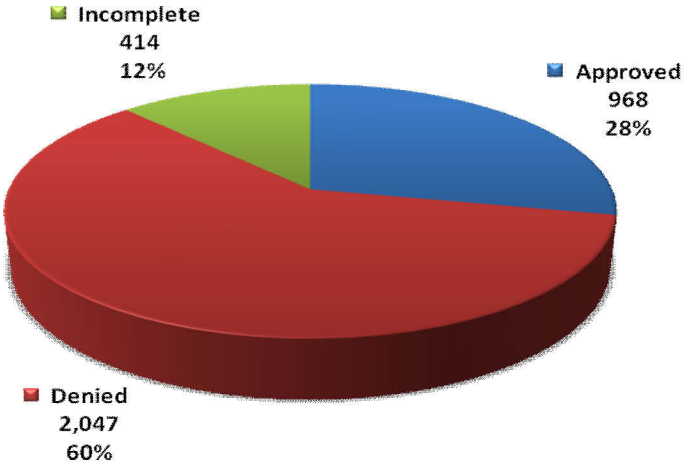
Demographics of Members Utilizing Antihypertensives: FY 2007



Prior Authorization of Antihypertensives

The following are the statistics on prior authorizations submitted for this PBPA category. Please note that for this PBPA category the system will automatically search for a tier-one in member's claims history within a certain timeframe and if detected, the member can automatically get the tier-two medication without submitting a prior authorization form. The bottom chart shows the details broken down by each major class.

Prior Authorization for the Class of Antihypertensives



	Approved	Denied	Incomplete	Totals
CCBs	178	621	108	907
ACEIs	132	162	32	326
ARBs	249	478	106	833
HTN Combos	80	154	31	265
Totals	639	1,415	277	2,331

Recommendations

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

CCB MEDICATIONS		
Tier 1	**Tier 2**	**Tier 3**
amlodipine (Norvasc)	(Supplemental rebated Tier 3)	amlodipine/atorvastatin (Caduet)
diltiazem (Cardizem)		bepridil (Vascor)
diltiazem (Tiazac, Taztia XT)		diltiazem (Cardizem LA)
diltiazem CD (Cardizem CD)		isradipine (Dynacirc)
diltiazem ER (Cartia XT, Diltia XT)		nicardipine (Cardene SR)
diltiazem SR (Cardizem SR)		nimodipine (Nimotop)
diltiazem XR (Dilacor XR)		nisoldipine (Sular)
felodipine (Plendil)		verapamil (Covera HS)
isradipine (Dynacirc CR)		verapamil (Verelan PM)
nicardipine (Cardene)		
nifedipine (Adalat, Procardia)		
nifedipine CC (Adalat CC)		
nifedipine XL (Nifedical XL, Procardia XL)		
verapamil (Calan, Isoptin, Verelan)		
verapamil SR (Calan SR, Isoptin SR)		
ACE INHIBITORS		
benazepril (Lotensin)	(Supplemental rebated Tier 3)	perindopril (Aceon)
captopril (Capoten)		ramipril (Altace)
enalapril (Vasotec)		trandolapril (Mavik)
enalaprilat (Vasotec IV)		
fosinopril (Monopril)		
lisinopril (Prinivil, Zestril)		
moexipril (Univasc)		
quinapril (Accupril)		
ACE/CCB COMBINATIONS		
Tier-1 ACEI + Tier-1 CCB	(Supplemental rebated Tier 3)	benazepril/amlodipine (Lotrel)
		enalapril/felodipine (Lexxel)
		trandolapril/verapamil (Tarka)
ACEI/HCTZ COMBINATIONS		
benazepril/HCTZ (Lotensin HCT)	(Supplemental rebated Tier 3)	quinapril/HCTZ (Accuretic)
captopril/HCTZ (Capozide)		moexipril/HCTZ (Uniretic)
enalapril/HCTZ (Vasoretic)		
fosinopril/HCTZ (Monopril HCT)		
lisinopril/HCTZ (Prinzide, Zestoretic)		
ARB AND ARB/HCTZ COMBINATION		
Tier-1 ACE inhibitor	(Supplemental rebated Tier 3)	All other ARBs & ARB combos
DIRECT RENIN INHIBITORS		
Tier-1 ACE inhibitor + diuretic	ARB or ARB combo	Aliskiren (Tekturna)

Appendix F

Prior Authorization Annual Review - Fiscal Year 2007
Ultram ER and Ultram ODT
Oklahoma Health Care Authority
October 2007

Manufacturer	Biovail Corporation
Distributor	PriCara, Unit of Ortho-McNeil, Inc.
Classification	Centrally acting synthetic opioid analgesic Status: prescription only

Summary

Ultram® ER is an extended release form of tramadol. It is indicated for the treatment of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time (up to 300mg/day).

Ultram® ODT* is an orally disintegrating formulation of tramadol. It is indicated for the treatment of moderate to moderately severe pain in adults and will be available in a 50mg dosage form.

*Ultram ODT (not yet available)

Current Criteria FY '07 (Implemented 03/2006)

Ultram ER® (FDA approved 09-08-2005)

- FDA approved diagnosis.
- Clinical supporting information for a diagnosis or health condition that requires extended pain treatment with around-the-clock dosing schedule, the reason immediate release tramadol is inappropriate and must include the physician's signature.
- Maximum covered dose of 300mg daily due to lack of efficacy and increased risk for adverse effects and seizures at higher doses.
- Quantity limit of 30 units per 30 days.

Ultram ODT® (FDA approved 05-05-2005)

- FDA approved diagnosis.
- Clinical supporting information indicating a medical condition which would make a member incapable of swallowing tablets and must include physician's signature.
- Quantity limit of 240 units per 30 days.

Approvals will be for 90 days, with the exception of members with a cancer related diagnosis where an approval will be granted for one year.

Utilization FY '07

Ultram (tramadol HCl) Fiscal Year Comparison			% Change
Cost FY '07		**$256,965.72**	**19.7↓**
	Cost FY '06	*$ 319,946.91*	
Claims FY '07		**31,638**	**18.6↓**
	Claims FY '06	*38,888*	
Per Diem FY '07		**$0.53**	**8.2↑**
	Per Diem FY '06	*$0.49*	
Members FY '07		**13,563**	**14.6↓**
	Members FY '06	*15,873*	
Units per Day FY '07		**4.34**	**N/C**
	Units per Day FY '06	*4.34*	

Product	Claims	Units	Days	Unit/Day	Cost	Members	PerDiem
Ultram ER 100mg	18	573	513	1.12	$1,712.27	8	$3.34
Ultram ER 200mg	40	1,126	1,126	1	$5,427.01	22	$4.82
Ultram ER 300mg	17	510	510	1	$3,450.07	4	$6.77
Total	75	2,209	2,149	1.03	$10,589.35	*31	$4.93

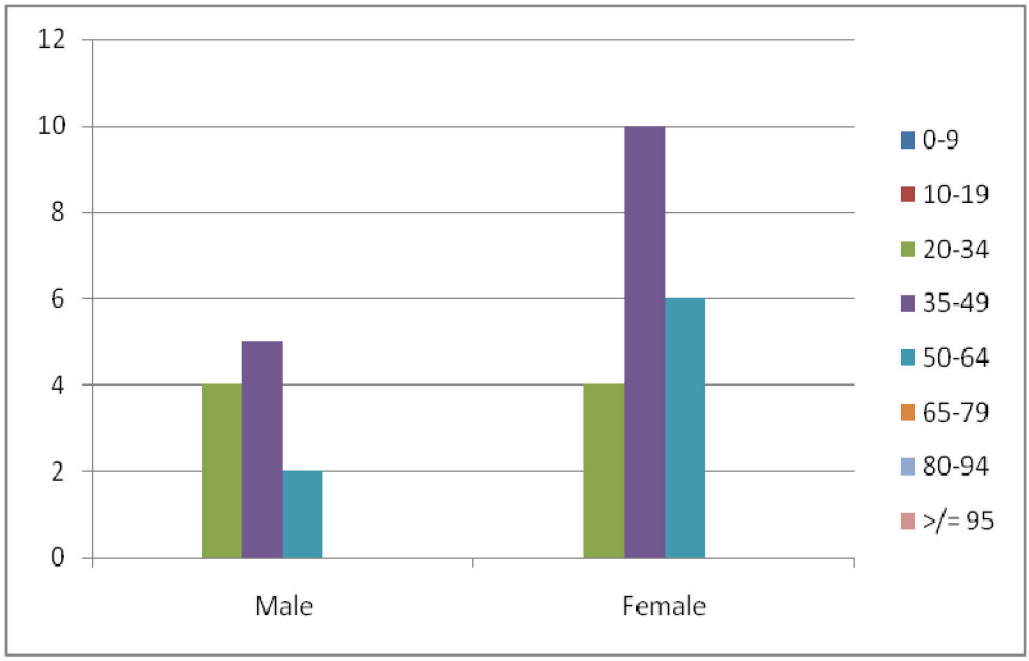
*Unduplicated members.

Petition Summary FY '07

Total Petitions: 263

Approved..... 74
Denied..... 134
Incomplete..... 34

Age and Gender FY '07



Recommendation

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

Appendix G

30 Day Notice to Prior Authorize
XYZAL® (levocetirizine dihydrochloride)
Oklahoma Health Care Authority
October 2007

Manufacturer	UCB, Inc
Classification	H1 receptor antagonist antihistamine
Status:	Prescription Only

Summary
XYZAL® is the R-enantiomer of cetirizine. It is available as a white, oval, scored 5mg tablet. It is indicated for the following conditions:

- The relief of symptoms associated with allergic rhinitis (seasonal and perennial) in adults and children 6 years of age and older.
- The treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older.

Dosing
Recommended dose is 5mg once daily in the evening for adults and children 12 years of age and older. The recommended dose for children 6 to 11 years of age is 2.5mg (1/2 tablet) once daily in the evening. A daily dose above 2.5mg for children 6 to 11 years of age is not recommended.

Warnings
- Avoid engaging in hazardous occupations requiring complete mental alertness such as driving or operating machinery when taking XYZAL®.
- Avoid concurrent use of alcohol or other central nervous system depressants with XYZAL® due to possible additional reductions in mental alertness.
- Avoid using more than the recommended dose of XYZAL® due to an increased risk of somnolence at higher doses.

Commonly Reported Adverse Effects

Subjects >12 years of age*	Children 6-12 years of age*
Somnolence 6%	Pyrexia 4%
Nasopharyngitis 4%	Cough 3%
Fatigue 4%	Somnolence 3%
Dry Mouth 2%	Epistaxis 2%
Pharyngitis 1%	

*dose of 5mg/day

Drug Interactions

Levocetirizine is metabolized primarily by CYP 3A4. It is not an inhibitor of CYP isoenzymes 1A2, 2C9, 2C19, 2A1, 2D6, 2E1, and 3A4. It is not an inducer of CYP isoenzymes 1A2, 2C9, and 3A4. *In vivo* drug-drug interaction studies have not been performed with levocetirizine. Drug-drug interactions studies have been performed with racemic cetirizine.

Market Changes in Category

- The following patents will expire this year: Clarinex® 10/2007 and Zyrtec® 12/2007. There is current speculation about one or more of these products seeking OTC status when this happens.

Cost Comparison

	Per Diem (based on EAC or SMAC)
Loratadine OTC 10mg	$0.50975
Fexofenadine 180mg	$1.44300
Zyrtec® 10mg	$2.44200
XYZAL® 5mg	$2.47504
Clarinex® 5mg	$3.04260

Current Criteria and Tier Chart

PA Criteria

- Tier 2 oral allergy products are covered after previous trials with an over-the-counter antihistamine. A 14 day trial of over-the-counter loratadine is required prior to coverage of a Tier 2 product for all age groups.
  - Trials should have been in the last month and be of adequate dose and duration,
  - Over-the-counter loratadine is a covered product for members under 21 years of age without prior authorization, and
  - For members 21 years of age and older, loratadine is available with prior authorization AFTER documented trial of a non-loratadine OTC product.
- For members six months to two years of age, cetirizine and desloratadine syrup is available without prior authorization.
- Diagnosis must be for a chronic allergic condition.
- Clinical exceptions include asthma and COPD. Prior authorization will not be approved for a time period greater than 90 days for members without a diagnosis which requires continuous coverage.

Tier 1	Tier 2
• Over-the-counter loratadine • Cetirizine and desloratadine syrup for members 6 months to 2 years of age	• Cetirizine • Desloratadine • Fexofenadine*

*Will move to Tier 1 when SMAC is comparable to loratadine.

Recommendations

The College of Pharmacy recommends the following:

1. Placing XYZAL® in the PBPA as a tier-2 agent. In addition to current tier-2 criteria, member will also have to meet the following criteria for approval of XYZAL therapy:
   a. Member must be 6 years of age or older.
   b. Member must have trials with at least two tier-1 oral allergy products. Trials must be fourteen days in duration or longer.

2. Moving desloratadine and cetirizine to tier-1 when these products are available as generics and have been assigned a SMAC.

REFERENCE

XYZAL® Product Information. UCB Inc. May 2007.

Appendix H

30 Day Notice to Prior Authorize Nuvigil™ (armodafinil)

Oklahoma Health Care Authority
October 2007

Manufacturer Cephalon, Inc.
Classification FDA classification: C-IV
Status: prescription only

Summary

Nuvigil™ (armodafinil) is an oral wakefulness-promoting medication which is the longer-lived R-enantiomer of modafinil (Provigil®). It is available in 50mg, 150mg and 250mg strengths and is indicated for obstructive sleep apnea/hypopnea syndrome (OSAHS), narcolepsy or shift work sleep disorder. In OSAHS, it is indicated as an adjunct to standard treatment. Nuvigil's effectiveness has not been studied in placebo-controlled trials for use longer than 12 weeks and has no indication for use in pediatric patients.

Revised ADHD/Narcolepsy Tier Table

Tier 1	Tier 2	Tier 3
methylphenidate SR, ER, and CR	Metadate CD	Daytrana
dexmethylphenidate IR (Focalin)	Ritalin LA	Desoxyn
Focalin XR	Strattera	Vyvanse
Concerta	methylphenidate IR*	dextroamphetamine
Adderall XR	amphetamine salt combos*	Dexedrine Spansule
		Provigil
		Nuvigil

Blue color denotes current supplemental rebate – individual products would move to Tier 2 if manufacturer chooses to no longer participate in program.
Products can move to lower tiers based on supplemental rebate participation.
*No PA will be required for a once daily dosing of these medications. Doses greater than once daily will require prior authorization.

Recommendations

The College of Pharmacy recommends placing Nuvigil™ into the ADHD/Narcolepsy PBPA category as a Tier 3. An FDA approved diagnosis of obstructive sleep apnea/hypopnea syndrome, narcolepsy or shift work sleep disorder would be required along with all other Tier 3 criteria. A quantity limit of 30 units for a 30 day supply and age restriction of 18 or older would also be applied. When approved, the initial authorization would be for 3 months, beyond that, additional information from the physician about member's response to the medication would be required for long term authorization.

REFERENCE

Nuvigil™, Product Information. Cephalon, Inc. 2007.

Appendix I

60 Day Notice and Potential Economic Impact for Product Based Prior Authorization of Topical Antifungals

Oklahoma Health Care Authority
October 2007

Introduction

The purpose of this review is to evaluate the safety, efficacy and cost effectiveness of all the available topical antifungal treatments. This category was introduced for possible inclusion in the Product Based Prior Authorization program in December 2006. See that packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Topical antifungals are used to treat a variety of infections, including tinea pedis, tinea cruris, tinea corporis, tinea versicolor, candidiasis of the skin, seborrheic dermatitis, onychomycosis, dandruff and diaper rash. There are various treatment options available to treat these conditions. The 3 main classes of topical antifungals are polyenes, imidazoles and allylamines.

Mechanisms of Action

Polyenes- bind irreversibly to ergosterol, an essential component of fungal cell membranes. This interaction results in production of aqueous pores, causing altered membrane permeability and leakage of vital cytoplasmic components. Examples include:

Nystatin

Imidazoles- inhibit ergosterol synthesis, causing defects in the fungal cell membrane. Imidazoles are relatively broad-spectrum antifungals that are primarily fungistatic. They specifically interfere with the ability of the cytochrome P-450 enzyme lanosterol I4-demethylase to catalyze the conversion of lanosterol to ergosterol. Examples include:

Clotrimazole	Econazole	Miconazole	Oxiconazole (Oxistat®)
Sulconazole (Exelderm®)	Terconazole	Tioconazole	Sertaconazole Nitrate (Ertaczo®)
Ketoconazole			

Allylamines- suppress the biosynthesis of ergosterol at an earlier stage of the metabolic pathway than the azoles by inhibiting the activity of squalene epoxidase, an action independent of the P-450 enzyme. At therapeutic drug concentrations, Allylamines are primarily fungicidal against dermatophytes and fungistatic against *C.albicans*. Examples include:

Amorolfine	Butenafine (Mentax®)	Naftifine (Naftin®)	Terbenafine

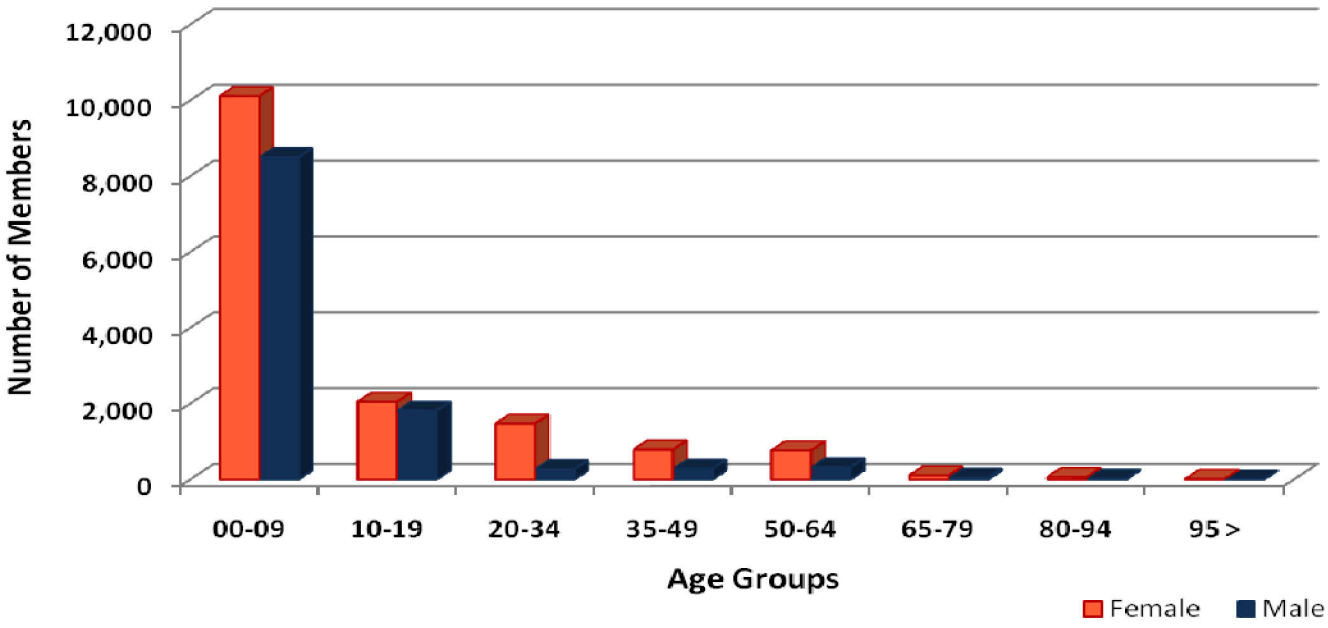
Ciclopirox gel (Loprox®) - a hydroxypyridone which differs from other antifungal agents in its chemical structure and it mechanism of action. Unlike most antifungal agents, cyclopirox does not affect sterol biosynthesis. The mode of action of this drug is very complex, targeting a variety of metabolic processes in the fungal cell.

Utilization of Topical Antifungals

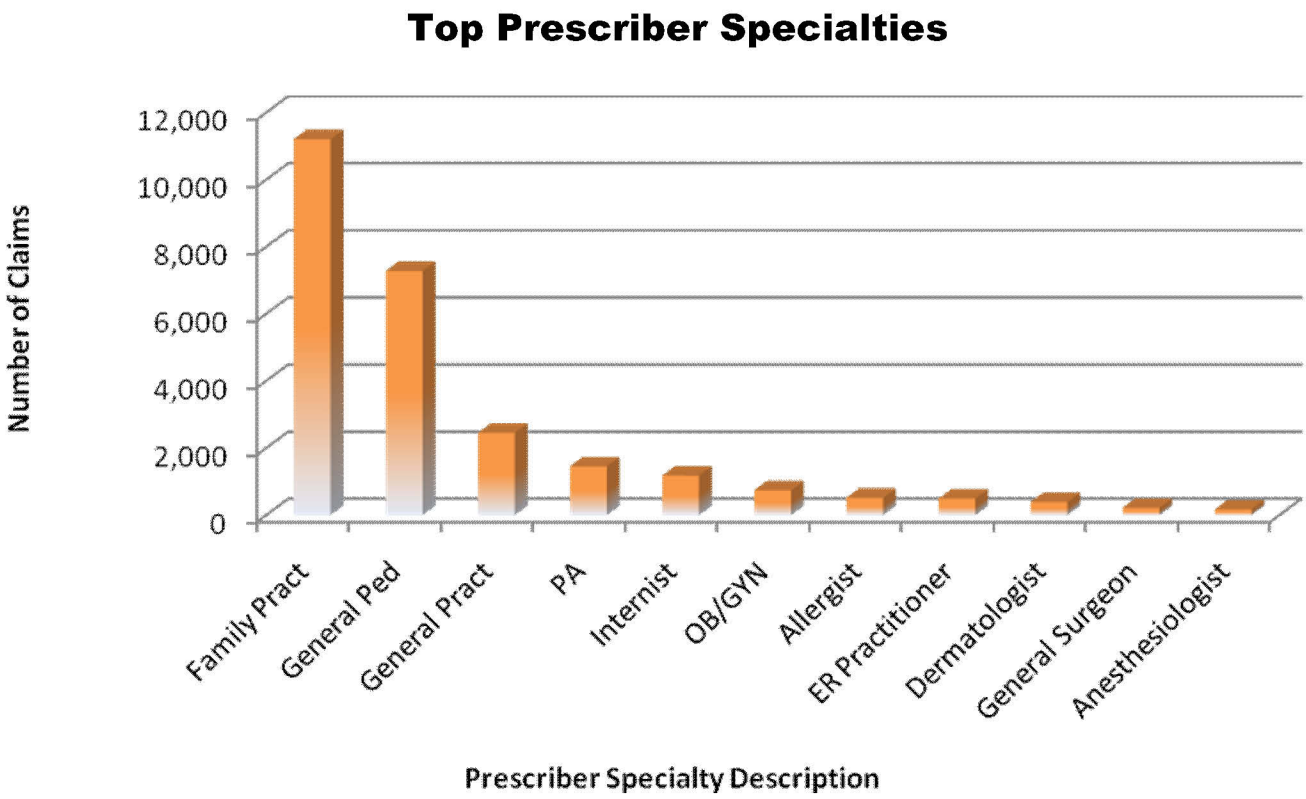
Trends in Utilization of Topical Antifungals

	Calendar Year 2005	Calendar Year 2006	Percent Change
Members	33,287	26,651	Decreased 19.9 %
Claims	56,516	39,323	Decreased 30.4 %
Cost	$1,335,575.79	$861,616.77	Decreased 35.5 %
Cost/Claim	23.63	21.91	Decreased 7.28 %
Perdiem	$2.14	$1.90	Decreased 11.2 %
Units	2,235,266	1,571,975	Decreased 29.7 %
Days	623,858	454,322	Decreased 27.2 %

Demographics of Members Utilizing Topical Antifungals



Age Groups	00-09	10-19	20-34	35-49	50-64	65-79	80-94	95 >	Totals
Female	10,112	2,050	1,472	789	766	108	64	10	15,371
Male	8,502	1,814	274	282	320	48	21	0	11,261



Recommendations

The College of Pharmacy recommends including the Topical Antifungals in the Product Based Prior Authorization (PBPA) programs.

The following Tier 1 drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Healthcare Authority.

Tier 1	Tier 2
Ciclopirox	Ciclopirox sol, shampoo, & gel **(Penlac® and Loprox®)**
Clotrimazole and Clotrimazole/Betamethasone	Miconazole/Zinc Oxide/White petrolatum **(Vusion®)**
Econazole	Oxiconazole **(Oxistat®)**
Ketoconazole	Sertaconazole nitrate **(Ertaczo®)**
Nystatin and Nystatin/Triamcinolone	Butenafine **(Mentax®)**
Hydrocortisone/Iodoquinol	Ketoconazole gel **(Xolagel®)**
All available generic antifungal products	Naftifine **(Naftin®)**
	Sulconazole **(Exelderm®)**
	Terbinafine **(Lamisil® Spray)**
	Clotrimazole **(Lotrimin Lotion 1%)**

Approval Criteria:

1. Approval of a branded antifungal product will be granted following trials of at least two other Tier 1 topical antifungal products within the last 30 days.

Potential Costs

Overall efficacy is considered to be equal across this class, but drug selection requires individual patient history which includes, but is not limited to: other illnesses, disease risk factors, and current symptoms.

Based on a potential shift of proposed Tier 2 products to a Tier 1 product of 100%, it is estimated that approximately 1,777 petitions would be required. The proposed tier changes would affect approximately 5% of the total population for this PBPA category.

Previously, it has been theorized that total cost per petition to the *healthcare system* (includes cost to physicians, pharmacists, and program) is between $7.12 and $13.78. Total cost per petition to the *healthcare system* is estimated to be between $12,652.24 and $24,487.06 annually. Anticipated actual administrative cost to the program is projected to be less than $10,000.

Potential pharmacy reimbursement savings to the program based on recommended tiers and a potential shift of 100% of market share from Tier 2 to Tier 1 is estimated to be $131,613.42 annually.

Potential Reimbursement Savings:	$131,613.42		$131,613.42
Potential Administrative Cost:	$12,652.24		$24,487.06
Total Potential Reimbursement Savings:	**$107,126.36**	**to**	**$118,961.18**
Percent of Current Reimbursement	**12.4%**	**to**	**13.8%**

Medication	Claims	Members	Units	Days	Cost	Perdiem
CLOTRIM/BETA CRE DIPROP	7,058	5,273	263,686	82,100	$164,729.83	$2.01
KETOCONAZOLE CRE 2%	2,685	2,131	93,891	33,751	$65,598.01	$1.94
NYSTATIN CRE 100000	9,925	7,611	321,011	96,672	$64,391.72	$0.67
CLOTRIMAZOLE CRE 1%	2,909	2,321	100,753	35,831	$64,200.19	$1.79
ECONAZOLE CRE 1%	1,413	1,098	61,700	18,204	$55,692.54	$3.06
CICLOPIROX CRE 0.77%	896	741	34,407	11,811	$44,094.76	$3.73
NYAMYC POW 100000	66	45	31,545	633	$39,989.48	$63.17
KETOCONAZOLE SHA 2%	1,475	844	186,118	24,156	$39,786.70	$1.65
NYSTAT/TRIAM CRE	4,883	3,835	181,776	55,269	$34,073.80	$0.62
NYSTATIN POW 100000	546	408	26,355	5,300	$33,602.17	$6.34
NYSTOP POW 100000	1,023	599	24,480	10,703	$31,735.30	$2.97
PENLAC SOL 8%	222	149	1,474	5,472	$31,431.87	$5.74
CICLOPIROX SUS 0.77%	354	251	19,320	5,573	$27,193.30	$4.88
MENTAX CRE 1%	372	293	10,215	4,394	$26,022.99	$5.92
OXISTAT CRE 1%	446	359	14,970	5,823	$24,554.88	$4.22
NYSTATIN OIN 100000	2,708	2,139	96,035	28,462	$19,721.25	$0.69
ALCORTIN GEL	267	198	12,197	3,598	$17,083.14	$4.75
MONISTAT CRE DERM 2%	218	163	10,238	2,568	$13,267.99	$5.17
CLOTRIM/BETA LOT DIPROP	365	273	13,135	5,192	$12,997.25	$2.50
LOPROX SHA 1%	152	79	19,770	2,771	$12,233.82	$4.41
LOPROX GEL TOPICAL	117	93	4,720	1,624	$10,506.27	$6.47
ERTACZO CRE 2%	92	52	3,480	1,413	$6,217.85	$4.40
NYSTAT/TRIAM OIN	647	505	20,359	6,617	$4,287.68	$0.65
NAFTIN CRE 1%	79	60	3,030	1,215	$4,247.76	$3.50
NAFTIN GEL 1%	33	19	1,480	651	$2,271.34	$3.49
EXELDERM CRE 1%	75	55	2,445	1,171	$1,978.82	$1.69
SPECTAZOLE CRE 1%	31	31	1,160	373	$1,628.07	$4.36
PEDI-DRI POW 100000	19	13	1,084	246	$1,376.28	$5.59
CLOTRIMAZOLE SOL 1%	78	30	2,350	595	$1,258.31	$2.11
LAMISIL SPR 1%	15	11	450	115	$1,224.20	$10.65
HYDROCORT/ CRE IODOQUIN	66	38	2,617	784	$1,043.45	$1.33
OXISTAT LOT 1%	16	14	480	242	$765.59	$3.16
NIZORAL SHA 2%	20	18	2,640	252	$670.76	$2.66
VUSION OIN	11	10	330	173	$611.38	$3.53
NYSTATIN POW USP	11	10	808	185	$238.84	$1.29
EXELDERM SOL 1%	6	6	210	90	$201.37	$2.24
NYSTAT-RX POW 50MU	2	2	59	30	$135.48	$4.52
NYSTAT-RX POW 500MU	1	1	86	15	$120.56	$8.04
HYDROC IODO CRE 1%	6	5	227	67	$120.06	$1.79
CLOTRIMAZOLE POW	5	5	374	80	$103.55	$1.29
LOTRIMIN LOT 1%	3	3	90	27	$90.44	$3.35
NYSTATIN POW 50MU	2	2	45	8	$58.21	$7.28
VERSICLEAR LOT	2	2	240	45	$41.62	$0.92
LOTRIMIN AF CRE 1%	1	1	120	10	$6.84	$0.68
MYCOGEN II OIN	1	1	15	10	$5.61	$0.56
NAFTIN-MP CRE 1%	1	1	1	1	$5.44	$5.44
Totals	**39,323**	**26,651***	**1,571,976**	**454,322**	**$861,616.77**	**$1.90**

*Total number of unduplicated members

BRAND NAME	*Indications*	*Dosing/Duration*
CLOTRIM/BETA CRE DIPROP	Tinea corporis, Tinea cruris, Tinea pedis	Apply to affected area twice daily MAX 2 wk (tinea corporis or tinea cruris) or MAX 4 wk (tinea pedis), 45 g cream/wk or 45 mL lotion/wk
KETOCONAZOLE CRE 2%	Candidiasis of skin, Pityriasis versicolor, Seborrheic dermatitis, Tinea corporis, Tinea cruris, Tinea pedis	Candidiasis of skin- apply 2% cream QD X 2 weeks Pityriasis versicolor- apply 2% cream to affected areas BID X 2 weeks Seborrheic dermatitis - apply 2% cream to the affected area BID X 4 weeks or 'til clinical clearing Tinea corporis or Tinea cruris, - apply 2% cream once daily for 2 weeks Tinea pedis - apply 2% cream QD X 6 weeks
NYSTATIN CRE 100000	Candidiasis of skin, Cutaneous and mucocutaneous infections	Apply liberally to affected areas twice daily until healing complete
CLOTRIMAZOLE CRE 1%	Topical Candidiasis, Pityriasis versicolor, Tinea corporis, Tinea cruris, Tinea pedis	apply thin layer of 1% cream twice daily for up to 4 wks
ECONAZOLE CRE 1%	Candidiasis of skin Tinea, Tinea pedis, tinea cruris, tinea corporis and tinea versicolor	Candidiasis of skin- apply to affected areas twice daily for 2 wk Tinea - apply to affected areas once daily for two weeks; tinea pedis for four weeks
CICLOPIROX CRE 0.77%	Tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm) caused by T. rubrum, T. mentagrophytes, E. floccosum, and M. canis; cutaneous candidiasis (moniliasis) caused by C. albicans; tinea (pityriasis) versicolor caused by M. furfur.	Gently massage gel into affected skin areas of scalp areas twice daily, morning and evening. If no improvement after 4 wk of treatment, reevaluate the diagnosis.
NYAMYC POW 100000	cutaneous or mucocutaneous mycotic infections caused by Candida albicans and other susceptible Candida species.	apply to candidal lesions topically 2 to 3 times daily until healing complete; for fungal infections of the feet, footwear should be dusted as well
KETOCONAZOLE SHA 2%	Pityriasis versicolor	apply 2% shampoo topically to damp skin and a wide surrounding margin, lather, leave on skin for 5 minutes then rinse. Shampoo twice a week for 4 weeks with at least 3 days between each shampooing, and then intermittently as needed to maintain control
NYSTAT/TRIAM CRE	Cutaneous candidiasis	Apply as a thin film to affected area(s) twice daily as indicated until healing is complete.
NYSTATIN POW 100000	Candidiasis of skin, Cutaneous and mucocutaneous infections	apply to candidal lesions topically 2 to 3 times daily until healing complete; for fungal infections of the feet, footwear should be dusted as well
NYSTOP POW 100000	Candidiasis of skin, Cutaneous and mucocutaneous infections	apply to candidal lesions topically 2 to 3 times daily until healing complete; for fungal infections of the feet, footwear should be dusted as well
PENLAC SOL 8%	Onychomycosis due to dermatophyte (Mild to Moderate), Fingernails and toenails	apply lacquer once daily to affected nails with applicator brush; remove with alcohol every 7 days. Use no more than 48 weeks.
CICLOPIROX SUS 0.77%	Tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm) caused by T. rubrum, T. mentagrophytes, E. floccosum, and M. canis; cutaneous candidiasis (moniliasis) caused by C. albicans; tinea (pityriasis) versicolor caused by M. furfur.	Gently massage gel into affected skin areas of scalp areas twice daily, morning and evening. If no improvement after 4 wk of treatment, reevaluate the diagnosis.

BRAND NAME	*Indications*	*Dosing/Duration*
MENTAX CRE 1%	Pityriasis versicolor, Tinea corporis, Tinea cruris Tinea pedis, Interdigital	apply to affected areas once daily for 2 wk apply twice daily for 7 days or once daily for 4 wk
OXISTAT CRE 1%	Pityriasis versicolor, Tinea, Superficial, Tinea corporis, Tinea cruris, Tinea pedis	apply to affected area and surrounding areas once or twice daily for 2 weeks; treat tinea pedis for 1 month
NYSTATIN OIN 100000	Candidiasis of skin, Cutaneous and mucocutaneous infections	ointment or cream, apply liberally to affected areas twice daily until healing complete
ALCORTIN GEL	Contact or atopic dermatitis,, impetiginized eczema, nummular eczema, endogenous chronic infectious dermatitis, stasis dermatitis Pyoderma, nuchal eczema, chronic eczematoid otitis externa, acne urticata, localized or disseminated neurodermatitis, lichen simplex chronicus, anogenital pruritus (vulvae, scroti, ani), Folliculitis, bacterial dermatoses, mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis), Monliasis, intertrigo.	Apply to affected area 3-4 times daily in accordance with physician's directions or as directed otherwise by a physician. (Only information available on package insert)
MONISTAT CRE DERM 2%	Tinea, Superficial	apply to affected areas twice daily for 2 weeks; treat tinea pedis for 1 month
CLOTRIM/BETA LOT DIPROP	Tinea corporis, Tinea cruris, Tinea pedis	Apply to affected area twice daily MAX 2 wk (tinea corporis or tinea cruris) or MAX 4 wk (tinea pedis), 45 g cream/wk or 45 mL lotion/wk
LOPROX SHA 1%	Seborrheic dermatitis of scalp	apply 5 mL to the wet scalp (up to 10 mL for long hair), lather, leave on for 3 minutes, then rinse; repeat twice per week for 4 weeks with at least 3 days between applications
LOPROX GEL TOPICAL	Seborrheic dermatitis of scalp Tinea, Superficial	apply gel twice daily to affected areas for 4 weeks Tinea, Superficial - gently massage gel into affected area twice daily for 4 weeks
ERTACZO CRE 2%	Tinea pedis, Interdigital	Apply cream topically twice daily for 4 weeks
NYSTAT/TRIAM OIN	Cutaneous candidiasis	Apply as a thin film to affected area(s) twice daily as indicated until healing is complete.
NAFTIN CRE 1%	Same as Naftin-MP 1% CRE	
NAFTIN GEL 1%	Same as Naftin-MP 1% CRE	
EXELDERM CRE 1%	Candidiasis of skin tinea pedis, tinea cruris, tinea corporis, tinea versicolor	Candidiasis of skin - apply once or twice daily for 3-4 wk Tinea, Superficial - apply once or twice daily for at least 3 wk; 4 wk for tinea pedis, with twice-daily application
SPECTAZOLE CRE 1%	Same as for Econazole CRE 1%	
PEDI-DRI POW 100000	Candidiasis of skin, Cutaneous and mucocutaneous infections	powder, apply to candidal lesions 2 to 3 times daily until healing complete; for fungal infections of the feet, footwear should be dusted as well
CLOTRIMAZOLE SOL 1%	Same as Lotrimin AF CRE 1%	
LAMISIL SPR 1%	Dermal mycosis, Onychomycosis due to dermatophyte	Dermal mycosis: (1% gel) tinea versicolor, tinea corporis, tinea cruris, tinea pedis; apply QD X 7 d. Dermal mycosis: (1% cream) tinea pedis; interdigital, apply BID X 1 week; plantar, apply BID X 2 weeks Dermal mycosis: (1% solution) tinea versicolor, apply twice daily for 1 week Onychomycosis due to dermatophyte: ORAL, 250 mg daily for 6 wk for fingernails; 12 wk for toenails

BRAND NAME	*Indications*	*Dosing/Duration*
HYDROCORT/ CRE IODOQUIN	Same as for Alcortin	
OXISTAT LOT 1%	Tinea pedis, Tinea cruris, Tinea corporis	tinea(pityriasis) versicolor: apply once daily Tinea corporis, tinea cruris, and tinea (pityriasis) versicolor should be treated for 2 weeks and tinea pedis for 1 month to reduce the possibility of recurrence.
NIZORAL SHA 2%	Dandruff, Pityriasis versicolor	apply shampoo to wet hair, lather, rinse thoroughly, and repeat; use every 3 to 4 days for up to 8 weeks; then as needed to control dandruff Pityriasis versicolor - apply 2% shampoo to damp skin and a wide surrounding margin, lather, leave on skin for 5 minutes then rinse. Shampoo twice a week for 4 weeks with at least 3 days between each shampooing, and then intermittently as needed to maintain control
VUSION OIN	Diaper rash, Complicated by candidiasis	Topical: gently apply at each diaper change for 7 full days; do not rub into skin
NYSTATIN POW USP	Same as for Nystatin Pow 50MU	
EXELDERM SOL 1%	Candidiasis of skin tinea cruris, tinea corporis, tinea versicolor.	Candidiasis of skin - apply once or twice daily for 3-4 wk Tinea, Superficial - apply once or twice daily for at least 3 wk; 4 wk for tinea pedis, with twice-daily application
NYSTAT-RX POW 50MU	Same as for Nystatin Pow 50MU	
NYSTAT-RX POW 500MU	Same as for Nystatin Pow 50MU	
HYDROC IODO CRE 1%	Same as for Alcortin	
CLOTRIMAZOLE POW	tinea pedis, tinea cruris, tinea corporis	should be sprinkled onto the affected area(s) for 2 weeks; 4 wk for tinea pedis
LOTRIMIN LOT 1%	Same as Lotrimin AF CRE 1%	
NYSTATIN POW 50MU	Candidal vulvovaginitis, Candidiasis of skin, Cutaneous and mucocutaneous infections, Gastrointestinal candidiasis, Non-esophageal, Oral candidiasis	apply to candidal lesions 2 to 3 times daily until healing complete; for fungal infections of the feet, footwear should be dusted as well
VERSICLEAR LOT	For topical use in the treatment of tinea versicolor	Apply a thin film of lotion to all affected areas and other susceptible areas twice a day or as directed by a physician. Finish the full course prescribed.
LOTRIMIN AF CRE 1%	Candidiasis, topical Pityriasis versicolor, tinea pedis, tinea cruris, tinea corporis	Candidiasis, topical - apply thin layer of 1% cream twice daily for up to 4 wks Pityriasis versicolor, tinea pedis, tinea cruris, tinea corporis - apply thin layer of 1% cream twice daily for up to 4 wks
MYCOGEN II OIN	Cutaneous candidiasis	Apply as a thin film to affected area(s) twice a day as indicated until healing is complete.
NAFTIN-MP CRE 1%	tinea pedis, tinea cruris, tinea corporis	A sufficient quantity should be gently massaged into the affected and surrounding skin areas once a day in the morning and evening. The hands should be washed after application. If no clinical improvement is detected within 4 weeks of therapy, the clinical condition should be reevaluated

Chemical Class Generic Name	Trade names	Manufacturers	Formulations	Indications
Polyenes				
Amphotericin B			C, L, O	CC
	Fungizone	Bristol Myers Squibb		
Nystatin			C, O, OS, P, VT, T	CC, OC, VC
	Mycostatin	Bristol Myers Squibb		
	Nilstat	Wyeth-Ayerst		
	Mykinac	Alpharma		
	Pedi-Dri	Pedinol Pharmacal		
Azoles (Imidazoles)				
Butoconazole			C	VC
	Femstat	Bayer		
Clotrimazole			C, L, S, T, VT	D, CC, OC, VC
	Fungoid	Pedinol Pharmacal		
	Lotrimin	Schering		
	Mycelex	Bayer		
	Gyne-Lotrimin	Schering		
Econazole			C	D, CC
	Spectazole	Ortho Dermatological		
Ketoconazole			C, S	D, CC
	Nizoral	Janssen Pharmaceu.		
Miconazole			C, L, S, P, VS	D, CC, VC
	Micatin	McNeil		
	Monistat-Derm	Ortho Dermatological		
	Monistat-7	Ortho Dermatological		
	Monistat-3	Ortho Dermatological		
Oxiconazole			C, L	D, CC
	Oxistat	Glaxo Wellcome		
Sulconazole			C, S	D, CC
	Exelderm	Westwood-Squibb		
Terconazole			C, VS	VC
	Terazole 3	Ortho McNeil		
	Terazole 7	Ortho McNeil		
Tioconazole			C, VO	VC
	Vagistat-1	Bristol-Myers Squibb		

Allylamines and other non-azole ergosterol synthesis inhibitors				
Amorolfine			NL	O
	Loceryl	Roche Laboratories		
Butenafine HCl			C	D
	Mentax	Penederm		
Naftifine			C, O, P	D
	Naftin	Allergan		
Terbinafine			C, S	D
	Lamisil	Sandoz Pharmaceu.		
Other agents				
Ciclopirox olamine	Loprox	Hoechst Marion Roussel	C, L	D, CC
	Penlac	Dermic	NL	O
Haloprogin			C	D, CC
	Halotex	Westwood Squibb		
Tolnaftate			C, S, P	D
	Aftate	Schering-Plough		
	NP-27	Thompson Medical		
	Tinactin	Schering-Plough		
	Ting	Fisons		
Undecylenate			C, P, O, S	D
	Cruex	Fisons		
	Desenex	Fisons		

C: cream L: lotion

NL: nail lacquer O: ointment

OS: oral suspension P: powder

S: solution/spray VO: vaginal ointment

VS: vaginal suppository T: troche VT: vaginal tablet

D: dermatophytosis CC: cutaneous candidiasis

OC: oropharyngeal candidiasis VC: vulvovaginal candidiasis

Appendix J

Early Communication of an Ongoing Safety Review

Bisphosphonates: Alendronate (Fosamax, Fosamax Plus D), Etidronate (Didronel), Ibandronate (Boniva), Pamidronate (Aredia), Risedronate (Actonel, Actonel W/Calcium), Tiludronate (Skelid), and Zoledronic acid (Reclast, Zometa)

This information reflects FDA's current analysis of available data concerning these drugs. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug products and the emerging safety issue. Nor does it mean that FDA is advising health care professionals to discontinue prescribing these products. FDA is considering, but has not reached a conclusion about whether this information warrants any regulatory action. FDA intends to update this document when additional information or analyses become available.

Publications in a recent issue of *The New England Journal of Medicine* have raised the question about the association of atrial fibrillation with the use of bisphosphonates. FDA has reviewed some safety data and requested additional data to further evaluate the risk of atrial fibrillation in patients who take bisphosphonates.

An article and an accompanying letter to the editor in the May 3, 2007, issue of *The New England Journal of Medicine* describe increased rates of serious atrial fibrillation (defined by the authors as life-threatening or resulting in hospitalization or disability) in two different studies of older women with osteoporosis treated with the bisphosphonates, Reclast and Fosamax. In both studies, more women who received one of the bisphosphonates (Reclast-1.3% or Fosamax-1.5%) reportedly developed serious atrial fibrillation as compared to women who received placebo (Reclast study-0.5%, Fosamax study-1.0%). In both studies, the rates of all atrial fibrillation (serious plus nonserious) were not significantly different between groups treated with bisphosphonate versus placebo.

What does FDA know about this concern?

The FDA reviewed spontaneous post-marketing reports of atrial fibrillation reported in association with oral and intravenous bisphosphonates and did not identify a population of bisphosphonate users at increased risk of atrial fibrillation. In addition, as part of the data review for the recent approval of once-yearly Reclast for the treatment of postmenopausal osteoporosis, the FDA evaluated the possible association between atrial fibrillation and the use of Reclast. Most cases of atrial fibrillation occurred more than a month after drug infusion. Also, in a subset of patients monitored by electrocardiogram up to the 11th day following infusion, there was no significant difference in the prevalence of atrial fibrillation between patients who received Reclast and patients who received placebo.

Atrial fibrillation is a heart rhythm disorder common in individuals 65 years old and older, the same age range of many of the patients studied in the article published in *The New England Journal of Medicine*. Upon initial review, it is unclear how these data on serious atrial fibrillation should be interpreted. Therefore, FDA does not believe that healthcare providers or patients should change either their prescribing practices or their use of bisphosphonates at this time.

This early communication is in keeping with FDA's commitment to inform the public about its

ongoing safety reviews of drugs. FDA is seeking additional data to allow for an in-depth evaluation of the atrial fibrillation issue for the entire class of bisphosphonates. It may take up to 12 months to complete the evaluation at which time FDA will communicate the conclusions and any resulting recommendations to the public. Moreover, FDA is continuing to monitor spontaneous post-marketing reports of atrial fibrillation reported in patients who have taken bisphosphonates.

Bisphosphonates are a class of drugs used primarily to increase bone mass and reduce the risk for fracture in patients with osteoporosis. Bisphosphonates are also used to slow bone turnover in patients with Paget's disease of the bone and to treat bone metastases and lower elevated levels of blood calcium in patients with cancer. There are 7 FDA-approved bisphosphonates: alendronate (Fosamax, Fosamax Plus D), etidronate (Didronel), ibandronate (Boniva), pamidronate (Aredia), risedronate (Actonel, Actonel W/Calcium), tiludronate (Skelid), and zoledronic acid (Reclast, Zometa).

The FDA urges both healthcare professionals and patients to report side effects from the use of bisphosphonates to the FDA's MedWatch Adverse Event Reporting program.

- on-line at www.fda.gov/medwatch/report.htm
- by returning the postage-paid FDA form 3500 (available in PDF format at www.fda.gov/medwatch/getforms.htm) to 5600 Fishers Lane, Rockville, MD 20852-9787
- faxing the form to 1-800-FDA-0178
- by phone at 1-800-332-1088

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Date created: October 1, 2007

FDA News

FOR IMMEDIATE RELEASE
September 28, 2007

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888-INFO-FDA

FDA Takes Action to Stop Marketing of Unapproved Hydrocodone Products

Action to impact approximately 200 cough-suppressant products

The U.S. Food and Drug Administration today announced its intention to take enforcement action against companies marketing unapproved prescription drug products containing hydrocodone, a narcotic widely used to treat pain and suppress coughs. The action does not affect other hydrocodone formulations, which have FDA approval.

Hydrocodone is one of the strongest medications available to treat pain or to suppress cough. The drug has also been an extremely popular drug of abuse and can lead to serious illness, injury, or death, if improperly used. Hydrocodone overdose can result in breathing problems or cardiac arrest, and its use may impair motor skills and judgment.

The FDA has received reports of medication errors associated with formulation changes in unapproved hydrocodone products and reports of confusion over the similarity of the names of unapproved products to approved drug products. As part of the drug approval process, the agency considers the possibility of medication errors and name confusion, so that potential safety issues associated with these factors can be minimized.

Some hydrocodone pain-relief products, such as Vicodin, are FDA-approved. However, most of the hydrocodone formulations now marketed to suppress coughs have not been approved. The agency is particularly concerned about improper pediatric labeling of unapproved hydrocodone cough suppressants (also known as antitussives), and the risk of medication error involving the unapproved products.

"Companies marketing these unapproved products have not demonstrated the safety and efficacy of these drugs," said Steven K. Galson, M.D., M.P.H., director of the FDA's Center for Drug Evaluation and Research (CDER). "A case in point – no hydrocodone cough suppressant has been established as safe and effective for children under 6 years of age and some of these unapproved products carry labels with dosing instructions for children as young as 2 years of age."

Today's action is part of FDA's broader initiative on marketed unapproved drugs that was announced in June 2006. At that time, the agency published a Compliance Policy Guide describing the FDA's risk-based enforcement approach to these products.

"This is another example of the kinds of safety risks that warrant priority enforcement under our Compliance Policy Guide," said Deborah M. Autor, J.D., director of CDER's Office of Compliance. "There are products on the market with inadequate safety information on their labeling improperly suggesting that the products may be used safely by very young children. In addition, these products may pose a higher risk of medication error than approved products. These products need to come off the market until they meet FDA approval standards."

There are a number of alternatives for patients who might be using unapproved hydrocodone cough suppressants. There are seven FDA-approved cough suppressant products containing

hydrocodone. There also are a variety of approved antitussive products that do not contain hydrocodone. Consumers should consult a health care professional for detailed guidance on treatment options.

Anyone marketing unapproved hydrocodone products that are currently labeled for use in children younger than 6 years of age must end further manufacturing and distribution of the products on or before October 31, 2007. Those marketing any other unapproved hydrocodone drug products must stop manufacturing such products on or before December 31, 2007 and must cease further shipment in interstate commerce on or before March 31, 2008. Further legal action could be taken against those failing to meet these deadlines.

For more information:
Hydrocodone Drug Products Information

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Information for Healthcare Professionals
Fentanyl Buccal Tablets (marketed as Fentora)

FDA ALERT [9/2007]: FDA has received reports of serious side effects including death in patients who have taken Fentora. These reports describe prescribing to non-opioid-tolerant patients, misunderstanding of dosing instructions, or inappropriate substitution of Fentora for Actiq by pharmacists and prescribers. The directions for using Fentora must be followed exactly to prevent death or other severe side effects from overdosing with fentanyl. FDA has asked Cephalon, the manufacturer of Fentora, to update the Fentora label and Medication Guide for patients with additional information on the safe use of Fentora.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program and complete a form on line at http://www.fda.gov/medwatch/report/hcp.htm or report by fax to 1-800-FDA-0178, by mail using the postage-paid address form provided on line, or by telephone to 1-800-FDA-1088.

Recommendations

Healthcare professionals who prescribe Fentora should be fully aware of all the prescribing information in the product label. Following are highlights of the important safety information from the product label:

- **Fentora contains fentanyl, a very potent opioid analgesic, that may cause death if not used in opioid-tolerant patients exactly as instructed in the product label.**
- **Fentora should only be used for breakthrough pain in opioid-tolerant patients with cancer.** Patients considered physiologically opioid-tolerant are those who are taking at least 60 mg daily of oral morphine, at least 25 mcg/hour of transdermal fentanyl, at least 30 mg daily of oxycodone, at least 8 mg daily of oral hydromorphone, or an equianalgesic daily dose of another opioid for at least one week.
- **Do not prescribe Fentora for patients who only need an opioid on an intermittent, as needed basis and who are not on around-the-clock opioids.**
- **Do not prescribe Fentora for the management of acute or postoperative pain including headaches, migraines, and pain due to injury.** Life-threatening respiratory depression can occur at any dose of Fentora in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients including patients who were given Fentora for headaches.
- **Fentora dosing is complex and must be thoroughly understood before prescribing.**
    - At the same microgram (mcg) dose, Fentora results in higher blood levels of fentanyl than Actiq. Therefore, for opioid-tolerant patients on around-the-clock opioids being treated with Actiq for their breakthrough cancer pain, **conversion to Fentora MUST include a dose reduction** according to the table in the

product label.
    - For opioid-tolerant patients on around-the-clock opioids being treated with any other pain medication for their breakthrough cancer pain, **the initial dose of Fentora is 100 mcg**
    - During titration and after a dose has been selected, patients **should never use more than 2 doses of Fentora** to treat an episode of breakthrough cancer pain. After the second dose of Fentora, **patients must wait a minimum of 4 hours** before treating another episode of breakthrough cancer pain with Fentora.
- **Fentora is not a generic version of Actiq.** Therefore, do not directly substitute Fentora for Actiq or other fentanyl-containing products.

Information for the patient: *Physicians who are prescribing fentanyl buccal tablets should ensure that their patients or their caregivers understand the following:*

- **Fentora can cause life-threatening breathing problems which can lead to death if it is not used correctly.** Use Fentora exactly as prescribed by your doctor.
- **Only take Fentora if you regularly use other opioid pain medicines around-the-clock (are opioid-tolerant).** Patients who take narcotic pain medications every day and around-the-clock develop *tolerance*, meaning that they are more resistant to the dangerous side effects of these medications including respiratory depression (severe trouble breathing), than patients who take narcotic pain medication only when needed. Ask your healthcare professional if you are opioid-tolerant before taking Fentora.
- **Only take Fentora for breakthrough pain due to cancer.** If this does not describe your situation, talk to your doctor about other options for managing your pain. Fentora must not be used to treat pain from injuries, surgery, headaches or migraines.
- **The Fentora dose prescribed to you may vary depending upon other opioid pain medicines you are receiving and the dose of these medicines. Make sure you read, follow, and understand your doctor's instructions and the Fentora Medication Guide for patients.**
- **Place Fentora in your mouth against the gum and allow the tablet to dissolve.** Do not chew or swallow the tablet.

Background Information

Since FDA approved Fentora in September 2006, FDA has received reports of serious adverse events including deaths in patients who received Fentora. These reports describe inappropriate prescribing to non-opioid tolerant patients, misunderstanding of dosing instructions, and inappropriate substitution by pharmacists or prescribers of Fentora for Actiq.

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Date created: September 26, 2007

Information for Healthcare Professionals
Haloperidol (marketed as Haldol, Haldol Decanoate and Haldol Lactate)

FDA ALERT [9/2007]: This Alert highlights revisions to the labeling for haloperidol (marketed as Haldol, Haldol Decanoate and Haldol Lactate). The updated labeling includes WARNINGS stating that Torsades de Pointes and QT prolongation have been observed in patients receiving haloperidol, especially when the drug is administered intravenously or in higher doses than recommended. Haloperidol is not approved for intravenous use.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program and complete a form on line at http://www.fda.gov/medwatch/report/hcp.htm or report by fax to 1-800-FDA-0178, by mail using the postage-paid address form provided on line, or by telephone to 1-800-FDA-1088.

This advisory addresses the risk of QT prolongation and Torsades de Pointes (TdP) in patients treated with haloperidol (a butryphenone antipsychotic), especially when given intravenously.

Recommendations and considerations for healthcare professionals:

Although injectable haloperidol is approved by the FDA only for ***intramuscular injection***, there is considerable evidence from the medical literature that ***intravenous administration*** of haloperidol is a relatively common "off-label" clinical practice, primarily for treatment of severe agitation in intensive care units. Due to a number of case reports of sudden death, TdP and QT prolongation in patients treated with haloperidol (especially when the drug is given intravenously or at doses higher than recommended), the sponsor has updated the labeling for haloperidol. The updated WARNINGS note that:

- Higher doses and intravenous administration of haloperidol appear to be associated with a higher risk of QT prolongation and TdP.
- Although cases of sudden death, TdP and QT prolongation have been reported even in the absence of predisposing factors, particular caution is advised in treating patients using any formulation of haloperidol who:
  - have other QT-prolonging conditions, including electrolyte imbalance (particularly hypokalemia and hypomagnesemia),
  - have underlying cardiac abnormalities, hypothyroidism, or familial long QT syndrome, or
  - are taking drugs known to prolong the QT interval.
- Because of this risk of TdP and QT prolongation, ECG monitoring is recommended if

haloperidol is given intravenously.

- Haloperidol is not approved for intravenous administration.

Clinical Data

There are at least 28 case reports of QT prolongation and TdP in the medical literature, some with fatal outcome in the context of off-label intravenous use of haloperidol. In addition to these cases, case-control studies have demonstrated a dose-response relationship between intravenous haloperidol dose and subsequent TdP. Based on this information, as well as the biologic plausibility of QT prolongation with intravenous haloperidol, FDA has strengthened warnings in the haloperidol labeling with regard to the risk of TdP and QT prolongation with intravenous haloperidol use.

At the request of the Pharmacovigilance Department of the Italian Drug Agency (AIFA), the sponsor (Johnson & Johnson) performed two post-marketing analyses of QT interval prolongation and TdP with haloperidol administration (oral or injectable). In one analysis, the sponsor searched their Benefit Risk Management worldwide safety database for QT prolongation -related adverse event reports received through June 30, 2005. This search identified 229 reports, many of which the sponsor described as confounded by concomitant QT-prolonging drugs or medical conditions. The reports included 73 cases of TdP, eleven of which were fatal. Eight of the eleven fatal cases involved intravenous administration of various doses of haloperidol.

In March 2007 the sponsor submitted to FDA the results of a second post-marketing investigation conducted for the Italian drug authority[1]. This report examined cardiac adverse events with haloperidol decanoate received by the sponsor as of July 30, 2005. The sponsor found thirteen reports including TdP, QT prolongation, ventricular arrhythmias and/or sudden death.

Based on case reports alone, we are unable to estimate the frequency with which QT prolongation or TdP occur following administration of these drugs.

Next Steps

Healthcare professionals should consider this new risk information when making individual treatment decisions for their patients. FDA will continue to monitor post-marketing reports for QT prolongation and Torsades de Pointes in patients treated with haloperidol, and will analyze any additional data for this as well as other important adverse events. FDA will consider further regulatory action and communication as additional information becomes available.

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[1] NDA 20-919 (Haloperidol). QT Prolongation in Association with the Use of Haloperidol Decanoate: a Response to the Pharmacovigilance Department of the Italian Drug Agency. Prepared by Johnson & Johnson Pharmaceutical Research and Development, L.L.C. Dated October 2005.

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FDA News

FOR IMMEDIATE RELEASE
September 14, 2007

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888-INFO-FDA

FDA Approves New Uses for Evista

Drug Reduces Risk of Invasive Breast Cancer in Postmenopausal Women

The U.S. Food and Drug Administration today approved Evista (raloxifene hydrochloride) for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis and in postmenopausal women at high risk for invasive breast cancer. Evista is only the second drug approved to reduce the risk of breast cancer.

Evista is commonly referred to as a selective estrogen receptor modulator (SERM). In reducing the risk of invasive breast cancer, SERMs may act by blocking estrogen receptors in the breast.

"Today's action provides an important new option for women at heightened risk of breast cancer," said Steven Galson, M.D., M.P.H., director, FDA's Center for Drug Evaluation and Research. "**Because Evista can cause serious side effects, the benefits and risks of taking Evista should be carefully evaluated for each individual woman.** Women should talk with their health care provider about whether the drug is right for them."

On July 24, 2007, FDA's Oncology Drugs Advisory Committee recommended approval of Evista for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis and in women at high risk for breast cancer.

In 1997, FDA approved Evista for the prevention of osteoporosis in postmenopausal women and, in 1999, for the treatment of postmenopausal women with osteoporosis.

Breast cancer is the second leading cause of cancer death in American women and accounts for 26 percent of all cancers among women. An estimated 178,480 new cases of invasive breast cancer are expected to occur among women in the United States during 2007. Invasive breast cancer develops when abnormal cells spread into the surrounding breast tissue.

Three clinical trials in 15,234 postmenopausal women comparing Evista to placebo (no drug) demonstrated that Evista reduces the risk of invasive breast cancer by 44 to 71 percent. A fourth clinical trial in 19,747 postmenopausal women at high risk for developing breast cancer compared Evista to tamoxifen. In this trial, the risk of developing invasive breast cancer was similar for the two treatments. The clinical trials were conducted over the last 10 years.

Evista can cause serious side effects including blood clots in the legs and lungs, and death due to stroke. Women with current or prior blood clots in the legs, lungs, or eyes should not take Evista. Other potential side effects include hot flashes, leg cramps, swelling of the legs and feet, flu-like symptoms, joint pain, and sweating. Evista should not be taken by premenopausal women and women who are or may become pregnant because it may cause harm to the unborn baby. In addition, Evista should not be taken with cholestyramine (a drug used to lower cholesterol levels) or estrogens.

The benefits and risks of taking Evista should be carefully weighed in each individual woman. Evista does not completely prevent breast cancer. Breast examinations and mammograms should be done before starting Evista and regularly thereafter.

The product is manufactured by Eli Lilly and Company, Indianapolis, Ind.

For more information, visit: http://www.hhs.gov/breastcancer/

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