THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – February 8, 2005**

DATE: February 3, 2005

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

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

Call to Order

Public Comment Forum

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

Update on DUR/MCAU Program - **See Appendix B.**

Update on Supplemental Rebate Program

State Maximum Allowable Cost (SMAC) Report

Action Item – Vote to Prior Authorize LUNESTA™ – **See Appendix C.**

Action Item – Vote to Prior Authroize Bladder Control Drugs - **See Appendix D.**

Annual Review of Growth Hormones – **See Appendix E.**

Annual Review of Antihypertensives – **See Appendix F.**

Follow-Up of Ondansetron (Zofran®) Utilization – **See Appendix G.**

Annual Review of Plavix – **See Appendix H.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – February 08, 2005 @ 6:00p.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. Whitsett, Chairman:

1. **Call To Order**
   A. Roll Call – Dr. Graham

Items to be presented by Dr. Whitsett, Chairman:

2. **Public Comment Forum**
   A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. Whitsett, Chairman:

3. **Action Item - Approval of DUR Board Meeting Minutes – See Appendix A.**
   A. January 11, 2005 DUR Minutes – Vote
   B. Memorandum of January 24, 2005

Items to be presented by Dr. Flannigan, Dr. Browning, Dr. Whitsett, Chairman:

4. **Update on DUR/MCAU Program – See Appendix B.**
   A. Retrospective Drug Utilization Review Report for October 2004
   B. Medication Coverage Activity Audit for January 2005
   C. Help Desk Activity Audit for January 2005

Items to be presented by Dr. Nesser, Dr. Whitsett, Chairman:

5. **Update on Supplemental Rebate Program**

Items to be presented by Mr. Easton, Dr. Whitsett, Chairman:

6. **State Maximum Allowable Cost (SMAC) Report**

Items to be presented by Dr. Browning, Dr. Whitsett, Chairman:

7. **Action Item - Vote to Prior Authorize LUNESTA™ – See Appendix C.**
   A. Product Comparison
   B. COP Recommendation

Items to be presented by Dr. Moore, Dr. Whitsett, Chairman:

8. **Action Item – Vote to Prior Authorize Bladder Control Drugs – See Appendix D.**
   A. Available Product Information
   B. COP Recommendations
   C. Nursing Home Provider Letter Draft

Items to be presented by Dr. Moore, Dr. Whitsett, Chairman:

9. Annual Review of Growth Hormones – See Appendix E.

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

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

10. Annual Review of Antihypertensives – See Appendix F.

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

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

11. Follow-Up of Ondansetron (Zofran®) Utilization – See Appendix G.

A. Review of 5-HT3 Receptor Antagonist Utilization
B. Effects of Quantity Limit Override Activity
C. COP Recommendations

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

12. Annual Review of Plavix® – See Appendix H.

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

13. FDA and DEA Updates – See Appendix I.

14. Future Business

A. PBPA Annual Reviews
B. Neurontin™ Follow-Up Review
C. Fuzeon® Follow-Up Review
D. Estrogen Replacement Products Review
E. Narcotics Follow-Up
F. New Product Reviews

15. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JANUARY 11, 2005

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Dorothy Gourley, D.Ph.		X
Cathy Hollen, D.Ph.	X	
Dan McNeill, Ph.D., PA-C	X	
Cliff Meece, D.Ph.	X	
Dick Robinson, D.Ph., Vice-Chair	X	
James M. Swaim, D.Ph.	X	
Thomas Whitsett, M.D., Chair	X	

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph./Clinical Pharmacist	X	
Metha Chonlahan, D.Ph./Clinical Pharmacist	X	
Karen Egesdal, D.Ph./Clinical Pharmacist/OHCA Liaison	X	
Kelly Flannigan, Pharm.D./Clinical Pharmacist	X	
Shellie Gorman, Pharm.D./Clinical Pharmacist	X	
Ronald Graham, D.Ph., Manager, Operations/DUR	X	
Chris Kim Le, Pharm.D./Clinical Pharmacist	X	
Ann McIlvain, Pharm.D./Clinical Pharmacist	X	
Carol Moore, Pharm.D./Clinical Pharmacist	X	
Neeraj Patel, Pharm.D./Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.		X
Visiting Pharmacy Student: Elon Jacobs	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A.; Pharmacy Operations Manager	X	
Mike Fogarty, J.D., M.S.W.; Chief Operating Officer	X	
Lynn Mitchell, M.D., M.P.H.; Medical Director		X
Nancy Nesser, Pharm D., J.D.; Pharmacy Director	X	
Howard Pallotta, J.D., Legal		X
Lynn Rambo-Jones, J.D., Legal	X	
Rodney Ramsey; Pharmacy Claims Specialist	X	

OTHERS PRESENT:

Scott Mullins, Sanofi	Angela Menchaca, Amgen	Jason Schwier, Amgen
Randy McGinley, Berlex	Mike Cofer, Pfizer	Deron Grothe, Solvay
Jeff West, Chiron	Greg Hoke, Wyeth	Jonathan Klock, GlaxoSmithKline
David Love, Sepracor	Tracy Copeland, Forest	Alex Imhoff, Pharma
Patrick Evans, BMS	Lonna Erwin, BMS	Jorge Nassar, BMS
Mark DeClerk, Lilly	Don Stevens, Novaratis	Richard Ponder, J&J
Warren Piesatt, Pfizer	Roger Enix, Merck	

PRESENT FOR PUBLIC COMMENT:
Samuel Allen, Sepracor; Agenda Item 10

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

1A: Roll Call

Dr. Whitsett 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**

2A: Acknowledgement of Speakers and Agenda Item

Dr. Whitsett acknowledged speaker for Public Comment.

ACTION: NONE REQUIRED.

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

3A: December 14, 2004 DUR Minutes

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **NEW LEGISLATURE UPDATE AND BUDGET ISSUES**

Reported by Nico Gomez: A new legislature goes to work on February 7, 2005. The House has filed over 1700 Bills, but will have to decrease that number by half before January 20, 2005. The Senate has no limit on the number of Bills that can be filed and there are 1700 Bills filed. Mr. Gomez handed copies of the OHCA budget request. An additional $154 million above current budget base of $482 million is requested to operate this program at maximum efficiency. The top three items of expenditure are Annualization, Maintenance, and Federal and State Mandates. These three items of $97 million are mandatory in order to operate the OHCA for the next year. In October 2005, the State of Oklahoma will lose Federal matching dollars in the amount of 2.27%, a $33 million loss.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **UPDATE ON DUR/MCAU PROGRAM**

5A: Therapy Management Quarterly Report: Second Quarter FY05

Year-to-date totals (July – December 2004) were reported as 576 new clients; 285 established clients; 3,793 total PA's; 1,736 letters to providers; and 464 phone calls to providers; presented by Dr. Flannigan.

5B: Medication Coverage Activity Report: December 2004

The December 2004 activity audit noted total number of petitions submitted was 18,093 including super-PA's and special circumstance PA's. Approval/denial/duplicate percentages were indicated on the reports included in the agenda packet for this meeting; monthly and 2nd Quarter reports presented by Dr. Browning.

5C: Help Desk Activity Report: December 2004

Total calls for December 2004 numbered 18,203 (87.22% pharmacies, 8.43% clients, 2.39% physicians, 1.96% other); monthly and 2nd Quarter reports presented by Dr. Browning.

Dr. McNeill asked for a more defined report on Smoking Cessation. The Annual report is scheduled within the next couple of months. Dr. Whitsett requested more information the proposal from the tobacco trust fund.. Dr. Whitsett asked what other states are doing and maybe give a short report on that. Dr. Whitsett thinks it a good idea to invite someone from the tobacco councils to our meeting. Maybe have this person present something to Board members. Two Board members wanted to acknowledge the outstanding job the pharmacy help desk provides for the pharmacy providers. One statement was related to never having to wait but a few seconds to get through to a customer service representative and the other statement referred to the solving the problem and giving the proper information back to the calling provider in a professional manner.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 6: **UPDATE AND VOTE ON PRIOR AUTHORIZATION STATUS OF ANTIDEPRESSANTS**

Materials included in agenda packet; presented by Dr. Le.
Dr. Robinson moved to approve; motion seconded by Dr. Bell.
Dr. Whitsett asked if all of the SSRI's will get the black box warning? Dr. Le explained that according to the FDA, all antidepressants will get black box warnings. Dr. Whitsett wanted to know how the patient medication guide will get to the patient? Dr. Le stated that she understands that every prescription for these products will require passing out the patient medication guide. Dr. Robinson wanted to know a date that this would take effect. Dr. Whitsett reminded that everyone else besides paroxetine scripts for children are getting it now without prior authorization. Dr. Whitsett wanted to know if there is a safe time after a patient has been on these drugs to not worry too much about this risk of suicide. Dr. Robinson moved to accept COP option 2 recommendation.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **NEW PRODUCT REVIEW - CYMBALTA®**

Materials included in agenda packet; presented by Dr. Chonlahan. Dr. Whitsett asked about comparable trials? Motion was made by Dr. McNeill to bring back this category to see what can be done as far as prior authorization category for these indications. Dr. Hollen asked to include KI binding affinity and the remission date including the number of weeks. Dr. McNeill asked why we couldn't take all antidepressants as a class for efficacy and toxicity and usage and costs to the state.
ACTION: NONE REQUIRED.

AGENDA ITEM No. 8: **30-DAY NOTICE OF INTENT TO PRIOR AUTHORIZE BLADDER CONTROL DRUGS**

Materials included in agenda packet; presented by Dr. Moore. Dr. McNeill wants to know when it would go into effect? Dr. Nesser said supplemental rebates would go into effect April 1st or by July 1st. Dr. Whitsett wanted to know about usage patterns? Dr. McNeill asked what happens when you have a person who cannot communicate and refuses to take it. As far as a side effect it needs to be opened up a bit. Dr. Whitsett said he would hope that someone would accept that as a side affect. Dr. Whitsett asked if we had the ability to communicate to the nursing homes. Dr. Whitsett asked that a draft of a letter be presented before the Board that would go out to the nursing homes. Grandfathering will be implemented prior to PA requirements.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF ANXIOLYTIC/HYPNOTIC PBPA CATEGORY**

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

AGENDA ITEM NO. 10: **30-DAY NOTICE OF INTENT TO PRIOR AUTHORIZE LUNESTA®**

For Public Comment, Samuel Allen: *Thank you Mr. Chairman. I'm here tonight, Dr. Samuel Allen from Sepracor Medicaid Affairs department. I am here to give you a very brief clinical only review of Lunesta®, our new agent which has recently been approved by the FDA. It's not currently on the market, but we expect it will be in the next thirty or sixty days. It has been FDA approved for the use of insomnia in adults and furthermore, it was FDA approved for both sleep onset and maintenance in adults, with no quantity limit thus far. We have 2, 120 patients we reviewed in six clinical trials as submitted in our NDA and one of those was a 12-month study on chronic use of our drug with abrupt discontinuation afterwards to test for withdrawal, addiction, tolerance and we found none of those. The FDA agreed with us so thus our label says we are able to treat chronically. It is an S-isomer of a racemic compound used in Europe, actually, not (unintelligible) of the world for almost twenty years now, and the drug has +20 million patients on it thus far. We licensed the drug, let me rephrase that . . . we took the drug and pulled off the S-isomer and thus received our own unique license . . . got the good half, I guess is the way you say that. The other half was largely inactive at the GABA site. The drug is metabolized primarily by 3A4 of the CYP3450 isoenzyme system. There is a little bit of 2E1 but it's negligible. Metabolite is largely inactive, it's actually two*

metabolites. One is completely inactive, one does have some receptor binding at the therapeutic site but so minimal it's thought to be non-reportable. The differences right now in the market is that we are the only drug that has no quantity limit by the FDA, that is approved both for sleep onset and sleep maintenance, so Ambien and Sonata both are very short half-life drugs, created a niche in the market for us if we could produce a drug that would help us, help a person get a good night's sleep and yet not have any next day side effect carryover effects, thus we think we have succeeded in that. We do not yet know the Schedule, if it will be Schedule IV or not. The FDA suggested we be listed as Schedule IV agent and those data are now at the DEA and apparently there is a debate as to whether it will be a higher Schedule or scheduled at all because of our copious amounts of safety data in long term use. That's my brief introduction. If I have any questions, I'd be happy to address them.
Dr. Whitsett: *Why would it be considered Schedule IV at all?*
Mr. Allen: *Well we don't know. The . . . there's a class . . .*
Dr. Whitsett: *Overdosing . . . feel like some of it ought to be over the counter.*
Mr. Allen: *Actually all the anxiolytic hypnotic sedatives are usually classed affecting the Schedule IV. So we expected it to be Schedule IV. We've only recently learned that it may not be Schedule IV.*
Dr. Swaim: *As of day before yesterday, it was being sold as that.*
Mr. Allen: *Absolutely, we found it out this morning. There was a press release this morning that found out that the DEA has not yet given us our Schedule.*
Dr. Hollen: *Have you had a chance to look through the information that was included in the packet? Was there anything . . .*
Mr. Allen: *I have not. I was the person that was brought in for the clinical presentation and have not seen the data that you have in front of you. It's the label? The 25-page label? Yeah, I'm very familiar with that.*
Dr. Whitsett: *Cost wise? What's . . .*
(unintelligible)
Dr. Whitsett: *. . . per tablet . . . $3.50 a day.*
(unintelligible)
Dr. Hollen: *Okay, but clarify because . . .*
(unintelligible)
Dr. Hollen: *What is your recommended adult dose going to be?*
Mr. Allen: *Recommended adult dose will start out at 2 mg for non-elderly adults, go to 3 mg if needed.*
Dr. Hollen: *If needed?*
Mr. Allen: *If needed.*
Dr. Hollen: *Okay, do you know what your estimated acquisition cost for 2 mg is going to be?*
Mr. Allen: *I cannot say, since the drug's not on the market yet, we haven't . . .*
Dr. Hollen: *So do we know any of the estimated acquisition costs, or do we . . .*
Mr. Allen: *I can't address any . . . issues . . . I'm only here to present clinical data. I'm sorry.*
Dr. Meece: *. . . $3.26 . . . $3.26 . . . 3 mg . . . says $3.26 . . . across the board . . . flat price . . . so it's flat base pricing? Does that sound about . . .*
Mr. Allen: *I know it's flat base pricing. It actually is, I should point out, a different dosing regimen for elderly adults, starting 1 mg and go to 2 mg if needed. It's because their PK kinetics are slightly different. They eliminate a little bit slower, thus the drug tends to be not washed out as quickly.*
Dr. Nesser: *Do you know what the average dose is for the 20 million other users? Since there's a lot of use.*
Mr. Allen: *It's a different drug, it's racemic mixture and actually their main dose is 7.5 mg, but since it's racemic we cut that in half so it would be 3.75 was the average normal maximal dose for the non . . .*
Dr. Whitsett: *I take it drug interactions are not a special issue?*
Mr. Allen: *No. We did quite a few interactions. It does go through 3A4 but it's neither inhibitor nor inducer of the system. It's just broken down by . . we did run it with Ketoconazole which is . . . interactor of 3A4 and it did not change the kinetics Ketoconazole. . . Ketoconazole did increase the area of the curve . . . otherwise we saw no notable interactions. There was a possible other . . . there was . . . pharmacodynamic interaction with olanzepine when it was tested, but it was more in effects of patient sedation and somnolence, which somnolence is means sleeping pill I guess. We have a goodly amount of data. Our next day effect data are excellent.*
Dr. Whitsett: *How are you getting away with that? How does that work?*
Mr. Allen: *How does it work? Well it's a 6-hour half life.*
Dr. Whitsett: *I understand that . . .*
(unintelligible)
Dr. Whitsett: *. . . the next day . . . medications . . . people do have carryover side effects even though theoretically it's gone. It may be out of the plasma but it may still be bound to receptors and leaching off a receptor much slower than it did from the plasma and so a prolonged duration of after effects occur.*

Mr. Allen: *Well that's true of most . . . first of all we're not a benzo. We don't stick to that receptor. We're not chemically related to anything else in that class. It's GABA-A, binds to an alpha sub-unit of GABA-A receptor. It binds to a different sub-unit more so than Ambien does. Ambien tends to be much more at the alpha-1 sub-unit. Our drug binds more at the alpha-3 sub-unit. The alpha-3 sub-unit is localized much more in the actual sleep producing centers instead of the limbic system and/or cortex of the brain where you would get more true sedative effect instead of a sleep inducement effect.*
Dr. Whitsett: *If someone is aroused during the night, do you have difficulty waking them or do they wake up fully alert . . .*
Mr. Allen: *I don't have any data as far as . . . it says in our label very clearly not to take the drug unless you are expecting a good eight hours' sleep, so . . .*
Dr. Whitsett: *So if someone is expected to get up during the night to go to the bathroom, I understand some people do, it would probably be, I don't know that it would be contraindicated . . . what are your contraindications?*
Mr. Allen: *We don't have any.*
Dr. Whitsett: *Don't have any? But if you get up and go to the bathroom two or three times during the night, then you wouldn't recommend it?*
Mr. Allen: *Well, yeah . . . the label plainly says if you . . . expecting a full night's sleep . . . for that matter, that's almost a classic . . . (unintelligible).*
Mr. Allen: *The data actually there is a published paper out there right now by Tom . . . out of the Henry Ford Center up in Michigan . . . (unintelligible) . . . and the number of arousals during the night, as far as the need to go to the restroom decreased significantly in someone whose insomnia is actually treated. That it may be a side effect of someone having to get up and go to the bathroom because they were awake already and . . . (unintelligible).*
Dr. Hollen: *Do we know, what's the half life of Sonata and Ambien? Do we know those?*
Mr. Allen: *Sonata is an hour and a half to two hours. Ambien is right around (untelligible). They're both very short half lifes. That's why neither is indicated for maintenance. They usually wear off . . . the effects wear off (unintelligible).*
Dr. Whitsett: *The onset you said was, onset of action thought to be . . .*
Mr. Allen: *The onset of action is very rapid. C-max is about one hour and our half life is about six hours. It's a very linear curve when you look at the plasma concentrations.*
Materials included in agenda packet; presented by Dr. Browning.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: REVIEW AND DISCUSS MULTIPLE SCLEROSIS MEDICATIONS
Materials included in agenda packet; presented by Dr. Patel. Dr. McNeill asked how these were being filled at retail pharmacies and if administered in the home.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 12: ANNUAL REVIEW OF ADHD/NARCOLEPSY PBPA CATEGORY
Materials included in agenda packet; presented by Dr. McIlvain. Dr. Hollen asked how many patients on Strattera had shown liver toxicity since it came out? Dr. McIlvain said that two patients had demonstrated this side effect. Dr. Hollen asked if the liver damage was reversible? Dr. Bell said it was. Dr. Whitsett asked how changes for example in black box warnings on a particular drug, do the pharmacist consult with the patient?
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 13: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED.

AGENDA ITEM No. 14: **FUTURE BUSINESS**

14A: PBPA Annual Reviews
14B: Neurontin™ Follow-Up Review
14C: Zofran® Follow-Up Review
14D: SMAC Update
14E: New Product Reviews
14F: Supplemental Rebate Update

Materials included in agenda packet; submitted by Dr. Graham.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 15: **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: January 24, 2005

To: Nancy Nesser, DPh, JD
Pharmacy Director
Oklahoma Health Care Authority

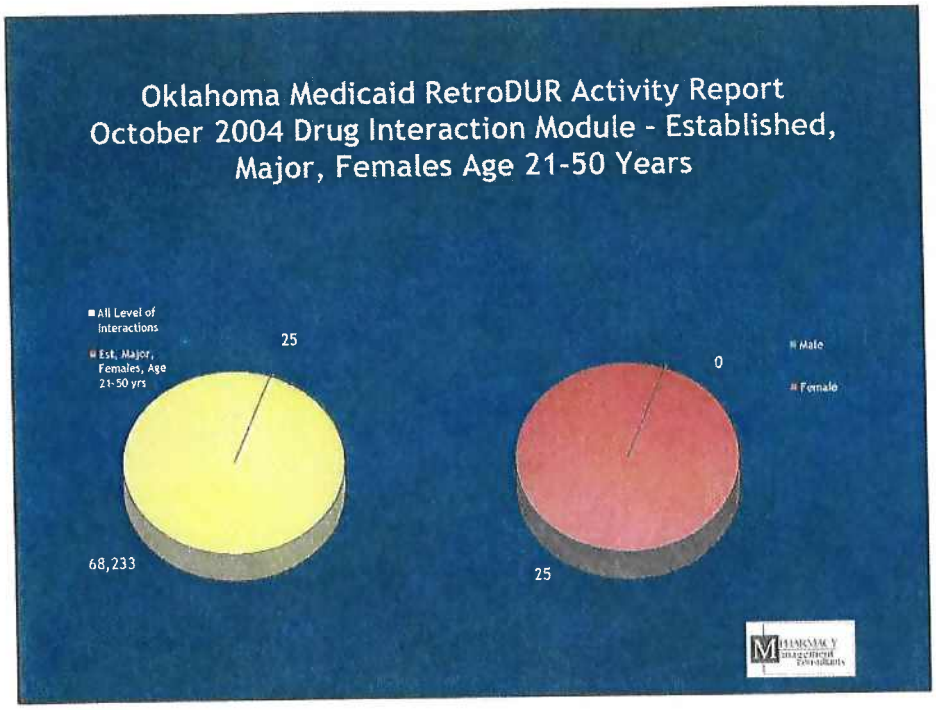
From: Ron Graham, DPh
Operations Coordinator / DUR Manager
Pharmacy Management Consultants

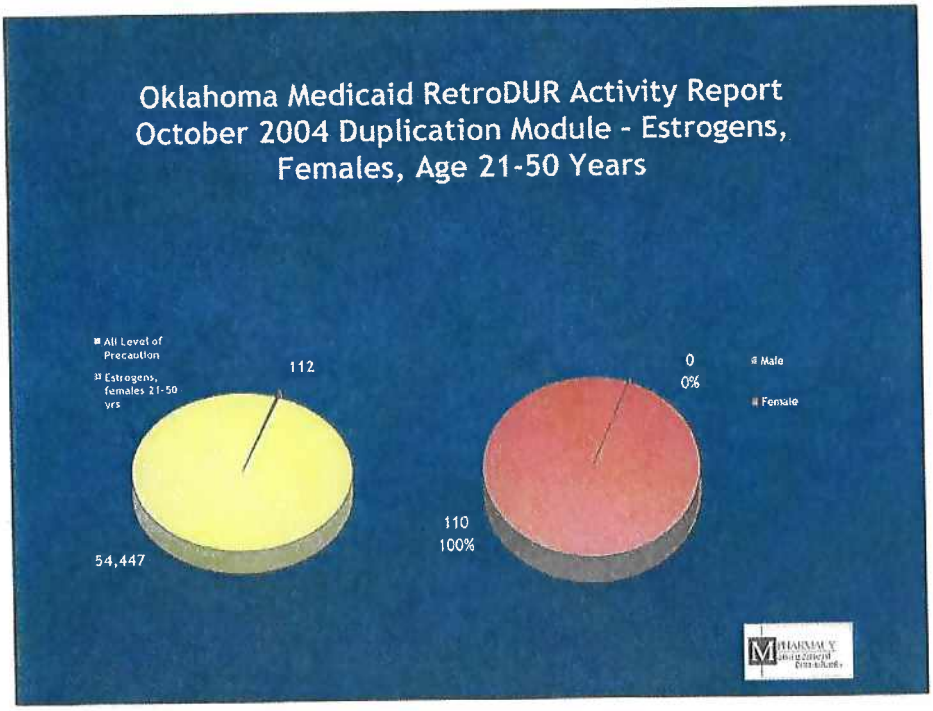
Subject: DUR Board Recommendations from Meeting of January 11, 2005.

Recommendation 1: Update and Vote on Prior Authorization Status of Antidepressants.

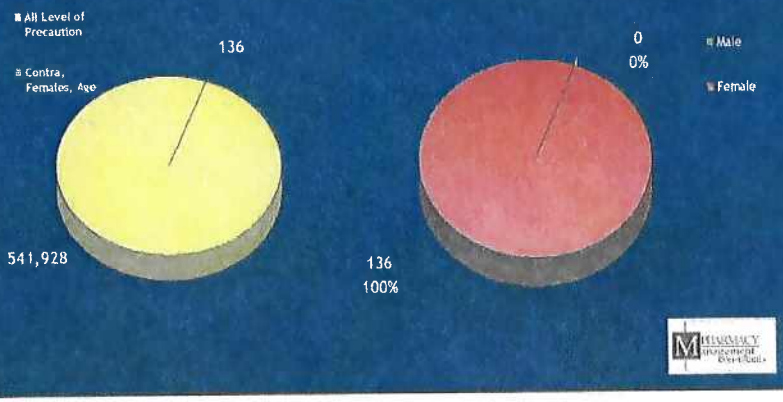
The DUR Board moved to approve Option (2) of the College of Pharmacy recommendations to remove the existing prior authorization of paroxetine as it is no longer singled out by the FDA to exhibit risks to the pediatric population. It appears the actions of the FDA, such as the black box warning requirement, implementation of the Patient Medication Guide, and all warnings issued in scientific and layman's language, may be sufficient in acknowledging the medical and patient communities of the risks associated with antidepressants.
MOTION CARRIED.

APPENDIX B

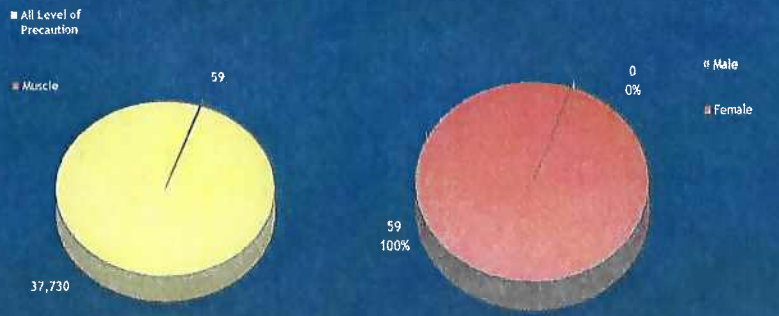

Oklahoma Medicaid RetroDUR Activity Report
October 2004 Drug Interaction Module - Established, Major, Females Age 21-50 Years
All Level of Interactions
Est, Major, Females, Age 21-50 yrs
25
68,233
0
25
Male
Female


Oklahoma Medicaid RetroDUR Activity Report
October 2004 Duplication Module - Estrogens, Females, Age 21-50 Years
All Level of Precaution
Estrogens, females 21-50 yrs
112
54,447
0
0%
110
100%
Male
Female

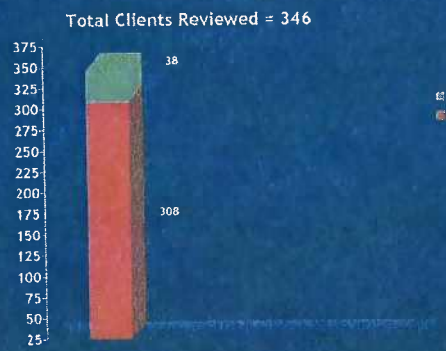
Oklahoma Medicaid RetroDUR Activity Report October 2004 Drug-Disease Level - Contraindicated, with Hypertension or Heart Failure, Females Age 21-50 Years, Non-Nursing Home



Oklahoma Medicaid RetroDUR Activity Report October 2004 Dosing & Duration Module - Muscle Relaxants, High Dose Only, Females Age 21-50 Years, Non-Nursing Home



Oklahoma Medicaid RetroDUR Activity Report
Follow-Up
October 2004 Female Clients Age 21-50 years - All Modules



Total Responses

Pharmacy	=	0 /15	0%
Physician	=	0/65	0%

Date Processed: Wednesday, February 02, 2005

Activity Audit for

January 01 2005 Through January 31 2005

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	ARB app.	ARB den.	Anti-depressants app.	Anti-depressants den.	Daily Total
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	3	236	47	43	20	0	0	44	15	11	10	4	4	1	3	1	14	38	20	2	1	29	29	575
4	1	2	271	43	57	28	0	0	37	22	3	12	5	11	1	2	5	17	51	16	1	1	23	19	628
5	1	1	192	24	38	21	0	0	44	13	3	7	4	2	2	0	5	16	46	9	0	0	21	7	456
6	0	2	173	25	24	12	0	0	31	4	3	10	1	2	0	0	8	14	26	10	1	0	14	9	369
7	0	1	195	29	33	10	5	0	38	19	10	8	3	5	0	1	5	14	42	7	0	0	18	9	452
8	1	0	27	2	15	3	0	0	10	3	3	1	2	2	0	0	0	3	4	0	0	1	2	2	81
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	181	13	41	22	4	0	41	8	0	11	5	3	0	0	4	12	24	10	0	0	17	0	396
11	0	0	177	24	50	25	0	0	51	12	9	6	2	5	2	1	9	8	31	8	0	0	24	5	449
12	0	1	152	39	48	27	0	0	43	11	5	9	5	2	1	0	9	13	37	8	0	1	20	6	438
13	0	0	139	29	34	19	4	0	48	11	1	12	3	3	1	0	1	9	23	10	1	0	26	9	383
14	1	0	138	21	45	15	0	0	40	13	10	15	0	1	1	0	3	8	27	9	0	0	14	4	365
15	1	0	30	10	6	4	0	0	10	6	1	0	0	0	0	0	3	0	6	1	0	0	2	1	81
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	0	1	139	31	27	15	1	0	28	18	5	8	2	2	1	0	6	7	36	9	0	0	11	5	352
18	0	1	145	11	25	17	0	0	35	16	8	6	2	7	1	1	8	11	35	5	1	0	12	3	350
19	0	0	163	13	41	15	0	0	46	10	7	11	5	4	0	0	6	7	24	3	0	0	14	5	375
20	1	0	136	16	36	20	0	0	40	9	5	7	6	3	1	0	2	11	27	10	1	1	16	4	352
21	1	1	137	23	34	20	4	0	51	14	2	5	2	5	0	0	3	6	24	3	4	0	8	4	351
22	0	0	14	5	7	4	0	0	7	5	0	2	0	0	0	0	0	1	6	0	0	0	0	1	52
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	145	15	43	14	0	0	37	8	9	6	0	1	0	0	4	7	17	3	1	0	13	1	324
25	0	0	134	20	48	15	0	0	45	12	7	9	1	4	0	0	11	3	43	6	2	1	18	3	382
26	2	1	160	15	47	14	6	0	52	10	7	4	4	2	0	0	5	8	28	8	1	0	17	4	395
27	0	2	103	10	32	9	0	1	41	3	6	5	2	3	0	0	5	6	23	7	2	1	12	3	276
28	1	1	136	6	39	18	3	0	61	9	5	7	2	4	0	1	5	10	28	3	0	1	18	4	362
29	1	0	33	3	9	9	0	0	13	3	1	1	0	0	0	0	1	3	10	1	1	0	3	0	92
30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	2	0	134	15	38	4	2	0	42	17	6	7	2	5	0	1	1	11	26	7	2	2	15	4	343

Date Processed: Wednesday, February 02, 2005

Activity Audit for

January 01 2005 Through January 31 2005

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	ARB app.	ARB den.	Anti-depressants app.	Anti-depressants den.	Daily Total
App.	13		3490		860		29		935		127		62		12		110		682		20		367		
Den.		17		489		380		1		271		179		80		10		219		173		10		141	
Average Length of Approvals in Days	3		95		94		157		223		325		218		244		294		284		294		150		

Changes to existing PA's	110
Total (Previous Year)	15688

*** Denial Codes**

762 = Lack of clinical Information	13.64%
763 = Medication not eligible	1.63%
764 = Existing PA	7.43%
772 = Not qualified for requested Tier	5.10%
773 = Requested override not approve	10.94%

SUPER PA's

Early Refill Attempts	50025
Dosing Change	557
Lost/Broken Rx	156
Stolen	35
Other	94
Wrong D.S. on Previous Rx	91
Quantity vs. Days Supply	335
Brand	307
-- Approved	141
-- Denied	166

Monthly Totals

	Number	Percent of Total
Approved	8120	57.23%
Additional PA's	10	0.07%
SUPER PA's	1575	11.10%
Emergency PA's	3	0.02%
Duplicates	586	4.13%
Incompletes	1445	10.18%
Denied *	2449	17.26%
Total	14188	100.00%

Daily Average of 567.52 for 25 Days

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

Additional PA's: Done by the help desk (doctor letter responses, PA ran for the wrong person)

Incompletes: Missing necessary information (NDC, SIG, Diagnosis, etc.)

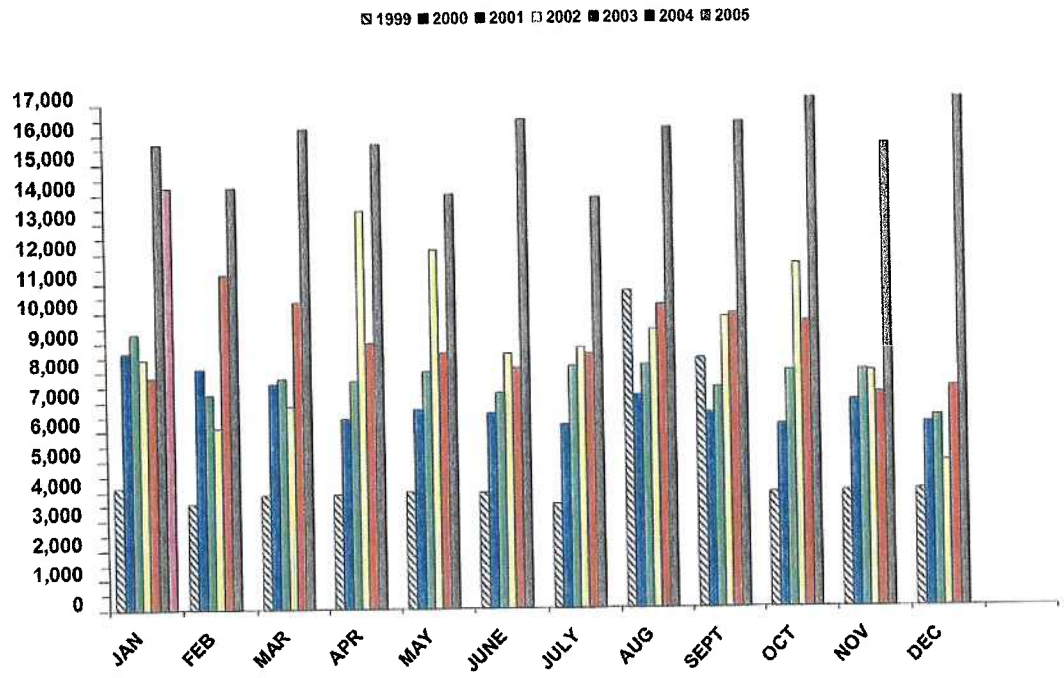
PRIOR AUTHORIZATION ACTIVITY AUDIT

Monthly Totals

MONTH	1999 Total *(approved/ duplicates/ denied)*	2000 Total *(approved/ duplicates/ denied)*	2001 Total *(approved/ duplicates/ denied)*	2002 Total *(approved/ duplicates/ denied)*	2003 Total *(approved/ duplicates/ denied)*	2004 Total *(approved/ duplicates/ denied)*	2005 Total *(approved/ duplicates/ denied)*
January	4,124	8,669	9,296	8,427	7,797	15,688	14,188
February	3,542	8,077	7,194	6,095	11,272	14,188	
March	3,856	7,588	7,748	6,833	10,358	16,138	
April	3,867	6,390	7,676	13,381	8,953	15,644	
May	3,959	6,711	7,980	12,082	8,589	13,960	
June	3,884	6,565	7,249	8,550	8,084	16,454	
July	3,523	6,181	8,133	8,775	8,565	13,813	
August	10,676	7,183	8,195	9,353	10,213	16,132	
September	8,387	6,585	7,438	9,793	9,918	16,305	
October	3,863	6,140	7,956	11,584	9,615	17,534	
November	3,919	6,961	7,949	7,921	7,201	15,554	
December	3,953	6,206	6,385	4,867	7,391	18,093	
Calendar Year Total	**57,553**	**83,256**	**93,199**	**107,661**	**107,956**	**189,503**	**14,188**

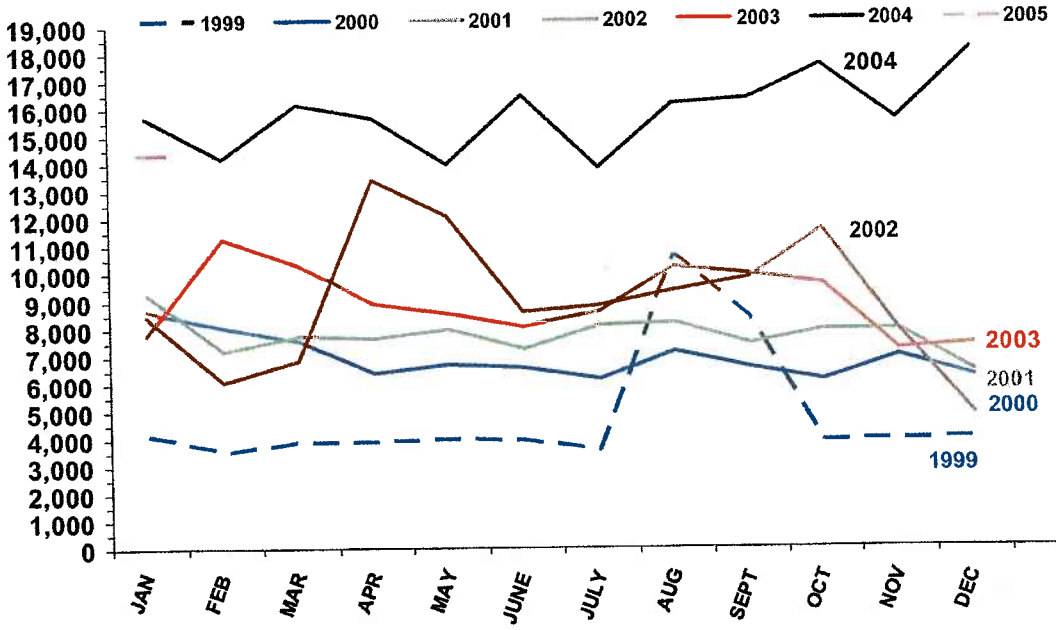
Monthly PA Activity

Calendar Years 2000-2005

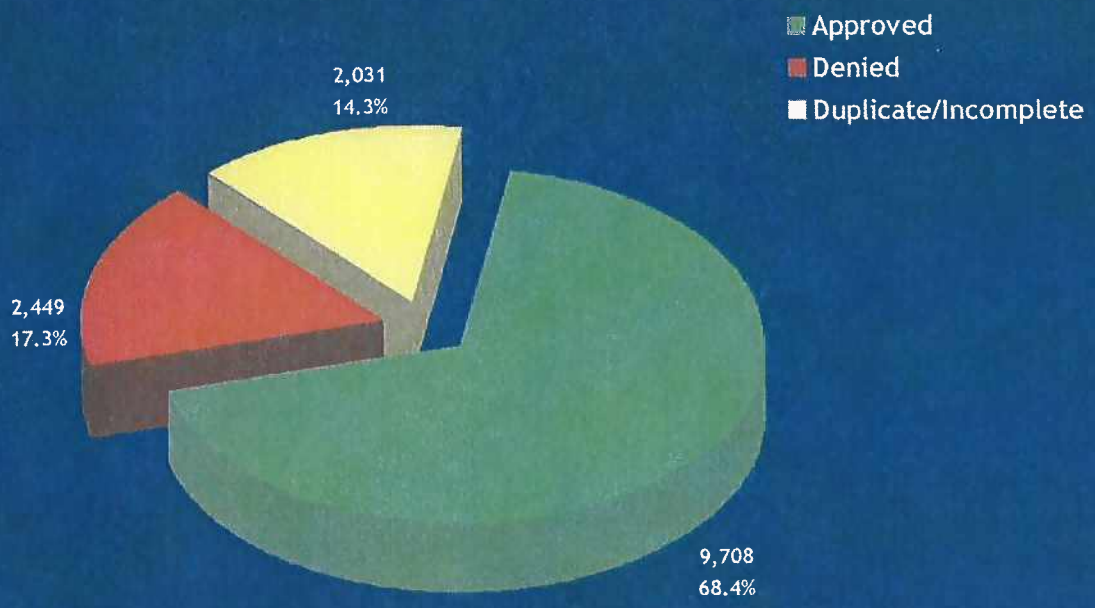


Monthly PA Activity

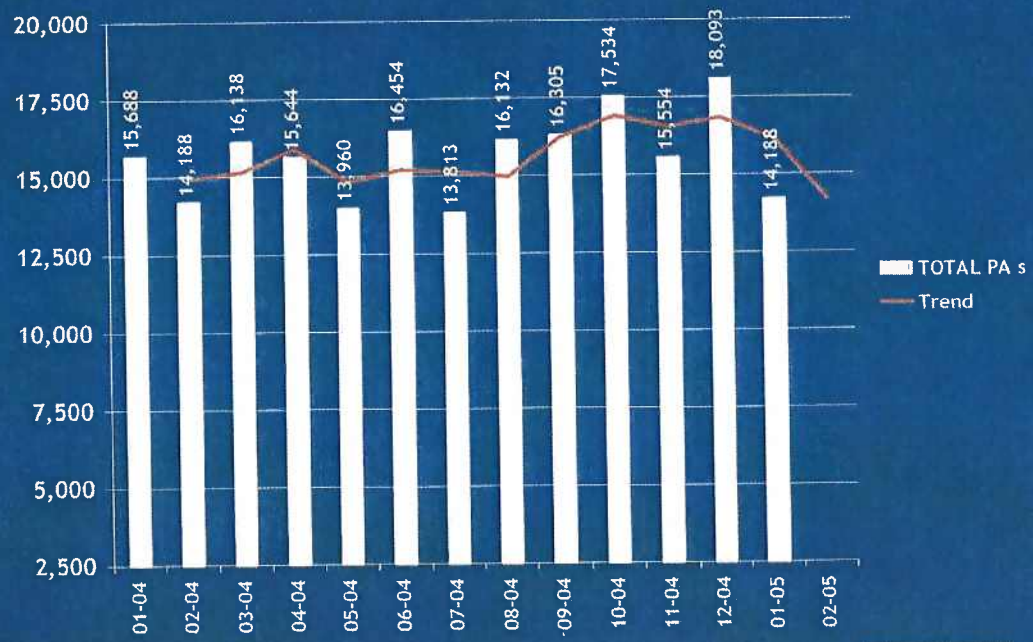
Calendar Years 2000-2005



PRIOR AUTHORIZATION ACTIVITY REPORT
January 2005



PRIOR AUTHORIZATION REPORT
January 2004 - January 2005



CALL VOLUME -JANUARY 2005

JANUARY 2005	CALLER					ISSUE					TYPE OF CALL					RESOLUTION							
																	Resolved						
	Call Volume	Physician	Pharmacies	Clients	Other	Eligibility	Claims	PA Issue	SMAC	Other	Regular	Callback	Proactive	ProDUR	Other	Helpdesk Resolved	Transferred Pharmacist	Transferred Supervisor	OHCA	Reversals/ Adjustments	EDS	Customer Service	Provider Contracts
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	812	9	705	81	17	108	420	83	0	201	785	7	0	19	1	790	1	0	0	0	0	14	7
4	807	20	712	61	14	94	373	136	0	204	766	3	0	37	1	776	6	1	0	0	1	14	9
5	597	9	531	42	15	76	313	75	0	133	564	6	1	21	5	583	3	1	1	0	0	8	1
6	602	22	504	59	17	66	291	92	1	152	594	1	2	2	3	589	5	1	0	0	0	6	1
7	610	13	517	76	4	65	292	98	0	155	595	6	0	9	0	581	6	3	0	1	0	12	7
8	156	0	155	1	0	30	81	12	0	33	154	0	0	1	1	151	0	0	0	0	0	3	2
9	56	0	55	1	0	14	28	2	0	12	54	0	0	2	0	55	0	0	0	0	0	1	0
10	764	10	641	89	24	118	363	100	0	183	738	5	0	16	5	739	9	0	1	0	0	9	6
11	770	21	667	68	14	105	342	98	1	224	741	2	0	23	4	740	5	1	0	1	0	10	13
12	746	17	626	85	18	76	350	88	0	232	713	8	2	20	3	716	3	3	0	0	0	14	10
13	756	20	681	40	15	77	448	86	0	145	736	6	1	12	1	739	2	0	0	3	0	7	5
14	642	14	549	61	18	79	297	86	2	178	620	5	0	14	3	618	4	1	0	0	0	9	10
15	162	0	155	7	0	25	87	9	0	41	161	0	0	1	0	161	0	0	0	0	0	0	1
16	58	0	55	3	0	15	31	3	0	9	55	0	0	3	0	58	0	0	0	0	0	0	0
17	488	5	449	22	12	68	257	57	0	106	469	2	0	12	5	479	0	2	0	0	0	3	4
18	747	17	634	69	27	193	289	94	0	171	725	4	1	9	8	719	0	0	0	0	0	14	14
19	600	11	513	63	13	135	223	83	0	159	578	6	0	13	3	580	3	0	0	1	0	6	10
20	602	18	509	61	14	70	299	78	0	155	577	3	0	19	3	583	3	1	1	0	0	9	5
21	684	11	570	71	32	78	332	96	0	178	652	5	1	18	8	648	6	0	0	0	0	18	12
22	156	0	150	6	0	20	78	6	0	52	156	0	0	0	0	148	0	0	0	0	0	2	6
23	53	0	49	3	1	14	28	3	0	8	53	0	0	0	0	53	0	0	0	0	0	0	0
24	678	7	575	83	13	94	330	86	0	168	663	3	0	9	3	656	5	5	0	0	0	7	5
25	705	17	609	68	11	98	358	93	0	156	691	2	0	11	1	671	8	0	0	1	1	8	16
26	643	18	545	60	20	92	294	82	0	175	620	5	0	15	3	625	2	0	1	0	2	10	3
27	715	9	628	59	19	190	291	72	0	162	696	3	1	7	8	682	2	1	0	0	2	18	10
28	626	10	534	61	21	84	319	74	0	149	615	5	0	3	3	609	2	1	0	0	1	6	7
29	173	0	163	8	2	31	85	15	0	42	162	1	0	8	2	165	0	0	0	0	0	3	5
30	54	0	51	2	1	11	32	3	0	8	52	0	0	1	1	54	0	0	0	0	0	0	0
31	614	13	535	55	11	166	234	56	0	158	600	3	0	7	4	597	5	0	0	0	0	7	5
Total	**15,076**	**291**	**13,067**	**1,365**	**353**	**2,292**	**7,165**	**1,866**	**4**	**3,749**	**14,585**	**91**	**9**	**312**	**79**	**14,565**	**80**	**21**	**4**	**7**	**7**	**218**	**174**
Percentage	**100.00%**	**1.93%**	**86.67%**	**9.05%**	**2.34%**	**15.20%**	**47.53%**	**12.38%**	**0.03%**	**24.87%**	**96.74%**	**0.60%**	**0.06%**	**2.07%**	**0.52%**	**96.61%**	**0.53%**	**0.14%**	**0.03%**	**0.05%**	**0.05%**	**1.45%**	**1.15%**

CALL VOLUME

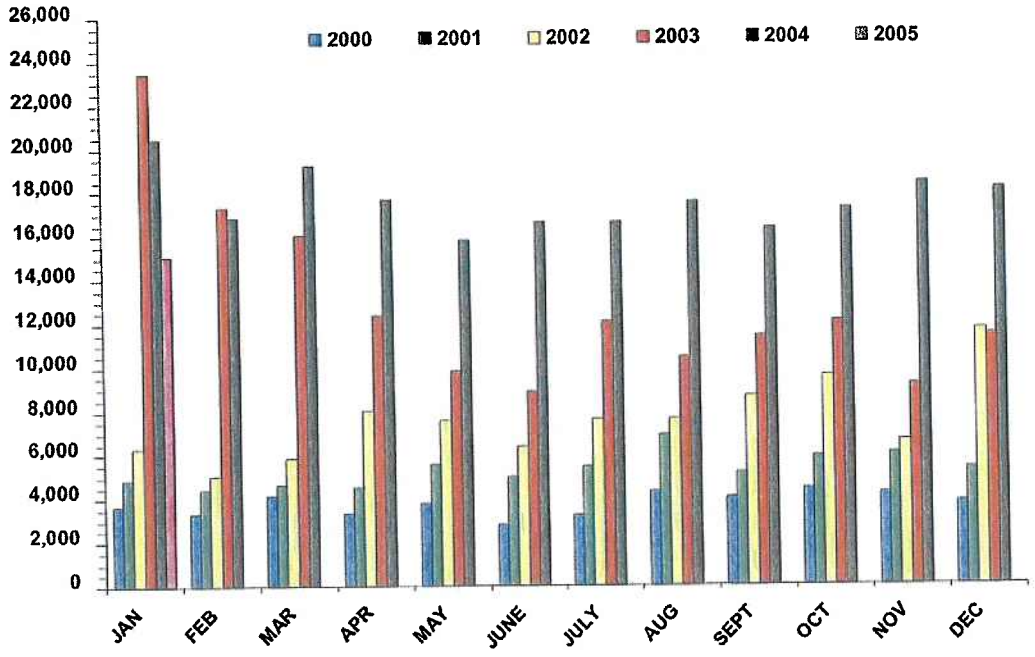
Monthly Totals

MONTH	1999 Total	2000 Total	2001 Total	2002 Total	2003 Total	2004 Total	2005 Total
January	* 0	3,697	4,905	6,295	23,499	20,498	15,076
February	* 0	3,335	4,393	5,049	17,354	16,857	
March	* 0	4,157	4,668	5,858	16,081	19,232	
April	* 0	3,337	4,556	8,047	12,378	17,660	
May	* 0	3,804	5,540	7,586	9,836	15,828	
June	* 0	2,820	4,982	6,368	8,917	16,634	
July	* 0	3,242	5,465	7,651	12,126	16,662	
August	3,883	4,333	6,881	7,629	10,454	17,563	
September	2,360	4,015	5,145	8,664	11,449	16,373	
October	1,963	4,398	5,912	9,608	12,102	17,300	
November	1,721	4,216	6,011	6,627	9,178	18,477	
December	2,475	3,804	5,314	11,710	11,461	18,203	
Calendar Year Total	**12,402**	**45,158**	**63,772**	**91,092**	**154,835**	**211,287**	**15,076**

* Help Desk Call Center implemented in August 1999.

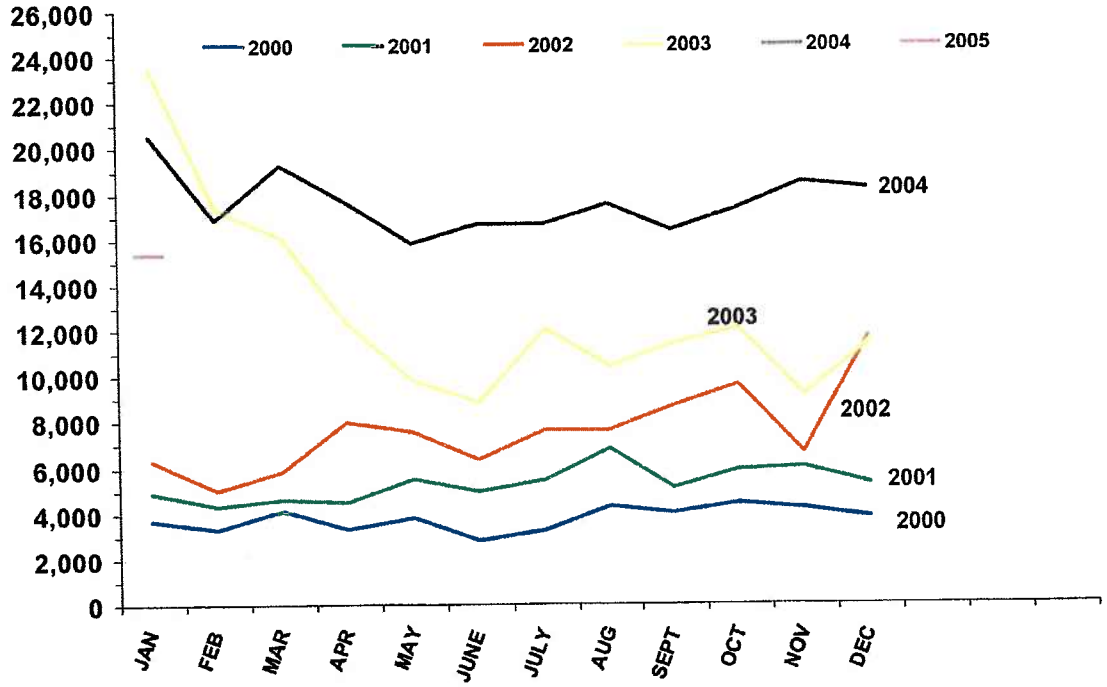
Monthly Call Volume

Calendar Years 2000-2005

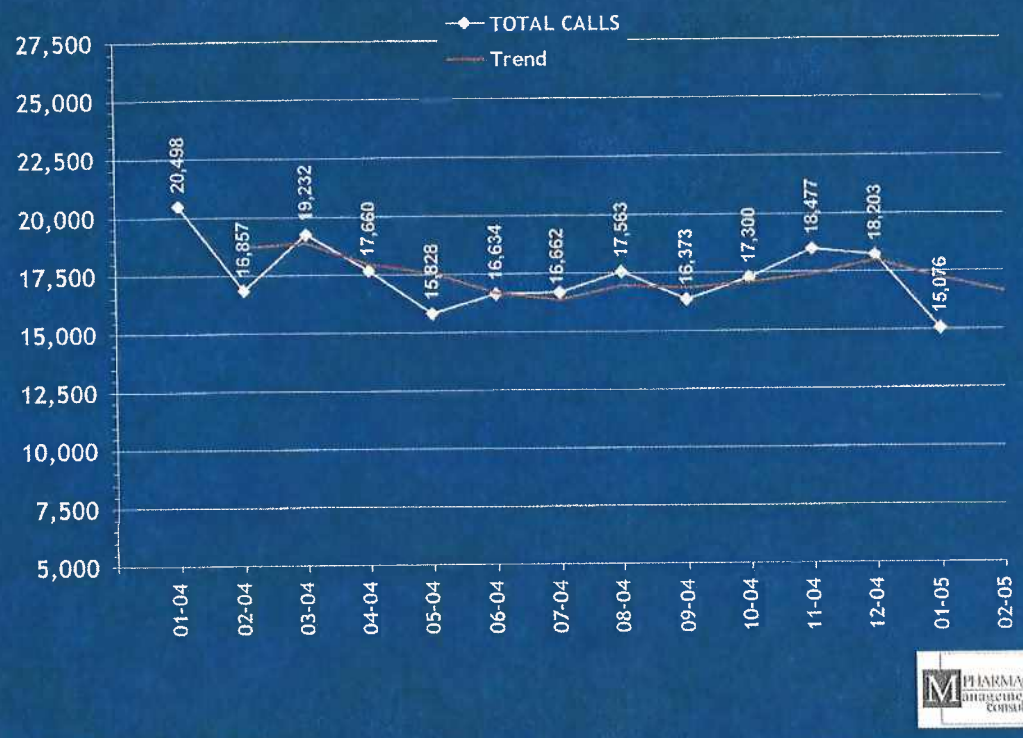


Monthly Call Volume

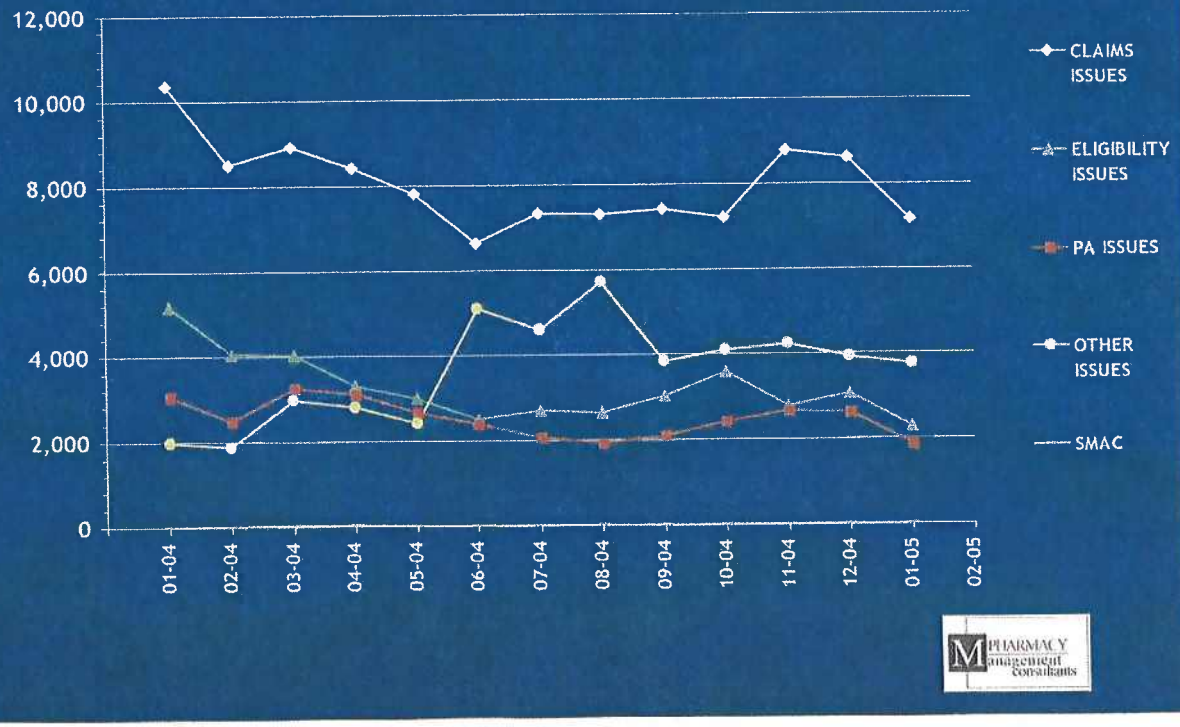
Calendar Years 2000-2005



CALL VOLUME MONTHLY REPORT
January 2004 - January 2005



CALL VOLUME ISSUES
January 2004 - January 2005



APPENDIX C

Vote to Prior Authorize LUNESTA™ (eszopiclone)

Oklahoma Medicaid
February 2005

Comparison of LUNESTA™, Ambien®, and Sonata®[1-3]

	LUNESTA™	Ambien®	Sonata®
Not indicated for clients under 18	X	X	X
Dosage adjustment for hepatic impairment		X	X
Dosage adjustment in older population	X	X	X
Dosage adjustment with renal impairment			
Sleep Onset	X	X	X
Sleep Duration	X	X	
Sleep Maintenance	X	X	
Renal Excretion	X	X	
Active Metabolites	X		
Tmax affected by food	X	X	X
Contraindications			
Schedule IV	X	X	X
Short term use*		X	X
Long term use*	X		

*All sleep medications recommend limited use for 7-10 days and a re-evaluation before continued use.

Clinical Trials of LUNESTA™ (eszopiclone)

2,700 patients participated in the clinical development program (Phases I-III).[4]

In placebo-controlled clinical effectiveness studies involving approximately 2,120 patients, approximately 1,550 were exposed to LUNESTA™.[4]

Studies assessed safety and efficacy for treatment of insomnia in adult (21-64 years) and elderly (65-86 years).[4]

Completed studies:[4]

- 16 - Phase I studies (n=593) drug interaction and special populations.
- 2 - Phase II studies (n=25) assess next-day residual effects in healthy subjects and those with chronic insomnia.
- 1 - Phase III study in transient insomnia (n=436) using First Night Effect Model in healthy subjects.
- 3 - Phase III studies (n=1,164) in adults with chronic, primary insomnia.
- 2 - Phase III studies (n=526) elderly patients with chronic, primary insomnia.

At the recommended adult dose of 2-3mg and the elderly dose of 1-2mg, the trials showed a significant decrease in sleep latency and improved measures of sleep maintenance (objectively-wake time after sleep onset and subjectively-total sleep time) and no evidence of tolerance or rebound insomnia. [1]

The most common adverse event associated with eszopiclone is unpleasant taste. [5]

LUNESTA™ was approved in mid-December 2004 and was expected to be available in early January 2005. However, there has been a delay in the drug's availability and it is now expected to be available in March 2005. [4]

The manufacturer is conducting additional Phase IIIB/IV studies of LUNESTA™ for the treatment of insomnia in women experiencing the hormonal changes due to perimenopause, in patients experiencing pain associated with rheumatoid arthritis, and a six- month, double-blind, placebo-controlled study in patients with chronic insomnia. [4]

Recommendations

The college of pharmacy has the following recommendation:

- Include LUNESTA™ in prior authorization category with anxiolytics and hypnotics.
- Place quantity limits on LUNESTA™: 30 units for a 30 day supply. Currently quantity limits are in place for Ambien® and Sonata®.

Summary of LUNESTA™ Studies[5-9]

Description	Study Objectives	Population	Drug(s) tested/ Regimens	Number of Subjects (M/F)	Treatment Duration	Conclusion
Randomized, double-blind, placebo controlled	evaluate efficacy and safety of ESZ in First Night Effect of transient insomnia	healthy males and females	single dose ESZ 2mg or 3 mg	n=293	one night	ESZ showed improvements in sleep onset, maintenance (including number of awakenings) quality and reduced morning sleepiness.
Randomized, double-blind, placebo controlled	evaluate efficacy and safety of ESZ in elderly patients with chronic insomnia	patients 65-85 years old diagnosed with primary insomnia	ESZ n=136 PBO n=128	n=264	2 weeks	ESZ 2mg produced consistent statistically significant improvement in both patient-reported measure of sleep (onset and maintenance) and Polysomnography (PSG). Reduced daytime napping and improvements in some QoL domains.
Randomized, double-blind, multi-center, placebo-controlled, followed by 2 nights of single-blind placebo	assess the efficacy and safety of ESZ in adults with chronic primary insomnia	adults	PBO ESZ 2 or 3mg	n=308	6 weeks	Compared to PBO, 3mg dose showed improvements in all areas (time to sleep onset, total sleep and efficiency, maintenance enhanced quality and depth of sleep). 2mg showed improvements in all areas except sleep maintenance. No evidence of tolerance or rebound insomnia or detrimental effects on next-day psychomotor performance using the Digit-Symbol Substitution Test (DSST).
6-month open-label extension phase of previous 6 month, double-blind	long-term efficacy and safety	M/F aged 21-64 sleeping no more than 6.5 hours per night and/or taking longer than 30 minutes to fall asleep	PBO n=111 ESZ n=360 3mg	n=471	6 months	12 months of continued therapy with 3mg ESZ provided and maintained sustained improvement in patient-reported sleep and daytime functioning, was well tolerated and showed no evidence of tolerance or withdrawal.

References

1. LUNESTA™. NDA 21-476 Approved Labeling Test. December 15, 2004.

2. Ambien® package insert.

3. Sonata® package insert.

4. Preliminary Results Show Improvement for Insomnia Patients with Co-Existing Depression Who Were Treated with Sepracor's LUNESTA™ [PR Newswire] Release Date: 1/12/2005.

5. Zammit GK, McNabb L, Caron J, Amato D and Roth T. Efficacy and safety of eszopiclone across 6-weeks or treatment for primary insomnia. *Curr Med Res Opin.* 2004;20(12)1917-1991.

6. Rosenberg R, Jamieson A, Caron J, Roth T. Eszopiclone (ESZ), A novel non-benzodiazepine anti-insomnia agent: efficacy and safety in a model of transient insomnia [Abstract]. *Sleep.* 2002;45:A68-69.

7. Roth T. Krystal A, Walsh J, Roehrs T, Wessel T, Caron J. Twelve months of nightly eszopiclone treatment in patients with chronic insomnia: assessment of long-term efficacy and safety. *Sleep.* 2004;27(suppl.):A260.

8. Erman M, Rosenberg R, Caron J. Polysomnographic and patient-reported evaluation of the efficacy and safety of eszopiclone in elderly subjects with chronic insomnia. *Sleep.*2004;27(suppl.):A257.

9. General Summary for LUNESTA™ (eszopiclone) Tablets.

APPENDIX D

Vote to Prior Authorize Bladder Control Drugs

Oklahoma Medicaid
February 2005

Available FDA Approved Treatment

Drug	How Supplied	Indications
Flavoxate (Urispas®)	100 mg Tablet	Symptomatic relief of dysuria, nocturia, suprapubic pain, urgency, and incontinence due to detrusor instability and hyper-reflexia in elderly with cystitis, urethritis, urethrocystitis, urethrotrigonitis, and prostatitis
Hyoscyamine (Anaspaz®, Cystospaz®, Cystospaz-M®)	0.15 mg Tablet (Cystospaz®), 0.375 mg Capsule, timed release (Cystospaz-M®)	Adjunctive therapy for neurogenic bladder/bowel*
Oxybutynin (Ditropan®, Ditropan XL®, Oxytrol®)	5 mg Tablet (Ditropan®), 5 mg/5 mL syrup (Ditropan®) 5 mg, 10 mg, 15 mg Tablet, extended release (Ditropan® XL): Transdermal system (Oxytrol®): 3.9 mg/ [39 cm^2; total oxybutynin 36 mg]	Antispasmodic for neurogenic bladder (urgency, frequency, urge incontinence) and uninhibited bladder
Tolterodine (Detrol®, Detrol LA®)	1 mg, 2 mg Tablet (Detrol®) 2 mg, 4 mg Caps, extended release (Detrol LA®)	Treatment of patients with an overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence
Trospium (Sanctura®) (App'd 5/04)	20 mg Tablet - EAC $1.31	Treatment of overactive bladder with symptoms of urgency, incontinence, and urinary frequency
Solifenacin (Vesicare®) (App'd 11/04)	5 mg, 10 mg tablet	Treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency
Darifenacin (Enablex®) (App'd 12/04)	7.5 mg, 15 mg tablet, extended release	Management of symptoms of bladder overactivity (urge incontinence, urgency, and frequency)

*Also used as adjunctive therapy for peptic ulcers, irritable bowel; treatment of infant colic, GI tract disorders caused by spasm; to reduce rigidity, tremors, sialorrhea, and hyperhidrosis associated with parkinsonism; as a drying agent in acute rhinitis.

Warnings/Side Effects

Drug	Contraindication	Caution	Side Effect
Flavoxate (Urispas®)	Hypersensitivity to flavoxate; pyloric or duodenal obstruction; GI hemorrhage; GI obstruction; ileus; achalasia; obstructive uropathies of lower urinary tract (BPH)	May cause drowsiness, vertigo, and ocular disturbances; administer cautiously in patients with suspected glaucoma	Tachycardia, palpitations, drowsiness, confusion (especially in the elderly), nervousness, fatigue, vertigo, headache, hyperpyrexia, rash, urticaria, constipation, nausea, vomiting, xerostomia, dry throat, dysuria, leucopenia, increased intraocular pressure, blurred vision
Hyoscyamine (Anaspaz®, Cystospaz®, Cystospaz-M®)	Hypersensitivity to belladonna alkaloids or any component of the formulation; glaucoma; obstructive uropathy; myasthenia gravis; obstructive GI tract disease, paralytic ileus, intestinal atony of elderly or debilitated patients, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis; unstable cardiovascular status in acute hemorrhage, myocardial ischemia	Use with caution in children with spastic paralysis. Use with caution in patients with autonomic neuropathy, coronary heart disease, CHF, cardiac arrhythmias, prostatic hyperplasia, hyperthyroidism, hypertension, chronic lung disease, renal disease, and hiatal hernia associated with reflux esophagitis. Use with caution in the elderly, may precipitate undiagnosed glaucoma and/or severely impair memory function (especially in those patients with previous memory problems). May increase the risk of heat prostration.	Palpitations, tachycardia, ataxia, dizziness, drowsiness, headache, insomnia, mental confusion/excitement, nervousness, speech disorder, urticaria, lactation suppression, bloating, constipation, dry mouth, loss of taste, nausea, vomiting, impotence, urinary hesitancy, urinary retention, weakness, blurred vision, cycloplegia, increased ocular tension, mydriasis, allergic reactions, decreased sweating
Oxybutynin (Ditropan®, Ditropan XL®, Oxytrol®)	Hypersensitivity to oxybutynin or any component of the formulation; untreated glaucoma; partial or complete GI obstruction; GU obstruction; urinary retention; megacolon; toxic megacolon	Use with caution in patients with urinary tract obstruction, angle-closure glaucoma (treated), hyperthyroidism, reflux esophagitis (including concurrent therapy with oral bisphosphonates or drugs which may increase the risk of esophagitis), heart disease, hepatic or renal disease, prostatic hyperplasia, autonomic neuropathy, ulcerative colitis (may cause ileus and toxic megacolon), hypertension, hiatal hernia, myasthenia gravis, ulcerative colitis, or intestinal atony. The extended release formulation consists of drug within a nondeformable matrix; following drug release/absorption, the matrix/shell is expelled in the stool. The use of nondeformable products in patients with known stricture/narrowing of the GI tract has been associated with symptoms of obstruction. Caution should be used in elderly due to anticholinergic activity (eg, confusion, constipation, blurred vision, and tachycardia). May increase the risk of heat prostration.	**Oral:** Dizziness, somnolence, xerostomia, constipation, Urination impaired, headache, confusion, insomnia, nervousness, dry skin, skin rash, nausea, dyspepsia, abdominal pain diarrhea, flatulence, gastrointestinal reflux, taste perversion, Post-void residuals increased, urinary tract infection, weakness, blurred vision, dry eyes, rhinitis, dry nasal and sinus membranes. **Transdermal:** Application site reaction, pruritus, xerostomia, diarrhea, constipation, dysuria, erythema, vesicles, rash, vision changes

Drug	Contraindication	Caution	Side Effect
Tolterodine (Detrol®, Detrol LA®)	Hypersensitivity to tolterodine or any component of the formulation; urinary retention; gastric retention; uncontrolled narrow-angle glaucoma; myasthenia gravis	Use with caution in patients with bladder flow obstruction, may increase the risk of urinary retention. Use with caution in patients with gastrointestinal obstructive disorders (ie, pyloric stenosis), may increase the risk of gastric retention. Use with caution in patients with controlled (treated) narrow-angle glaucoma; metabolized in the liver and excreted in the urine and feces, dosage adjustment is required for patients with renal or hepatic impairment. Patients on CYP3A4 inhibitors require lower dose. Safety and efficacy in pediatric patients have not been established.	Dry mouth (35%; extended release 23%), Chest pain, headache (7%; extended release 6%), somnolence (3%; extended release 3%), fatigue (4%; extended release 2%), dizziness (5%; extended release 2%), anxiety (extended release 1%) dry skin, abdominal pain (5%; extended release 4%), constipation (7%; extended release 6%), dyspepsia (4%; extended release 3%), diarrhea, weight gain, dysuria (2%; extended release 1%), arthralgia, abnormal vision (2%; extended release 1%), dry eyes (3%; extended release 3%), bronchitis, sinusitis (extended release 2%)
Trospium (Sanctura®) (App'd 5/04)	Hypersensitivity to trospium or any component of the formulation; urinary retention; gastric retention; uncontrolled narrow-angle glaucoma; myasthenia gravis	Use with caution in patients with bladder flow obstruction, may increase the risk of urinary retention. Use with caution in patients with GI obstructive disorders (eg, pyloric stenosis); may increase the risk of gastric retention. Use with extreme caution in patients with controlled (treated) narrow-angle glaucoma. Use with caution in renal dysfunction; dosage adjustment is required. Monitor closely when used concurrently with other medications that are eliminated by active tubular secretion (eg, digoxin, procainamide, pancuronium, morphine vancomycin, metformin, tenofovir); may increase levels of trospium and/or the coadministered drug. Use caution in Alzheimer's patients. Use caution in patients with moderate-to-severe hepatic dysfunction. Use caution in the elderly (≥ 75 years); increased anticholinergic side effects are seen. Safety and efficacy in pediatric patients have not been established.	Xerostomia, tachycardia, headache, fatigue, dry skin, constipation, abdominal pain, dyspepsia, flatulence, abdominal distention, vomiting, dysgeusia, urinary retention, dry eyes, blurred vision, angioneurotic edema

Drug	Contraindication	Caution	Side Effect
Solifenacin (Vesicare®) (App'd 11/04)	Contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients who have demonstrated hypersensitivity to the drug substance or other components of the product.	Use with caution in patients with clinically significant bladder outflow obstruction due to risk of urinary retention. Use with caution in patients with decreased gastrointestinal motility. Use with caution in patients being treated for narrow-angle glaucoma. Use with caution in patients with reduced renal function. Doses of VESIcare greater than 5 mg are not recommended in patients with severe renal impairment (CLcr < 30 mL/min). Use with caution in patients with reduced hepatic function. Doses of VESIcare greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B). VESIcare is not recommended for patients with severe hepatic impairment (Child-Pugh C).	Dry Mouth, constipation, nausea, dyspepsia, upper abdominal pain, vomiting, urinary tract infection, influenza, pharyngitis, dizziness, blurred vision, dry eyes, urinary retention, edema lower limb, fatigue, depression, cough, hypertension
Darifenacin (Enablex®) (App'd 12/04)	Hypersensitivity to darifenacin or any component of the formulation; uncontrolled narrow-angle glaucoma; paralytic ileus, GI or GU obstruction	Use with caution with hepatic impairment; dosage limitation is required in moderate hepatic impairment (Child-Pugh Class B). Not recommended for use in severe hepatic impairment (Child-Pugh Class C). Use with caution in patients with clinically-significant bladder outlet obstruction, prostatic hyperplasia (nonobstructive), or urinary retention. Use caution in patients with decreased GI motility, constipation, hiatal hernia, reflux esophagitis, and ulcerative colitis. Use caution in patients with myasthenia gravis. In patients with controlled narrow angle glaucoma, darifenacin should be used with extreme caution and only when the potential benefit outweighs risks of treatment. Safety and efficacy have not been established in pediatric patients.	Xerostomia, constipation Headache, dizziness, dyspepsia, abdominal pain, nausea, diarrhea, urinary tract infection, asthenia, dry eyes, flu-like syndrome, accidental injury, abnormal vision, acute urinary retention, arthralgia, back pain, bronchitis, dry skin, flu-like syndrome, hypertension, pain, peripheral edema, pharyngitis, rash, rhinitis, sinusitis, weight gain, urinary tract disorder, vaginitis, vomiting

Geriatric Effects

Flavoxate: Caution should be used in the elderly due to anticholinergic activity (eg, confusion, constipation, blurred vision, and tachycardia).

Hyoscyamine: Avoid long-term use. The potential for toxic reactions is higher than the potential benefit, elderly are particularly prone to CNS side effects of anticholinergics (eg, confusion, delirium, hallucinations). Side effects often occur before clinical response is obtained. Generally, not recommended because of side effects.

Oxybutynin: Caution should be used in the elderly due to anticholinergic activity (eg, confusion, constipation, blurred vision, and tachycardia). Start with lower doses. Oxybutynin may cause memory problems in the elderly. A study of 12 health volunteers with an average age of 69 showed cognitive decline while taking the drug (*J Am Geriatr Soc*, 1998, L46:8-13).

Tolterodine: Safety and efficacy in patients >64 years was found to be similar to that in younger patients; no dosage adjustment is needed based on age

Trospium: In studies, the incidence of anticholinergic side effects was higher in patients ≥75 years of age as compared to younger adults.

Solifenacin: No dosage adjustment is needed based on age.

Darifenacin: No dosage adjustment is needed based on age.

Recommendations

The College of Pharmacy recommends prior authorizing this class of drugs utilizing the PBPA program. Authorization will be given for 1 year.

- Tier-1 – Detrol®, oxybutynin, hyoscyamine*
- Tier-2 - Detrol LA®, Ditropan XL®, flavoxate, Oxytrol®, Sanctura®, VESIcare®, Enablex®

*hyoscyamine can be used as adjuvant therapy only; by itself, it will not count toward a tier-2

Prior authorization criteria:

In order to get a tier-2 drug, client must meet one of the following criteria:

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

DRAFT

Dear Nursing Home Provider

OHCA will be initiating Product Based Prior Authorization on bladder control drugs. Currently available drugs will be divided into the following tiers:

- Tier-1 – Detrol®, oxybutynin, hyoscyamine*
- Tier-2 - Detrol LA®, Ditropan XL®, flavoxate, Oxytrol®, Sanctura®, VESIcare®, Enablex®

*hyoscyamine can be used as adjuvant therapy only; by itself, it will not count toward a tier-2

Please remind staff involved in direct patient care that the following symptoms are some of the most commonly associated side effects of these drugs:

dry mouth, constipation, dizziness, confusion, weakness, blurred vision , somnolence, impaired urination, urinary tract infection, headache, confusion, and insomnia.

Because these side effects can lead to noncompliance, falls, and other adverse outcomes, particularly in the elderly, it is imperative that they be reported and that steps are taken to alleviate them.

Patients who are stabilized on a Tier-2 medication will be allowed to continue their current treatment without prior authorization.

New Tier-2 drug prescriptions will be subject to the following criteria prior to approval for payment:

- tier-1 drug failure (i.e. inadequate clinical response or adverse effect), or
- contraindication to the tier-1 drugs , or
- need for the tier-2 drug for a unique indication which the tier-1 drugs lack.

Thank you for your continued service to Oklahoma's Medicaid clients. If you have questions, please call the Pharmacy Help Desk at 405-271-6349 or 1-800-831-8921.

Notes:

- Letters could be sent 30 days in advance of the policy going into effect
- Manufacturers will have the opportunity to participate in the supplemental rebate prior to the policy going into effect, and the drugs listed as Tier 1 and 2 will reflect the status after rebate participation

APPENDIX E

Annual Review of Growth Hormones - Fiscal Year 2004

Oklahoma Medicaid
February 2005

Definition of Prior Authorization Category for FY '04
COVERED INDICATIONS

- Classic hGH Deficiency
- Short Stature (including Prader-Willi Syndrome)
- Short Stature associated with chronic renal insufficiency
- Small for Gestational Age (SGA)
- Turner's Syndrome or 45 X, 46 XY mosiacism in males
- Hypoglycemia associated with hGH insufficiency
- AIDS wasting (Serostim only)

Utilization

For the period of July 2003 through June 2004, a total of 168 clients received growth hormone products through the Medicaid fee-for-service program. Sixty-nine (41%) of these clients transferred to fee-for-service from the HMO's in January 2004.

Product	# of Claims	Total Units	Total Days	Units /Day	Total Cost	Total Clients	Cost/mg***
Protropin 10 mg	6	82	187	0.44	$37,514.03	2	$45.72
Nutropin AQ 5mg	256	2,391	4,138	0.58	$549,206.27	44	$45.95
Humatrope 5 mg	82	742	2,438	0.30	$117,609.95	12	$31.70
Nutropin 5 mg	29	215	431	0.50	$49,775.47	4	$46.30
Genotropin 5.8 mg	93	597	2,810	0.21	$135,333.23	14	$39.08
Humatrope 6 mg	96	248	2,607	0.10	$68,974.58	12	$46.35
Humatrope 12 mg	57	163	1,686	0.10	$90,797.13	12	$46.42
Genotropin 13.8 mg	53	390	789	0.49	$212,315.89	12	$39.45
Nutropin 10 mg	139	822	3,885	0.21	$379,329.73	20	$46.15
Humatrope 24 mg	26	115	827	0.14	$127,786.07	6	$46.30
Genotropin 0.2 mg	13	684	293	2.33	$4,740.19	2	$34.65
Genotropin 0.4 mg	6	182	182	1.00	$3,335.30	2	$45.81
Genotropin 0.6 mg	32	881	881	1.00	$24,136.94	7	$45.66
Genotropin 0.8 mg	9	252	252	1.00	$8,276.72	4	$41.05
Genotropin 1 mg	12	339	339	1.00	$15,707.12	3	$46.33
Genotropin 1.2 mg	6	168	168	1.00	$9,084.94	2	$45.06
Genotropin 1.4 mg	7	196	196	1.00	$12,558.14	2	$45.77
Genotropin 1.6 mg	37	1,034	1,034	1.00	$75,198.57	4	$45.45
Genotropin 1.8 mg	13	364	364	1.00	$30,321.85	3	$46.28
Genotropin 2 mg	1	28	28	1.00	$2,591.21	1	$46.27
Nutropin Depot	6	12	12*	0.03	$7,191.90	1	$44.39
Nutropin Depot	24	41	37*	0.04	$32,205.43	4	$43.64
Nutropin Depot	17	35	23*	0.04	$34,967.84	5	$44.40
Saizen 5 mg	20	194	387	0.50	$41,987.66	3	$43.29
Serostim 6 mg	8	224	224	1.00	$49,691.44	2	$36.97
Saizen 8.8 mg	26	233	503	0.46	$81,528.58	6	$39.76
Total	**1,074**	**10,632**	**24,721**	**0.43**	**$2,256,166.18**	**168****	**$43.39**

*Total days x 30 days. **Total unduplicated clients for FY04.
***Cost calculations include dispensing fee, but not rebate information.

Total Cost FY '04	**$2,256,166.18**
Total Cost FY '03	*$1,420,703.88*
Total Claims FY '04	**1,074**
Total Claims FY '03	*776*
Total Clients FY '04	**168**
Total Clients FY '03	*102*
Per Diem FY '04	**$84.16**
Per Diem FY '03	*$66.32*

PA Activity

Total petitions submitted in for this category during specified time period: 389

Approved 314
Denied 17
Incomplete 56
Overrides 2

Demographics

Age	Female	Male	Totals
0 to 9	24	34	58
10 to 19	26	68	94
20 to 34	3	5	8
35 to 49	3	2	5
50 to 64	1	2	3
65 to 79	0	0	0
80 to 94	0	0	0
95 and Over	0	0	0
Totals	**57**	**111**	**168**

Claims were reviewed to determine the age/gender of the clients.

Changes in FY '04

Nutropin depot (Genentech) was taken off the market in June. Six of the eight clients using the depot product have been changed to a daily injection. The last two are aware, but have not moved to another product yet.

Protropin (Genentech) has been phased out because of a market shift to Nutropin products. Clients have been switched to other products.

Changes in FY '05

A new product, TEV-TROPIN (GATE Pharmaceuticals), was introduced to the market in January, 2005. It is indicated for classic hGH deficiency.

Recommendations
The college of pharmacy has the following recommendation(s) for Fiscal Year 2004:

The College of Pharmacy recommends no changes to the Growth Hormone category at this time.

APPENDIX F

Annual Review of Antihypertensives - Fiscal Year 2004
Oklahoma Medicaid
February 2005

Product Based Prior Authorization – Antihypertensives

Four classes of antihypertensive drugs were included in the Product Based Prior Authorization program during fiscal year 2004. The classes are as follows:

- Calcium Channel Blockers (CCBs)
- ACE inhibitors (ACEIs)
- ACEI/CCB combinations drugs
- ACEI/HCTZ combination drugs

Criteria for Authorization

To qualify for a tier-2 medication, there must be:

- documented failure of a tier-1 drug of the same class
- contraindication to the tier-1 drugs
- previous stabilization on the tier-2 drug
- a unique indication for the tier-2 drug which the tier-1 drugs lack

Calcium Channel Blockers (CCBs)

Tier 1	*Tier 2*
diltiazem (Cardizem) diltiazem CD (Cardizem CD) diltiazem ER (Cardia XT, Diltia XT) **diltiazem (Tiazac, Taztia XT)** diltiazem SR (Cardizem SR) diltiazem XR (Dilacor XR) **isradipine (Dynacirc CR)** nifedipine (Adalat, Procardia) nifedipine CC (Adalat CC) nifedipine ER nifedipine XL (Nifedical XL, Procardia XL) nicardipine (Cardene) verapamil (Calan, Isoptin, Verelan) verapamil SR (Calan SR, Isoptin SR)	nicardipine (Cardene SR) diltiazem (Cardizem LA) verapamil (Covera HS) isradipine (Dynacirc) nimodipine (Nimotop) amlodipine (Norvasc) felodipine (Plendil) nisoldipine (Sular) bepridil (Vascor) verapamil (Verelan PM)

Angiotensin Converting Enzyme Inhibitors (ACEIs)

Tier 1	*Tier 2*
captopril (Capoten) **benezepril (Lotensin)** enalapril (Vasotec) enalaprilat (Vasotec IV) **fosinopril (Monopril)** lisinopril (Prinivil, Zestril)	perindopril erbumine (Aceon) quinapril (Accupril) ramipril (Altace) trandolapril (Mavik) moexipril (Univasc)

ACE/HCTZ Combinations

Tier 1	*Tier 2*
benazepril/HCTZ (Lotensin HCT) captopril/HCTZ (Capozide) enalapril/HCTZ (Vasoretic) lisinopril/HCTZ (Prinzide, Zestoretic)	fosinopril/HCTZ (Monopril HCT) moexipril/HCTZ (Uniretic) quinapril/HCTZ (Accuretic)

ACE/CCB Combinations

Tier 1	*Tier 2*
benazepril/amlodipine (Lotrel) **trandolapril/verapamil (Tarka)**	enalapril/felodipine (Lexxel)

Products Moved to Tier One During FY 2004 and 2005:

- isradipine (Dynacirc CR) during FY 2004
- diltiazem (Tiazac, Taztia XT) during FY 2005
- benezepril (Lotensin) during FY 2005
- fosinopril (Monopril) during FY 2004
- benazepril/HCTZ (Lotensin HCT) during FY 2004
- benazepril/amlodipine (Lotrel) during FY 2005
- trandolapril/verapamil (Tarka) during FY 2005

Utilization

For the period of July 2003 through June 2004, a total of 41,075 clients received antihypertensive drugs from the PBPA categories through the Medicaid fee-for-service program.

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*	
Total Clients	36,642	41,075	Increased	12.1 %
Total Claims	238,517	237,576	Decreased	0.40 %
Total Cost	$10,359,510.81	$9,093,828.34	Decreased	12.2 %
Total Days	9,208,713	9,681,912	Increased	5.13 %
Per Diem	$1.16	$0.94	Decreased	19.0 %

Comparison of Cost vs. Claims between Antihypertensive Classes

Class	*Cost*	*% Cost*	*Claims*	*% Claims*
Calcium Channel Blockers	$5,330,840.63	59%	92,579	39%
ACE Inhibitors	$2,488,411.59	27%	123,147	52%
ACE/HCTZ Combinations	$377,103.47	4%	13,741	6%
ACE/CCB Combinations	$897,472.56	10%	8,109	3%
Totals	$9,093,828.25	100%	237,576	100%

Calcium Channel Blockers

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2004**	13,604	64,441	3,239,352	2,649,721	$3,075,846.59	$0.95	$1.16
	FY 2003	12,430	66,316	3,172,428	2,577,857	$3,287,999.21	$1.07	$1.32
Tier 2	**FY 2004**	5,582	28,138	1,333,296	1,197,262	$2,254,994.04	$1.69	$1.88
	FY 2003	5,945	33,407	1,490,913	1,323,880	$2,294,995.24	$1.59	$1.79

ACE Inhibitors

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2004**	22,698	108,024	5,491,337	4,225,346	1,547,901.90	$0.28	$0.37
	FY 2003	18,568	96,905	4,810,613	3,606,212	$2,330,738.83	$0.50	$0.67
Tier 2	**FY 2004**	3,151	15,123	787,927	648,993	$940,509.69	$1.19	$1.45
	FY 2003	4,123	22,141	1,082,212	885,257	$1,175,266.56	$1.13	$1.38

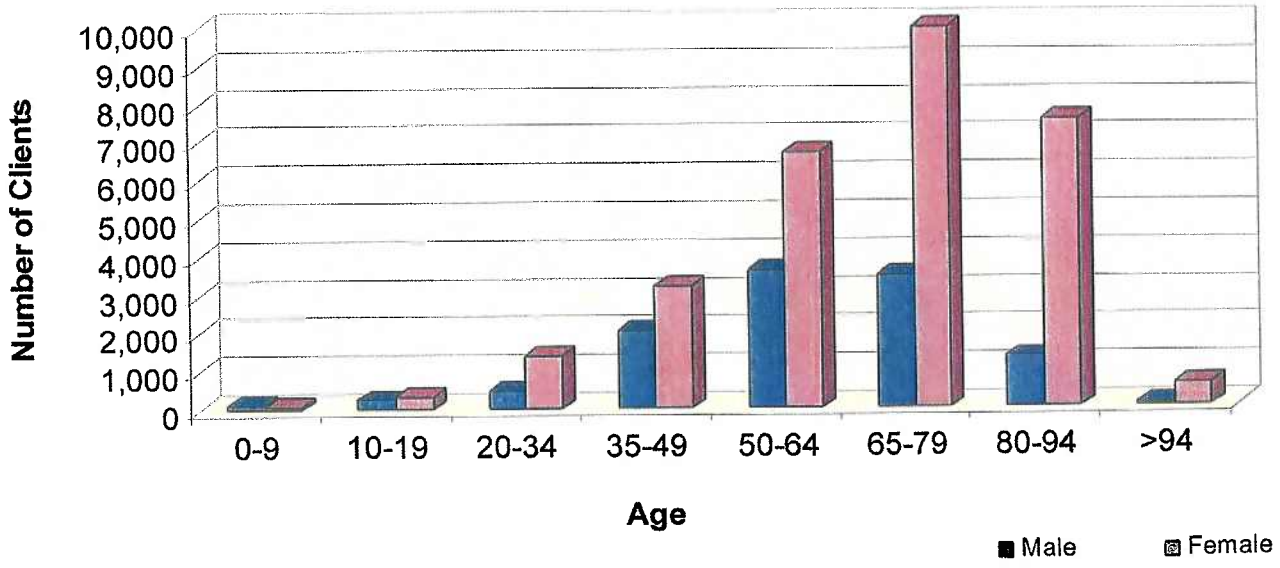
ACE Inhibitor/HCTZ Combinations

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2004**	3,004	12,948	681,816	566,434	$329,897.42	$0.48	$0.58
	FY 2003	2,005	9,905	507,114	410,008	$423,240.28	$0.88	$1.09
Tier 2	**FY 2004**	195	793	41,547	34,938	$47,206.14	$1.14	$1.35
	FY 2003	348	1,794	83,810	72,995	$81,248.40	$1.00	$1.15

ACE Inhibitor/Calcium Channel Blocker Combinations

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 2	**FY 2004**	1,613	8,109	419,183	359,218	$897,472.56	$2.14	$2.50
	FY 2003	1,452	8,049	397,862	332,504	$757,022.29	$1.96	$2.35

Client Age and Sex



Recommendations

The College of Pharmacy has the following recommendation(s) for Fiscal Year 2005:

- Continue to move drugs from tier-2 to tier-1 as they become available in generic and have a SMAC applied.

APPENDIX G

Follow-Up of Ondansetron (Zofran®) Utilization

Oklahoma Medicaid

February 2005

5-HT3 Receptor Antagonists Utilization

In September of 2004 a drug utilization review revealed that the 5-HT3 receptor antagonists were the most expensive class of anti-emetics in regards to cost per claim. This class accounted for only 30% of the claims, yet incurred 88% of the cost. Ninety-three percent of the 5-HT3 receptor antagonist claims were for Zofran®. The results of the drug utilization review suggested that Zofran® was utilized inappropriately for non-approved diagnoses. The following are the currently available 5-HT3 receptor antagonists and their FDA approved indications.

Medication		CINV*	RINV+	PONV@
Ondansetron[i]	(Zofran®)	Yes	Yes	Yes
Granisetron[ii]	(Kytril®)	Yes	Yes	Yes
Dolasetron[iii]	(Anzemet®)	Yes	No	Yes
Palonosetron[iv]	(Aloxi®)	Yes	No	No

*CINV – chemotherapy induced nausea and vomiting, +RINV – radiation induced nausea and vomiting, @PONV – post operative nausea and vomiting.

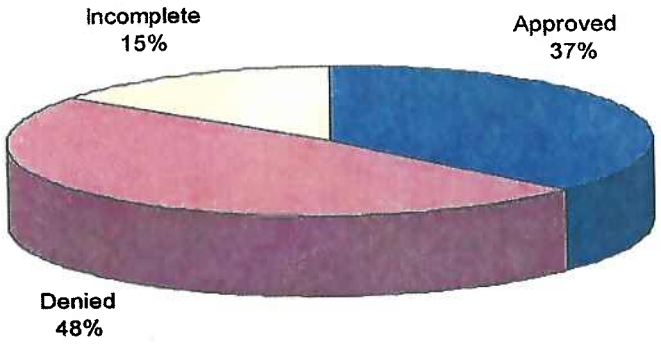
Zofran® Quantity Limit Override Activity

Implementation of quantity limits is among the cost-cutting methods utilized by various health-care systems. The Drug Utilization Review Board voted to approve quantity limits for certain medications covered by the Oklahoma Medicaid System in October 2003. In June 2004, quantity limits were implemented on all of the 5-HT3 receptor agonists, including a quantity limit of 12 tablets per 30 days for Zofran®. If a claim exceeded this amount a Quantity Limit Override petition may be submitted for further consideration. From June through December of 2004, a total of 78 clients accounted for 137 petitions within the class of 5-HT3 receptor antagonists. Of these petitions 95% were for Zofran®.

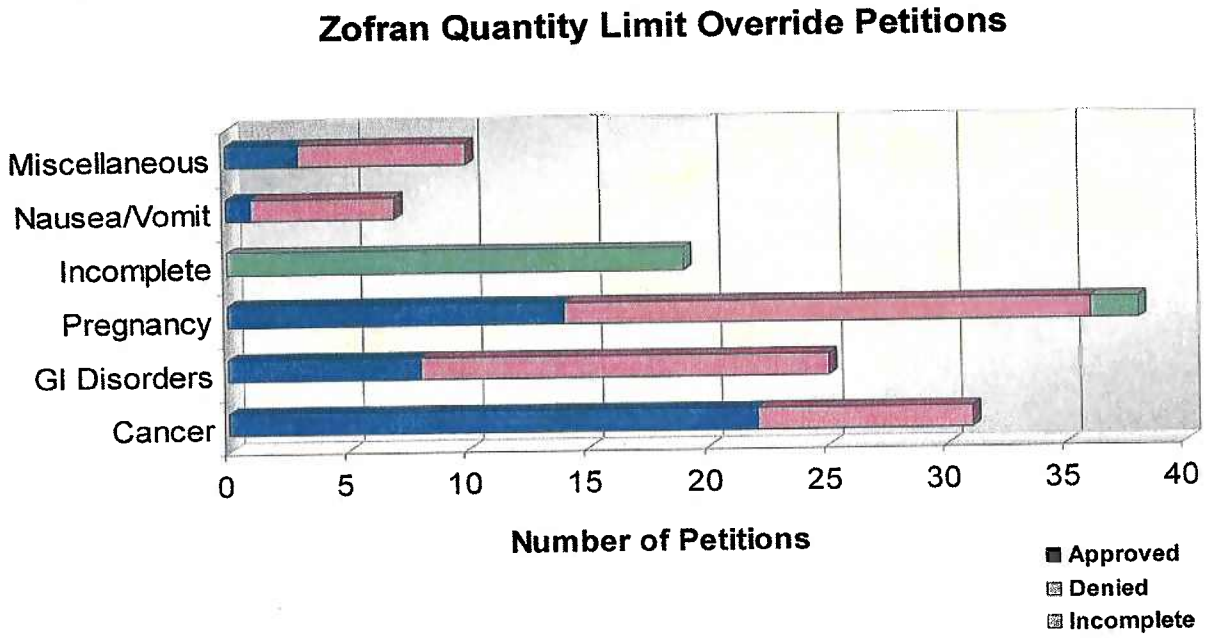
Zofran® Quantity Limit Override Petitions

Clients	*Petitions*	*Approved*	*Denied*	*Incomplete*
74	130	48	63	19

Status of Petitions Submitted for Zofran
June - December 2004



All Quantity Limit Override petitions submitted for Zofran® were manually reviewed to gather data regarding the diagnosis or reason for exceeding the quantity limit. The diagnoses and the status of the petitions are displayed in the following chart.



A total of 19 clients submitted 31 petitions with the diagnosis of cancer. Of those, all clients were ultimately approved except one client. That client's petition only requested 8 tablets per month and the pharmacy was advised on proper claim submission.

Impact of Quantity Limits on Utilization of Zofran®

Claims data were reviewed for Calendar Year 2004 to analyze the impact of quantity limits. Keep in mind the quantity limits were applied during June of 2004.

Zofran® Utilization for Calendar Year 2004

	Jan-Jun 2004	*Jul-Dec 2004*	*Percent Change*	
Total Clients	926	1008	Increased	8.85 %
Total Claims	1,794	1,744	Decreased	2.79 %
Total Cost	$957,805.36	$636,104.37	Decreased	33.6 %
Total Units	44,878	28,874	Decreased	35.6 %

Since the implementation of the quantity limit on Zofran®, only approximately 7% of the clients submitted a Quantity Limit Override petition. This may seem like a small impact, since the previous data showed a much greater percentage of inappropriate use. However, this data shows a 33% decrease in total costs paralleled by a similar decrease in total units. The results show that the quantity limit effectively decreases costs, while only minimally increasing petition load for providers and clients. On the other hand, Quantity Limit Override petitions offer flexibility for cancer clients with special treatment regimens requiring more than the monthly limit of Zofran®.

Availability of Generic Zofran®

Zofran® first entered the market in 1991. The patents for Zofran® oral tablets are expected to expire in 2005. Applications have been submitted from various pharmaceutical companies specializing in production of generic products. The generic form, ondansetron, is expected to be available in the latter parts of 2005 or early 2006.

Conclusion & Recommendation

The OU College of Pharmacy recommends no further action at this time. It appears that the implementation of the quantity limit on Zofran® has helped regulate inappropriate use of this product. The quantity limits have also reduced the number of tablets that can be filled per month, thereby reducing the overall costs, even if the inappropriate use is undetected. The upcoming availability of generic ondansetron will also help control costs for this drug category.

[i] GlaxoSmithKline Pharmaceuticals. Package literature Zofran®. May 2004.
[ii] Roche Pharmaceuticals. Package Literature Kytril®. June 2001.
[iii] Aventis Pharmaceuticals, Inc. Package Literature Anzemet®. October 2003.
[iv] Helsinn Healthcare. Package Literature Aloxi®. July 2003.

APPENDIX H

Annual Review of Plavix® - Fiscal Year 2004

Oklahoma Medicaid
February 2005

Category Criteria for FY '04

Plavix® requires prior authorization for all clients. Plavix® therapy will be approved for clients meeting approved diagnostic criteria that have failed aspirin therapy (due to either side effects or event recurrence), or have a documented aspirin allergy, or use Plavix® concomitantly with aspirin. The approved diagnoses are as follows:

- Recent stroke
- Recent myocardial infarction
- Established peripheral artery disease
- Acute coronary syndrome (unstable angina/non-Q-wave MI)
- Percutaneous coronary intervention with stent placement (aspirin trial not required)
- Transient ischemic attacks

Clients, with the exception of stent placement, are eligible for up to a year of therapy per authorization. Post stent placement clients are eligible for up to 90 days of therapy *per* authorization.

Utilization

For the period of July 2003 through June 2004, a total of 5,429 clients received Plavix® through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Plavix® 75 mg	24,721	1,015,766	1,007,189	1.02	$3,956,165.24	5,429	$ 3.92

Total Cost FY '04	**$3,956,165.24**	**- 1.3%**
Total Cost FY '03	*$4,009,980.32*	
Total Claims FY '04	**24,721**	**- 17.1%**
Total Claims FY '03	*29,827*	
Total Clients FY '04	**5,429**	**- 15.1%**
Total Clients FY '03	*6,396*	
Total Units FY '04	**1,015,766**	**- 11.1%**
Total Units FY '03	*1,142,384*	
Per Diem FY '04	**$3.93**	**+ 10.0%**
Per Diem FY '03	*$3.57*	

Total petitions submitted in for this category during specified time period:

Approved	*5,606*
Denied	1,656
Incomplete	2,247
Number of denied/incomplete petitions later approved	2,806

Claims were reviewed to determine the age/gender of the clients.

Age	Female	Male	Totals
0 to 9	0	0	0
10 to 19	0	3	3
20 to 34	12	12	24
35 to 49	215	148	363
50 to 64	863	501	1,364
65 to 79	1,513	608	2,121
80 to 94	1,175	272	1,447
95 and Over	95	12	107
Totals	**3,873**	**1,556**	**5,429**

Changes in Market Share, Per Diem, and Total Dollars for Therapeutic Category

Drug Name	Total Days/ Product FY '03	Total Days/ Product FY '04	Percent Change
Clopidogrel	1,124,086	1,007,189	**- 11.6%**
Dipyridamole	69,171	65,365	**- 5.5%**
Ticlopidine	21,154	19,430	**- 8.1%**
Cilostazol	163,185	167,866	**+15.1%**
Anagrelide	5,375	5,961	**+10.9%**
Dipyridamole/Aspirin	101,954	152,887	**+49.9%**

Drug Name	Per Diem FY '03	Per Diem FY '04	Percent Change
Clopidogrel	$3.57	$3.93	**+10.0%**
Dipyridamole	$0.80	$0.48	**- 40.0%**
Ticlopidine	$2.72	$1.93	**- 29.0%**
Cilostazol	$2.84	$3.13	**+10.2%**
Anagrelide	$19.35	$20.78	**+7.4%**
Dipyridamole/Aspirin	$3.21	$3.65	**+13.7%**

Drug Name	Total $/ Product FY '03	Total $/ Product FY '04	Percent Change
Clopidogrel	$ 4,009,980.32	$ 3,956,165.24	- 1.3%
Dipyridamole	$ 55,262.77	$ 31,603.21	- 42.8%
Ticlopidine	$ 57,603.39	$ 37,534.24	- 34.8%
Cilostazol	$ 463,716.09	$ 524,823.23	+13.2%
Anagrelide	$ 104,029.33	$ 123,858.36	+19.1%
Dipyridamole/Aspirin	$ 327,332.62	$ 558,229.62	+70.5%

Recommendations

Due to the increased use of drug eluting stents and changes in the American College of Chest Physicians recommendations for anti-platelet therapy post stent, the criteria should be amended. To decrease paperwork and improve access, the length of approval *per* authorization for stent patients should be extended to one year.

APPENDIX I

U.S. Food and Drug Administration

FDA Statement

FOR IMMEDIATE RELEASE
Statement
January 14, 2005

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

FDA Announces Dates for Public Meeting on Non-Steroidal Anti-Inflammatory Drugs

The Food and Drug Administration (FDA) has announced a joint public meeting of the agency's Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee to be held February 16, 17 and 18, 2005.

The committees will discuss the overall benefit-to-risk considerations (including cardiovascular and gastrointestinal concerns) for COX-2 selective non-steroidal anti-inflammatory drugs (NSAIDs) and related medicines.

Members of the public are encouraged to participate in this meeting. Interested persons may present data, information or views, orally or in writing, on issues pending before the committees. Oral presentations from the public will be scheduled between 1:00 p.m. and 3:00 p.m. on February 17. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should register to speak at the meeting before February 4, 2005. No registration is required for those only planning on attending the meeting.

The three-day meeting will be held at the Hilton Washington DC North, 620 Perry Parkway, Gaithersburg, Md. The proceedings will start at 8:00 a.m each day. Agendas and other background materials will be posted online no later than one business day before the meeting.

For more information regarding this meeting, including contact information for members of the public interested in making presentations or submitting written comments please go to: http://www.fda.gov/oc/advisory/accalendar/2005/cder12532ddd0216171805.html.

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THE HENRY J. KAISER FAMILY FOUNDATION kaisernetwork.org
Health Policy As It Happens

Kaiser Daily Health Policy Report

Monday, January 24, 2005

Prescription Drugs

Many People Taking COX-2 Inhibitors Could Have Been Prescribed Older, Less-Expensive Pain Medications, Study Indicates

Almost two-thirds of individuals who took COX-2 inhibitors in 2002 had a low risk for gastrointestinal problems -- the "main selling point" for the use of such medications -- according to a study published on Monday in the *Archives of Internal Medicine*, *USA Today* reports (Rubin, *USA Today*, 1/24). For the study, researchers from Stanford University and the University of Chicago examined data from two studies conducted by the National Center for Health Statistics and found that between 1999 and 2002 only 2% of participants were at "high risk" for gastrointestinal side effects and should have taken COX-2 inhibitors rather than older nonsteroidal anti-inflammatory drugs (Dai et al., *Archives of Internal Medicine*, 1/24). NSAIDs, such as ibuprofen and naproxen, are linked with gastrointestinal side effects, which prompted some physicians to favor COX-2 inhibitors after they entered the market in 1999. COX-2 inhibitors cost 10 to 15 times more than NSAIDs (Ritter, *Chicago Sun-Times*, 1/24). However, recent concerns about the safety of COX-2 inhibitors prompted Merck in September 2004 to voluntarily withdraw Vioxx from the market and Pfizer last month to end all direct-to-consumer advertisements for Celebrex (*Kaiser Daily Health Policy Report*, 1/18).

Additional Results

According to the new study, the percentage of participants at low risk for gastrointestinal side effects who received COX-2 inhibitors increased from 40% in 1999 to 66% in 2002 (*Archives of Internal Medicine*, 1/24). The study said that such individuals "could have obtained just as much pain relief" from NSAIDs, the *Chicago Sun-Times* reports (*Chicago Sun-Times*, 1/24). In addition, the study found that physicians prescribed COX-2 inhibitors to participants with congestive heart failure or liver or kidney dysfunction -- "conditions that should have prompted restricted use of the drugs," the *Los Angeles Times* reports (Maugh, *Los Angeles Times*, 1/22). Population studies have indicated that COX-2 inhibitors "generally are no better at relieving arthritis and other painful conditions than older anti-inflammatory drugs," the *Sun-Times* reports (*Chicago Sun-Times*, 1/24).

Analysis

Randall Stafford, a Stanford University internist and an author of the study, said that marketing efforts by Merck, which in 2000 spent $161 million to promote Vioxx, contributed to the increased number of COX-2 inhibitor prescriptions. Stafford said, "There's an assumption that newly approved drugs somehow have proven themselves to be better than what's already available" (*USA Today*, 1/24). G. Caleb Alexander, a University of Chicago professor and an author of the study, said, "What we saw was widespread, rapid adoption of an interesting and promising but expensive and largely untested medication by millions of people with little or nothing to gain from long-term use" (*Los Angeles Times*, 1/22).

Drugs and Chemicals of Concern

Hydromorphone
(Trade names: Dilaudid, Palladone™)

October, 2004
DEA/ODE/041001

Introduction

Hydromorphone is one of the most potent Schedule II opioid analgesic drugs available on the market. It is marketed as injectable ampoules (1, 2, and 4 mg/mL) and multiple dose vials (20 mL of 2 mg/mL), tablets (2, 4, and 8 mg) and suppositories (3 mg). On September 24, 2004, the Food and Drug Administration (FDA) approved for marketing an extended release capsule formulation (Palladone™) containing 12, 16, 24 and 32 mg hydromorphone. The prescriptions for hydromorphone products have increased by 106 percent, from about 470,000 in 1998 to 970,000 in 2003. Recently physicians have been prescribing hydromorphone as an alternative to OxyContin®. Aggregate production quota for hydromorphone as established by DEA for legitimate national needs increased from 766 kilograms in 1998 to 1,651 kilograms in 2003. Recent data indicate that the diversion and abuse of hydromorphone and its resultant health consequences are increasing. According to the Drug Abuse Warning Network (DAWN), the estimated number of emergency department (ED) episodes involving hydromorphone increased from 937 in 1996 to 2,667 in 2002.

Licit Uses

Hydromorphone is indicated for the relief of moderate to severe pain in patients where an opioid analgesic is appropriate. Like morphine, adequate doses of hydromorphone will relieve even the most severe pain. Palladone™, the extended release hydromorphone product, is indicated for the management of persistent, moderate to severe pain. Its use is restricted to opioid-tolerant patients requiring continuous, around-the-clock analgesia with a high potency opioid for an extended period of time (weeks to months) or longer. Patients need to swallow Palladone™ capsules whole because breaking, chewing, opening, dissolving or crushing of the capsules can lead to the absorption of potentially lethal doses.

Chemistry/Pharmacology

Hydromorphone, [4,5-epoxy-3-hydroxy-17-methylmorphinan-6-one, dihydrohydroxycodeinone; dihydromorphinone; dimorphone] is a semi-synthetic opioid agonist derived from morphine. Hydromorphone HCl will test positive for an opiate in the available field test kits. Pharmacological and toxic effects, clinical indications and contraindications, abuse and dependence liabilities of hydromorphone are essentially similar to those of other Schedule II opioid analgesics such as morphine, oxycodone, etc. In humans, the doses of 1.3 and 7.5 mg hydromorphone produces analgesia equivalent to that produced by 10 and 30 mg morphine when taken by the intramuscular and oral routes, respectively. The analgesic action of hydromorphone is perceived within 15 and 30 minutes following its administration through injection and oral routes, respectively. The analgesic action usually lasts for more than five hours. Palladone™, as an extended-release product, has a longer duration of action and requires only once a day administration. Similar to other

opioids, hydromorphone produces euphoria, feelings of relaxation, reduced anxiety, respiratory depression, constipation, papillary constriction, and cough suppression. Acute overdose of hydromorphone can produce severe respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, reduction in blood pressure and heart rate, and death. Pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from hydromorphone overdose. Palladone™ exposure has a risk of producing fatal respiratory depression in children, especially small children.

Illicit Uses

Hydromorphone abuse has been a continuing problem in the United States. Hydromorphone, similar to other Schedule II opioids, has a high abuse and dependence potential and produces tolerance. Prior to the current popularity of hydrocodone and oxycodone among drug abusers, low dose (2 and 4 mg) immediate release hydromorphone formulations (i.e., Dilaudid) were the leading opioid products for abuse and diversion during the 1970's and 1980's. As early as 1979, the DEA initiated a targeted investigation program for hydromorphone. Some street names for Dilaudid are Dust, Juice, Dillies, Smack, D and Footballs. The abuse of hydromorphone, similar to other prescription opioids, is mainly among rural and suburban populations. The large amount of hydromorphone (12 to 32 mg) present in Palladone™ makes this product highly susceptible for diversion and abuse by opioid abusers and doctor shoppers.

Illicit distribution

The main sources of hydromorphone diversion have been through forged prescriptions, "doctor-shoppers", unscrupulous pharmacists and physicians, and armed robberies and night break-ins of pharmacies and nursing homes. Recently, the diversion of Dilaudid has been reported by a number of DEA field offices including, New York, Chicago, St. Louis, San Antonio, Atlanta, Boston, Dallas, Detroit, Houston, Los Angeles, and Washington, DC. The street price of a 4 mg tablet of Dilaudid, the most common dosage strength reported, ranges from $5 to $100 per tablet depending on the region. According to the System to Retrieve Information from Drug Evidence, a Federal database for drug seizures, there were 39 and 31 hydromorphone seizure records in 2002 and 2003, respectively. State/local seizures of hydromorphone products as reported in the National Forensic Laboratory Information System were 621 and 485 in 2002 and 2003, respectively.

Control status

Hydromorphone products are in Schedule II of the Controlled Substances Act of 1970.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section, FAX 202-353-1263 or telephone 202-307-7183.

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Drugs and Chemicals of Concern

Tramadol (Trade Name: Ultram®)

July 2004
DEA/OD/ODE/200407/27

Introduction:

Tramadol was approved for marketing as a noncontrolled analgesic in 1995 under the trade name of Ultram®. Although the company initially claimed that this substance produced only very weak narcotic effects, recent data demonstrates that opioid activity is the overriding contributor to the drug's pharmacological activity. Because of inadequate product labeling and lack of established abuse potential, many physicians felt this drug was perfectly safe to prescribe to recovering narcotic addicts and to known narcotic abusers. As a consequence, a large number of reports of abuse and dependence have been received.

Licit Uses:

Tramadol is approved for the treatment of moderate to moderately severe pain in adults. Although FDA has still not recommended the scheduling of this substance in the Controlled Substances Act (CSA), a requirement necessary for DEA to place a substance under control, they have required the company to inform physicians about recent abuse data and to include new information under the "Drug Abuse and Dependence" section in the approved labeling. The labeling now contains the following language:

> "Ultram® has a potential to cause psychic and physical dependence of the morphine-type (μ-opioid). The drug is associated with craving, drug-seeking behavior and tolerance development. Cases of abuse and dependence on Ultram® have been reported. Ultram® should not be used in opioid-dependent patients. Ultram® can reinitiate physical dependence in patients that have been previously dependent or chronically using other opioids. In patients with a tendency to drug abuse, a history of drug dependence, or are chronically using opioids, treatment with Ultram® is not recommended."

Chemistry/Pharmacology:

Tramadol is a centrally acting synthetic opioid. Opioid activity is due to both the parent compound and the more active O-desmethylated metabolite. Apart from analgesia, tramadol may produce a number of symptoms including dizziness, somnolence, nausea, and constipation similar to other opioids.

Tramadol is well absorbed orally. It can be administered in 50 to 100 mg doses as needed for pain relief every 4 to 6 hours, not to exceed 400 mg/day. Seizures have been reported in patients receiving recommended doses but are more likely in high doses associated with abuse of this medication.

Poison Control data (2002 AAPCC Annual Report) indicates that there were 2,400 exposures of tramadol reported to poison control centers. Of those, 108 resulted in a major medical outcome and 8 resulted in death.

Illicit Uses:

Tramadol is abused for its opiate effects. The Drug Abuse Warning Network (DAWN) is a database which provides data on drug related episodes reported by hospital emergency rooms. In 2002, there were 1,714 episodes for tramadol and a total of 7,890 episodes from 1998 through 2002. DAWN medical examiners reported that tramadol was involved in 95 drug-related deaths in 2002 and a total of 382 deaths from 1998 through 2002.

The National Forensic Laboratory System (NFLIS) and System to Retrieve Drug Evidence (STRIDE) are both DEA databases that collect scientifically verified data on analyzed samples in state/local and DEA forensic laboratories, respectively. In 2003, there were 267 exhibits of tramadol in NFLIS and 2 exhibits in STRIDE. These relatively small numbers are most probably a reflection of the uncontrolled status of tramadol in the U.S.

User Population:

The current pattern of tramadol abuse in the US involves street drug addicts, chronic pain patients, and health professionals. The lack of control and lack of urine toxicology screen for this medication have probably contributed significantly to the availability of this drug.

Illicit distribution:

Like other legal pharmaceuticals with abuse potential, diversion of this medication occurs in a number of ways including prescription fraud. As an uncontrolled substance, there are no CSA regulations regarding manufacturing, distribution, or prescription of this medication.

Control status:

Tramadol is not controlled under the CSA but is under review for possible control.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section, FAX 202-353-1263 or telephone 202-307-7183.

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