Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

Wednesday

June 13, 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 – June 13, 2007**

DATE: June 6, 2007

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

Enclosed are the following items related to the June 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 Tekturna® – **See Appendix C.**

Action Item – Vote to Prior Authorize Amrix® and Fexmid™ – **See Appendix D.**

Action Item – Vote on Prior Authorization Changes to Xopenex® **– See Appendix E.**

Action Item – Vote on Prior Authorization Changes to Anxiolytics – **See Appendix F.**

60 Day Notice to Prior Authorize Ophthalmic Anti-Infectives **– See Appendix G.**

30 Day Notice to Prior Authorize Ophthalmic Glaucoma Products – **See Appendix H.**

30 Day Notice to Prior Authorize Tovalt™ ODT **– See Appendix I.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – June 13, 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. May 9, 2007 DUR Minutes – Vote
B. May 10, 2007 DUR Recommendations Memorandum
C. Provider Correspondence

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 January 2007
B. Retrospective Drug Utilization Review for February 2007
C. Medication Coverage Activity Audit for May 2007
D. Help Desk Activity Audit for May 2007

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

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

A. Product Summary
B. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Amrix® and Fexmid™– See Appendix D.

A. Product Summary
B. COP Recommendations

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

7. Action Item – Vote on Changes to Xopenex® Prior Authorization – See Appendix E.

A. Current Prior Authorization Criteria
B. Utilization Review
C. Potential Costs and Savings
D. COP Recommendations

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

8. Action Item – Vote on Changes to Anxiolytics Prior Authorization – See Appendix F.

A. Coverage Options
B. Current Criteria
C. COP Recommendations

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

9. 60 Day Notice to Prior Authorize Ophthalmic Anti-Infectives and Steroid Combinations – See Appendix G.

A. Utilization Review
B. COP Recommendations

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

10. 30 Day Notice to Prior Authorize Ophthalmic Anti-Glaucoma Products – See Appendix H.

A. Introduction
B. Therapy and Management
C. COP Recommendations

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

11. 30 Day Notice to Prior Authorize Tovalt™ ODT – See Appendix I.

A. Product Summary
B. COP Recommendations

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Utilization Review of Narcotics
B. Utilization Review of ESAs
C. Review of New Nasal Allergy Products
D. New Products

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MAY 9, 2007

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	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.	X	
James Rhymer, D.Ph	X	
VACANT – OMA	n/a	n/a

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.	X	
Visiting Pharmacy Students: None	n/a	n/a

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:

Pat Trahan, Taro Pharmaceuticals	Josh Treadway, Alcon Laboratories	John Omick, Novartis
Cheryl McIntosh, Novartis	Toby Thompson, Pfizer	Matt Hobbs, Pfizer
Jim Dunlap, Eli Lilly	Courtney Walker, Eli Lilly	Mark DeClerk, Eli Lilly
Jim Fowler, Astra Zeneca	Jason Neely, Sepracor	Aliza Tomlinson, OrthoMcNeilJanssen
Edward Diaz, Shire	Juanita Green, Sepracor	Steve Whiten, Taro Pharmaceuticals
Michael Mason, Alcon	Bobby White, UCB	Steve Higgins, Takeda
M. Patty Laster, Genentech	Bill Cook, Astra Zeneca	Fred Morse, BMS
Brian Mores, Pfizer	Richard Ponder, J&J	Janie Huff, TAP
Joseph Medina, Sepracor		

PRESENT FOR PUBLIC COMMENT:

Lon Lowrey, Novartis	Agenda Item No. 10
Valerie Pennington, Novartis	Agenda Item No. 10
Riaz Sirajuddin, Novartis	Agenda Item No. 10

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: April 11, 2007 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: October 2006

4B: Retrospective Drug Utilization Review Response: September 2006

4C: Medication Coverage Activity Report: April 2007

4D: Help Desk Activity Report: April 2007

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE FLECTOR®**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE QUALAQUIN®**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE OCULAR ALLERGY PRODUCTS**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **(A) DISCUSS & VOTE ON PROPOSED CHANGES TO ADHD/NARCOLEPSY PBPA**
(B) VOTE ON PRIOR AUTHORIZATION OF VYVANSE™

Materials included in agenda packet; presented by Drs. Gorman and Moore.

(A) Dr. Meece moved to approve; seconded by Dr. Gourley.

ACTION: MOTION CARRIED.

(B) Dr. Gourley moved to approve; seconded by Dr. Meece.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **60-DAY NOTICE TO PRIOR AUTHORIZE OPTHALMIC GLAUCOMA PRODUCTS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE TEKTURNA®

For Public Comment, Valerie Pennington: Good evening everyone. I'd just like to take a brief moment to introduce myself. My name is Valerie Pennington and my purpose here tonight is two-fold. I am here representing Novartis Pharmaceuticals who I'm currently employed by and I've been with them for about the past seven months. But I'm also a pharmacist and prior to joining Novartis, practiced here in the community for fifteen years, most recently at Deaconess. So I'm here, like I said, there's a two-fold purpose. But I'm here to talk to you tonight about Tekturna. Aliskiren is the generic name and this represents a new entity that is in a new class of antihypertensives. It's the first new class that's been introduced in over a decade to the market. And Tekturna is actually within the group called direct renin inhibitors. That's the name of this new class, or DRI's for short. And so in terms of the mechanism of action of Tekturna, it works by binding directly to the renin molecule which is the point of activation for the renin angiotensin aldosterone system; thereby rendering renin inactive and not allowing the conversion of angiotensinogen to angiotensin I. So this is the rate limiting step in that cascade. And because of that inhibition, angiotensin II cannot be formed and thereby the RAAS system is left quiet and no longer over activated in those patients where it was over activated. And this is really important because we know that over activation of the RAAS system contributes greatly to hypertension and therefore cardiovascular morbidity and mortality. So we know also that RAAS depression has been proven to provide and/or give protection beyond just blood pressure lowering itself. In terms of Tekturna, it's approved by the FDA for monotherapy for hypertension as well as in combination with other antihypertensive agents. It's available in two strengths, 150 and 300 milligrams. With regards to efficacy, it has been studied for monotherapy in greater than 4,900 patients and showed superior results to placebo with systolic blood pressure reductions in the 13 to 16 range, and diastolic blood pressure reductions in the 8 to 12 range. And the mean baseline blood pressures on average was 150's over 100, in terms of the patients that were studied in the monotherapy arms. In terms of combination therapy, Tekturna has been studied with ACE inhibitors, ARB's, calcium channel blockers and hydrocholorathiazide in more than 2,900 patients. And in the combination therapy trials, each individual compared or showed, Tekturna showed comparable blood pressure reductions to the comparators and actually showed synergistic effects when used in combination with these agents for blood pressure lowering. In terms of the pharmacokinetics, pharmacodynamics, you have information in your handout, so I'm not going to go through each item, but I'd like to make a couple of points. First of all, Tekturna does have a very long half-life which does allow for smooth blood pressure reduction, true 24-hour efficacy and we also have clinical data following withdrawal of the agent that shows sustained blood pressure and no rebound hypertension. So that's very important. In addition, Tekturna does not induce nor inhibit the P450 system; therefore there are no contraindications with other medications. I will point out, however, that when Tekturna was administered concurrently with Lasix, there were reductions in both the AUC and the Cmax of Lasix. We don't know the clinical significance of this, but a patient that was on those two agents concurrently, you would want to monitor and they might need an adjustment in their Lasix dose. Tekturna doesn't require a dose adjustment for renal or hepatic impairment, nor in elderly patients and in terms of safety, it's been studied now in greater than 10,000 patients, including 1,700 treated for greater than six months; 1,200 treated for greater than a year. And study discontinuation rates across all studies were 2.2% for Tekturna, versus 3.5% for placebo. So it has demonstrated great tolerability. The most common adverse effects reported I think you have in your handout, but primarily nasopharyngitis, headache, diarrhea, dizziness. And basically in conclusion, again I'd like to summarize that Tekturna is the first agent in a new class called the direct renin inhibitors. It has a unique mechanism of action, working at the point of activation of the RAAS system and provides effective 24-hour blood pressure lowering with no rebound hypertension, and it demonstrates placebo-like tolerability in the patients it was studied in. And now Dr. Sirrajuddin, I believe . .

Dr. McNeill: Let me ask the Board if they have any questions for you first. Okay. Thank you very much. Dr. Sirrajuddin?

For Public Comment, Dr. Riaz Sirajuddin: Good evening. I'm Dr. Riaz Sirajuddin. I'm a private practice cardiologist in south Oklahoma City. I currently have a lot of my patient population under Oklahoma Health Care Authority, almost 20% of my patients. I deal with very difficult to treat hypertensive patients, and the reason I'm here is to share a little bit of my clinical data and experience with Tekturna, and I just wanted to fill you in on that. For me, I'm really a very big advocate of prevention, preventative cardiology, although I am involved with interventional cardiology as well. I take great pride saying aggressive control, blood pressure lowering, has really played a key role in having my patients in a very healthy state. Despite that, it has been very tough to treat patients who have been on multiple medications, being on ACE inhibitors, beta-blockers, angiotensin receptor blockers. And then you come to a brick wall where you say, where do we go now with blood pressures still 150's, 160's. And it's always nice to have a new class come out, the first time in the last ten years. The question is that is it really as good? The research data says that it lowers the blood pressure significantly. My main goal is to share a little bit of my clinical experience and how it's being used. I've had patients who had coronary artery disease, really bad vascular path, again on all the right drugs. You know, you can't do anything further, and blood pressure is still 150's. Basically, she's already on ACE inhibitor and I added on Tekturna, you know, along with an ACE inhibitor. From 150's and 160's, within three weeks' time, she was down to 117/68. Significant drop, significant tolerance to the drug. Similarly I've had another incidence where I had another elderly lady who was significantly hypertensive and was maxed on an angiotensin receptor blocker, namely candasartan, and in combination with a thiazide diuretic. She could not tolerate an ACE inhibitor due to the cough. And she did not want to, you know, she was having more worsening problems, although her blood pressure as still in the 140's to 160's range. I saw it slowly creeping up, despite what we did. When she came in and I saw her, and she had worsening edema and shortness of breath, I said, you know we really have to do something different. But just then Tekturna got approved. I said renin angiotensin system is very, you know, very close to my heart, no pun intended, but you know, I, what I did was, I changed, she was already maxed out on candasartan so I said, you know, let me just get out of this whole therapy. I changed it over to a different angiotensin receptor blocker, much lower dose because of the mechanics, how it works, and I added on Tekturna, higher dose, a little bit higher, about 300 mg. Within three weeks of time, her swelling was improved; the daughter came and thanked me. The

daughter was actually a nurse. She came and thanked me, Doctor, thank you so much. So it does, you know, it dropped from 160's down to 117. A significant drop. More than 40 mm drop with a very reasonable amount of time, without significant side effects or anything. At the same time, you know, it depends on does it work on every patient or not? It's a very new drug. Our experience is very limited, but I feel that where it works in the renin angiotensin pathway. It works right on the initiation of the whole pathway. It's very well known for many, many years that the renin pathway is really bad for cardiovascular mortality and morbidity. It's been proven by the success of ACE inhibitors and angiotensin receptor blockers. I feel this is going to be, it's working great from the limited experience we've had. I think it will greatly benefit, especially the tough to control antihypertensives and also as Dr. Pennington already discussed with the long half-life period, it really becomes a key element with regard to compliance where you're not worried about rebound effects and the fact that it stays in your bloodstream for a long period of time. So I just wanted to brief on that and then I just want to open up for questions so that you guys might have anything to ask me or anything related to the drug, as Dr. Pennington already covered most of the other points.

Dr. Kuhls: Well, I have one quick question. Can you envision in terms of how you've used it so far, you've used it in very tough to control patients. Can you envision new hypertensives coming in and right from the start, starting on this medication without trials of the more common or more experienced drugs?

Dr. Sirajuddin: That's a good question because if you're going to (unintelligible) details, the question is can you use it first-line, is that what you're asking me .....

Dr. Kuhls: Would you in your practice?

Dr. Sirajuddin: Would I use it first-line.

Dr. Kuhls: You can use it first-line, but my question is how do you envision using it yourself in your clinical practice?

Dr. Sirajuddin: In my clinical practice, I'd tell you how I would practice. My practice is I still stick with the guidelines. My first preference is ACE inhibitors, and I use it because it's been well proven for many, many years. When you go on to the angiotensin receptor blockers, although they've been proven to reduce the blood pressure as such, the ACE inhibitors have better cardiovascular protectant data. And the way I envision this, I like to use it in combination with ACE inhibitors in people who don't tolerate ACE's; I plan to use either Tekturna by itself, or in combination with angiotensin receptor blockers. That's what I plan to use. And I think that mechanistically, it should work great and it's already proven it's working that way in my practice so far.

Dr. McNeill: Thank you, sir. Dr. Lowrey?

For Public Comment, Lon Lowrey: Thanks for the promotion, sir. I appreciate it. It's Lon. I'm a lobbyist but I never told my mother what I did. I wanted to bring to your attention tonight maybe potentially a policy issue. Let me go back just a little bit. In 2005, there was a preferred drug list program here for all the ARB's and all the products, and then the Medicare eligibles moved over to Medicare Part D, leaving you with a smaller population to treat. As a result of that, the department last year, as I remember, about this time, maybe a little bit later, asked the manufacturers to participate in a new bid program, and there were incredibly low prices. They were more the generic oriented price. So as a result, I think virtually all the ARB's except for one of the products, I think, moved to a Tier-2 status. Because you have, and almost all Medicaid programs have continuity of care, the patient stabilized, they're grandfathered and remain on, but now you've got a situation in which after ACE failure or because of grandfathering from the old PDL that we had, that the department's not gaining any rebates on these products. And that's a good thing, from my perspective. But what I'm proposing or what I would like you to think about is maybe, I hadn't thought about it until I saw the ADHD proposal tonight. Maybe you want to think about a three tier system. Let manufacturers voluntarily work with the department, if we can come to an agreement, maybe we can set up some kind of a modified tier system for those that want to work with the department and help them out. So that's my proposal, I'd like you to put that on the table. I don't know whether that's something that the Board would need to discuss, but I think you catch what I'm trying to say here. I think it's a valid point that any company could voluntarily come forward and work with the department if they so chose. We could do that with Tekturna. We are developing into a company. We're going to have another antihypertensive coming out here in a few months, so we're now becoming a company that's going to have a lot of products. So I just throw it out for your consideration. I appreciate your time. Any questions for me?

Dr. McNeill: Well I think we're actually, we're going to see this again next month, so I mean I would hope that you would talk with the folks on the other side of the table to, if a three tier system makes sense to the Agency or how you get a new product into this system .....

Mr. Lowrey: No brand name, I can speak for Novartis. Whatever the number was it was fairly low. We won't come to that level. That's pretty .....

Dr. McNeill: Okay, well ....

Mr. Lowrey: What I'm saying is we're willing to work with the department if there's a way, should I, I'd like to ask a question if I may, maybe of Dr. Nesser or Dr. Graham. How does it work, they're tried on an ACE, according to the proprosal. The computer will go back six months to see if they've been on an ACE, then what does the doctor have to do to get Tekturna, Diovan, Micardis, anything? How does that work?

Dr. Nesser: Have they been on an ACE?

Mr. Lowrey: Yes, well I'm assuming that they have.

Dr. Nesser: They don't have to do anything.

Mr. Lowrey: No paperwork at all? Okay. I thought that there was paperwork.

Dr. Nesser: No paperwork if it's when they're in the tiers, if you have already hit a tier-1, that's on a file, you know, that shows in the claims, then the tier-2 goes right through.

Mr. Lowrey: I thought there was paperwork .....

Dr. Nesser: Not when we put them in this kind of a program. When they're in step therapy, if you get step-1, if it's already on the file, then you can slip right into step-2. So, yeah.

Mr. Lowrey: Thanks for your time. Any other questions?
Dr. Kuhls: I'd just like to make the statement that having the three tier system always makes a lot more sense than two tier system, so to me in general, that makes a lot of sense to me.
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE AMRIX® AND FEXMID™**
Materials included in agenda packet; presented by Dr. Patel.
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: Xopenex® Changes
13B: Anxiolytics
13C: Opthalmic Anti-Infectives
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: May 10, 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 May 09, 2007.

Recommendation 1: Vote to Prior Authorize Flector®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Flector® and placement with the Tier-2 NSAID products.

- Approvals will be granted with FDA approved diagnosis.
- Clinical documentation supporting use for acute short-term therapy.
- Quantity limit for a maximum of 28 patches for 14 days of therapy per month.
- Approval based on current NSAID criteria and supporting information regarding the medical necessity of topical formulation.

Recommendation 2: Vote to Prior Authorize Qualaquin®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Qualaquin®. Approval based on an FDA approved diagnosis of malaria. Off label use for the prevention/treatment of leg cramps and other related conditions will not be covered.

Recommendation 3: Vote to Prior Authorize Ocular Allergy Products

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of the Ocular Allergy products to the Product Based Prior Authorization program.

Tier 1	Tier 2
cromolyn sodium	Alomide® Alocril® Alamast®
Zaditor OTC®	Optivar® Elestat® Patanol® Pataday® Ketotifen Emadine® Alrex®

Criteria for Tier 2 Product:

1. FDA approved diagnosis.
2. A trial of at least one Tier 1 product of a similar type (ie: cromolyn sodium prior to use of a mast cell stabilizer product or OTC ketotifen prior to use of an antihistamine, dual action, or corticosteroid product) for a minimum of two weeks in the last 30 days.
3. Documentation of clinical need for Tier 2 product over Tier 1 should be noted on the petition.
4. Clinical exceptions granted for products with allergic reaction or contraindication.

Recommendation 4: Vote to Prior Authorize Vyvanse™

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Vyvanse™ and placement with the Tier-2 ADHD products.

Recommendation 4: Vote on Proposed Changes to ADHD/Narcolepsy Product Based Prior Authorization Category

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the ADHD/Narcolepsy PBPA Category:

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

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 requireprior authorization.
†Price unavailable – may be eligible for Tier 2 status based on final price.

For Tier 2 Products:

- ☑ Trial with one Tier 1 drug (should include a longer-acting product).
  - Trial should have been within the last 30 days.
  - Dosing up to maximum or provide information regarding side effects at higher dose.
  - If trials are not in members claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
- ☑ Diagnosis of ADHD or Narcolepsy.
- ☑ Clinical exception for Strattera if tics or substance abuse is present.
- ☑ Only use of one long-acting product (regardless of tier level) is allowed concurrently – except for a maximum of a two month titration period.
- ☑ An immediate release product of the same drug type may be used concurrently if an afternoon dose is required.

For Tier 3 Product:

- ☑ Trial with one Tier 1 drug and one Tier 2 drug **OR** two trials of either a Tier 1 or Tier 2.
  - Both trials should have been within the last 60 days.
  - Dosing of Tier 1 up to the FDA maximum or provide information regarding side effects at higher dose.
  - If trials are not in members claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
- ☑ Diagnosis of ADHD or Narcolepsy.
- ☑ All other Tier 2 criteria apply.

For all Tiers:

- ☑ Dosing cannot exceed 1.5 times the FDA maximum.
- ☑ Prior Authorization is required for all tiers for members greater than 20 years of age. Must have a diagnosis of ADHD or Narcolepsy.

From: JFRONKMD@aol.com [mailto:JFRONKMD@aol.com]
Sent: Thursday, May 31, 2007 7:49 AM
To: Graham, Ronald D. (HSC)
Subject: Vigamox ophthalmic drops

Dear Mr. Graham:

I am writing to recommend that Vigamox ophthalmic drops be placed on the PDL.
It has excellent broad spectrum coverage for common ocular pathogens, and studies have shown that it has the best corneal penetration of the topical ocular antibiotics; which makes it particularly useful for patients who have undergone ophthalmic surgery and for patients with corneal infections.

Thank you for your consideration.

Sincerely,

James F. Ronk, M.D.

Respiratory Specialists, Inc.
1265 S. Utica, Suite 102 Tulsa, Oklahoma 74104 918/582-7007

Fred Garfinkel, M.D., F.C.C.P.
Andrew Gottehrer, M.D., F.C.C.P.
John C. Vallandigham, M.D., F.C.C.P.

April 9, 2007

Oklahoma Health Care Authority,

The s-isomer of racemic albuterol is pro inflammatory. The literature has shown that it stimulates the production of some of the same inflammatory mediators that are known to cause the obstructive airway diseases. When racemic albuterol is used regularly, the s-isomer accumulates with preferential retention in the lung. This makes the underlying disease much more difficult to manage. It leads to more decompensations as well as longer hospitalizations. This actually leads to an increased cost of care as well as inferior care in the reactive airway diseases.

F. Garfinkel

Dr. Fred Garfinkel

May 9, 2007

Dr. Ron Graham,

I am writing to you about the need for a new drug tekturna to be approved for Medicaid. According to JNC7 guidelines most hypertension patients will require more than two drugs to meet their goal. With tekturna's unique mode of action MOA it allows us to treat hypertension with an additional drug. My practice is in a rural high Native American population. I see a large number of Native Americans with diabetes as well as renal failure. I treat many patients with hypertension and I treat a large population of Medicaid patients. I would appreciate your support in this matter.

Thank you,

Dr. Darrell R. Mease, M.D.

Richard T. Brittingham, MD

Internal Medicine
Board Certified, American Board of Internal Medicine

May 7, 2007

Drug Utilization Review Board
Oklahoma Health Care Authority
4545 N. Lincoln Blvd, Ste 124
Oklahoma City, OK 73105

RE: Tekturna

To Whom It May Concern:

It has been brought to my attention that Tekturna (aliskiren) will be reviewed before your board this Wednesday, May 9, to discuss Tekturna's formulary status on Medicaid. As a prominent Medicaid provider, I want to express my sincere opinion how imperative it is that Tekturna remain affordable to my Medicaid patients at the price of two dollars per month.

Tekturna is the first new class of hypertension medication in over 10 years. It has an innovative mechanism of action by suppressing the entire rennin-angiotensin-aldosterone system. Tekturna also has a 40-hour half-life. One of the unique advantages/results of Tekturna's mechanism of action and long half-life is that there is a low-risk of hypertension rebound if a patient does not take the medication at the indicated time (this is not the case with other classes of hypertension medications). A lot of my Medicaid patients fall into this realm of noncompliance either due to forgetting to take their meds or forgetting to refill their prescriptions in a timely manner. Tekturna will help me treat these patients by delivering over 24-hour efficacy. It takes 2 weeks for Tekturna patient's hypertension to return to baseline-hypertension after the patient has stopped taking the drug!

Tekturna is also unique because it decreases plasma rennin activity (PRA), whereas all the other classes of hypertension medications that act on the RAAS increase RNA. Studies show that increased PRA leads to heart disease and end-organ damage/failure. I strongly believe that in the near future Tekturna will get approved for the indication of hea4rt and/or renal protection.

3201 West Gore Boulevard, Suite 304 Lawton, Oklahoma 73505 (580) 353-6760 Fax (580) 248-3760

As you can see, Tekturna will help me manage my hypertension patients where other medications fail. Tekturna is cutting-edge for the treatment of hypertension. Please continue to make Tekturna affordable to my Medicaid patients.

Cordially,

Richard T. Brittingham, MD

FAMILY MEDICAL CENTER

May 9, 2007

Attn: Ron Graham
Pharmacy Management Consultant

www.familymedicalctr.com

MARK W. COTTON, D.O.
Certified by American Board of Family Practice

KRISTA GORDON, M.D.
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IVANKA A. VASSILEVA, M.D.
Certified by American Board of Family Practice

1122 NE 13th St., Oklahoma City, OK 73117

Fax: (405) 271-2615

Re: Tekturna

Mr. Graham,

It is my understanding that Tekturna will be reviewed by your board today, Wednesday, May 9, to discuss Tekturna's formulary status on Medicaid. I have a lot of Medicaid patients so I want to take this opportunity to express how necessary it is that Tekturna remain affordable to these patients.

Tekturna is the first new class of blood pressure medication in 10 years. It has an ground-breaking mechanism of action by suppressing the entire RAAS (renin-angiotensin-aldosterone system) by 60%-80%. As a result, there will be lower amounts of angiotensin I and II produced in the body of a person who is taking Tekturna which leads to lower blood pressure. Tekturna also has an accumulation half-life that exceeds 24-hours. One of great advantages of Tekturna is low risk of rebound hypertension if a patient does not take the medication as indicated. Tekturna's low risk of rebound hypertension is due to its superior mechanism of action along with the long accumulation half-life. Other hypertension medication that work on the RAAS do not share a low risk of hypertension rebound like Tekturna. For example, if a patient is taking an ARB, there is a lot of angiotensin II circulating in her body. If she misses a dose, there will be a lot of naked AT1 receptors upon which Angiotensin II can bind. The result of this is rebound hypertension. The same can be said for a patient who is on an ACE. Studies show that is takes 2 weeks for a patient's hypertension to return to baseline-hypertension after the patient has stopped taking Tekturna.

A lot of my Medicaid patients are not compliant when it comes to taking their medications as indicated due to simply forgetting, forgetting to refill their prescriptions in a timely manner, or not being able to afford their refills when needed. Tekturna will help me treat these patients successfully.

Tekturna is also unique because it decreases plasma renin activity (PRA), whereas all other classes of hypertension medications that act on the RAAS increase PRA. Increased PRA can lead to heart disease (i.e. myocardial infarctions) and end-organ damage. I believe that Tekturna will get approved for other indications (e.g. heart protection, renal protection, diabetes), besides hypertension, in the future. This is another reason why Tekturna should remain affordable on Medicaid.

Tekturna will help me treat my hypertension patients where other hypertension medications fail. Tekturna is a great advancement in the treatment of hypertension. Please maintain Tekturna's affordability on Medicaid.

Sincerely,

Ivanka Vassileva, MD

5/9/07

Sharad S. Swami, M.D.
PRIME CARE FAMILY PRACTICE
INTERNAL MEDICINE BOARD CERTIFIED
533 S. 30TH, SUITE A • CLINTON, OK 73601
TELEPHONE: (580) 323-4600 FAX: (580) 323-7722

May 9, 2007

Oklahoma Board of Pharmacy:

On my behalf I feel that Tekturna can fill a void in treating patients with hypertension and because of this I see there is value in keeping it on the Medicaid Formulary. If I could further express my opinion through a phone call please feel free to contact my office.

Sincerely,

Sharad Swami, MD

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for January 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	41,699	62,543	137,865	36,018
Limits which were applied	Established, Major, Males and Females, Age 22-35	Antianxiety Agents, Males and Females, age 51-57 years	Contraindicated, Males and Females 0-150 years, Hyperthyroidism	High dose, Strattera, Males and Females, 0-7 years
Total # of messages after limits were applied	40	171	62	13
Total # of members reviewed after limits were applied	40	145	58	13

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
71		17	

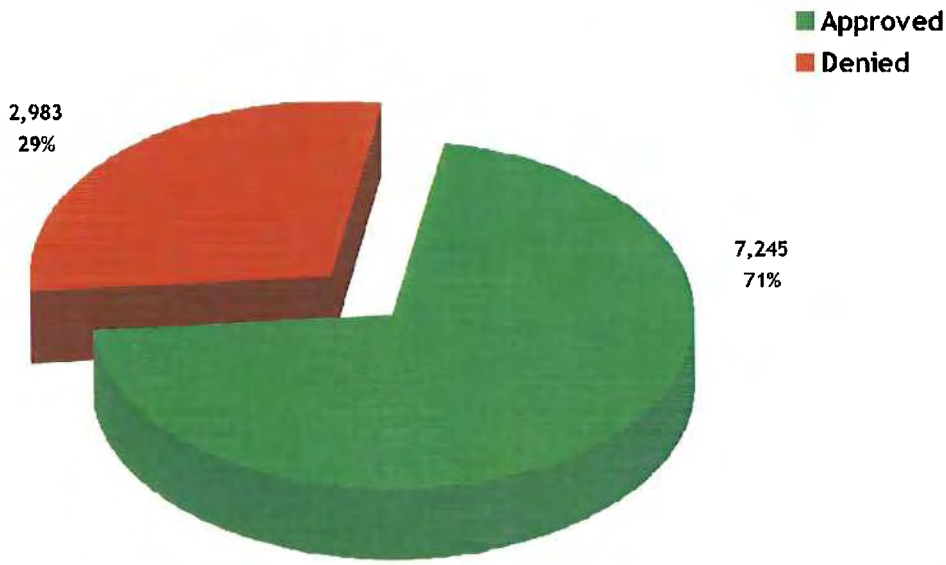
Retrospective Drug Utilization Review Report

Claims Reviewed for February 2007

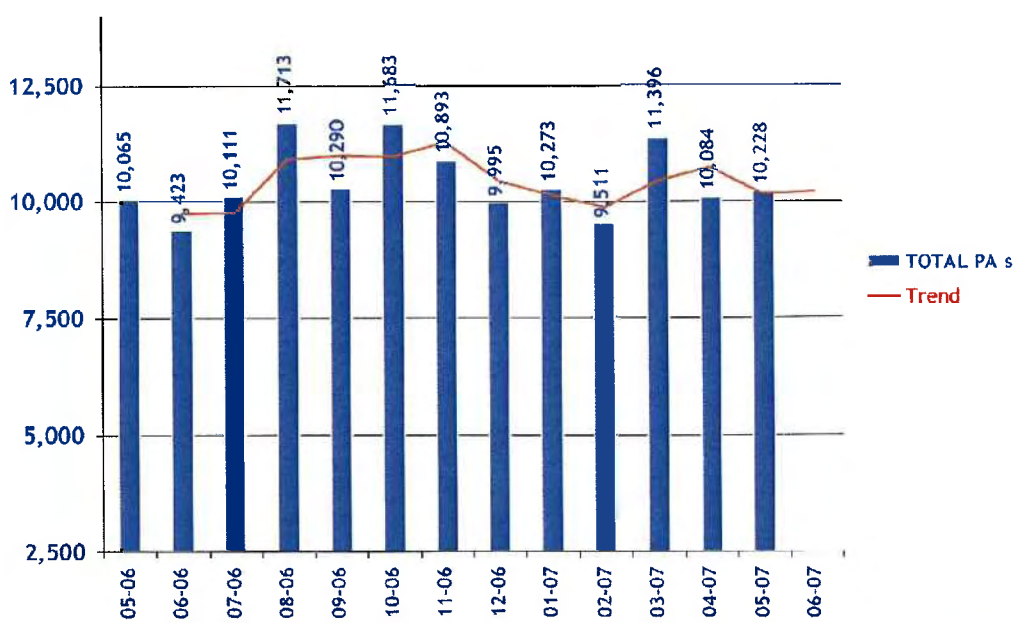
Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	38,109	59,896	131,138	38,253
Limits which were applied	Established, Major, Males and Females, Age 36-45	Antianxiety Agents, Males and Females, age 58-65 years	Contraindicated, Males and Females 0-150 years, Glaucoma	High dose, Strattera, Males and Females, 8-10 years
Total # of messages after limits were applied	40	142	52	44
Total # of members reviewed after limits were applied	40	113	38	44

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
59		25	

PRIOR AUTHORIZATION ACTIVITY REPORT
May 2007



PRIOR AUTHORIZATION REPORT
May 2006 - May 2007



Activity Audit for

May 01, 2007 Through May 31, 2007

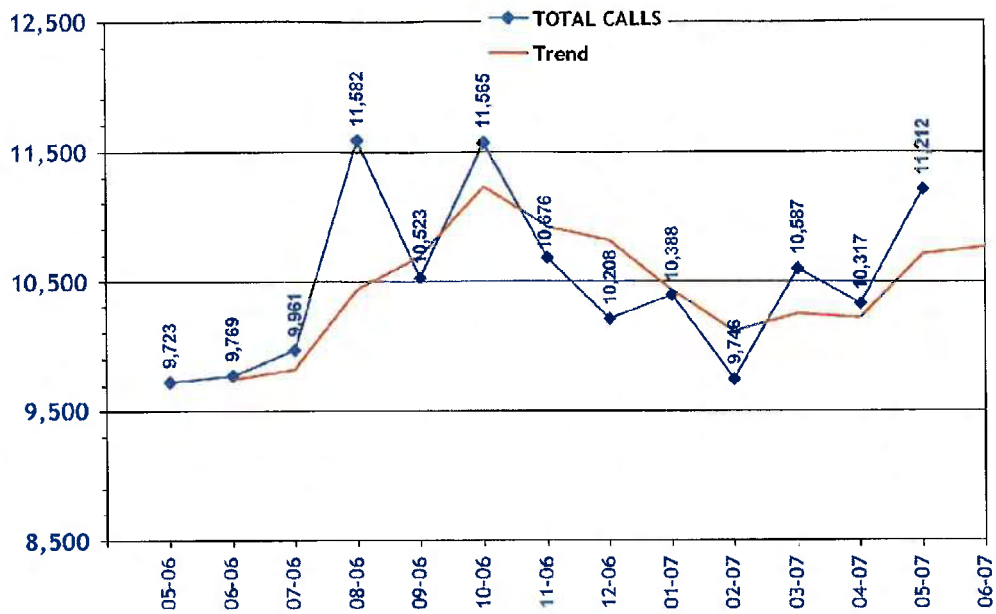
	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	64	14	4	18
Angiotensin Receptor Antagonist	365	39	53	92
Antidepressant	268	241	445	686
Antihistamine	102	1,273	729	2,002
Antiulcers	25	24	22	46
Anxiolytic	94	3,388	423	3,811
Calcium Channel Blockers	281	4	5	9
Growth Hormones	145	59	3	62
HTN Combos	304	6	21	27
Hypnotics	92	378	129	507
Nsaids	280	23	78	101
Plavix	359	199	11	210
Stimulant	195	651	231	882
Others	112	945	829	1,774
Emergency PAs		1	0	1
Total		**7,245**	**2,983**	**10,228**
Overrides				
Brand	232	36	35	71
Dosage Change	18	308	18	326
High Dose	137	2	0	2
Lost/Broken Rx	16	85	5	90
Nursing Home Issue	14	56	1	57
Other	13	29	19	48
Quantity vs. Days Supply	191	250	158	408
Stolen	8	14	1	15
Wrong D.S. on Previous Rx	3	1	4	5
Overrides Total		**781**	**241**	**1,022**

Denial Reasons

Lack required information to process request.	2,972
Unable to verify required trials.	1,130
Not an FDA approved indication/diagnosis.	198
Considered duplicate therapy. Member has a prior authorization for similar medication.	115
Does not meet established criteria.	89
Requested dose exceeds maximum recommended FDA dose.	75
Member has active PA for requested medication.	51
Medication not covered as pharmacy benefit.	12
Duplicate Requests	593
* Changes to existing	791

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

CALL VOLUME MONTHLY REPORT
May 2006 - May 2007



04-06 thru 03-07: corrected totals

PHARMACY Management consultants

Appendix C

Vote to Prior Authorize Tekturna ® (aliskiren)

Oklahoma Healthcare Authority

June 2007

Manufacturer:	Novartis Pharmaceuticals Corp.
Classification:	Direct Renin Inhibitor
Dosage forms:	150mg and 300mg oral tablet
FDA Indications:	Treatment of hypertension, alone or in combination with other anti-hypertensive agents

Place in Therapy[i]

- Aliskiren is the first agent in a new class of Direct Renin Inhibitors.
- Aliskiren has been observed in clinical trials to lower systolic blood pressure an average of 10-15 mmHg and diastolic blood pressure an average of 5-12 mmHg.
- Aliskiren has been shown to further decrease systolic (average ~ 5-10 mmHg) and diastolic (2-4 mmHg) blood pressure when added to hydrochlorothiazide, ramipril, or valsartan.
- Currently, there are no known clinical advantages of aliskiren when compared with other agents that act upon the rennin-angiotensin-aldosterone system.
- According to the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[ii] (JNC VII), thiazide diuretics and ACE inhibitors are recommended as first line agents for the initial treatment of hypertension, followed by other antihypertensive agents such as beta blockers, calcium channel blockers, etc.

Recommendations

The College of Pharmacy recommends the addition of Tekturna® (aliskiren) to the Antihypertensive PBPA category with the following approval criteria:

1. FDA approved indication.
2. 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.
3. Aliskiren may be used in either monotherapy or combination therapy.

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[i] Novartis Pharmaceuticals Corporation. Tekturna Product Prescribing Information. Available at: http://www.pharma.us.novartis.com/product/pi/pdf/tekturna.pdf. March 2007.

[ii] The National Heart Lung and Blood Institute. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - Complete Report. Available at: http://www.nhlbi.nih.gov/guidelines/hypertension/ 2004.

Appendix D

Vote to Prior Authorize Amrix® (cyclobenzaprine hydrochloride) Extended Release Capsules and Fexmid™ (cyclobenzaprine hydrochloride)

Oklahoma Health Care Authority
June 2007

Amrix® ECR Pharmaceuticals, Inc	Fexmid™ Victory Pharmaceuticals, Inc
Amrix® is an **extended-release form** of cyclobenzaprine hydrochloride designed for once daily administration. Amrix® is indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful, musculoskeletal conditions. It is available in **15mg and 30mg capsules.** Pricing not currently available	Fexmid™ is indicated for as an adjunct to rest and physical therapy for relief of muscle spasms associated with acute, painful musculoskeletal conditions. It is available in **7.5mg strength**. AWP= $2.05

Recommendations

The College of Pharmacy recommends prior authorization of Amrix® and Fexmid™. Approval based on clinical documentation of inability to take other generically available forms of cyclobenzaprine hydrochloride. A quantity limit of 30 capsules for 30 days would be placed on Amrix® and 90 tablets for 30 days on the Fexmid™.

REFERENCE

Amrix® Product Information. ECR Pharmaceuticals, Inc. 2004.

Fexmid® Product Information. Victory Pharmaceuticals, Inc. 2007.

Appendix E

Vote on Changes to Xopenex® Prior Authorization

Oklahoma Health Care Authority
June 2007

Current Prior Authorization Category

Xopenex® (levalbuterol) use in excess of 90 days of therapy in a floating 360-day period will require prior authorization.

1. In the prior authorization request, the prescriber should explain why the member is unable to use long acting bronchodilators and/or inhaled corticosteroid (ICS) therapy for long-term control per NAEPP guidelines.
2. Clinical exceptions will be made for members with COPD.

Quantity limits apply as follows:

- For nebulization – 288units/30 day supply
- For HFA inhaler – 30units/30 day supply

Utilization for January 2006 through December 2006

Nebules

	Members	*Cost*	*Claims*	*Days/ Member*	*Cost/ Day*	*Cost/ Claim*	*Cost/ Member*	*Claims/ Member*
1 Claim	5,436	$ 712,372.27	5,436	19.43	$ 6.75	$131.05	$ 131.05	1.00
2- 3 Claims	2,567	$ 776,412.33	5,918	44.81	$ 6.75	$131.20	$ 302.46	2.31
> 3 Claims	918	$ 746,310.21	5,504	111.68	$7.28	$135.59	$ 812.97	6.00
Total	**8,921***	**$2,235,094.81**	**16,858**	**36.22**	**$ 6.92**	**$132.58**	**$ 250.54**	**1.89**

HFA

	Members	*Cost*	*Claims*	*Days/ Member*	*Cost/ Day*	*Cost/ Claim*	*Cost/ Member*	*Claims/ Member*
1 Claim	1,777	$ 92,955.97	1,777	25.27	$ 2.07	$52.31	$ 52.31	1.00
2- 3 Claims	658	$ 81,270.29	1,519	58.06	$ 2.13	$53.50	$ 123.51	2.31
> 3 Claims	86	$ 22,287.09	420	113.66	$ 2.28	$53.06	$ 259.15	4.88
Total	**2,521***	**$196,513.35**	**3,716**	**36.83**	**$ 2.12**	**$52.88**	**$ 77.95**	**1.47**

*Unduplicated members = 11,020. 422 members utilized both types.

Projected Program Savings/Cost Calculations

30 Day Option

	Members	*Current Reimbursement*	*PA Cost*[1]	*Members Approved*[2]	*30 Day No PA*[3]	*Post 30 Days*[4]	***Projected Savings***[5]
No PA	7,213	$ 805,328.24	$ 0.00	7,213	$ 805,328.24	$ 0.00	$ 0.00
PA	4,229	$1,626,279.92	$(58,275.62)	1,147	$ 502,663.85	$ 569,162.53	$ 496,177.92
Totals	**11,442**	**$2,431,608.16**	**$(58,275.62)**	**8,360**	**$1,307,992.09**	**$ 569,162.53**	**$ 496,177.92**

[1]The average cost to the *healthcare system* for processing petitions is calculated at $7.12 per petition with the maximum cost at $13.78 per petition. The maximum cost was used in the estimation of administrative costs.
[2]Approved members based on those requiring less than 30 days of therapy (four 24 count boxes of nebulizer and 2 HFA units) and an approximate approval rate of 20% for members with 2 to 3 claims and 50% for clients with greater than 3 claims.
[3]Cost for members with less than 30 days of therapy.
[4]Cost for approved members with greater than 30 days of therapy.
[5]Projected Savings = Current Reimbursement – Pre and Post 30 Day Cost - PA Cost.

Recommendation

The College of Pharmacy recommends the following change to the Xopenex® prior authorization criteria:

Xopenex® (levalbuterol) use in excess of 30 days of therapy in a floating 360-day period will require prior authorization.

1. In the prior authorization request, the prescriber should document why the member is unable to use racemic albuterol. For those members with asthma, members should also be utilizing inhaled corticosteroid (ICS) therapy for long-term control per NAEPP guidelines.
2. Dose of levalbuterol requested cannot be less than the racemic equivalent documented on the prior authorization request.

Quantity limits apply as follows:

- For nebulization – 288units/30 day supply
- For HFA inhaler – 30units/30 day supply

Appendix F

Vote on Changes to Anxiolytic Prior Authorization Category

Oklahoma Health Care Authority
June 2007

Background:

The current coverage for anxiolytic benzodiazepines has been in effect since 1993. With many additional products now available for treatment of anxiety and related disorders, a change is sought for coverage of these products. The goal of the new coverage criteria is to reduce inappropriate utilization of this class of drugs, while maintaining coverage for those who require this medication on a long-term basis.

The 2005 Annual Report of the American Association of Poison Control Centers' National Poisoning and Exposure Database reported 67,593 exposures with benzodiazepines with 54,953 treated in a health care facility. There were 3,018 major outcomes and 243 deaths. In comparison, ibuprofen had 71,109 exposures, 21,377 treated in a health care facility, 348 major outcomes, and 25 deaths.

Coverage Options:

1. Discontinue coverage of benzodiazepines: States may exclude or restrict coverage of benzodiazepines from Medicaid coverage as part of the Medicaid Drug Rebate Program, created by OBRA 1990 in section 1927(d)(2)(4,5).
2. Continue current non-hypnotic benzodiazepine coverage.
3. Create new coverage criteria.

Current Anxiolytic Coverage Criteria:

- First 90 days of therapy do not require a prior authorization.
- Members may receive two benzodiazepines if one is used during the day for one diagnosis and the other is used at night as a hypnotic agent; or if they are using two different strengths to reach a target dose not available in a single unit.
- Clarification of dosing schedule and diagnosis are important to assure that the member is not receiving duplicate therapy (e.g. an anxiolytic and hypnotic both dosed at bedtime).
- Additional information regarding recent attempts at dose reductions is requested on recurrent petitions for high dose anxiolytics.

Proposed Criteria:

Long-Term (**PA Exempt**) Diagnoses:

For these physical medicine diagnoses, *DUR +* will automatically generate a yearly approval:

- Seizures,
- Epilepsy,
- Paralysis,
- MS,
- CP, and
- Muscular Dystrophy.

Drug Grouping:

1 14 Days – No Pa	2 14 Days – No Pa	3 Hard PA
Chlordiazepoxide	Alprazolam	Alprazolam XR
Clorazepate	Diazepam	Niravam
Oxazepam	Lorazepam	
Clonazepam		
Midazolam		

Coverage Summary:

Currently Prior Authorized Members:

- Automatic yearly approval for members with PA exempt diagnoses listed above.
- All other diagnoses require periodic authorization similar to current coverage.

New Starts:

- Short term (14 days or less) receive automatic approval based on drug group and criteria listed below.
- Automatic annual approval for those with PA exempt diagnoses listed above.
- All other diagnoses would require a manual prior authorization for long-term usage similar to current coverage.

Approval Criteria:

1. DUR+ Criteria:
    a. Long-Term (PA Exempt) Diagnosis = Automatic Paid Claim.
    b. No Long-Term Diagnosis (Group 1 and 2) and claim is for 14 day supply or less:
        i. No benzodiazepine claim in last 90 days *AND*
        ii. Member between 19 and 64 years old or less than 19 and prescription is from a psychiatrist *AND*
        iii. No concurrent ADHD medications (except Strattera) *AND*
        iv. No contraindicated indications *AND*
        v. Total units do not exceed 4 per day = Automatic Paid Claim.

2. Manual Prior Authorization Criteria (All Groups):
    a. Diagnosis from the long-term behavioral health list *AND*
    b. Documentation of recent (past 90 days) SSRI or other non-benzodiazepine treatment when appropriate, including treatment outcome and reason benzodiazepine is required *AND*
    c. If Group 2, reason must be given for not using a Group 1 medication – if Group 3, clinical documentation and previous trial information must be given to support the use of a Group 3 drug instead of a Group 1 or Group 2 medication *OR*
    d. Prescription by a Psychiatrist.

3. Limitations to Prior Authorization:
    a. Review by pharmacy Lock-In Program staff for members using Group 2 or Group 3 medications if other controlled substances are utilized.
    b. Approval granted for 90 days per authorization.
    c. Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.

Current Prior Authorized Members:

1. Continue current regimen unless a 90 day therapy gap exists.
    a. If gap exists, member will be subject to "New Start" criteria.
2. Review by pharmacy Lock-In Program staff for members using Group 2 or Group 3 medications if other controlled substances are utilized.
3. Request downward dosage titration every 180 days.
4. Approval granted for 90 days per authorization.
5. Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.
6. No concurrent ADHD medications.

Contra-Indicated Co-Morbid Conditions:

- History of Substance Abuse/Dependence including Alcoholism.
- Antisocial Personality Disorder
- Cigarette Use

Long-Term Behavioral Health Diagnoses:

- Post Traumatic Stress Disorder
- Panic Disorder
- Obsessive Compulsive Disorder
- Social Phobia
- Severe Generalized Anxiety Disorder
- Major Depression Recurrent
- Bipolar Disorder

Appendix G

60 Day Notice to Prior Authorize Ophthalmic Anti-Infectives and Steroid Combinations

Oklahoma HealthCare Authority

June 2007

Utilization

Utilization of Ophthalmic Anti-infectives: Liquid Dosage Forms CY 2006

Medication	Claims	Units	Days	Members	Cost	Cost/ Unit	Units/ Claim	Cost/ Claim
VIGAMOX DRO 0.5%	9,310	28,366	94,105	8,122	$532,234.85	$18.76	3.05	$57.17
CIPROFLOXACN SOL 0.3% OP	1,693	8,516	15,479	1,533	$39,548.61	$4.64	5.03	$23.36
NEO/POLY/GRA SOL OP	1,560	15,563	17,677	1,450	$37,640.18	$2.42	9.98	$24.13
ZYMAR DRO 0.3%	668	3,373	7,726	543	$37,627.75	$11.16	5.05	$56.33
SOD SULFACET SOL 10% OP	4,109	61,635	50,655	3,916	$25,743.71	$0.42	15.00	$6.27
GENTAMICIN SOL 0.3% OP	3,813	21,872	34,750	3,516	$25,323.66	$1.16	5.74	$6.64
OFLOXACIN SOL 0.3%	1,202	7,301	11,084	1,079	$22,432.78	$3.07	6.07	$18.66
TOBRAMYCIN SOL 0.3% OP	2,551	13,231	23,306	2,376	$18,058.73	$1.36	5.19	$7.08
POLYMYXIN B/ SOL TRIMETHP	2,270	22,812	27,888	2,130	$14,049.32	$0.62	10.05	$6.19
QUIXIN SOL 0.5%	243	1,235	2,487	211	$13,173.13	$10.67	5.08	$54.21
TRIMETHOPRIM SOL POLYMYXN	1,571	15,712	16,342	1,490	$9,919.42	$0.63	10.00	$6.31
TRIFLURIDINE SOL 1% OP	78	578	995	59	$7,008.64	$12.13	7.41	$89.85
SULFACET SOD SOL 10% OP	725	10,800	8,826	699	$4,576.49	$0.42	14.90	$6.31
GENTAK SOL 0.3% OP	340	1,870	3,149	324	$2,213.08	$1.18	5.50	$6.51
NATACYN SUS 5% OP	5	75	50	2	$797.05	$10.63	15.00	$159.41
AK-TOB SOL 0.3% OP	90	475	936	89	$648.47	$1.37	5.28	$7.21
VIROPTIC SOL 1% OP	5	38	85	5	$517.80	$13.63	7.60	$103.56
BLEPH-10 SOL 10% OP	68	365	578	65	$333.11	$0.91	5.37	$4.90
OCUTRICIN SOL OP	1	10	7	1	$24.40	$2.44	10.00	$24.40
CHIBROXIN SOL 0.3% OP	1	5	7	1	$23.98	$4.80	5.00	$23.98
TOTALS	**30,303**	**213,832**	**316,132**	**31,993***	**$791,895.16**	**$3.70**	**7.06**	**$26.13**

*Total number of unduplicated members utilizing an anti-infective from both dosage forms.

Utilization of Ophthalmic Anti-infectives: Ointment Dosage Forms CY 2006

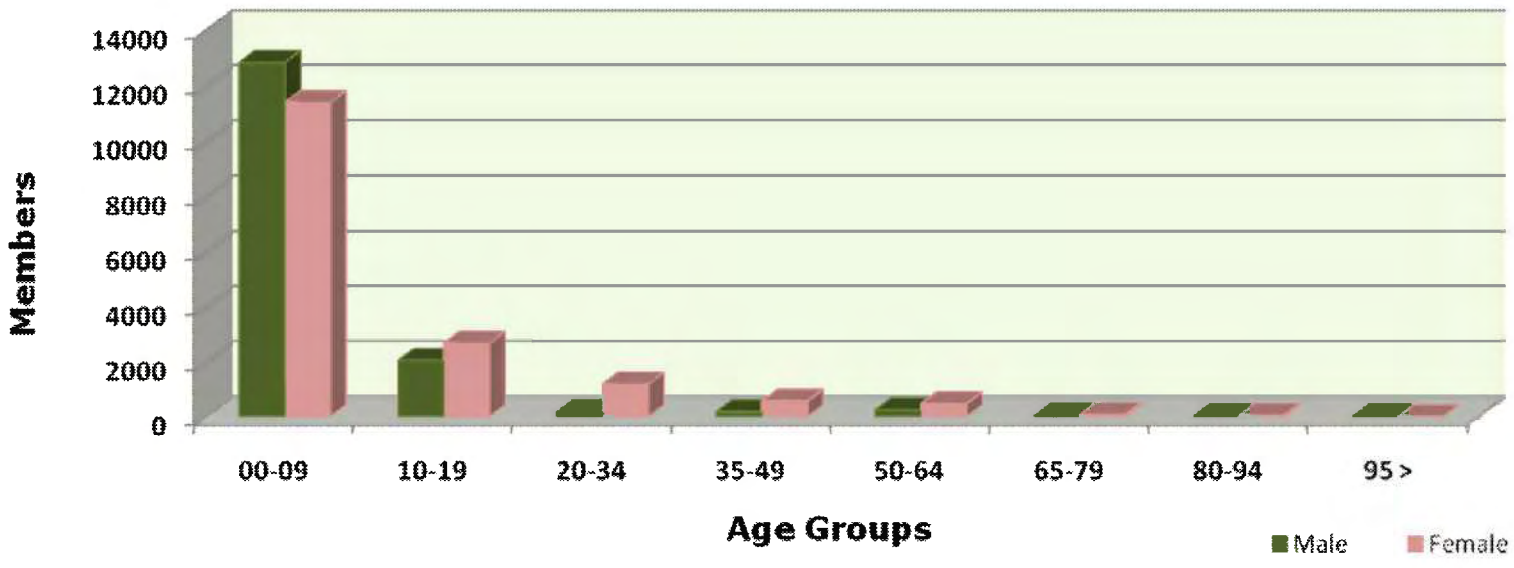
Medication	Claims	Units	Days	Members	Cost	Cost/ Unit	Units/ Claim	Cost/ Claim
ERYTHROMYCIN OIN OP	5,518	20,541	42,525	5,063	$37,992.32	$1.85	$3.72	$6.89
TOBREX OIN 0.3% OP	204	722	1,614	184	$11,901.81	$16.48	$3.54	$58.34
CILOXAN OIN 0.3% OP	185	653	1,471	147	$11,553.65	$17.69	$3.53	$62.45
BACIT/POLYMY OIN OP	513	1,892	4,342	455	$10,263.96	$5.42	$3.69	$20.01
GENTAK OIN 0.3% OP	481	1,718	3,985	451	$8,712.12	$5.07	$3.57	$18.11
SULFACET SOD OIN 10% OP	288	1,028	2,398	266	$3,112.06	$3.03	$3.57	$10.81
GENTAMICIN OIN 0.3% OP	150	548	1,123	138	$2,760.59	$5.04	$3.65	$18.40
NEO/BAC/POLY OIN OP	164	578	1,253	154	$2,632.84	$4.56	$3.52	$16.05
BAC/NEO/POLY OIN OP	137	490	948	127	$1,721.89	$3.51	$3.58	$12.57
BACITRACIN OIN OP	255	929	2,206	206	$1,664.44	$1.79	$3.64	$6.53
AK-POLY-BAC OIN OP	49	172	392	48	$1,016.67	$5.91	$3.51	$20.75
TOTALS	7,944	29,271	62,257	31,993*	$93,332.35	$3.19	$3.68	$11.75

*Total number of unduplicated members utilizing an anti-infective from both dosage forms.

Trends in Utilization of Ophthalmic Anti-infective Agents

Calendar Year	Members	Claims	Cost	Cost/Claim	Per-Diem	Units	Days
2005	35,641	44,872	$961,355.21	$21.42	$2.16	292,145	444,927
2006	31,993	38,247	$885,227.51	$23.15	$2.34	243,100	378,389
Percent Change	-10.20%	-14.80%	-7.90%	8.10%	8.30%	-16.80%	-15.00%

Demographics of Members Utilizing Ophthalmic Antibiotics for CY 2006



Demographic Details

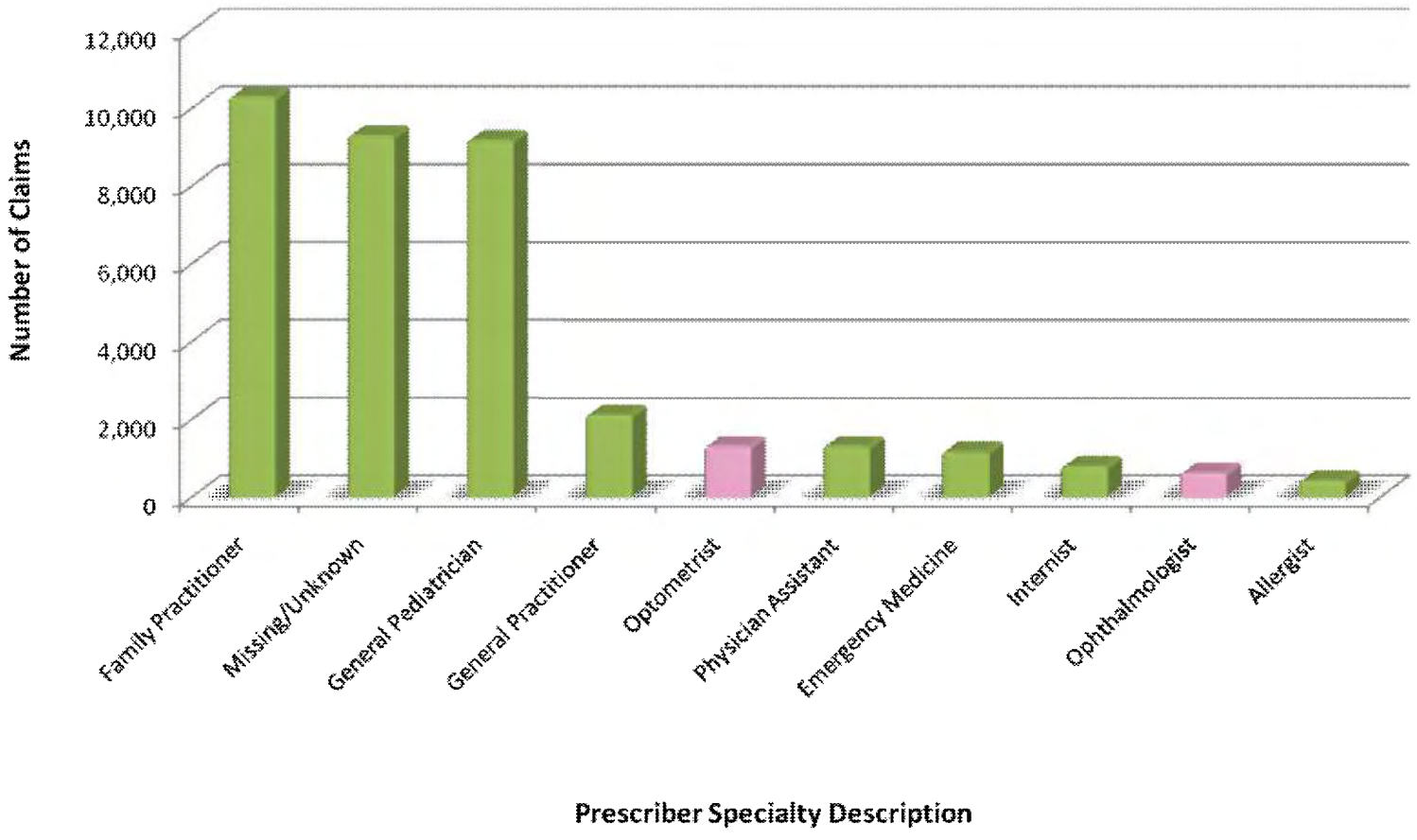
Age Groups	Male	Female
00-09	12,843	11,393
10-19	2,043	2,673
20-34	172	1,197
[illegible]	[illegible]	[illegible]
50-64	246	468
65-79	30	84
80-94	11	53
>95	3	7

Claims per Member for CY 2006

Claims Count	Number of Members
> 10 Claims	14
6-10 Claims	33
3-5 Claims	926
1-2 Claims	31,020

Of the 31,993 members,
47 members had 6 or more claims for an ophthalmic anti-infective product.

Top 10 Prescriber Specialty of Ophthalmic Antibiotic Claims: CY 2006



Utilization of Ophthalmic Antibiotic-Steroid Combination Products: CY 2006

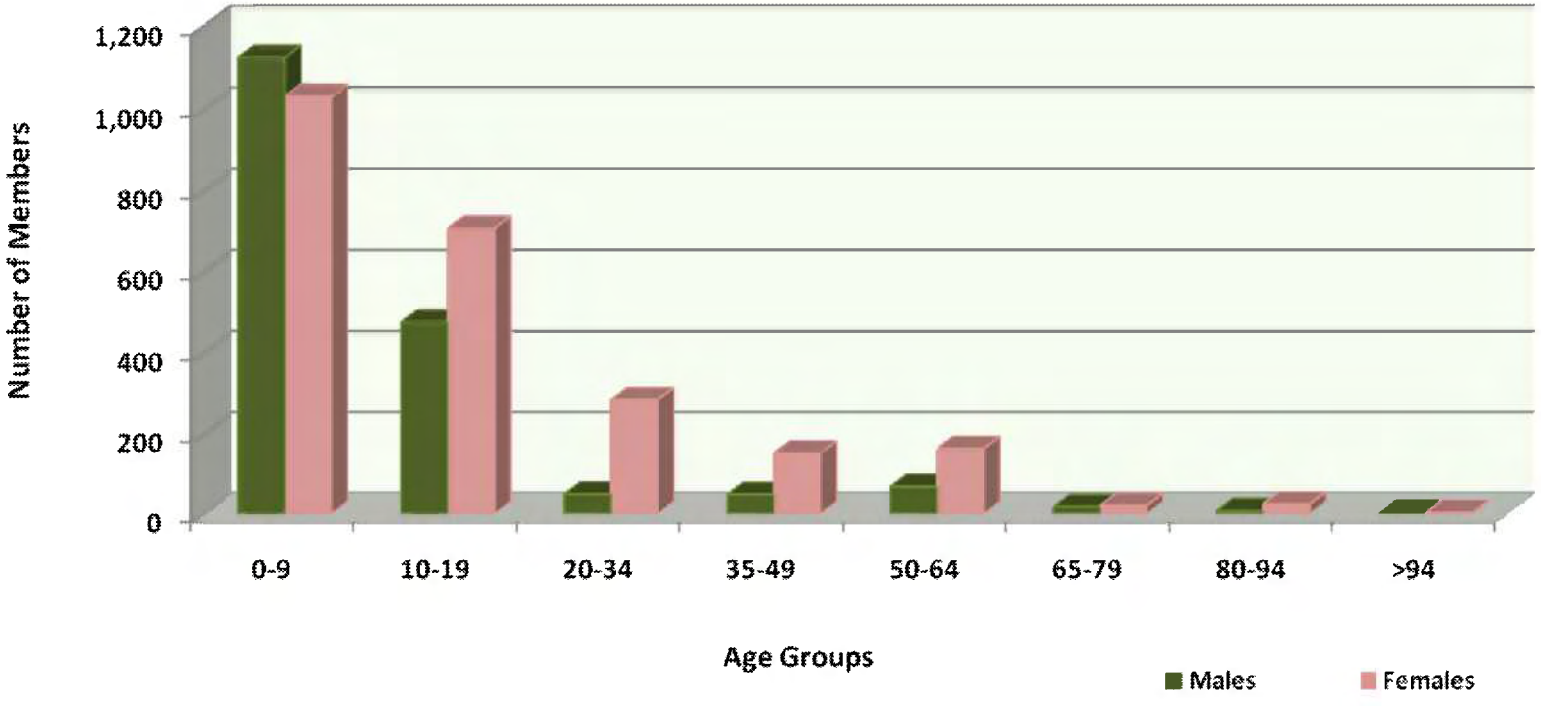
Medication	Claims	Units	Days	Members	Cost	Cost/ Unit	Units/ Claim	Cost/ Claim
TOBRADEX SUS OP	1,781	9,572	19,096	1,603	$124,121.86	$12.97	5.37	$69.69
NEO/POLY/HC SUS OP	914	7,073	9,638	845	$49,080.66	$6.94	7.74	$53.70
TOBRADEX OIN OP	363	1,289	2,953	313	$26,475.82	$20.54	3.55	$72.94
BLEPHAMIDE SUS OP	172	1,180	1,841	154	$9,947.38	$8.43	6.86	$57.83
ZYLET SUS 0.5-0.3%	93	488	894	83	$6,395.04	$13.10	5.25	$68.76
NEO/POLY/DEX SUS 0.1% OP	855	4,458	9,160	737	$5,414.35	$1.21	5.21	$6.33
BLEPHAMIDE OIN S.O.P.	107	377	983	88	$5,135.97	$13.62	3.52	$48.00
NEO/POLY/DEX OIN 0.1% OP	327	1,196	2,709	287	$2,020.52	$1.69	3.66	$6.18
SULF/PRED NA SOL OP	40	350	481	36	$980.69	$2.80	8.75	$24.52
BAC/POLY/NEO OIN /HC OP1%	102	358	824	90	$755.96	$2.11	3.51	$7.41
PRED-G SUS OP	14	75	90	14	$424.63	$5.66	5.36	$30.33
NEO/POLY/BAC OIN /HC OP1%	51	195	450	48	$388.95	$1.99	3.82	$7.63
POLY-PRED SUS OP	6	45	70	5	$224.06	$4.98	7.50	$37.34
FML-S SUS LIQUIFLM	3	20	32	3	$84.84	$4.24	6.67	$28.28
PRED-G S.O.P OIN OP	3	11	33	2	$83.78	$7.62	3.67	$27.93
TOTALS	4,831	26,687	49,254	4,165*	$231,534.51	$8.68	5.52	$47.93

*Total number of unduplicated members utilizing ophthalmic antibiotic-steroid combination products.

Trends in Utilization of Ophthalmic Antibiotic-Steroid Combination Products

Calendar Year	Member	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2005	6,012	7,691	$337,511.62	$43.88	$4.34	41,702	77,786
2006	4,165	4,831	$231,534.51	$47.93	$4.70	26,687	49,254
Percent Change	-30.70%	-37.20%	-31.40%	9.20%	8.30%	-36.00%	-36.70%

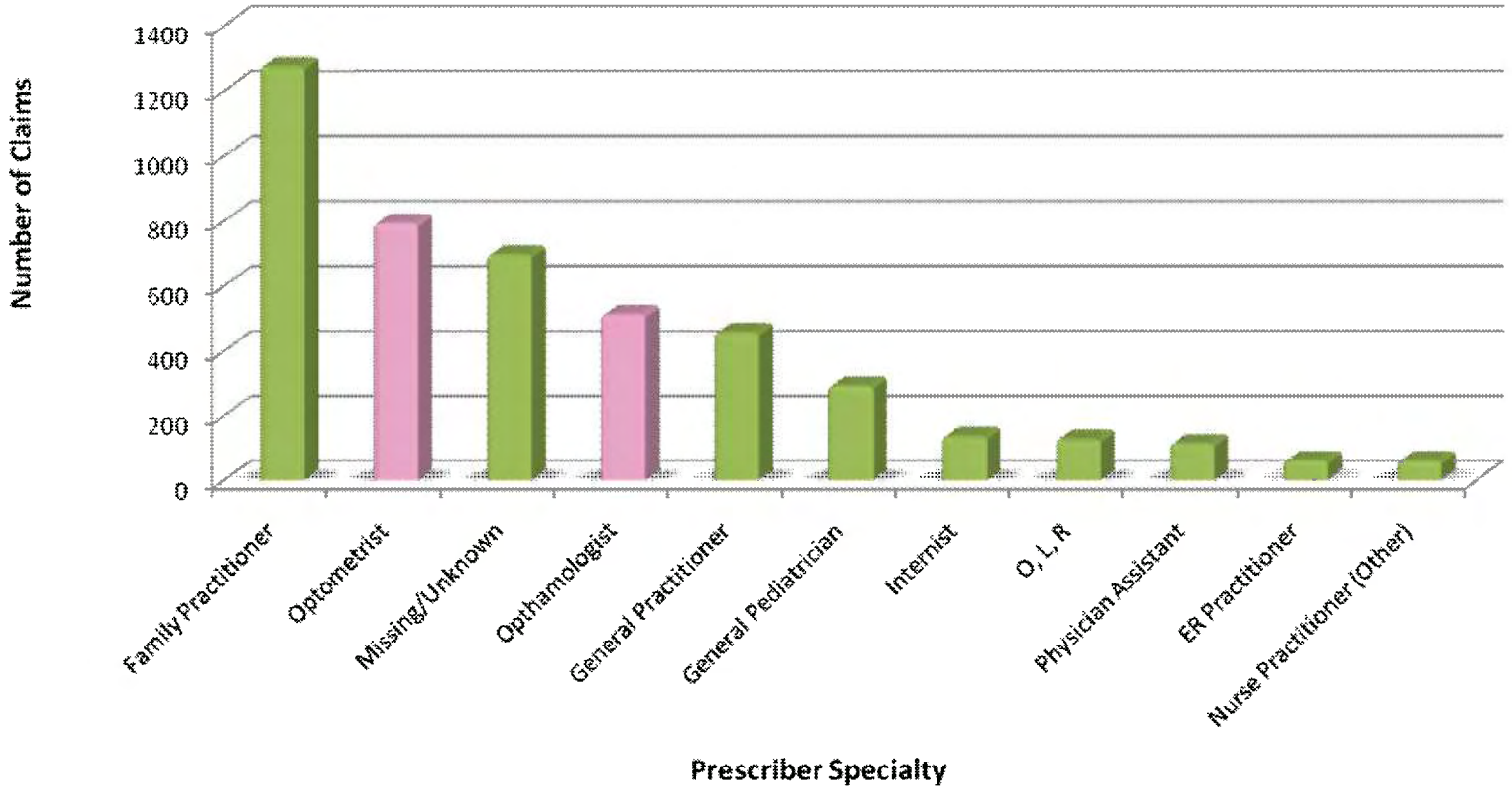
Demographics of Members Utilization
Ophthalmic Antibiotic-Steroid Combination Products: CY 2006



Demographic Details

Age Groups	0-9	10-19	20-34	35-49	50-64	65-79	80-94	>94
Males	1,124	474	48	47	67	17	7	0
Females	1,030	705	282	151	162	20	24	3

Top 10 Prescriber Specialty of Ophthalmic Antibiotic-Steroid Combination Products: CY 2006



Recommendations

The College of Pharmacy recommends the addition of the Ophthalmic Anti-infective Classes to the Product Based Prior Authorization program. The following Tier-1 drug lists have 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.

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:

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

Ophthalmic Antibiotic–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

Approval Criteria:

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

Potential Economic Impact

This category was introduced for possible inclusion in the Product Based Prior Authorization program in February 2007. See the February DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Potential Administrative Costs

Based on a potential shift of proposed Tier 2 products to a Tier 1 product of ~90 %, it is estimated that approximately 3,500 petitions would be required. The proposed tier changes would affect approximately 30 % of the total population for this 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 of prior authorization to the *healthcare system* is estimated to be between $24,920 and $48,230 annually. Anticipated actual administrative cost to the program is projected to be less than $20,000.

Potential Program Savings

Potential net pharmacy *ingredient* cost savings to the program based on recommended tiers is estimated to be $271,919.4 annually.

Total Potential Savings

Potential Savings:	$ 271,919		$ 271,919
Potential Administrative Cost:	$ - 48,230		$ - 24,920
Total Potential *Ingredient* Savings	$ 223,689	to	$ 246,999
Percent of Current *Reimbursement*	20.0%	to	22.1%

Product Information

The following is a list of ophthalmic anti-infective products included in this utilization review along with available generics, FDA approved indications and dosing.

Brand Name	Generic Name*	FDA approved Indications
AK-tracin Ointment **3.5g OIntment**	**Bacitracin Ointment**	Bacterial infection of eye: apply thin ribbon of ophthalmic ointment every 3-4 hr for 7-10 days. Superficial bacterial infection of skin: apply TOPICALLY 2-5 times/day No Pediatric dosing available.
A/T/S, Roymicin, Ilotycin Oint. **5 mg/gm (1 tube, 3.5 gm)**	**Erythromycin Ointment 0.5%**	Bacterial infection of eye: 1 cm ribbon applied up to 6 times daily X 7-10 days.
Azasite 1% Solution **2.5mL dropper bottle**	Azithromycin 1% Solution	Bacterial conjunctivitis: days 1-2, 1 drop BID; days 3-5, 1 drop QD
Ciloxan Solution 0.3% **5mL plastic Drop-Tainer® Dispensers**	**Ciprofloxacin Solution 0.3%**	Conjunctivitis: Adults and Children (above the age of 1 year) Instill one or two drops into the conjunctival sac(s) every two hours while awake for two days and then two drops every four hours while awake for 5 days. Corneal Ulcer: Adults and Children (above the age of 12 years) Instill two drops into the affected eye every 15 min for the first 6 hours and then two drops into the affected eye every 30 minutes for the remainder of the first day. On the second day, instill two drops in the affected eye hourly. On the 3-14th day, place two drops in the affected eye q4 hours.
Ciloxan Ointment 0.3% **3.5g metal ophthalmic tubes**	Ciprofloxacin Ointment 0.3%	Conjunctivitis: Adults and Children (above the age of 1 year) Apply a 1/2" ribbon TID on the first two days and then apply a 1/2" ribbon BID for the next 5 days. Corneal ulcer: Adults and Children (above the age of 12 years) Apply a 1/2" ribbon every 1-2 hours around the clock on the first two days, then apply a 1/2" ribbon q4 hours for up to 12 days.
Quixin 0.5 %, Iquix 1.5% Solution **5mL dropper bottle**	Levofloxacin Solution 0.5%	Bacterial conjunctivitis: day 1-2, 1-2 gtt q 2 hr while awake (MAX 8 times/day); day 3-7, 1-2 gtt q 4 hrs while awake (MAX 4 times/day) Corneal ulcer: day 1-3, 1-2 gtt q 30 min to 2 hr while awake and 4 hr and 6 hr after retiring; day 4 to treatment end, 1-2 gtt q 1-4 hrs while awake. Pediatric dosing available.

Brand Name Medication	Generic Name	FDA approved Indications
Vigamox Solution 0.5 % **3mL dropper bottle**	Moxifloxacin Solution 0.5%	Bacterial conjunctivitis: 1 drop to affected eye(s) TID X 7 days. Pediatric dosing available.
Zymar Solution 0.3 % **5mL dropper bottle**	Gatifloxacin Solution 0.3 %	Bacterial conjunctivitis: 1 gtt OS/OD QID Start: 1 gtt OS/OD q2h x2 days, up to 8x/day x 7 days total. Pediatric dosing available.
Chibroxin Solution 0.3 % **5mL dropper bottle**	Norfloxacin Solution 0.3%	Bacterial conjunctivitis: 1-2 gtt IAE QID for up to 7 days. No Pediatric dosing available.
Ocuflox Solution 0.3 % **5mL, 10mL dropper bottle**	**Ofloxacin Solution 0.3%**	Bacterial conjunctivitis: 1-2 gtt OS/OD q2-4h x2 days, then 1-2 gtt qid x 5d Corneal ulcer 1-2 gtt OS/OD q30min x2 days, then 1-2 gtt q1h on days 3-7 and 1-2 gtt QID on days 7-9. Pediatric dosing available.
Gentak, Garamycin Solution & Ointment 0.3% **5mL, 15mL Sol, 3.5g Ointment**	**Gentamicin Solution & Ointment 0.3%**	Gram – such as Pseudomonas: **ointment**, apply a small amount twice to three times a day; **solution**, instill 1-2 drops every 4 hr, up to 2 drops every hour for severe infections. Pediatric dosing available.
AK Tob, Tobrex Solution & Ointment 0.3% **5mL Sol, 3.5g Oint**	**Tobramycin Solution** & Ointment 0.3%	Gram – such as Pseudomonas: 1-2 gtts OS/OD q4-6h, for severe infections, 2 gtts q1h or apply ointment tid/qid. Pediatric dosing available.
Bleph-10 Solution 10, 15, & 30% Ointment 10% **5mL, 15mL Sol, 3.5g Ointment**	**Sulfacetamide Na Sol & Oint**	Bacterial infection of eye: 1-2 gtt OS/OD q2-3h x7-10 days, 0.5 inch ribbon oint OS/OD q3-4h and qhs x7-10 days; may use combination of ointment and solution Corneal ulcer: 2 gtt OS/OD q2h. Pediatric dosing available.
Viroptic Solution 1 % (antiviral) **7.5mL dropper bottle**	**Trifluridine Solution 1%**	HSV keratoconjunctivitis: 1 gtt OS/OD q2h, continue until re-epithelialized, then 1 gtt q4h x7 days. Pediatric dosing available>6 yo
Vira-A Ointment 3 % (antiviral) (discontinued)	Vidarabine Ointment 3%	Keratoconjunctivitis, acute: ½ in. into conjunctival sac(s) of affected eye(s) q 3 hr (5 times daily); treat for an additional 7 days at a reduced dose (such as twice daily) after re-epithelialization.
Natacyn Suspension 5 % **15mL glass dropper bottle**	Natamycin Suspension 5%	Blepharitis: 1 gtt OS/OD 4-6x/day, continue for 14-21 days or until resolution Fungal conjunctivitis: 1 gtt OS/OD 4-6x/day, for 14-21 days or until resolution Mycotic keratitis, 1 gtt OS/OD 6-8x/day, Start: 1 gtt q1-2h x3-4 days, then incr., Info, continue x14-21 days or until resolution. No Pediatric dosing available.
AK-Poly-Bac Ointment	**Bacitracin/PolymyxinB**	Superficial infections caused by susceptible organisms
Polytrim Solution 0.1% **10mL dropper bottle**	**PolymyxinB/Trimethoprim**	Superficial bacterial infections: 1 gtt OS/OD q3h x7-10 days, max 6 doses/day. Pediatric dosing available.
Neosporin Ointment, Ocutricin, Ointment 3.5g Ointment	**Neomycin/polymyxinB/ bacitracin**	Superficial bacterial infections: apply OS/OD q3-4h x7-10 days. Pediatric dosing available.
AK-Spore Solution **2mL, 10mL dropper bottle**	**Neomycin/ polymyxinB/gramicidin**	Superficial bacterial infections: 1-2 gtt OS/OD q4h x7-10 days, 2 gtt q1h for severe infections. No Pediatric dosing available.

Generic available if bolded in red.

Brand Name	Generic Name*	Use
Pred-G 3.5g Ointment **Pred-G** 2mL, 5mL, 10mL Suspension	Gentamicin 0.3% - Prednisolone 0.6% Gentamicin 0.3% - Prednisolone 1%	Apply in the affected eye(s) q4 h.
Zylet 2.5mL, 5mL, 10mL Suspension	Tobramycin 0.3% - Loteprednol 0.5%	1 to 2 gtt into the conjunctival sac of the affected eye(s) every 4 to 6 h.
FML-S 5mL, 10mL Suspension and Ointment	Na Sulfacetamide 10% - Flourometholone 0.1%	Instill 1 drop into the conjunctival sac 2 to 4 times daily Apply one-half inch ribbon into the conjunctival sac every 4 hrs, may use TID for maintenance
Blephamide 5mL, 10mL Suspension **Blephamide S.O.P.** 3.5g Ointment	**Na Sulfacetamide 10% & Prednisolone 0.25% Sol** Na Sulfacetamide 10% & Prednisolone 0.25% Oint	2 gtt OS/OD q4h while awake Alt: 0.5 inch ribbon oint OS/OD to conjunctival sac tid-qid and qhs
Tobradex 2.5mL, 5mL, 10mL Suspension, 3.5g Ointment	Tobramycin 0.3% - Dexamethasone 0.1%	1-2 gtt OS/OD q4-6h Apply 0.5 inch oint to conjunctival sac tid-qid
Poly-Pred 5mL, 10mL Suspension	Neomycin - Polymyxin - Prednisone 0.5%	apply OS/OD q3-4h
Cortisporin 3.5gm, 15gm Ointment	**Neomycin-Polymyxin-Bacitracin-Hydrocortisone**	Apply ointment in affected eye(s) every 3 to 4 h depending on condition severity
Cortisporin 7.5mL Suspension	**Neomycin – Polymyxin – Hydrocortisone**	1-2 gtt OS/OD q3-4h
Poly-Dex, Maxitrol 3.5gm Ointment	**Neomycin – Polymyxin – Dexamethasone**	1-2 gtt OS/OD q4-6h
Neo-Decadron 5mL Suspension	**Neomycin 0.35% - Dexamethasone 0.1%**	apply OS/OD q3-4h

Generic available if bolded in red.

Antibacterial Coverage of Select Ophthalmic Agents

	Ciprofloxacin[i] (Ciloxan®)	Oflaxacin[ii] (Ocuflox®)	Levofloxacin[iii] (Quixin®)	Moxifloxacin[iv] (Vigamox®)	Gatifloxacin[v] (Zymar®)	Azithromycin[vi] (Azasite®)
Acinetobacterium lwoffii			√	√*		
Chlamydia trachomatis				√		
Corynebacterium species			√	√*	√*	
CDC coryneform group G						√*
Enterobacter species						
Enterobacter cloacae		√				
Escherichia coli						
Haemophilus influenza	√	√	√	√	√	√
Haemophilus parainfluenzae				√		
Klebsiella species						
Micrococcus luteus				√*		
Mycoplasma pneumonia						
Neisseria gonorrhoeae						
Propionibacterium acnes		√				
Proteus mirabilis		√				
Pseudomonas aeruginosa	√	√				
Serratia marcescens	√	√*	√			
Staphylococcus aureus	√	√	√	√	√	√
Staphylococcus epidermidis	√	√	√	√	√	
Staphylococcus haemolyticus				√		
Staphylococcus hominis				√		
Staphylococcus warneri				√		
Streptococcus mitis					√	√
Streptococcus pneumonia	√	√	√	√	√	√
Streptococcus pyogenes						
Streptococcus (Group C/F)			√			
Streptococcus (Group G)			√			
Treponema pallidum						
Viridans group streptococci	√		√	√		

*Efficacy for this organism was studied in less than 10 infections.

[i] Alcon Laboratories. Ciloxan Prescribing Information. Acessed at: http://www.fda.gov/cder/foi/label/2006/019992s020lbl.pdf. September 2004.
[ii] Allergan Pharmaceuticals. Ocuflox Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/nda/99/019921_S008_Ocuflox_Approval_Package.pd. August 1999.
[iii] Daiichi Pharmaceuticals. Quixin Prescribing Information. Accessed at http://www.fda.gov/cder/foi/label/2002/21199s2lbl.pdf. August 2000.
[iv] Alcon Laboratories. Vigamox Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2004/21598slr002_vigamox_lbl.pdf. 2004.
[v] Allergan, Inc. Zymar Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2005/021493s006,007lbl.pdf. August 2004.
[vi] Inspire Pharmaceuticals. Azasite Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2007/050810lbl.pdf April 2007.

Appendix H

30-Day Notice to Prior Authorize Ophthalmic Anti-Glaucoma Products

Oklahoma Health Care Authority
June 2007

Introduction[1,2,3]

Glaucoma is a group of ocular disorders associated with optic neuropathy that affects approximately 2% of the U.S. population. Abnormal anatomical features and functionality of the eye can cause optic nerve damage leading to an irreversible loss of retinal ganglion cell axons. This can result in visual field loss and blindness if left untreated. Initially, peripheral vision is reduced followed by a gradual loss of central vision. Visual impairment can affect both eyes but the majority of cases occur unilaterally. Glaucoma is most commonly associated with chronic progression of vision loss but severe acute episodes can occur which require immediate treatment. Glaucoma is often referred to as the "the silent thief of sight" because of the lack of early warning signs and symptoms and half of the people affected are not aware that they have it.[1] Presence of elevated ***intraocular pressure*** (IOP) is an identifiable and modifiable risk factor but it is not an absolute indicator of glaucoma. Elevated intraocular pressure above 21 mmHg without signs and symptoms of glaucoma is referred to as ***ocular hypertension*** (OHT) .[1,4] Glaucoma can affect people of all ages and it is preventable with early diagnosis and treatment to preserve visual function and maintain quality of life.

Types of Glaucoma

Primary vs Secondary (with or without preexisting disease)
Open-angle (asymptomatic and chronic onset)
Angle-Closure (symptomatic and acute onset)
Inflammatory
Pseudoexfoliative
Pigmentary
Neovascular
Traumatic
Intraocular Surgery (cataract or retinal)
Infantile
Juvenile
Congenital

Therapy and Management[1,3,4,5]

Differential diagnosis and severity of disease must be performed to assess risk and determine appropriate therapy and management plan. Intraocular pressure (IOP) associated with optical nerve damage and visual field loss in a patient determines the 'target treatment pressure' which guides disease management. Target intraocular pressure may be set lower according to severity of disease.

Goals of Treatment:

- Stabilize optic nerve and retinal nerve-fiber-layers
- **Control IOP** (20% reduction of the pretreatment) [2]
- Stabilize ocular aqueous flow
- Stabilize visual fields
- Alleviate sign symptoms (i.e. blurred vision, halos around light, - aching eye, brow ache, eye redness, nausea)

Treatments Available:[2]

- **Pharmacologic (monotherapy or combination)**
- Laser (temporary: 30 to 50% require follow-up surgery)
- Surgical

Recommended Management and Follow-up

Target IOP met	Progression	Duration of Control	Recommended Follow-up
Yes	No	≤ 6 months	6 months
Yes	No	>6 months	12 months
Yes	Yes	n/a	4 months
No	n/a	n/a	4 months

Adapted from AAO Guidelines[2]

Adjustments to therapy in the following cases:

- Target IOP not reached (may use another medication in the same drug class)
- Progression despite IOP control
- Patient tolerability and compliance issues
- Consider down titration with long-term control

Market Update:

- March 2007- Tentative approval for generic Xalatan (latanoprost)
- February 2007 - Prostaglandins off-label usage as eye lash enhancer

Conclusion:

As one of the leading causes of blindness, glaucoma can be prevented or delayed with early detection and treatment. People with glaucoma should have annual dilated eye exams, especially those with one or more risk factors as recommended by the National Eye Institute. With adequate treatment and compliance to therapy, lowering intraocular pressure and reestablishing ocular fluid flow has been shown to reduce incidence and progression of disease. Treatment should be selected on an individual basis with regard to patient age, risk factors, concomitant diseases and severity of disease. **Sooner*Care*** members and healthcare providers will be provided glaucoma awareness outreach materials to ensure a high standard of vision care is provided to those diagnosed and treated for glaucoma.

Proposed Criteria

1. FDA approved diagnosis.
2. Member must attempt at least one Tier-1 trial of a minimum of 4 weeks duration within the last 90 days. Tier-1 trial may be from any pharmacologic class.
3. Approval may be granted if there is a documented adverse effect, drug interaction, or contraindication to Tier-1 products.
4. Approval may be granted if there is a unique FDA approved indication not covered by Tier-1 products.
5. Member must have had a comprehensive dilated eye exam within the last 365 day period as recommended by the National Institute of Health.
6. Approval duration will be for 1 year.

Tier 1	Tier 2
Beta-Blockers	
Betagan 0.25%,0.5% (Levobunolol) Optipranolol 0.3% (Metipranolol) Timoptic, Betimol, Istalol, Timoptic Ocudose, Timoptic XE 0.25,0.5% (Timolol Maleate) Cartrol, Ocupress 1% (Carteolol) Betoptic-S 0.5% (betaxolol)	Betoptic-S (betaxolol) Cosopt (Dorzolamide and Timolol)* Timoptic 0.5% Dropperette
Prostaglandin Analogs	
Xalatan (Latanoprost)**	Lumigan (Bimatoprost) Travatan, Travatan Z (Travoprost)
Adrenergic Agonists#	
Propine (Dipivefrin)	
Alpha-2 Adrenergic Agonists	
Brimonidine 0.2%	Alphagan P 0.1, 0.15% (Brimonidine) Iopidine 1% Apraclonidine
Carbonic Anhydrase Inhibitor@	
	Azopt (Brinzolamide) Trusopt (Dorzolamide) Cosopt (Dorzolamide and Timolol)*
Cholinergic Agonists[1]/Cholinesterase Inhibitors[2]	
Isopto Carpine, Pilopine HS 0.5,1,2,4,6 %(Pilocarpine)	Isopto, Miostat 1.5, 3% (Carbachol)[1] Phospholine Iodide (Echothiophate Iodide)[2]

@ Oral formulations of Carbonic Anhydrase Inhibitors also available

*Combination product

**Tentative generic approval by FDA 03/09/2007; supplemental rebate agreement participation

Glaucoma Medications

	Mechanism	Dosing	IOP Lowering[5]	Guidelines[2,7,1]
Beta-Blockers	Decrease aqueous production	Daily or twice daily	20-25% 10-20% Betaxolol	AOA: *Initial 1st Line* AAO: 1st Line AJHP: 1st Line
Prostaglandins	Increase aqueous flow	Daily	25-35%	AOA: *1st Line/Alternative* AAO: 1st Line AJHP: 1st Line
Adrenergic Agonists	Decrease aqueous production; Increase aqueous flow	**Nonselective:** daily to twice daily **Selective:** Three times daily	20-25%	AOA: Alternative/Adjunctive AAO: Alternative/Adjunctive AJHP: 2nd Line
Carbonic Anhydrase Inhibitors	Decrease aqueous production	**Oral:** daily, twice daily, three times daily, or four times daily. **Topical:** three times daily	10-20%	AOA: Alternative/Adjunctive AAO: Alternative/Adjunctive AJHP: 2nd Line
Cholinergic Agonists	Increase aqueous flow	Twice daily to four times daily **Pilopine HS gel:** daily **Ocusert Pilo:** weekly	20-25%	AOA: Alternative/Adjunctive AAO: Alternative/Adjunctive AJHP: 3rd LIne
Anticholinesterases	Increase aqueous flow	Daily to twice daily	20-25%	AOA: Alternative/Adjunctive AAO: Alternative/Adjunctive AJHP: 3rd Line
Combination	**Cosopt:** Decrease aqueous production **E-Pilo-1,2,3,4,6:** Improve aqueous outflow	Twice daily Four times daily	10-25% 20-25%	AOA: Alternative/Adjunctive AAO: Alternative/Adjunctive AJHP: Alternative

Adverse Effects and Safety

Pharmacologic Class	Side Effects[10]	Precautions[10]	Other[10]
Beta-Blockers	**>10 %** Stinging, burning eyes(i.e. Betaxolol) **1-10%** Bradycardia, arrhythmia, hypotension, dizziness, headache, alopecia, erythema, blepharoconjunctivitis, conjunctivitis, bronchospasm, hallucinations, malaise, depression, blurred vision, browache, infection, corneal staining, conjunctival hyperemia, nausea, diarrhea, edema, sexual ability decreased, insomnia.	Use with caution in asthma, COPD, bradycardia, second or third degree heart block, CHF,renal impairment, diabetes, psychiatric illness.	Betoptic-S is beta-1 selective and has less severe cardio-pulmonary adverse reactions.
Carbonic Anhydrase Inhibitors	**1-10%** Dermatitis, taste disturbances, blurred vision, blepharitis, dry eye, foreign body sensation, eye discharge, pain, rhinitis, photophobia, ocular allergic reaction, superficial punctate keratitis.	Use with caution in hepatic/renal impairment and sulfa allergies.	Avoid excessive use of aspirin products.
Prostagladin Analogs	**>10%** Conjunctival hyperemia, growth of eyelashes, ocular pruritus, blurred vision, burning, stinging, foreign body sensation **1-10%** Headache, Chest pain, rash, myalgia, arthralgia, dry eye, hirsutism, liver function tests abnormal, weakness, eye redness, burning, cataract, blepharitis, pain, pigmentation of periocular skin, visual disturbance, photophobia, tearing, allergic conjunctivitis, iris pigmentation, upper respiratory infection, depression, anxiety, hyper/hypotension.	May cause permanent changes in eye color. Risk of bacterial keratitis. Use with caution in patients with macular edema, intraocular inflammation, aphakic patients, renal impairment.	Latanoprost has lower hyperemia and eyelash changes compared to timolol, bimatoprost, travoprost. (Gandolfi[11])
Cholinergic Agonists/ Cholinesterase Inhibitors	**>10%** Flushing, chills, dizziness, headache, nausea, urinary frequency, weakness, rhinitis, diaphoresis, edema, hypertension, palpitations, tachycardia, pain, fever, somnolence, rash, pruritis, diarrhea, dyspepsia, vomiting, constipation, myalgia, syncope, flatulence, glossitis, salivation, taste perversion, tremor, tinnitus, cough, epistaxis, dysphagia, sinusitis, voice alteration, allergic reaction, vaginitis, urinary incontinence, stomatitis, diaphoresis, asthma, burning, abdominal cramps, diarrhea, corneal clouding, constrict pupil	Use with caution in cardiovascular disease. Phospholine Iodide: Use with caution with anesthesia, organophosphates/carbamate pesticides exposure, history of uveitis, retinal detachment, GI disturbances, epilepsy, parkinsonism, ophthalmic surgery.	Miostat, Isopto Carbachol, Phospholine, adverse effect frequency not defined.
Adrenergic Agonists	**1-10%** Headache, burning, stinging, photophobia, mydriasis, blurred vision, ocular pain, blepharoconjunctivitis, cystoids macular edema.	Use with caution in hypertension.	
Alpha-2 Adrenergic Agonists	**10%** Somnolence, allergic conjunctivitis, conjunctival hyperemia, pruritis. **1-10%** Hyper/hypotension, rash, dizziness, fatigue, headache,hypercholesterolemia, dry mouth, dyspepsia, burning, visual disturbance, decreased alertness, insomnia, ocular allergic reaction, conjunctival folliculosis, cataract, blepharoconjunctivitis, infection, cough, watery eyes, dry eye, foreign body sensation.	Use with caution in cardiovascular disease, depression, Raynaud's phenomenon, thromboangiitis obliterans, hepatic/renal impairment.	Iopidine: in some IOP-lowering efficacy decreases over time longer than 1 month.

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Appendix I

30 Day Notice to Prior Authorize Tovalt™ ODT (zolpidem tartrate)

Oklahoma Health Care Authority
June 2007

Manufacturer	Bioavail Pharmaceuticals, Inc
Classification	FDA classification: Non-benzodiazepine hypnotic Status: prescription only

Summary

Tovalt™ ODT is an orally disintegrating tablet containing 5mg or 10mg of zolpidem tartrate. Tovalt™ ODT is bioequivalent to Ambien® tablets. It is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation.

Revised Tier Table

Tier 1	Tier 2	Tier 3
estazolam	Lunesta®	Tovalt™ ODT
temazepam	Sonata®	
flurazepam	Rozerem®	
triazolam	Restoril® 7.5 and 22.5 mg	
zolpidem	Ambien CR®	

Recommendations

The College of Pharmacy recommends placing Tovalt® into the Hypnotic PBPA category as a Tier 3. Approval would require a diagnosis of insomnia and an additional diagnosis indicating that the member has a condition that prevents him/her from swallowing tablets. A quantity limit of 30 units for a 30 day supply would also be applied.

REFERENCE

Tovalt™ Product Information. Bioavail Pharmaceuticals, Inc. 2007.

Appendix J

FDA News

FOR IMMEDIATE RELEASE
P07-77
May 2, 2007

Media Inquiries:
Sandy Walsh, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications

The U.S. Food and Drug Administration (FDA) today proposed that makers of all antidepressant medications update the existing black box warning on their products' labeling to include warnings about increased risks of suicidal thinking and behavior, known as suicidality, in young adults ages 18 to 24 during initial treatment (generally the first one to two months).

The proposed labeling changes also include language stating that scientific data did not show this increased risk in adults older than 24, and that adults ages 65 and older taking antidepressants have a decreased risk of suicidality. The proposed warning statements emphasize that depression and certain other serious psychiatric disorders are themselves the most important causes of suicide.

"Today's actions represent FDA's commitment to a high level of post-marketing evaluation of drug products," said Steven Galson, M.D., MPH, director of FDA's Center for Drug Evaluation and Research. "Depression and other psychiatric disorders can have significant consequences if not appropriately treated. Antidepressant medications benefit many patients, but it is important that doctors and patients are aware of the risks."

People currently prescribed antidepressant medications should not stop taking them. Those who have concerns should notify their health care providers.

The proposed labeling changes apply to the entire category of antidepressants. Results of individual placebo-controlled scientific studies are reasonably consistent in showing a slight increase in suicidality for patients taking antidepressants in early treatment for most of the medications. Available data are not sufficient to exclude any single medication from the increased risk of suicidality

The proposed labeling update follows similar labeling changes made in 2005 that warned of a suicidality risk in children and adolescents who use antidepressants. At that time, FDA asked manufacturers to add a black box warning to the labeling of all antidepressants to describe this risk and to emphasize the need for appropriate monitoring and close observation, particularly for younger patients taking these medications. In addition, FDA directed manufacturers to develop Medication Guides, FDA-approved user-friendly information for patients, families and caregivers, that could help improve monitoring. Medication Guides are intended to be distributed at the pharmacy with each prescription or refill of a medication

Also in 2005, FDA began a comprehensive review of 295 individual antidepressant trials that included over 77,000 adult patients with major depressive disorder (MDD) and other

psychiatric disorders, to examine the risk of suicidality in adults who are prescribed antidepressants.

In December 2006, FDA's Psychopharmacologic Drugs Advisory Committee agreed that labeling changes were needed to inform health care professionals about the increased risk of suicidality in younger adults using antidepressants. Additionally, the committee noted product labeling needed to reflect the apparent beneficial effect of antidepressants in older adults and to remind health care professionals that the disorders themselves are the most important cause of suicidality.

FDA has been developing language to revise product labeling and update the Patient Medication Guides for these products. Manufacturers of antidepressants will now have 30 days to submit their revised product labels and revised Medication Guides to FDA for review

Products involved in today's action include:

Anafranil (clomipramine)
Asendin (amoxapine)
Aventyl (nortriptyline)
Celexa (citalopram hydrobromide)
Cymbalta (duloxetine)
Desyrel (trazodone HCl)
Elavil (amitriptyline)
Effexor (venlafaxine HCl)
Emsam (selegiline)
Etrafon (perphenazine/amitriptyline)
fluvoxamine maleate
Lexapro (escitalopram hydrobromide)
Limbitrol (chlordiazepoxide/amitriptyline)
Ludiomil (maprotiline)
Marplan (isocarboxazid)
Nardil (phenelzine sulfate)
nefazodone HCl
Norpramin (desipramine HCl)
Pamelor (nortriptyline)
Parnate (tranylcypromine sulfate)
Paxil (paroxetine HCl)
Pexeva (paroxetine mesylate)
Prozac (fluoxetine HCl)
Remeron (mirtazapine)
Sarafem (fluoxetine HCl)
Seroquel (quetiapine)
Sinequan (doxepin)
Surmontil (trimipramine)
Symbyax (olanzapine/fluoxetine)
Tofranil (imipramine)
Tofranil-PM (imipramine pamoate)
Triavil (perphenazine/amitriptyline)
Vivactil (protriptyline)
Wellbutrin (bupropion HCl)
Zoloft (sertraline HCl)
Zyban (bupropion HCl)

For more information:

Antidepressant use in children, adolescents, and adults, including the draft labeling and draft Medication Guides www.fda.gov/cder/drug/antidepressants/default.htm

FDA's Psychopharmacologic Drugs Advisory Committee, including transcripts from the December 2006 meeting

This press release was revised on May 14, 2007 to incorporate changes throughout the release.

FDA News

FOR IMMEDIATE RELEASE
P07-85
May 10, 2007

Media Inquiries:
301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Announces Results of Investigation Into Illegal Promotion of OxyContin by The Purdue Frederick Company, Inc.

Company Misrepresented Prescription Pain Reliever to Health Care Professionals

The U.S. Food and Drug Administration's (FDA) Office of Criminal Investigations (OCI) announced today that The Purdue Frederick Company, Inc. has agreed to pay more than $600 million to resolve criminal charges and civil liabilities in connection with a long-term illegal scheme to promote, market and sell OxyContin, a powerful prescription pain reliever that the company produces.

An investigation by OCI uncovered an extensive, long-term scheme by The Purdue Frederick Company, Inc. to generate the maximum amount of revenues possible from the sale of OxyContin. To further this goal, Purdue trained its sales representatives to make false representations to health care providers about the difficulty of extracting oxycodone, the active ingredient, from the OxyContin tablet; trained its sales force to represent to health care providers that OxyContin did not cause euphoria and was less addictive than immediate-release opiates; and allowed health care providers to entertain the erroneous belief that OxyContin was less addictive than morphine. In addition, Purdue falsely labeled OxyContin as providing "fewer peaks and valleys than with immediate-release oxycodone," and falsely represented that patients taking lower dosages of the drug can always be discontinued abruptly without suffering withdrawal symptoms or tolerance.

"FDA will not tolerate practices that falsely promote drug products and place consumers at health risk," said Margaret O.K. Glavin, Associate Commissioner for Regulatory Affairs. "We will continue to do all we can to protect the public against drug companies and their representatives who are not truthful and bilk consumers of precious health care dollars."

To resolve the criminal charges, Purdue pled guilty to a felony count of misbranding a drug with intent to defraud and mislead. As part of the plea, Purdue will pay a $600 million settlement. That amount includes a criminal fine, restitution to government agencies, over $276 million in forfeiture, and a related civil settlement under which Purdue will pay $100.6 million to the United States.

In addition, Purdue's current and former executive employees, Michael Friedman, Howard Udell and Dr. Paul Goldenheim, pled guilty to a misdemeanor violation of misbranding OxyContin as being the responsible corporate officers during the long-term illegal promotion of the drug.

This case was prosecuted by the U. S. Attorney's Office for the Western District of Virginia

and investigated by FDA's Office of Criminal Investigations; the Internal Revenue Service's Criminal Investigations Division; the U.S. Department of Health and Human Services' Office of Inspector General; and the State Police Departments of Virginia and West Virginia. This case serves as an excellent example of federal and state law enforcement cooperation.

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Rosiglitazone maleate (marketed as Avandia, Avandamet, and Avandaryl) Information

FDA ALERT [5/21/2007]: FDA is aware of a potential safety issue related to rosiglitazone maleate. Safety data from a pooled analysis of controlled clinical trials have shown a significant increase in the risk of heart attack and heart-related deaths in patients taking Avandia. However, other published and unpublished data from long-term clinical trials of Avandia provide contradictory evidence about the risk of ischemic cardiovascular events in patients taking Avandia. FDA's review of all available data is ongoing. FDA has not confirmed the clinical significance of the reported increased risk of ischemic cardiovascular events in the context of other studies. Myocardial ischemic events are currently described in the WARNINGS section of the rosiglitzsone label. FDA does not know whether the other approved medication in the same pharmacologic class or other oral drugs for treating type 2 diabetes have less, the same, or greater risks. Switching diabetic patients to other therapies also confers its own risks. For those reasons, FDA is providing this emerging information to prescribers so that they and their patients can make individualized treatment decisions. This information reflects FDA's current analysis of available data concerning this drug. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug product and the emerging drug safety issue. Nor does it mean that FDA is advising health care professionals to discontinue prescribing the product. FDA is considering, but has not reached a conclusion about, whether this information warrants any regulatory action. FDA intends to update this sheet when additional information or analyses become available.

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

Healthcare Professional Information

- Information for Healthcare Professionals [PDF] [HTML]
- Prescribing Information (Avandia Label)

Other Information

- FDA News
- Regulatory History of rosiglitazone from Drugs@FDA
- Patient Information Sheet
- Consumer Update: New Safety Information on Diabetes Drug Rosiglitazone

Report Adverse Events to MedWatch

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PDF requires the free Adobe Acrobat Reader

Date created: May 21, 2007, updated May 31, 2007

FDA News

FOR IMMEDIATE RELEASE
P07-92
May 25, 2007

Media Inquiries:
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Consumer Inquiries:
888-INFO-FDA

FDA Takes Action to Stop Marketing of Unapproved Timed-Release Guaifenesin Drug Products

The U.S. Food and Drug Administration (FDA) today announced its intention to take action against companies that market unapproved drug products in timed-release dosage form that contain guaifenesin, a substance commonly used in medicines to relieve cough and cold symptoms by stimulating removal of mucous from the lungs.

Approximately 20 firms make timed-release products containing guaifenesin that have not undergone FDA review and as a result are considered by the agency to be unapproved drugs.

"Today's action is another example of our commitment to ensure all drugs marketed in the United States that require FDA approval have that approval," said Steven K. Galson, M.D., M.P.H., director of the FDA's Center for Drug Evaluation and Research (CDER). "This benefits consumers because drugs that skirt the approval process may be unsafe, may not work, and often have inadequate labeling or are improperly manufactured."

This action does not affect products containing guaifenesin in immediate release form, but rather only affects timed-release forms, often described as extended-release, long-acting or sustained-release. These dosage forms release their active ingredients over an extended period of time, reducing the number of doses needed per day. Many of the products that contain guaifenesin also contain other active ingredients that are intended to relieve nasal congestion, suppress cough, reduce fever or relieve pain.

Timed-release drugs require FDA approval because the FDA must ensure that the product releases its active ingredients safely and effectively, sustaining the intended effect over the entire time in which the product is intended to work.

To date, only Adams Respiratory Therapeutics has obtained FDA approval for timed-release products containing guaifenesin (600 milligrams and 1200 milligrams) under the trade names of Mucinex and Humibid. These include over-the-counter products containing guaifenesin alone (Mucinex and Humibid), with the decongestant pseudoephedrine (Mucinex-D), and with the cough suppressant dextromethorphan (Mucinex-DM).

Companies marketing unapproved products containing guaifenesin in timed-release form are expected to stop manufacturing them within 90 days and must cease shipping them in interstate commerce within 180 days. A small amount of these products is expected to be available after these dates until supplies are exhausted.

After these dates, companies wishing to market products containing guaifenesin in timed-release form that do not have the required FDA approval must obtain approval or face

regulatory action. FDA is committed to working with companies to facilitate the process of ensuring that products are safe and effective, and meet appropriate standards for manufacturing and labeling.

Today's action is part of FDA's broader initiative on marketed unapproved drugs that was launched in June 2006. At that time, the agency published a Compliance Policy Guide describing FDA's risk-based enforcement approach to unapproved drugs. The guidance explains that FDA intends to give priority to enforcement actions involving unapproved drugs with potential safety risks, that lack evidence of effectiveness and that constitute health fraud.

Additional Information about Guaifenesin

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FDA's Unapproved Drugs Web site

RSS Feed for FDA News Releases [what's this?]

Drugs Marketed in the United States That Do Not Have Required FDA Approval

The Federal Food, Drug, and Cosmetic Act generally requires that drugs marketed in the United States be shown to be both safe and effective prior to marketing and widespread use in the general population. Drugs that are marketed without required FDA approval may not meet modern standards for safety, effectiveness, quality, and labeling.

However, for a variety of historical reasons, some drugs, mostly older products, continue to be marketed illegally in the United States without required FDA approval. Many healthcare providers are unaware of the unapproved status of some drugs and have continued to unknowingly prescribe unapproved drugs because the drugs' labels do not disclose that they lack FDA approval. Often these drugs are advertised in reputable medical journals or are included in widely used pharmaceutical references such as the Physicians' Desk Reference (PDR).

While some unapproved drugs may have benefits, there may also be risks. Patients and health professionals should carefully consider the medical condition being treated, the patient's previous response to the drug, and the availability of approved alternatives as part of discussing the benefits and risks of any unapproved treatment.

FDA has issued a guidance entitled "Marketed Unapproved Drugs--Compliance Policy Guide" designed to make sure that all drugs marketed in the U.S., prescription and over-the-counter, have been shown to be safe and effective. This guidance is the next step in an FDA initiative to ensure that all marketed U.S. drugs have required approval. The guidance clearly articulates FDA's expectation that manufacturers of products requiring FDA approval submit applications to FDA to show that their products are safe and effective. The guidance also outlines the agency's enforcement policies aimed at efficiently and rationally bringing all such drugs into the approval process.

Important Documents

- FDA Press Release: FDA Acts to Improve Drug Safety and Quality; Manufacturing of Unapproved Drug Products Containing Carbinoxamine Must Cease (Issued June 8, 2006)
- Remarks by Andrew C. von Eschenbach, M.D, Acting Commissioner of Food and Drugs, Regarding Unapproved Drugs (Issued June 8, 2006, posted July 13, 2006)
- Statement of Steven K. Galson, M.D., M.P.H., Director, Center for Drug Evaluation and Research, Regarding Unapproved Prescription Drugs (issued June 8, 2006, posted June 9, 2006)
- Questions and Answers About Unapproved Drugs and FDA's Enforcement Action Against Carbinoxamine Products
- Guidance Document: Marketed Unapproved Drugs - Compliance Policy Guide (June 8, 2006)
- Federal Register Notice of Availability [HTML] [PDF] (June 9, 2006). FDA announced the availability of a guidance entitled "Marketed Unapproved Drugs-Compliance Policy Guide." The guidance describes how the FDA intends to exercise its enforcement

discretion with regard to drugs marketed in the United States that do not have required FDA approval for marketing.

- Letter to Branded Pharmaceutical Association Regarding Unapproved Drugs Coordinator
- Congressional Report - Feasibility and Cost of a New Monograph System for Marketed Unapproved Drugs (July 2004)

Consumer Information

- Questions and Answers for Consumers About Unapproved Drugs
- Drugs@FDA -- Brand and Generic Drugs: Labels, Approval Histories, and More
- Information About the Products We Regulate
- Division of Drug Information Homepage
- Drug Information Pathfinder-- Provides links to information on specific drugs, drug development, drug application process, drug imports, and other topics

Selected Enforcement Actions on Unapproved Drugs

- Timed-Release Drug Products Containing Guaifenesin
- PharmaFab Inc.
- Trimethobenzamide Hydrochloride Suppositories
- Ergotamine-Containing Drug Products
- Quinine Sulfate Drug Products
- Vita-Erb, Ltd.
- C. R. Canfield Co., Inc.
- Actavis Totowa, LLC
- Syntho Pharmaceuticals, Inc. and Intermax Pharmaceuticals, Inc.
- Sheffield Laboratories, Division of Faria Limited LLC
- Concord Laboratories, Inc.
- Carbinoxamine Drug Products
- Neil Laboratories, Inc.
- Scientific Laboratories, Inc.
- Pharmakon Laboratory, Inc.
- Propharma, Inc.
- Lane Labs-USA, Inc.
- Exocrine Pancreatic Insufficiency Drug Products
- Carolina Pharmaceuticals, Inc.
- Forest Laboratories, Inc.
- Single Ingredient Guaifenesin Drug Products
- Digoxin Products for Oral Use
- Sage Pharmaceuticals, Inc.
- Levothyroxine Sodium Drug Products

January 9, 2007 Marketed Unapproved Drugs Workshop

- Meeting Agenda
- Meeting Presentations
- Transcript

Drug Approval Application Process

- Drug Approval Application Process
- Over-the-counter (OTC) Drug Products
- Chemistry, Manufacturing, and Controls
- Abbreviated New Drug Application (ANDA)
- New Drug Application (NDA)
- Investigational New Drug (IND) Application
- Demonstrating Clinical Drug Safety
- Pediatric Considerations
- User Fees and Waivers
- Small Business

Related Links

- The FDA's Drug Review Process: Ensuring Drugs are Safe and Effective-- FDA Consumer magazine article, July, 2002.
- How to Report Problems With Products Regulated by FDA
- About FDA's New Drug Safety Initiative
- The Critical Path to New Medical Products -- The Critical Path Initiative is FDA's effort to stimulate and facilitate a national effort to modernize the scientific process through which a potential human drug, biological product, or medical device is transformed from a discovery or "proof of concept" into a medical product.

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Date created: June 8, 2006, updated: May 25, 2007
