Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

December 14, 2005 @ 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 – December 14, 2005**

DATE: December 7, 2005

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

Enclosed are the following items related to the December 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 Xopenex HFA ™ – **See Appendix C.**

Action Item – Vote to Prior Authorize Darvocet A500™ and Balacet 325™ – **See Appendix D.**

60 Day Notice to Prior Authorize Nasal Allergy Products – **See Appendix E**

Review and Discuss Muscle Relaxant Utilization – **See Appendix F**

Action Item – Annual Review of Non-Steroidal Anti-Inflammatory Drugs – **See Appendix G**

Action Item – Annual Review of Anti-Ulcer Drugs – **See Appendix H.**

Action Item – Annual Review of Forteo® and Osteoporosis Utilization Review – **See Appendix I.**

New Product Reviews and Notices – **See Appendix J.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – December 14, 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. November 9, 2005 DUR Minutes – Vote
B. Memorandum of November 9, 2005 DUR Recommendations
C. Provider Correspondence

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

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

A. Retrospective Drug Utilization Review for August 2005
B. Medication Coverage Activity Audit for November 2005
C. Help Desk Activity Audit for November 2005

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

5. Action Item – Vote to Prior Authorize Xopenex HFA™ – See Appendix C.

A. Product Summary
B. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Darvocet A500™ and Balacet 325™ – See Appendix D.

A. Product Summary
B. COP Recommendations

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

7. 60 Day Notice to Prior Authorize Nasal Allergy Products – See Appendix E.

A. Recommendations
B. Potential Economic Impact

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

8. Review and Discuss Muscle Relaxant Utilization – See Appendix F.

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

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

9. Action Item – Annual Review of Non-Steroidal Anti-Inflammatory Drugs – See Appendix G.

A. Current Prior authorization Criteria
B. Utilization Review
C. Market Changes to Class
D. COP Recommendations

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

10. Action Item – Annual Review of Anti-Ulcer Medications – See Appendix H.

A. Product Information
B. Utilization Review
C. Market Changes to Class
D. COP Recommendations

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

11. Action Item – Annual Review of Forteo® and Osteoporosis Utilization Review – See Appendix I.

A. Product Information
B. Utilization Review
C. Market Changes to Class
D. COP Recommendations

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

12. New Product Reviews and Notices – See Appendix J.

A. New Product Summaries

13. FDA and DEA Updates – See Appendix K.

14. Future Business

A. Antipsychotic Utilization Review
B. Anticonvulsant Review
C. Contraceptive Utilization Review
D. Antidiabetic Utilization Review
E. Antiinfectives Utilization Review
F. Analgesic/Narcotic Utilization Review
G. Annual Reviews
H. New Product Reviews

15. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of NOVEMBER 9, 2005

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Dorothy Gourley, D.Ph.	X	
Kyle Hrdlicka, D.O.		X
Dan McNeill, Ph.D., PA-C	X	
Clif Meece, D.Ph.	X	
James Rhymer, D.Ph	X	
Dick Robinson, D.Ph., Vice-Chair	X	
Thomas Whitsett, M.D., Chair		X

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

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A./ Pharmacy Operations Manager	X	
Mike Fogarty, J.D., M.S.W./Chief Executive Officer		X
Nico Gomez/Director of Governmental & Public Affairs		X
Lynn Mitchell, M.D., M.P.H/Director of Medical Services		X
Nancy Nesser, D.Ph., 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:

Lana Stewart, Merck	Mike German, Sanofi-Aventis	Michelle Martinez, Santaris
Dale Roof, Takeda	Jim Delatte, Takeda	Sandra O. Brazil, Sanofi-Aventis
Ron Benjamin, Schering-Plough	Daniel Garcis, Takeda	James Osborne, GSK
Carol Beyes, Alpharma	Jorge Nassar, Bristol-Myers Squibb	Justin Springfield, Sepracor
Jerry Gomez, King Pharma	Ray Carter, King Pharma	Rebecca Waldrop, Sanofi-Aventis
Jerry Witcher, Forest Labs	Greg Hoke, Wyeth	Kimberly Williams, Schering-Plough
Jim Dunlap, Eli Lilly	Matt Anderson, Alpharma	Chris Caggrao, TAP

PRESENT FOR PUBLIC COMMENT:

Marain Pawk, M.D., Sanofi-Aventis	Agenda Item 6
Dr. Fran Kaiser, Merck	Agenda Item 8

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

1A: Roll Call

Dr. Robinson 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. Robinson acknowledged speakers for Public Comment.

ACTION: NONE REQUIRED.

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

3A: September 14, 2005 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report for July 2005

4B: Medication Coverage Activity Report: September, October 2005

4C: Help Desk Activity Report: September, October 2005

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

ACTION: NONE REQUIRED.

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

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

Motion made by Dr. Meece to approve COP recommendations; seconded by Dr. Gourley.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE AMBIEN CR™**

For Public Comment, Dr. Marain Pawk: *Good evening everybody. It's my pleasure to be here tonight to talk with you about Ambien CR. It's a new drug on the market for insomnia. Before I proceed with. . . I need just to clarify one issue when we talk about insomnia (unintelligible) you have different type of insomnia so we have to give the right medication for the right patient. In general we have four types. We have sleep onset insomnia, sleep latency insomnia. We have early awakening and poor sleep. In general 50 to 60% of patients with insomnia, they would be complaining of waking up in the middle of the night and having difficulty falling back asleep. And these patients need something to cover the whole night in term of sleep. Old Ambien basically was good for sleep onset insomnia because of the half life was 2.5 hours. Patients (unintelligible) from here and in thirty minutes they fall asleep and there is no problem for those patients who have only sleep onset insomnia because they don't have any problem cruising through the night. However for those patients complaining of sleep maintenance problem, those patients used to suffer a lot because (unintelligible) one, two, three a.m. these patients would wake up and did not have anything to help them fall back asleep. That's why Ambien CR was formulated. We still have the same molecule so it's not another molecule or something (unintelligible) been formulated in way that now comes in dual layer. We have an outer layer (unintelligible) quickly as the old Ambien and 7.5 will induce sleep as the old Ambien, however (unintelligible) you will see another 5 mg will be slower release so instead of having a drop in the level of Ambien in the plasma and the patient with poor sleep maintenance will wake up now we have a higher level of Ambien in the patient blood and so the patient will benefit from two to three hours extra sleep. As you see on the second page down, the second, basically graph, you don't see (unintelligible) Ambien time to, the level of Ambien time to drop after 24 hours but with Ambien CR, this level would continue to be at the higher level so the patient will benefit from having more sleeping hours during the night. Ambien CR has been tested against placebo and in clinical trials patients who took Ambien CR have higher sleep efficiency and sleep efficiency means the total sleep time divided by the total time in bed, they did have less awake after sleep onset and didn't have the same sleep loss efficiency so they were able to fall asleep quickly, to cruise through the night, to wake up the second day with a minimal residual effect. Actually, clinical trials show also that compared with placebo, there was no significant daytime sleepiness after eight hours of the medication one was given. Patients also, there was other trials that compared Ambien and Ambien CR in terms of sleep maintenance. Again the sleep maintenance and the patients who took Ambien, they had a hard time to fall back asleep, however the patients who took Ambien CR they were able to fall back asleep after scheduled awakening. So those patients were awake from that sleep, active awakening at three, four and five hours and when they were asked to go back to sleep the patient who took Ambien CR it was easy for him to go back to sleep. The patient who took Ambien, they were unable to do that after three, four and five hours because they did not have any Ambien in their blood. In terms of safety Ambien CR is a category C, it did not show on the clinical trials that it will affect any psychomotor test. In term of price, has the same price if not cheaper than old Ambien. Any questions from the Board?*

Materials included in agenda packet; presented by Dr. Gorman.
Dr. Gourley moved to approve COP recommendations as submitted; seconded by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **ANALYSIS OF NON-DUAL CLAIM UTILIZATION**
Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 8: **REVIEW AND DISCUSS ASTHMA UTILIZATION**
For Public Comment, Dr. Fran Kaiser: *Good evening. I'm Dr. Fran Kaiser. I'm Executive Medical Director with Merck and Clinical Professor of medicine (unintelligible) Southwestern. I know you're about to be talking about asthma utilization but I think it's important to remember that none of the medications for asthma are going to work unless people take them and take them appropriately. Asthma is one of the most common chronic diseases in the United States affecting over twenty million Americans including five million school children. And people with uncontrolled asthma miss school, work, need to curtail their exercise activities of daily living and those that miss school who are of school age miss 14 million days, not to mention what happens to the productivity of the parents who are stuck taking care of them. Asthma exacerbations lead to increasing numbers of emergency department visits, hospitalization and death. In the year 2000, asthma accounted for nearly two million ER visits, over 500,000 hospitalizations and over 1,500 deaths. And children have the highest hospitalization rate among people with asthma. And from a health economic standpoint in the year 2000, asthma accounted for 14.5 billion dollars in direct costs for an estimated twenty million patients, but in contrast, the direct cost for forty million patients with allergic rhinitis was 4.5 billion. Patients who have mild disease, mild asthma, make up the largest group of patients who have persistent asthma. And up to 65% of children are classified as having mild persistent asthma. The NHLBI guidelines which were last updated by the expert panel in 2002 recommended low dosed inhaled corticosteroid therapy as the preferred treatment for patients with mild persistent asthma, but recognizing that adherence to controlling therapies absolutely critical to the disease control. The expert panel also recommended alternative goals including leukotriene receptor antagonists for those patients who are unable or unwilling to use inhaled steroids. Montelukast or Singulair is a leukotriene antagonist that is indicated for prophylaxis in chronic treatment of asthma in both adults and pediatric patients twelve months of age and older. Singulair results have indicated for the relief of symptoms and seasonal allergic rhinitis which also may be a comorbid factor in asthma in both adults and pediatric patients two years of age and older and for perennial allergic rhinitis treatment in adult and pediatric patients six months of age and older. The efficacy of Singulair as an asthma controller was demonstrated in adults by large numbers of studies including two double blind placebo controlled trials in RPI in over 1,500 patients with mild to moderate asthma.And these studies showed significant increase in lung function, significant decrease in asthma symptoms compared to placebo. And in children with asthma, the results of double blind controlled studies were consistent with the findings of the adult studies. In addition, two additional trials revealed that the additional of Singulair to inhaled corticosteroid therapy resulted in further lung improvement, further improvement in lung function tests and symptom control and actually allowed for the reduction in dose or discontinuation of inhaled corticosteroid therapy in patients who had asthma. The adverse profile for Singular is comparable to that of placebo. The most common adverse experiences are headaches. Singulair does not alter the growth velocity in children and Singulair is supplied four different appropriate dose forms including granules and chewable tablets for children, and can be taken without regard to meals. The inability or unwillingness to use inhaled steroids which clearly do benefit some patients for those that can take it, can adversely affect appearance and lead to uncontrolled asthma, especially in pediatric populations. Having options for asthma, especially for children, is important and unrestricted access to Singulair provides both efficacious and easy to use alternative and is part of the alternative guideline for moderate asthma therapy, according to the NHL (unintelligible), so we ask that you give Singulair some consideration in your deliberations on asthma. Thank you.*
Materials included in agenda packet; presented by Dr. Flannigan.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF NON-SEDATING ANTIHISTAMINES**
Materials included in agenda packet; presented by Dr. Gorman.
Dr. McNeill moved to approve COP recommendations as submitted; seconded by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 10: **REVIEW AND DISCUSS NASAL ANTI-ALLERGY PRODUCTS**
Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **NEW PRODUCT REVIEWS AND NOTICES**
Materials included in agenda packet; presented by Drs. Flannigan, Moore, and Gorman.
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: **Antipsychotic Utilization Review**
13B: **Anticonvulsant Review**
13C: **Muscle Relaxant Review Review**
13D: **Osteoporosis Review**
13E: **Contraceptive Utilization Review**
13F: **Antidiabetic Utilization Review**
13G: **Antiinfectives Utilization Review**
13H: **Annual Reviews**
13I: **New Product Reviews**
Materials included in agenda packet; submitted by Dr. Graham.
ACTION: NONE REQUIRED.

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

The University of Oklahoma
College of Pharmacy

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

Memorandum

Date: November 11, 2005

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 November 9, 2005.

Recommendation 1: Vote to Prior Authorize Rozerem™

MOTION CARRIED by unanimous approval.

- Include Rozerem™ in the prior authorization category with anxiolytics and hypnotics.
- Place a quantity limit on Rozerem™: 30 units for a 30 day supply.

Recommendation 2: Vote to Prior Authorize Ambien CR™

MOTION CARRIED by majority approval.

- Require prior authorization for Ambien CR™ from first date of use. Must have documented reason for use of this product over the immediate release zopidem.
- Place a quantity limit on Ambien CR™: 30 units for a 30 day supply.

Recommendation 3: Annual Review of Non-Sedating Antihistamines

MOTION CARRIED by unanimous approval.

Addition of desloratadine syrup to Tier 1 consistent with cetirizine criteria and the following changes once SMAC pricing has been applied to fexofenadine:

Prior authorization is approved up to 90 days for non-chronic conditions, and may be approved for over 90 days for conditions which require continuous coverage throughout the year.

- Tier 2 non-sedating antihistamine only products are covered after a previous trial failure with an over-the-counter antihistamine and fexofenadine. A 14 day trial of over-the-counter loratadine and fexofenadine is required prior to coverage of a tier 2 product for all age groups.
    - Trials should have been in the last month and be of adequate dose and duration,
    - Over-the-counter loratadine and fexofenadine is a covered benefit for clients under the age of 21 years without prior authorization, and
    - For clients 21 years of age or greater, loratadine and fexofenadine is available with prior authorization AFTER documented over-the-counter failure of a non-loratadine product.
- For clients six months to two years of age, cetirizine syrup and desloratadine syrup are available without prior authorization.
- Diagnosis must be for a chronic allergic condition.
- Clinical exceptions include asthma and COPD.
    - For diphenhydramine, exceptions are made for EPS and insomnia.

Tier 1: OTC loradatine, fexofenadine, cetirizine sryup & desloratadine syrup (6 mo to 2 yrs)
Tier 2: cetirizine, desloratadine, Singulair

Nancy

Santiago Reyes, M.D.

Respiratory Diseases of
Children and Adolescents

Suite 330 Baptist Medical Plaza Bldg. D
3366 N.W. Expressway
Oklahoma City, Oklahoma 73112
Telephone (405) 945-4495
Fax (405) 945-4376

October 5, 2005

Linn Mitchell, M.D.
Medical Director of Oklahoma Medicaid Program
4545 N. Lincoln
Oklahoma City, OK 73105
fax: 530-3315

Dear Dr. Mitchell,

The issue of approval for synagis to be used as a very effective medication for RSV prophylaxis should be based on evidence demonstrated in the medical literature and be used in those patient that have increased susceptibility and risk related not only to the low gestational age but as well as related to different exposures who will make the patient more prone to the level which could become a fatal infection. Iris study by Carbonell clearly demonstrated risk factors which would increase the possibility of hospitalization of a child at risk. Some of the factors are lack of breast feeding, exposure to cigarette smoke, school age sibling, crowdedness in the home environment as well as family history of wheezing. The study by Anderson published in 1988 also demonstrated very similar risks factors in addition to low maternal education. Exposure to cigarette smoke constitutes, in my point of view, a very important risk factor for these children to develop RSV infection and possible hospitalization. These risk factors increase the chance of a child to be hospitalized between three and four times.

Hopefully, the DUR board will take into consideration this factor so more children in our state can be protected against RSV. Although synagis is an expensive medication it is very cost effective when you analyze the expenses of hospitalization in these high risk patients.

Sincerely yours,

Santiago Reyes de la Rocha, M.D.

cc: Nancy Nesser, DPH, JD.
Medicaid Pharmacy Director

Paula Rott
Medical Director Blue Links
Blue Cross and Blue Shield of Oklahoma

APPENDIX B

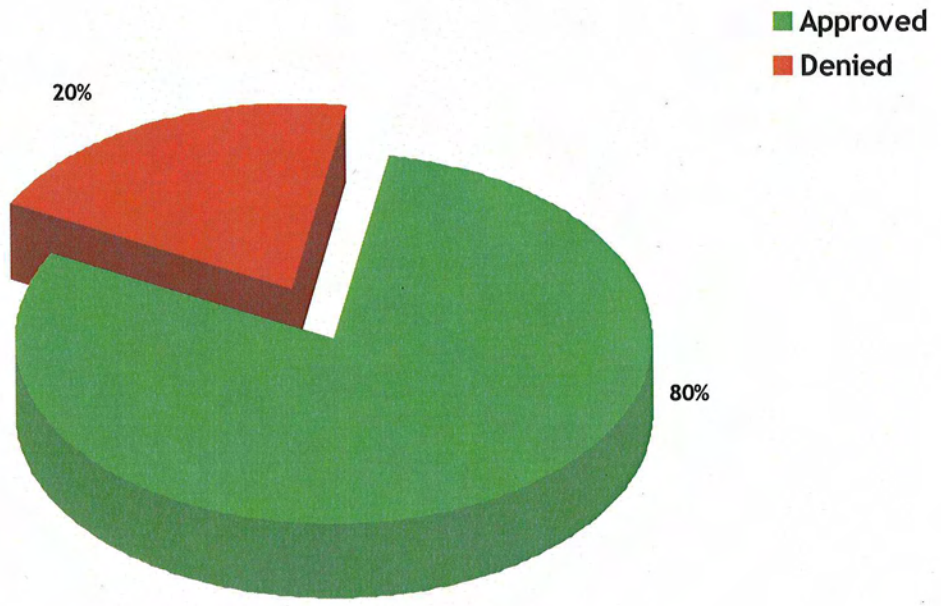
Retrospective Drug Utilization Review Report

Claims Reviewed for August 2005

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	113,048	114,582	956,808	37,993
Limits which were applied	Established, Major, age 22-50	Narcotics, Abuse potential, Males, age 22-35	Contraindicated, age 22-150, with Epilepsy	High dose, Direct Muscle Relaxants
Total # of messages after limits were applied	121	309	75	3
Total # of clients reviewed after limits were applied	121	187	57	3

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
178	45	70	17

PRIOR AUTHORIZATION ACTIVITY REPORT
November 2005



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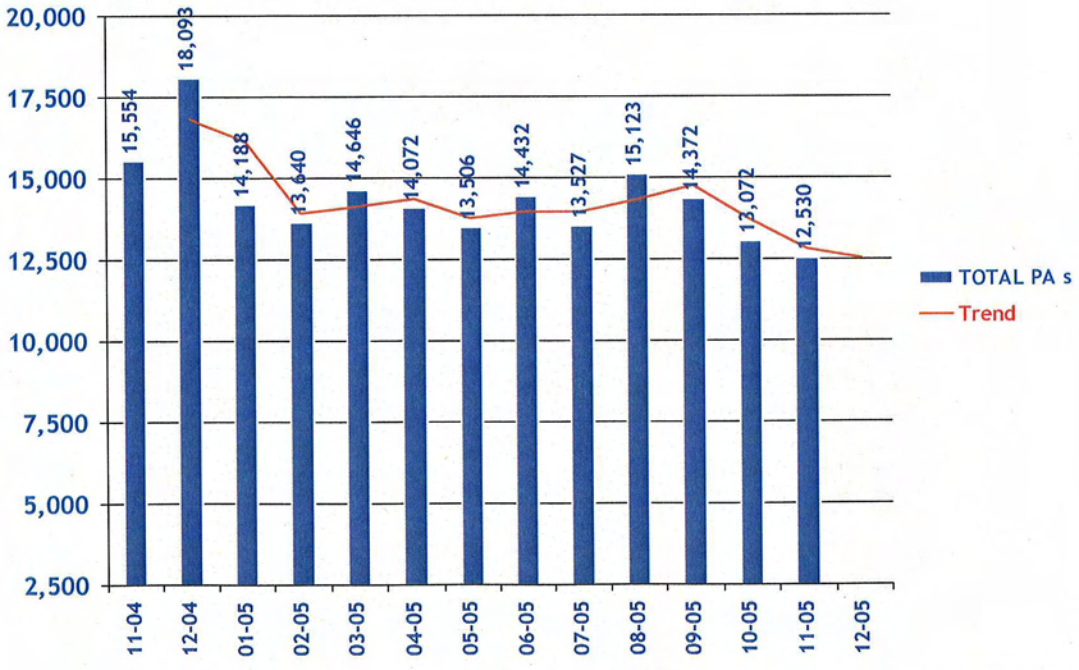
PRIOR AUTHORIZATION REPORT
November 2004 - November 2005



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Activity Audit for

November 01 2005 Through November 30 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.	21		2915		1014		42		843		184		38		5		103		644		20		307		
Den.		3		226		380		3		173		231		56		1		172		38		2		195	
Average Length of Approvals in Days	21		95		95		157		195		161		109		20		150		184		73		124		

Changes to existing PA's	1013
Total (Previous Year)	15554

*** Denial Codes**

762 = Lack of clinical information	11.19%
763 = Medication not eligible	1.55%
764 = Existing PA	1.15%
772 = Not qualified for requested Tier	10.39%
773 = Requested override not approved	16.83%

SUPER PA's

Admitted to Nursing Home	109
Early Refill Attempts	45953
Dosing Change	575
High Dose	31
Lost/Broken Rx	141
Stolen	25
Other	71
Wrong D.S. on Previous Rx	12
Quantity vs. Days Supply	1710
Brand	160
-- Approved	70
-- Denied	42

Monthly Totals

	Number	Percent of Total
Approved	7932	63.30%
Additional PA's	8	0.06%
Emergency PA's	11	0.09%
Duplicates	607	4.84%
Incompletes	1970	15.72%
Denied *	2002	15.98%
Total	12530	100.00%

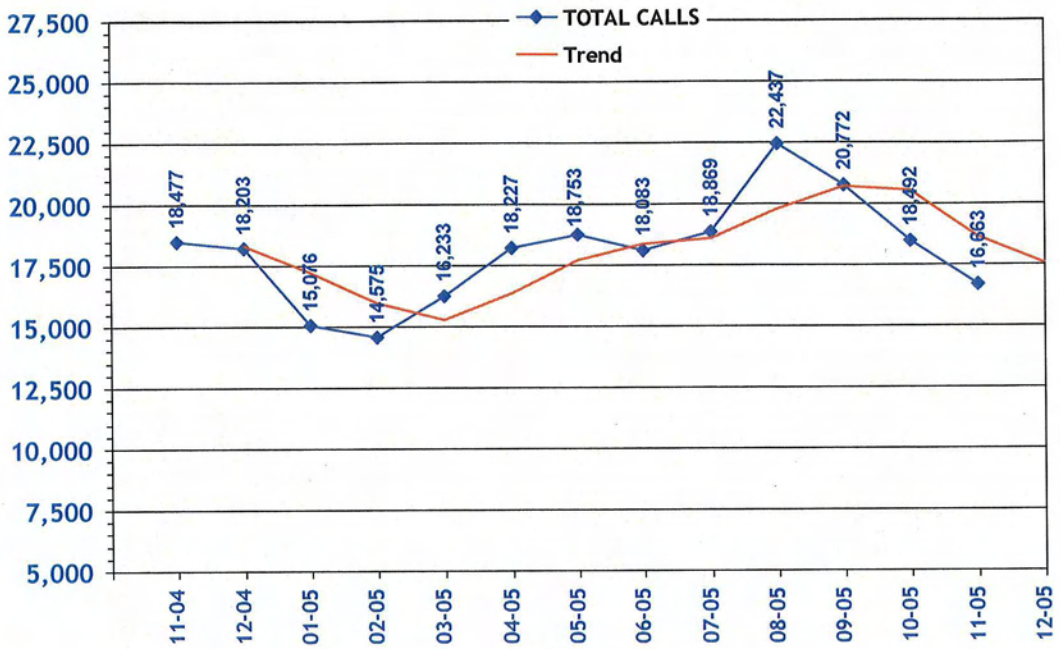
Daily Average of 596.67 for 21 Days

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.)

CALL VOLUME MONTHLY REPORT
November 2004 - November 2005



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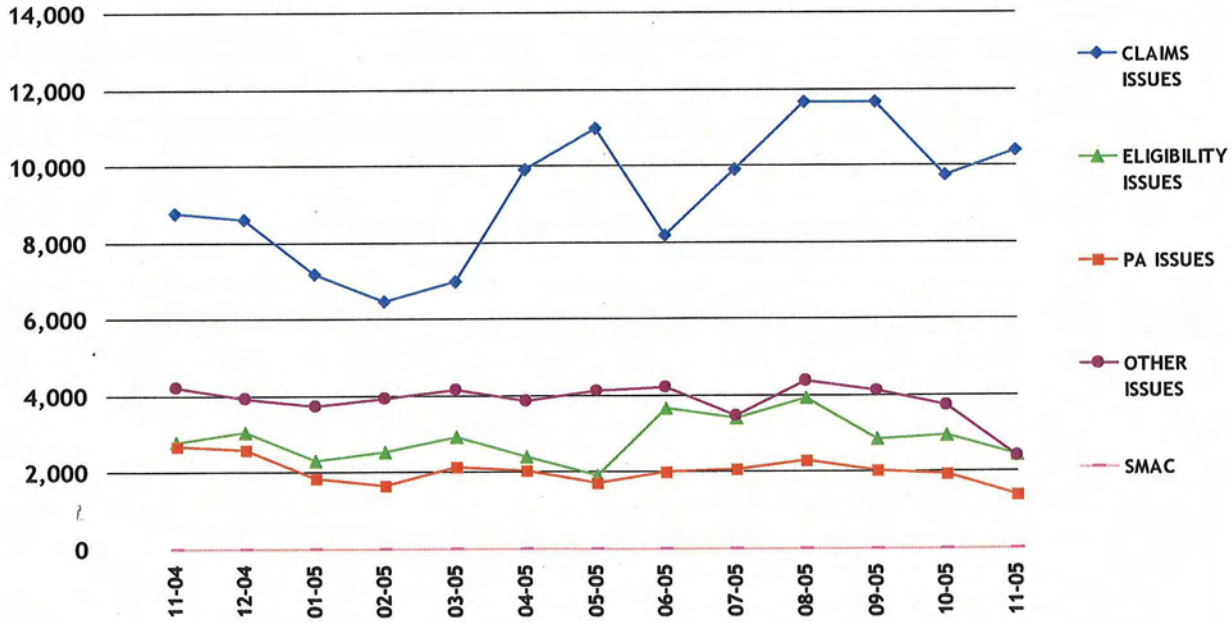
CALL VOLUME ISSUES
November 2004 - November 2005



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APPENDIX C

Vote to Prior Authorize Xopenex HFA™ (levalbuterol)

Oklahoma Medicaid
December 2005

Manufacturer Sepracor
Classification Short-acting inhaled bronchodilator
Status: prescription only

Summary

Levalbuterol tartrate, (R)-albuterol tartrate, is currently available as an inhalant solution and has been approved by the FDA to be marketed as an HFA inhalation aerosol. The metered-dose inhaler is approved for the treatment or prevention of bronchospasm in adults, adolescents and children 4 years of age and older with reversible obstructive airway disease. The product is expected to be available by the end of 2005. Each actuation will deliver 59 mcg of levalbuterol tartrate (equivalent to 45 mcg of levalbuterol free base). The 15 gm canister will provide 200 actuations per unit. Dosing for adults and children is 2 inhalations every 4 to 6 hours (1 inhalation every 4 hours may be sufficient).

Recommendation

The College of Pharmacy recommends Xopenex HFA™ be included with Xopenex® Inhalation Solution to require prior authorization for chronic use.

- Use of this product in excess of 90 days of therapy in a 360 day period will require prior authorization.
  - In the prior authorization request, the prescriber should explain why the client is unable to use long acting bronchodilators and/or inhaled corticosteroid (ICS) therapy for long-term control as recommended in the NAEPP guidelines. Also the need for use of this product over an albuterol MDI should be stated.
  - Clinical exceptions will be made for clients with COPD.
- A quantity limit of 30 g (2 units) every 30 days will also apply.

Product	Size	EAC/SMAC*
Xopenex HFA™	15 gm	$ 43.78
Proventil® HFA	6.7 gm	$ 38.69
Ventolin® HFA	18 gm	$ 33.11
Albuterol HFA	8.5 gm	$ 32.31
Albuterol MDI	17 gm	$ 3.91

*Price per container.

References

1. Prescribing Information: Xopenex HFA™ (levalbuterol tartrate); Sepracor Inc., Marlborough, MA; March 2005.

APPENDIX D

Vote to Prior Authorize:
Darvocet A500™ (Propoxyphene napsylate/acetaminophen)
Balacet 325™ (Propoxyphene napsylate/acetaminophen)
Oklahoma Medicaid
December 2005

Manufacturer Darvocet A500™ - aaiPharma Inc.
Balacet 325™ - Cornerstone BioPharma, Inc.

Classification FDA classification: Narcotic, mixed
Status: prescription only
DEA status: Schedule IV

Summary
Propoxyphene /acetaminophen combine a peripherally acting analgesic (acetaminophen) and a centrally acting opioid agonist (propoxyphene) in a fixed dose. Balacet 325™ contains 100 mg propoxyphene and 325 mg of acetaminophen. Darvocet A500™ contains 100 mg propoxyphene and 500 mg of acetaminophen. Dosing of both drugs is 1 tab q4h, not to exceed 6 tabs/day. The dose limiting component is the propoxyphene at 600 mg/day. Acetaminophen, in any form, should not exceed 4 g/day.

Recommendations
- Prior authorize Darvocet A500™ and Balacet 325™
  - Criteria:
    - Documented need to restrict acetaminophen use
    - Concurrent use of acetaminophen-containing products
    - Documented renal insufficiency or hepatic impairment
- Place a quantity limit of 180/30 on each of the products.

Drug	Propoxyphene	Acetaminophen	Reimbursement
Darvocet N-100®	100 mg	650 mg	$0.52
Propoxyphene/ acetaminophen	100 mg	650 mg	$0.06 (SMAC)
Darvocet N-50®	50 mg	325 mg	$0.58
Propoxyphene/ acetaminophen	50 mg	325 mg	$0.11 (FMAC)
Darvocet A500™	100 mg	500 mg	$1.10
Balacet 325™	100 mg	325 mg	$1.04
Darvon-N®	100 mg	n/a	$0.89

References

1. MICROMEDEX(R) Healthcare Series Vol. 125 expires 9/2005

APPENDIX E

60 Day Notice of Product Based Prior Authorization of Nasal Allergy Products and Potential Economic Impact

Oklahoma Medicaid
December 2006

Recommendation

The College of Pharmacy recommends the addition of the Nasal Allergy Products to the Product Based Prior Authorization program. The following Tier-1 Drug List has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of clients. The College of Pharmacy recommends this list to the Drug Utilization Review Board for consideration before approval and referral to the Oklahoma Healthcare Authority for final limitations or additions based on cost effectiveness.

Nasal Allergy Products	
*Tier One**	*Tier Two*
Flonase®	Nasonex®
flunisolide	Beconase® AQ
Ipratropium bromide	Nasacort® AQ
	Rhinocort® AQ
	Astelin®

*Brand products are subject to the Brand Name Override where generic is available.

The following criteria are recommended for approval of a tier-2 product:

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

Total Reimbursed for Nasal Allergy Products – 4th Qtr FY '05

Class	Total Claims	Total Reimbursement
Anticholinergics	209	$ 5,379.40
Antihistamines	1,226	$ 77,552.06
Corticosteroids	19,323	$ 1,364,921.13
Total	**20,758**	**$ 1,447,852.59**
Total Non-Duals	**16,577**	**$ 1,166,983.13**

Client Demographics - 4th Qtr FY '05

Age	Female	Male	Totals
0 to 9	2,111	2,739	4,850
10 to 19	2,270	2,320	4,590
20 to 34	821	136	957
35 to 49	564	166	730
50 to 64	478	176	654
65 to 79	35	14	49
80 to 94	20	5	25
Totals	**6,299**	**5,556**	**11,855**

Market Share and Cost for Non-Duals

Product	Total Claims	Total Days	Total Reimbursement	% Market Share	% Cost
Beconase AQ	73	2,142	$ 5,638.76	0.40%	0.48%
Rhinocort AQ	1,515	50,499	$ 116,153.32	9.35%	9.95%
Flunisonlide 0.025%	424	12,589	$ 18,482.72	2.33%	1.58%
Nasarel 0.25%	50	1,344	$ 2,651.50	0.25%	0.23%
Flonase	7,596	248,966	$ 530,761.72	46.11%	45.48%
Nasonex	3,928	130,894	$ 287,463.54	24.25%	24.63%
Nasacort AQ	1,888	60,005	$ 139,144.82	11.11%	11.92%
Ipratropium 0.3%	42	1,325	$ 1,162.75	0.25%	0.10%
Ipratropium 0.6%	48	1,213	$ 1,074.96	0.22%	0.09%
Astelin	1,013	30,911	$ 64,449.04	5.73%	5.52%
Total	**16,577**	**539,888**	**$ 1,166,983.13**		

Anticipated Market Changes

* There are no unexpired patents for Flonase® or Beconase® AQ, however currently no generic products are available.

Potential Administrative Costs

Based on a potential shift of proposed tier two products to a tier one product of 25 %, it is estimated that approximately 4,500 to 5,000 petitions would be required. The proposed tier changes would affect approximately 25 % of the total population for this PBPA category.

Previously, it has been theorized that total cost per petition to the healthcare system (includes cost to physicians, pharmacists, and program) is between $6.75 and $12.97. Total cost to the healthcare system for implementation of this PBPA

category is estimated to be between $30,375 and $64,850. Anticipated actual administrative cost to the program is projected to be less than $30,000.

Potential Program Savings

Potential savings to the program based on recommended tiers and a potential shift of 25% of market share from tier two to tier one is estimated to be $255,000 annually. This is the net *ingredient* cost savings after accounting for current rebates and dispensing fees.

Total Potential Savings

Potential Savings:	$ 255,000.00		$ 255,000.00
Potential Administrative Cost:	30,375.00		64,850.00
Total Potential Program Savings:	**$ 224,625.00**	**to**	**$ 190,150.00**

APPENDIX F

Drug Utilization Review of Skeletal Muscle Relaxants

Oklahoma Medicaid

December 2005

Overview of Musculoskeletal Conditions[1]

Musculoskeletal disorders are the leading cause of disability and work absenteeism and one out seven primary care visits are prompted by musculoskeletal pain for dysfunction. In persons under the age of 45, low-back problems are the most common cause of disability.

Musculoskeletal conditions can result from many causes as shown on the table below. However, musculoskeletal pain is most commonly associated with injury or trauma of the muscles and ligaments caused by sprains and strains. Pain, bruising, and inflammation are common symptoms of sprains while muscle spasm, muscle weakness, swelling, and cramping are symptomatic of strains, depending on the severity. Below is an overview of other etiologies of musculoskeletal conditions:

Musculoskeletal Conditions	Description
Mechanical back pain	Caused by strains of the paraspinal muscles, strains of ligaments of the spine, or diseases of joints between the bones of the spine.
Sciatica	Caused by irritation of a nerve root of the sciatic nerve resulting in pain radiating into the buttocks, back of the thigh, and often into the calf or foot.
Radiculopathy	Caused by any type of dysfunction of the nerve root resulting in weakness, pain (sciatica), numbness, and/or paresthesias.
Herniated Disc	Also called disc rupture, disc prolapse, herniated nucleus pulposus, or damage of the annulus fibrosis caused by age or injury. The location of the pain depends on which disc is weak but usually can include the back down to the toes.
Spinal Stenosis	Caused by the narrowing of the spinal canal (spondylosis) typically in the neck (cervical stenosis) or lower back (lumbar stenosis), resulting in pain in the back and neck that is aggravated by standing or walking and relieved by sitting or forward bending.
Myofascial Pain	Soft tissue pain caused by trauma, repetitive activities, or poor posture, resulting in muscle spasms, pain in neck, across shoulders, or sleeping difficulties and headaches.
Scoliosis	Abnormal curvature of spine due commonly to idiopathic causes. Most forms of scoliosis are not painful, but may depend on the severity of the curvature.
Fibromyalgia	Soft tissue pain presenting as generalized myalgia, stiffness, or soreness, and may disseminate to different areas of the body at different times. Pain may fluctuate and may occur concurrently with fatigue, sleep disorders, and as many as 50% of these patients will have clinical depression in their lifetime.

Treatment of Musculoskeletal Conditions[2]

Treatment is dependent upon the etiology and severity of the musculoskeletal condition. Most treatment modalities have been shown to be ineffective. Relief of pain and or discomfort is the primary initial concern and conservative treatment is often successful. The best and most cost-effective treatments are acetaminophen, NSAIDs, skeletal muscle relaxants, short term opioid analgesics, hot or cold packs, and bedrest for several days. The most common complaint is low-back pain due to one of the above causes, and 90% of these cases resolve in about 4-6 weeks. In certain severe cases, corrective surgery may be necessary and recovery may take several months to years, requiring immobilization and therapy.

Place in Therapy of Skeletal Muscle Relaxants[3]

Skeletal muscle relaxants have not been shown to have direct effects on skeletal muscles nor do they act at the neuromuscular junction. These agents are believed to exert actions on the central nervous system or spinal motor neurons to alter muscle tone.[4]

There is a lack of high quality studies to suggest that any skeletal muscle relaxant is more efficacious than the other.[5] Trials are usually of short duration and tend to show only modest advantage when compared to placebo or diazepam, with some trials showing no difference between the comparator drugs vs. placebo. A number of clinical trials show the treatment effects favored skeletal muscle relaxants over placebo at initiation, but treatment effects were similar to placebo at 4-7 days or beyond.[6]

The available clinical trials show oral skeletal muscle relaxants can be effective when used for acute symptomatic relief of pain and discomfort caused by various skeletal muscle conditions, but there is little evidence to support the use of skeletal muscle relaxants for chronic musculoskeletal conditions.

- **Baclofen (Lioresal®)**
  - A derivative of gamma aminobutyric acid (GABA) and acts specifically at the spinal end of the upper motor neurons to cause muscle relaxation.
  - May be useful in the treatment of muscular spasm due to conditions such as multiple sclerosis and spinal cord lesions.

- **Carisoprodol (Soma®)**
  - The mechanism of action of carisoprodol is unclear. Carisoprodol produces only mild effects on spasticity and is not considered effective for spastic or dyskinetic movement disorders.
  - Carisoprodol is metabolized to meprobamate, a sedative-hypnotic with highly addictive properties.
  - Use is generally not recommended due to its unclear benefit profile versus its adverse effect profile.

- **Chlorzoxazone (Parafon Forte®, Paraflex®)**
  - The mechanism of action of chlorzoxazone is not fully understood. Chlorzoxazone may act at the spinal cord and the subcortical levels of the brain to inhibit the reflexes associated with muscle spasm, however much of the therapeutic effects of chlorzoxazone are from its sedative effects.
  - It is most effective when used with acetaminophen as some researchers have found the effects of chlorzoxazone by itself to be too weak to exert clinical efficacy.[7]
  - Has, in rare instances, been associated with cases of serious hepatotoxicity.

- **Cyclobenzaprine (Flexeril®)**
  - Structurally related to the tricyclic antidepressants and exhibits similar pharmacological effects.
  - Has propensity for greater relief in the first 4 days of use which declines thereafter.[8]
  - CNS depression resulting in drowsiness and dizziness occurs with an incidence of up to 60% in clinical trials.
  - Possesses anticholinergic activity as well as tachycardia or dysrhythmic effects.

- **Metaxalone (Skelaxin®)**
  - The therapeutic effects of metaxolone come from actions on the central nervous system as it does not have a direct effect on skeletal muscles.
  - Limited data shows mixed results regarding efficacy when compared to placebo.

- **Methocarbamol (Robaxin®)**
  - Methocarbamol is a centrally acting skeletal muscle relaxant that is the carbamate derivative of guaifenesin.
  - Data shows efficacy over placebo, but there is little data showing efficacy over other skeletal muscle relaxants.

- **Orphenadrine (Norflex®)**
  - Orphenadrine is structurally similar to diphenhydramine. Its mechanism of action is not fully understood, but data seems to suggest efficacy over placebo.

- **Tizanidine (Zanaflex®)**
  - Mechanism of action is believed be produced by actions on the basal ganglia, especially the substantia nigra reticulata and entopeduncular nucleus.
  - May also enhance the efficacy of concomitantly-given non-steroidal anti-inflammatory drugs.

The most common side effects of these muscle relaxants are:

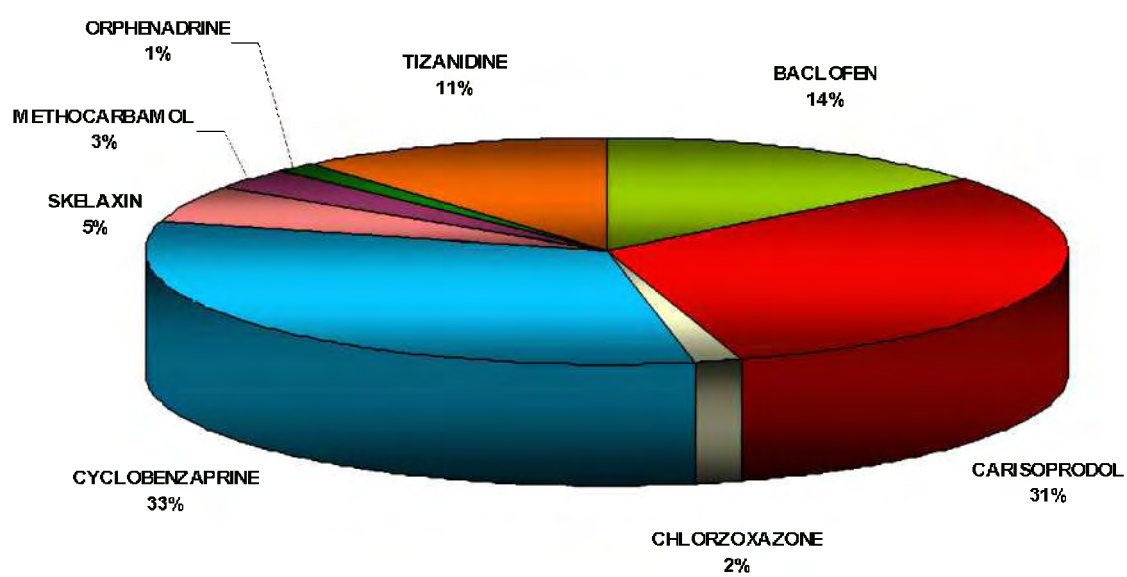
- drowsiness
- dizziness
- gastrointestinal upset
- hypotonia
- paresthesia
- somnolence
- tremor
- asthenia
- blurred vision
- mild muscular incoordination

Utilization of Skeletal Muscle Relaxants

Trends in Utilization of Muscle Relaxants

	Fiscal Year 2004	*Fiscal Year 2005*	*Percent Change*	
Total Clients	25,445	32,744	Increased	28.7 %
Total Claims	84,151	120,995	Increased	43.8 %
Total Cost	$ 2,443,000.34	$ 3,139,122.35	Increased	28.5 %
Cost per Claim	$ 29.03	$ 25.94	Decreased	10.6 %
Per- Diem Cost	$ 1.20	$ 1.07	Decreased	10.8 %
Total Units	6, 280,358	8,673,457	Increased	38.1 %
Total Days	2,034,076	2,936,406	Increased	44.4 %

Market Share by Therapy Days



Percent Increased between Fiscal Year 2004 and 2005

Name and Strength	*Claims*	*Units*	*Days*	*Cost*
CYCLOBENZAPRINE TAB 10MG	49.4%	52.0%	52.5%	50.8%
FLEXERIL® TAB 5MG	180.4%	193.9%	190.9%	213.9%
CARISOPRODOL TAB 350MG	48.6%	45.3%	51.5%	5.8%
BACLOFEN TAB 10MG	25.8%	11.6%	25.0%	11.5%
BACLOFEN TAB 20MG	27.5%	29.7%	26.3%	22.6%
SKELAXIN® TAB 800MG	97.0%	94.4%	107.4%	125.6%
METHOCARBAM TAB 750MG	43.2%	43.8%	46.0%	5.6%
ROBAXIN® TAB 500MG	200.0%	800.0%	350.0%	479.5%

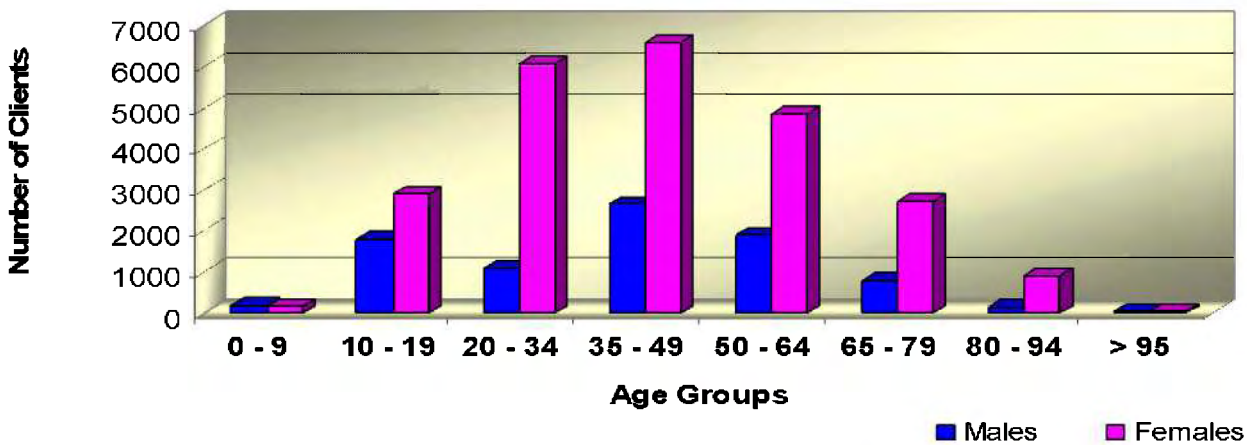
Utilization of Oral Formulations Skeletal Muscle Relaxants: FY 2005

DRUGNAME		CLAIMS	UNITS	DAYS	CLIENTS	COST	UNITS/ DAY	CLAIMS/ CLIENT	COST/ DAY
Cyclobenzaprine	TAB 10MG	40,073	2,123,683	861,637	17,304	$497,843.69	2.46	2.3	$0.58
Flexeril®	TAB 5MG	4,619	202,960	78,114	2,953	$259,391.91	2.60	1.3	$3.32
Flexeril®	TAB 10MG	39	2,372	1,031	30	$2,409.30	2.30	1.6	$2.34
Carisoprodol	TAB 350MG	34,164	2,693,935	909,442	6,612	$248,821.23	2.96	5.2	$0.27
Soma®	TAB 350MG	31	3,024	1,021	15	$10,525.60	2.96	2.1	$10.31
Baclofen	TAB 10MG	9,883	1,060,812	284,635	2,022	$238,986.01	3.73	4.9	$0.84
Baclofen	TAB 20MG	4,382	500,466	128,469	734	$207,664.43	3.90	6.0	$1.62
Tizanidine®	TAB 2MG	1,648	123,347	46,050	457	$60,621.32	2.68	3.6	$1.32
Tizanidine®	TAB 4MG	9,932	894,272	279,068	2,568	$468,144.04	3.20	3.9	$1.68
Zanaflex®	TAB 2MG	2	150	65	2	$85.01	2.31	1.0	$1.31
Zanaflex®	TAB 4MG	46	4,506	1,390	22	$4,979.30	3.24	2.1	$3.58
Skelaxin®	TAB 400MG	959	65,370	17,526	576	$90,713.36	3.73	1.7	$5.18
Skelaxin®	TAB 800MG	6,403	364,885	136,126	3,192	$863,598.09	2.68	2.0	$6.34
Methocarbamol	TAB 500MG	1,869	143,841	19,114	846	$20,193.57	7.53	2.2	$1.06
Methocarbamol	TAB 750MG	3,043	250,649	65,125	1,287	$34,417.20	3.85	2.4	$0.53
Robaxin®	TAB 500MG	3	540	90	1	$56.73	6.00	3.0	$0.63
Robaxin®	TAB 750MG	8	1,830	240	3	$1,514.15	7.63	2.7	$6.31
Chlorzoxazone	TAB 500MG	2,029	149,282	45,730	837	$15,501.25	3.26	2.4	$0.34
Parafon Forte®	TAB DSC	2	120	45	2	$59.02	2.67	1.0	$1.31
Orphenadrine	TAB 100MG CR	16	840	410	7	$774.43	2.05	2.3	$1.89
Orphenadrine	TAB 100MG ER	1,787	80,394	40,079	942	$71,623.74	2.01	1.9	$1.79
Norflex®	TAB 100MG CR	2	70	35	2	$113.98	2.00	1.0	$3.26
TOTALS		**120,940**	**8,667,348**	**2,915,442**		**$3,098,037.36**	**2.97**	**2.9**	**$1.06**

Utilization of Non-oral Formulations of Muscle Relaxants: FY 2005

DRUGNAME		CLAIMS	UNITS	DAYS	CLIENTS	COST	UNITS/DAY	COST/DAY
Lioresal® INT	INJ .05MG/ML	3	4	4	1	$308.13	1.00	$77.03
Lioresal® INT	INJ 0.05MG/1	1	2	1	1	$151.99	2.00	$151.99
Lioresal® INT	INJ 40MG/20	15	69	223	4	$28,382.11	0.31	$127.27
Baclofen	POW	29	5,643	557	8	$11,316.36	10.13	$20.32
Cyclobenzaprine	POW USP	3	270	112	1	$306.15	2.41	$2.73
Norflex®	INJ 30MG/ML	1	12	12	1	$120.95	1.00	$10.08
Orphenadrine	INJ 30MG/ML	2	50	25	2	$499.30	2.00	$19.97
TOTALS		**54**	**6,050**	**934**		**$41,084.99**	**43.99**	**$43.99**

Demographics of Clients Utilizing Skeletal Muscle Relaxants



Conclusions and Recommendations

- Data shows there is a decrease in cost per claim, however, the number of claims increased by over 40% between 2004 and 2005, suggesting a significant increase in utilization of skeletal muscle relaxants.
- The claims/client for carisoprodol and baclofen are high and is not consistent with recommendations for this disease process. However, baclofen may be used for chronic conditions.
- The mandatory generic plan has minimized utilization of brand name product associated with higher perdiem costs where generics are available.
- The patent exclusivity for Flexeril® 5mg is anticipated to expire February 2006.

The College of Pharmacy recommends the addition of the Skeletal Muscle Relaxant class to the Product Based Prior Authorization program. The following Tier-1 Drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of clients. The College of Pharmacy recommends this list to the Drug Utilization Review Board for consideration before approval and referral to the Oklahoma Healthcare Authority for final limitations or additions based on cost effectiveness.

Skeletal Muscle Relaxants	
Tier One*	***Tier Two***
Cyclobenzaprine (Flexeril®)	Carisoprodol (Soma®)
Baclofen (Lioresal®)	Metaxolone (Skelaxin®)
Tizanidine(Zanaflex®)	
Methocarbamol (Robaxin®)	
Chlorzoxazone (Parafon Forte®, Paraflex®)	
Orphenadrine (Norflex®)	

The following criteria are recommended for approval of a tier-2 product:

1. Documented adverse effect or contraindication to the preferred products.
2. Failure with at least two tier one medications defined as no beneficial response after at least two week of use during which time the drug has been titrated to the recommended dose.
3. Approvals will be for the duration of three months, except for clients with chronic diseases such as multiple sclerosis, in which case authorizations will be for the duration of one year.

[1] Beebe FA, Barkin RL, Barkin S. **A Clinical and Pharmacological Review of Skeletal Muscle Relaxants for Musculoskeletal Conditions**. Am J Ther. 2005;12:151-171.

[2] Devereaux, Michael W. **Low Back Pain.** Prim Care Clin Office Pract 31 (2004) 22-51.

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[4] Cohen SP, Mullings R, Abdi, S. **The Pharmacologic Treatment of Muscle Pain**. Anesthesiology. Aug 2004; 101: 495-526.

[5] **Chou** R. **Peterson** K. Helfand M. **Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review. [Review] [160 refs]** [Meta-Analysis. Review. Tutorial] *Journal of Pain & Symptom Management. 28(2):140-75, 2004 Aug.*

[6] Cohen SP, Mullings R, Abdi, S. **The Pharmacologic Treatment of Muscle Pain**. Anesthesiology. Aug 2004; 101: 495-526.

[7] Domino EF. **Centrally acting skeletal-muscle relaxants.** [Journal Article] *Archives of Physical Medicine & Rehabilitation. 55(8):369-73, 1974 Aug.*

[8] Browining R, Jackson JL, O'Malley PG. **Cyclobenzaprine and back pain: a meta-analysis.** Arch Intern Med 2001.; 161: 1613-1620.

APPENDIX G

Prior Authorization Annual Review - Fiscal Year 2005

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Oklahoma Medicaid
December 2005

Product Based Prior Authorization

With respect to the non-steroidal, anti-inflammatory drugs (NSAIDs), there are two tiers of drugs in this therapeutic classification.

(A) Tier-2 NSAIDs are approved if the individual has had two tier-1 NSAIDs within the current continuous NSAID therapy. This consists of all NSAID claims that have been sequentially acquired within 120 days of each other and provide medication coverage for the current date. The current continuous NSAID therapy shall then be retrospectively reviewed up to a maximum of 360 days for tier-1 NSAIDs.

(B) After an individual has received tier-2 NSAID coverage, the individual has tier-1 and tier-2 coverage for the duration of their continuous NSAID therapy.

(C) Individuals who have not acquired an NSAID for 120 days will be considered to have discontinued their continuous NSAID therapy and the previous approval will no longer be in effect.

The clinical exceptions for the non-steroidal, anti-inflammatory drugs in tier-2 are demonstrated by the following conditions:

(A) history of upper GI bleeding; or
(B) history of NSAID-induced ulcer, or
(C) active peptic ulcer disease, or
(D) concurrent use of warfarin, or
(E) concurrent chronic use of oral corticosteroids, or
(F) chronic NSAID therapy in elderly or debilitated patients, or
(G) diagnosis of gout – indomethacin only.

These clinical conditions are demonstrated by the documentation sent by the prescribing physician and pharmacist.

NSAIDS	
(Arthritis Medications or Non-Steroidal Anti-Inflammatory Drugs)	
Tier 1	**Tier 2**
diclofenac ER (Voltaren XR®)	diclofenac sodium/misoprostol (Arthrotec®)
diclofenac potassium (Cataflam®)	celecoxib (Celebrex®)
diclofenac sodium (Voltaren®)	indomethacin (Indocin®)
etodolac (Lodine®)	naproxen sodium (Naprelan®)
etodolac ER (Lodine XL®)	piroxicam (Feldene®)
fenoprofen (Nalfon®)	lansoprazole/naproxen (Prevacid® NapraPAC™)
flurbiprofen (Ansaid®)	meloxicam (Mobic®)
ibuprofen (Motrin®)	
ketoprofen (Orudis®)	
ketoprofen ER (Oruvail®)	
meclofenamate (Meclomen®)	
mefanamic acid (Ponstel®)	
nabumetone (Relafen®)	
naproxen (Naprosyn®)	
naproxen sodium (Anaprox®)	
naproxen EC (Naprosyn EC®)	
oxaprozin (Daypro®)	
sulindac (Clinoril®)	
tolmetin (Tolectin®)	

Changes for Fiscal Year 2005

July 1, 2004: meloxicam (Mobic®) was moved to a tier-1 status due to a supplemental rebate agreement,
September 30, 2004: voluntary withdrawal of rofecoxib (Vioxx®) from market.
April 7, 2005: valdecoxib (Bextra®) removed form market.

Changes for Fiscal Year 2006

July 1, 2005: meloxicam (Mobic®) was moved back to tier-2 status

Utilization – Fiscal Year 2005

For the period of July 2004 through June 2005, a total of 71,158 clients received non-steroidal, anti-inflammatory drugs through the Oklahoma Medicaid fee-for-service program.

Tier	# of Claims	Total Units	Total Days	Units /Day	Total Cost	Total Clients	Cost /Client	Cost /Claim
Tier-1	139,646	7,904,052	3,332,047	2.37	$2,045,418.41	60,625	$ 33.74	$ 14.65
Liquids	5,071	1,823,793	62,470	29.19	$ 107,441.74	3,057	$ 35.15	$ 21.19
Tier-2	44,940	2,087,608	1,624,452	1.29	$5,655,032.08	11,431	$ 494.71	$ 125.84
Liquids	6	900	180	5	$ 759.82	3	$ 253.27	$ 126.64
Total	**189,663**	**11,816,353**	**2,019,149**	**5.85**	**$7,808,652.05**	**71,158***	**$ 109.74**	**$ 41.17**

*Total unduplicated clients for FY05

Total Cost FY '05	**$7,808,652.05**
Total Cost FY '04	*$6,569,516.58*
Total Claims FY '05	**189,663**
Total Claims FY '04	*144,363*
Total Clients FY '05	**71,158**
Total Clients FY '04	*53,621*
Per Diem FY '05	**$3.87**
Per Diem FY '04	*$1.64*

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

Age	Female	Male	Totals
0 to 9	1,517	1,639	3,156
10 to19	10,938	6,560	17,498
20 to 34	15,637	1,379	17,016
35 to 49	7,721	2,932	10,653
50 to 64	6,577	2,902	9,485
65 to 79	6,301	2,011	8,312
80 to 94	4,058	688	4,746
95 and Over	264	28	292
Totals	**53,013**	**18,145**	**71,158**

Claims were also divided into the two tiers and reviewed by age and gender

Tier 1 Claims

Age	Female	Male	Totals
0 to 9	9	10	19
10 to19	315	187	502
20 to 34	593	125	718
35 to 49	1,277	529	1,806
50 to 64	2,032	717	2,749
65 to 79	2,579	625	3,204
80 to 94	2,019	277	2,296
95 and Over	128	12	140
Totals	**8,952**	**2,482**	**11,434**

Tier 2 Claims

Age	Female	Male	Totals
0 to 9	1,512	1,630	3,142
10 to19	10,774	6,445	17,219
20 to 34	15,373	1,308	16,681
35 to 49	7,025	2,634	9,659
50 to 64	5,336	2,437	7,773
65 to 79	4,399	1,561	5,960
80 to 94	2,395	467	2,862
95 and Over	15	18	168
Totals	**46,964**	**16,500**	**63,464**

	# of Claims	Total Units	Total Days	Total Cost	Per Diem
Tier -1 Duals	59,004	4,351,580	1,678,077	1,087,868.15	$0.65
Tier-2 Duals	34,622	1,600,258	1,254,183	4,324,891.16	$3.45
	93,626	5,951,838	2,932,260	5,412,759.31	$1.85
Tier-1 Non-Duals	85,713	5,376,265	1,716,440	1,064,992.00	$0.62
Tier-2 Non Duals	10,324	488,250	370,449	1,330,900.74	$3.59
	96,037	5,864,515	2,086,889	2,395,892.74	$1.14

Recommendations

The College of Pharmacy has the following recommendations for this prior authorization category:

No changes to the current criteria and continued monitoring of this category.

APPENDIX H

Prior Authorization Annual Review - Fiscal Year 2005

Anti-Ulcer Drugs

Oklahoma Medicaid
December 2005

Product Based Prior Authorization

With respect to the anti-ulcer medications there are two tiers of medications in the therapeutic category. A failed trial with a tier-1 anti-ulcer medication within the past 120 consecutive days is required before a tier-2 anti-ulcer medication can be approved.

Criteria required before moving to tier-2 medications include a failure of a maximum 40mg dose of omeprazole and trial of at least one tier-1 product (including omeprazole) or a clinical exception to the use of a tier-1 product.

Clinical exceptions to tier-1 anti-ulcer trials are the following:

1. H pylori eradication
2. Prophylaxis or treatment of NSAID induced ulcer
3. Erosive esophagitis or maintenance of healed erosive esophagitis
4. GERD complications (e.g. esophageal strictures, dysphagia, Barrett's esophagus)
5. Scleroderma

Anti-Ulcer Medications	
Tier 1	**Tier 2**
esomeprazole magnesium (Nexium)**	ranitidine (Zantac) capsules & effervescent tablets except generic tablets and other forms*
lansoprazole (Prevacid) capsules	Brand Rx (Prilosec)***
generic Rx omeprazole and Prilosec OTC*#	lansoprazole (Prevacid) oral disintegrating tablets & granules
Omeprazole (Zegerid)**	
pantoprazole sodium (Protonix)**	
rabeprazole sodium (Aciphex)**	

All versions of the prescription only product will remain Tier 2 until a SMAC can be applied or a supplemental rebate is established.

* Conversion to tier-1 drug for fiscal year 2004.
** Conversion to tier-1 drug on 07/01/2004 due to supplemental rebate program.
*** Brand-name prior authorization implemented on 11/01/2004.
 # Prilosec OTC does not count against 3-brand limit.

Update on Fiscal Year 2005

Product(s) moved from tier-2 to tier-1: Omeprazole (Zegerid), Pantoprazole sodium (Protonix) and rabeprazole sodium (Aciphex) due to supplemental rebate.

Brand-name override implemented 11/11/2004 which would effect those anti-ulcer medications available in generic. OTC Omeprazole (Prilosec) is covered without a PA and does not count against 3-brand limit.

Utilization

For the period of July 2004 through June 2005, a total of 54,253 clients received anti-ulcer products through the Medicaid fee-for-service program.

FY 2004 versus FY 2005			% Change
Cost FY '05		**$ 20,606,356.08***	**32.1 ↑**
	Cost FY '04	*$ 13,981,609.51*	
Claims FY '05		**343,851**	**44.1 ↑**
	Claims FY '04	*192,326*	
Per Diem FY '05		**$ 2.36**	**9.3 ↑**
	Per Diem FY '04	*$ 2.14*	
Clients FY '05		**54,253**	**20.8 ↑**
	Clients FY '04	42,965	

*Does not include any rebate information

Selected-Tiered Products	# of Claims	Total Units	Total Days	Units per Day	Total Cost	Per Diem
Tier 1 PPI's	151,139	5,413,406	4,975,339	1.09	$ 17,989,457.57	3.62
Tier 2 PPI's	951	29,973	28,539	1.05	$ 74,432.78	2.61
OTC Prilosec	9,753	393,840	316,407	1.25	$ 256,238.82	0.81
Tier 1 Ranitidine Tabs	73,899	2,721,570	1,509,522	1.80	$ 617,019.01	0.41
Tier 2 Ranitidine Caps & Effervescent Tabs	24	1,610	725	2.22	$ 3,327.99	4.59
Totals*	**235,766***	**8,560,399***	**6,830,532***	**1.25***	**$ 18,940,476.17***	**2.77***

*Excludes (I.V., liquids, combination products, remaining H2's, and/or supplemental rebate information)

Total petitions submitted in for this category during FY05: 3,793.

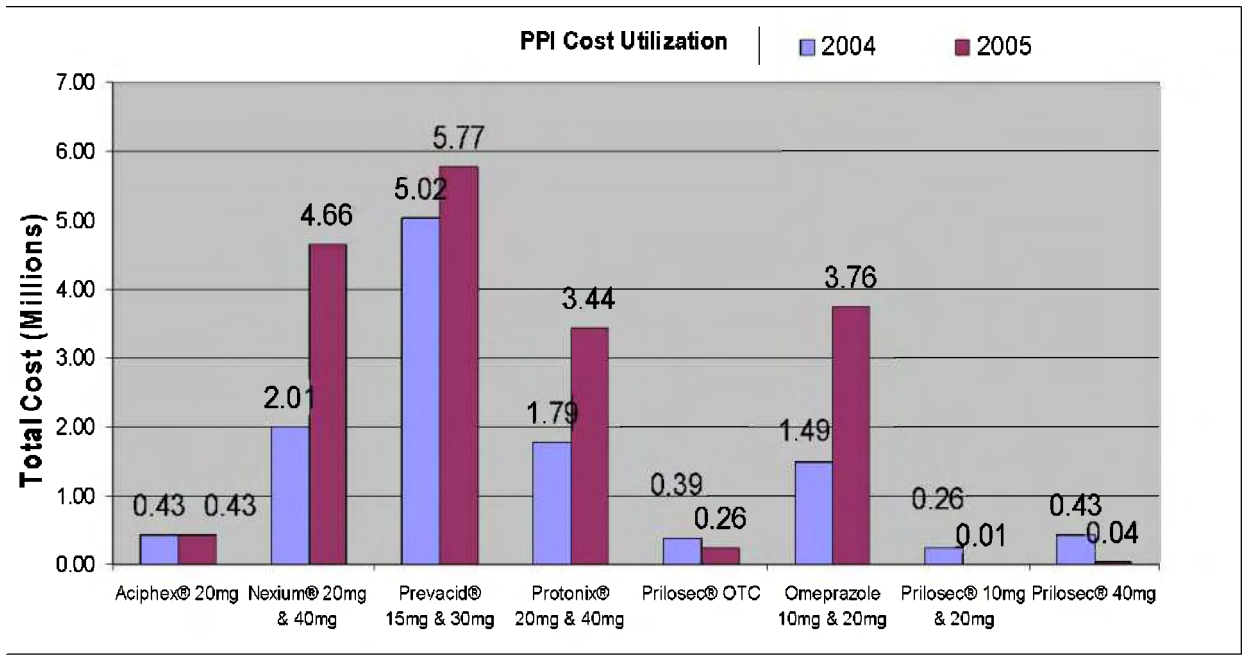
Approved	1,380
Denied	2,141
Incomplete	272
Super PA	1,030
Incomplete/Denied = Approved	606
Total Clients with Regular PA	1,827

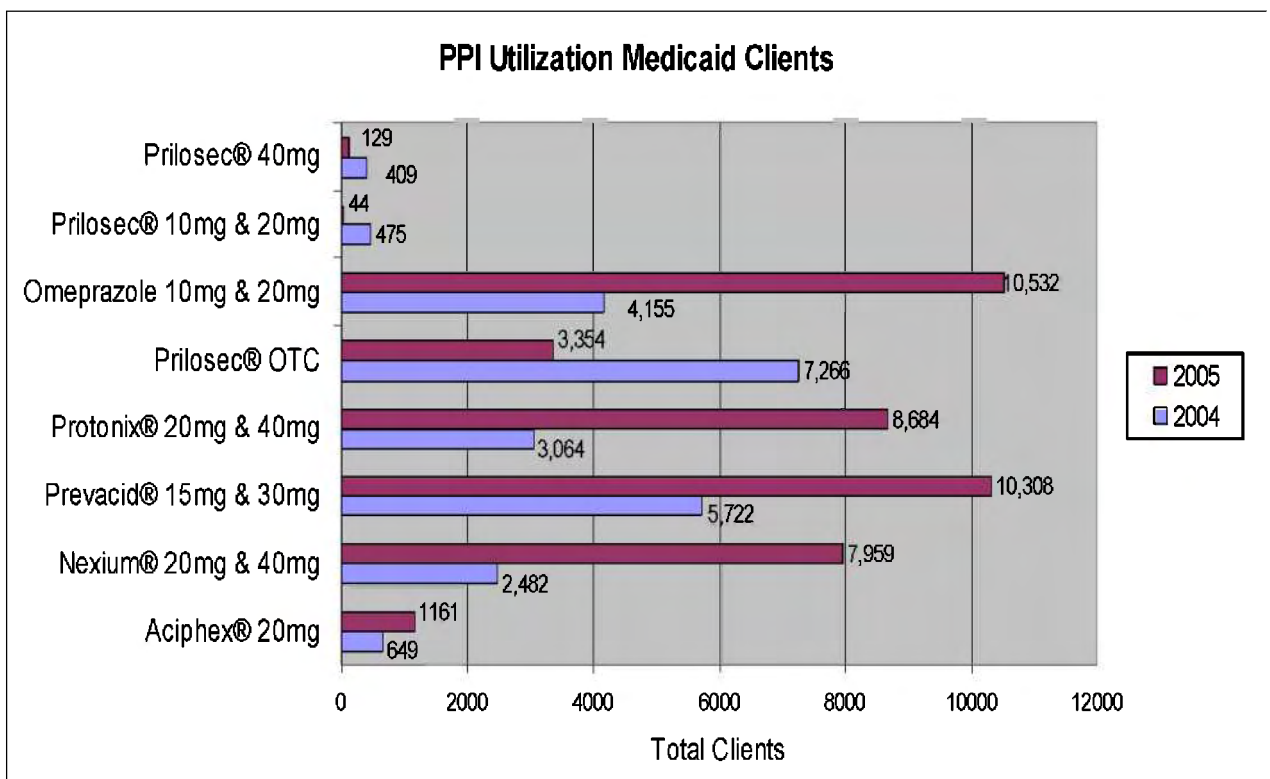
Age/Gender FY05

Age	Female	Male	Totals
0 to 9	2,478	2,723	5,201
10 to 19	3,684	2,449	6,133
20 to 34	4,979	1,083	6,062
35 to 49	5,440	2,704	8,144
50 to 64	6,798	3,262	10,060
65 to 79	7,495	2,789	10,284
≥80	6,938	1,431	8,369
Totals	**37,812**	**16,441**	**54,253***

*unduplicated clients

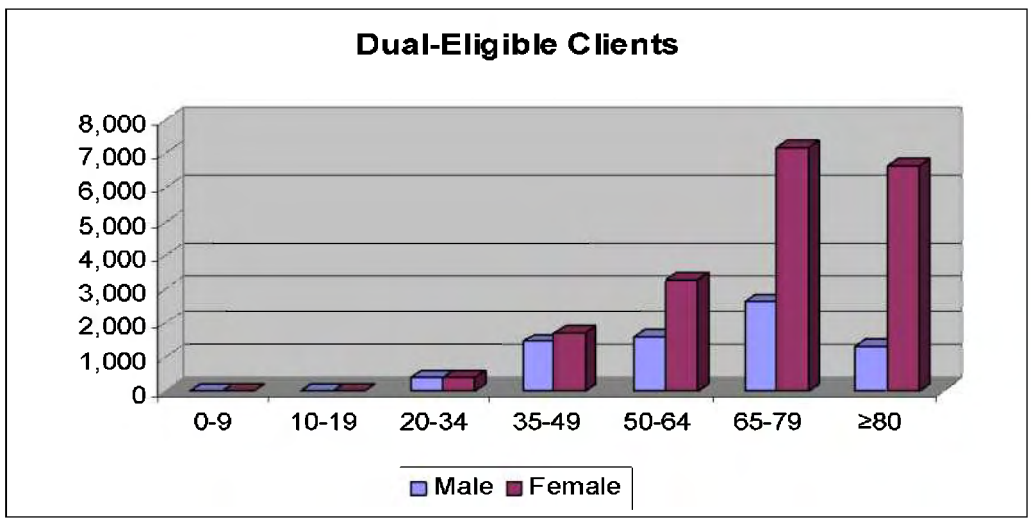
PPI Utilization for Medicaid Fee-for-service FY05

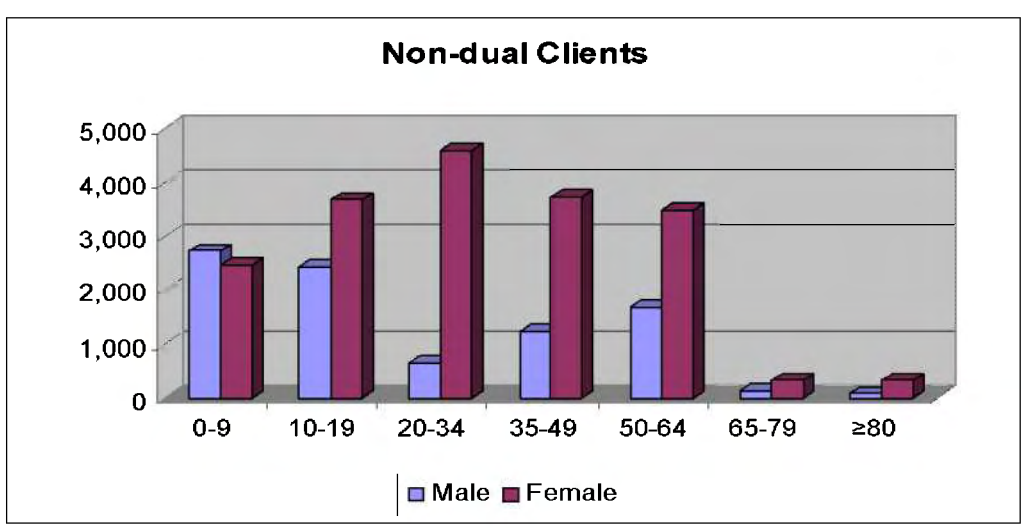




Medicaid-Medicare Dual-Eligibles FY05

FY 2005	# of Clients	# of Claims	Total Units	Total Days	Total Cost	Per Diem
Duals	26,640	240,099	8,159,371	5,579,733	13,100,699.93	2.35
Non-Duals	27,613	103,752	5,445,223	3,170,502	7,505,656.15	2.37





PPI vs H2 Utilization

	# of Claims		Total Cost*
	PPIs	H2s	
Dual-Eligible	116,343	123,379	13,001,543.36
Non-Duals	58,027	45,253	7,388,549.87
*Totals**	174,370	168,632	20,390,093.23

*Excludes (combination products and supplemental rebate information)

Current News for Anti-Ulcer Prior Authorization Category

Omeprazole (Zegerid) packets recently approved as tier-1 due to supplemental rebate as of 12/01/2004.

Esomeprazole (Nexium) received approved indication for risk reduction of non-steroidal anti-inflammatory drug (NSAID)-associated gastric ulcers as of 11/24/2004.

Patent expirations: Nexium (esomeprazole)……04/19/2006
Prevacid (lansoprazole)……05/10/2009
Protonix (pantoprazole)……07/19/2010

Recommendations

The College of Pharmacy recommends no action at this time. In the meantime, we will continue to monitor and evaluate the anti-ulcer category.

APPENDIX I

Prior Authorization Annual Review of Forteo® - Fiscal Year 2005

Oklahoma Medicaid
December 2005

Current Prior Authorization Criteria

Continue prior authorization of Forteo®:

- Postmenopausal women at high risk for fractures, or that cannot tolerate, are allergic to, or have failed to improve while on other agents.
- Men with primary or hypogonadal osteoporosis.
- Appropriate ICD-9 code (733.00, 733.01, etc).
- No concurrent use of Forteo® with other agents until more information is available regarding the safety and efficacy of such use.
- Minimum 3 month trial with one other agent (Fosamax®, Evista®, estrogen, Calcimar® or Miacalcin® unless contraindicated, intolerant, or allergic) ending in the past 30 days.
- PA approval for one month's supply per fill for duration of 1 year, with a maximum duration of 2 years.

Product Summary

Forteo® - approved December 2002 and available since January 2003.

- The first agent approved for the treatment of osteoporosis that stimulates new bone formation.
- Administered 20mcg/dose SQ once per day.
- Increases BMD, reconstructs bone architecture and has the same effects on the bone and kidney as endogenous parathyroid hormone.
- FDA labeled indications:
  - men with primary or hypogonadal osteoporosis,
  - postmenopausal women with osteoporosis, and
  - both men and women who
    - are at high risk for fractures,
    - have a history of fractures,
    - have multiple risk factors for the development of fractures,
    - cannot tolerate other therapies, or
    - have failed other therapies.
- Adverse effects similar to other osteoporosis medications.

Utilization

For the period of July 2004 through June 2005, a total of 117 clients received Forteo®.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Forteo® 750 sol	631	2,059	17,190	0.12	$391,804.75	117	$22.80

Total Cost FY '05	**$ 391,804.75**
Total Cost FY04	*$ 234,554.96*
Total Claims FY '05	**631**
Total Claims FY04	*327*
Total Clients FY 05	***117***
Total Clients FY04	*86*

379 total petitions were submitted for Forteo® during specified time period for 187 clients:

Approved 149
Denied 138
Incomplete 92
142 Denied or Incomplete subsequently Approved.

	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Duals	545	1,759	15,068	0.12	$339,827.60	103	$22.55
Non-Duals	86	300	2,122	0.14	$51,977.15	14	$24.50

Review of Osteoporosis Medications - Fiscal Year 2005

Oklahoma Medicaid
December 2005

Utilization

For the period of July 2004 through June 2005, a total of 8,658 clients received Forteo®, calcium regulators, or Evista® through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Fosamax® 5mg	136	3,995	4,040	0.98	$10,044.78	30	$2.49
Fosamax® 10mg	1,154	33,625	34,404	0.98	$84,058.62	195	$2.44
Fosamax® 35mg	683	2,748	19,881	0.14	$48,799.91	133	$2.45
Fosamax® 40mg	10	256	352	0.73	$1,445.58	2	$4.11
Fosamax® 70mg	18,738	74,714	534,507	0.14	$1,322,966.06	3,281	$2.48
Fosamax® Sol	206	60,533	5,787	10.46	$15,694.90	48	$2.71
Fosamax® Plus	6	24	172	0.14	$443.16	6	$2.58
Didronel® 200mg	24	1,242	593	2.09	$3,922.59	5	$6.61
Didronel® 400mg	48	2,230	1,222	1.82	$9,729.35	13	$7.96
Boniva®	8	10	290	0.03	$726.29	7	$2.50
Actonel® 5mg	779	22,804	23,547	0.97	$56,405.47	6	$2.40
Actonel® 30mg	247	2,306	9,381	0.25	$39,251.60	66	$4.18
Actonel® 35mg	12,433	49,646	352,176	0.14	$858,827.85	2,076	$2.44
Calcitonin 200	3	24	41	0.58	$350.23	3	$8.54
Miacalcin® 200 inj	221	1,085	3,606	0.30	$21,505.82	60	$5.96
Miacalcin® 200spry	9,572	74,791	268,075	0.28	$857,712.35	2,988	$3.20
Forteo® 750 sol	631	2,059	17,190	0.12	$391,804.75	117	$22.80
Evista® 60mg	7,485	327,431	326,217	1.00	$878,916.63	1,378	$2.70
Total	**52,384**	**659,523**	**1,601,481**		**$4,602,605.94**	**8,658***	

*Total unduplicated clients for FY05

Total Cost FY '05 **$4,602,605.94**
Total Cost FY04 *$3,938,944.01*
Total Claims FY '05 **52,384**
Total Claims FY04 *42,750*
Total Clients FY 05 ***8,658***
Total Clients FY04 *8,093*

Age	Female	Male	Totals
0 to 9	7	6	13
10 to 19	19	23	42
20 to 34	62	36	98
35 to 49	404	89	493
50 to 64	1,443	198	1,641
65 to 79	3,061	181	3,242
80 to 94	2,765	137	2,902
95 and Over	221	6	227
Totals	**7,982**	**676**	**8,658**

	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Duals	45,774	575,128	1,399,544	0.41	$4,025,787.88	7,409	$2.90
Non-Duals	6,610	84,394	201,937	0.42	$576,818.06	1,249	$2.86

Duals

Age	Female	Male	Totals
0 to 9	0	0	0
10 to 19	0	1	1
20 to 34	21	20	41
35 to 49	211	61	272
50 to 64	877	136	1,013
65 to 79	2,939	173	3,112
80 to 94	2,630	131	2,761
95 and Over	203	6	209
Totals	**6,881**	**528**	**7,409**

Non-Duals

Age	Female	Male	Totals
0 to 9	7	6	13
10 to 19	19	22	41
20 to 34	41	16	57
35 to 49	193	28	221
50 to 64	566	62	628
65 to 79	122	8	130
80 to 94	135	6	141
95 and Over	18	0	18
Totals	**1,101**	**148**	**1,249**

Market Changes for FY05

Boniva® (ibandronate) is a nitrogen-containing bisphosphonate that inhibits osteoclast-mediated bone resorption and is indicated for the treatment and prevention of osteoporosis in postmenopausal women. It is available in a once monthly tablet.

Fosamax Plus D® includes a weekly dose of vitamin D in the once weekly preparation.

Recommendations

The College of Pharmacy recommends continuation of the current criteria for the PA of Forteo® and continued monitoring of the osteoporosis category. The College of Pharmacy also recommends that a quantity limit be placed on Boniva® of 3 tablets every 84 days. There are already quantity limits on Fosamax® and Actonel®.

APPENDIX J

New Product Summaries

Oklahoma Medicaid
December 2005

Drug	Manufacturer	Indications	Dosage	Adverse Effects	Contraindications	New Molecular Entity	AWP / unit
Exjade (deferasirox) tablet	Novartis	Treatment of chronic iron overload due to multiple blood transfusions in adults and pediatric patient at least 2 years old	**Initiation**: 20 units of PRBC (~100mL/kg), >1000 mcg/L of serum ferritin **Starting dose**: 20mg/kg/d (also consider 10 and 30mg/kg/d based on frequency of transfusion) **Maintenance dose**: Adjusted based on monthly monitoring of serum ferritin	Nausea, abdominal pain, increase in kidney and liver functions, hearing and visual disturbances, rash	Hypersensitivity to deferasirox or any components of Exjade	Yes	$89 per gram
Arranon (nelarabine) liquid injection	GlaxoSmithKline	Arranon is indicated for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.	**Adult dose**:1,500 mg/m^2 IV over 2 hours on days 1, 3, & 5; repeat every 21 days. **Pediatric dose**: 650 mg/ m^2 IV over 1 hour daily for 5 days; repeat every 21 days.	hematologic toxicity, febrile neutropenia, infection complicating neutropenia, laboratory abnormalities including increased transaminase, gastrointestinal toxicity, fatigue, and asthenia.	History of hypersensitivity to nelarabine or any components of Arranon	Yes	

APPENDIX K

FDA Public Health Advisory

Serevent Diskus (salmeterol xinafoate inhalation powder), Advair Diskus (fluticasone propionate & salmeterol inhalation powder), Foradil Aerolizer (formoterol fumarate inhalation powder)

Today, FDA requested manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus to update their existing product labels with new warnings and a Medication Guide for patients to alert health care professionals and patients that these medicines may increase the chance of severe asthma episodes, and death when those episodes occur. All of these products contain medicines belonging to the class known as "long-acting beta 2-adrenergic agonists" (LABA), which are long-acting bronchodilator medicines. Bronchodilator medicines, such as LABAs, help to relax the muscles around the airways in the lungs. Wheezing (bronchospasm) happens when the muscles around the airways tighten. Even though LABAs decrease the frequency of asthma episodes, these medicines may make asthma episodes more severe when they occur.

FDA is issuing this public health advisory to highlight recommendations about use of a LABA medicine for asthma:

- LABAs should not be the first medicine used to treat asthma. LABAs should be added to the asthma treatment plan only if other medicines do not control asthma, including the use of low-or-medium dose corticosteroids.
- Do not stop using your LABA or other asthma medicines that your health care professional has prescribed for you unless you have discussed with your health care provider whether or not to continue treatment.
- Do not use your LABA to treat wheezing that is getting worse. Call your health care professional right away if wheezing worsens while using a LABA.
- LABAs do not relieve sudden wheezing. Always have a short acting bronchodilator medicine with you to treat sudden wheezing.

The information in FDA's proposed changes to the product labels explains that, even though LABAs decrease the number of asthma episodes, these medicines may increase the chances of a severe asthma episode when they do occur. In one asthma medicine study, an increased number of people taking a LABA in addition to their usual asthma care died from their asthma compared to people taking a placebo in addition to their usual asthma care, although the number of asthma deaths in the study was small. The Medication Guide has information about these risks for patients and caregivers in language approved by FDA and will be given to patients when a prescription for a LABA is filled or refilled.

LABAs are used for long-term control and prevention of asthma symptoms, for preventing wheezing (bronchospasm) caused by exercise in adults and children and for long-term control of

wheezing (bronchospasm) in adults with chronic obstructive pulmonary disease. The new warnings are about LABA-use for asthma. Information is not available to know whether there are similar concerns when LABAs are used for exercise-induced wheezing (bronchospasm) or chronic obstructive pulmonary disease.

Back to Top Serevent Diskus, Advair Diskus and Foradil

Date created: November 18, 2005

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www.lilly.com

Lilly

Lilly Research Laboratories
A Division of Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285 U.S.A.

Phone 317 276 2000

October 5, 2005

Re: Safety data on Cymbalta® (duloxetine hydrochloride) – Hepatic Effects

Dear Health Care Professional,

Eli Lilly and Company would like to inform you of new safety information regarding hepatotoxicity with Cymbalta® (duloxetine hydrochloride). This information comes from postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice). Some of these reports indicate that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the Precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease.

The following is updated language in the PRECAUTIONS of the Cymbalta package insert, and will be reflected in other materials. The language that has been added is underlined. Language that was deleted is shown in ~~strikethrough~~.

PRECAUTIONS

General

Hepatotoxicity — Cymbalta increases the risk of elevation of serum transaminase levels. Liver transaminase elevations resulted in the discontinuation of 0.4% (31/8454) of Cymbalta-treated patients. In these patients, the median time to detection of the transaminase elevation was about two months. In controlled trials in MDD, elevations of alanine transaminase (ALT) to >3 times the upper limit of normal occurred in 0.9% (8/930) of Cymbalta-treated patients and in 0.3% (2/652) of placebo-treated patients. In controlled trials in DPN, elevations of ALT to >3 times the upper limit of normal occurred in 1.68% (8/477) of Cymbalta-treated patients and in 0% (0/187) of placebo-treated patients. In the full cohort of placebo-controlled trials in any indication, 1% (39/3732) of Cymbalta-treated patients had a >3 times the upper limit of normal elevation of ALT compared to 0.2% (6/2568) of placebo-treated patients. In placebo-controlled studies using a fixed-dose design, there was evidence of a dose-response relationship for ALT and AST elevation of >3 times the upper limit of normal and >5 times the upper limit of normal, respectively. Postmarketing reports have described cases of hepatitis with abdominal pain, hepatomegaly and elevation of transaminase levels to more than twenty times the upper limit of normal with or without

jaundice, reflecting a mixed or hepatocellular pattern of liver injury. Cases of cholestatic jaundice with minimal elevation of transaminase levels have also been reported.
The combination of transaminase elevations and elevated bilirubin, without evidence of obstruction, is generally recognized as an important predictor of severe liver injury. In clinical trials, three Cymbalta patients had elevations of transaminases and bilirubin, but also had elevation of alkaline phosphatase, suggesting an obstructive process; in these patients, there was evidence of heavy alcohol use and this may have contributed to the abnormalities seen. Two placebo-treated patients also had transaminase elevations with elevated bilirubin. ~~Severe elevations of liver enzymes (>10 times the upper limit of normal) or liver injury with a cholestatic or mixed pattern have been rarely reported, in some cases associated with excessive alcohol use.~~ Postmarketing reports indicate that elevated transaminases, bilirubin and alkaline phosphatase have occurred in patients with chronic liver disease or cirrhosis. Because it is possible that duloxetine and alcohol may interact to cause liver injury or that duloxetine may aggravate pre-existing liver disease, Cymbalta should ordinarily not be prescribed to patients with substantial alcohol use or evidence of chronic liver disease.

Prior to approval, and as described in PRECAUTIONS of the previous package insert, it was known that use of duloxetine was associated with mild to moderate and usually transient elevation of hepatic enzymes that infrequently led to Cymbalta discontinuation. In addition, some cases of severe hepatic injury in patients consuming large quantities of alcohol were observed during duloxetine clinical trials, as is described in the original package insert.

Since approval on August 3, 2004, approximately one million patients have taken duloxetine. Among these, several cases of hepatic injury have been spontaneously reported. Some of these patients had underlying liver disease. Review of these cases suggests that patients with underlying chronic liver disease may be at increased risk of hepatotoxicity with duloxetine. In addition to hepatocellular and mixed liver injury, cases of cholestatic jaundice have been reported.

Patients and prescribers should be aware of the signs and symptoms of liver damage (pruritus, dark urine, jaundice, right upper quadrant tenderness, or unexplained "flu-like" symptoms) and health care professionals are encouraged to investigate such symptoms and signs promptly.

Should you have any questions or concerns regarding this important safety information, please contact your Eli Lilly and Company sales representative or contact the Lilly medical department at 1-800-Lilly-Rx. Please refer to the full prescribing information for Cymbalta included with this letter. As always, we request that serious adverse events be reported to Lilly at 1-800-Lilly-Rx or to the FDA MedWatch program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178) or by email (www.fda.gov/medwatch).

Paul Eisenberg, MD
Vice-President, Global Product Safety
Eli Lilly and Company

FDA Alert for Healthcare Professionals
Alemtuzumab (marketed as Campath)

FDA Alert [11/05]:

The Food and Drug Administration (FDA) has learned of three patients with multiple sclerosis (MS) who developed severe idiopathic thrombocytopenic purpura (ITP) while participating in a clinical study of Campath for treatment of MS. One of these individuals died from an intracranial hemorrhage. In the randomized clinical study, ITP developed approximately one to 11 months after the receipt of the last treatment with Campath. Dosing with Campath in this study is suspended at this time.

Campath is **not** approved for the treatment of MS. Campath is approved for treating B-cell chronic lymphocytic leukemia (CLL) in patients who have been treated with alkylating agents and who have failed fludarabine therapy. The Campath package insert currently includes a boxed warning about serious and rare hematologic toxicities, including autoimmune ITP, pancytopenia, marrow hypoplasia, and autoimmune hemolytic anemia associated with the use of Campath. The boxed warning also states: "**single doses of Campath greater than 30 mg or cumulative doses greater than 90 mg per week should not be administered because these doses are associated with a higher incidence of pancytopenia.**" In clinical studies of patients with CLL, autoimmune thrombocytopenia has been reported in two percent of patients with one reported fatal case of Campath-related autoimmune thrombocytopenia.

In the MS clinical study, two of the cases with ITP, including the patient who died, had received cumulative doses of Campath that exceeded the recommended cumulative weekly dosing limit in the boxed warning (see additional information about the dosing below). Both individuals had received 24 mg per day for 5 days (total dose 120 mg), followed by a second round of therapy of 24 mg per day for 3 days (total dose 72 mg) administered 12 months later. The third ITP case had received a lower dose of Campath.

This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.

Recommendations

As stated in the package insert (see electronic link to the approved package insert below), complete blood counts (CBC) and platelet counts should be obtained at weekly intervals during Campath therapy and more frequently if worsening anemia, neutropenia, or thrombocytopenia is observed on therapy. Campath should be discontinued in any patient with evidence of autoimmune hematologic toxicity or for severe hematologic toxicity

Data Summary

Idiopathic thrombocytopenia purpura (ITP) occurred in 3 patients with MS in the clinical study. The 3 patients are described below:

Case #1 – A patient received a 5 day course of Campath 24 mg/day, followed one year later by 24 mg/day for 3 days. Approximately 7 months after the second treatment, ataxia and ecchymoses developed, followed by obtundation and death from intracranial hemorrhage. The

platelet count had been in the normal range except for the month following the first cycle. At the time of hospital admission, the platelet count was 4000 cells/μL and antibodies to GPIIb/IIIa receptors on platelets were detected. Petechiae had been noted 1 month prior to the development of neurological symptoms.

Case #2 – A patient received Campath at a dosing schedule of 24 mg/day for 5 days, then 12 months later 24 mg/day for 3 days. Approximately 11 months following the second cycle of Campath, ecchymoses developed. Previous platelet counts had been in normal range, but on admission the count was 2000/μL, with platelet-associated IgG. After treatment with platelets, steroids, immunoglobulin and Danazol, the platelet count improved to the normal range on continued steroid treatment.

Case #3 – A patient received Campath at a dosing schedule of 12 mg/day for 5 days, then 12 and 24 months later 12 mg/day for 3 days. One month after receiving the third cycle of Campath, the platelet count was 81,000 cells/μL and the patient felt well. Petechiae subsequently developed. The platelet count at that time was 1000 cells/μL. Anti-platelet antibodies were not detected. The patient was then treated with steroids, platelet transfusion and WinRho with improvement in the platelet count.

Frequent close monitoring of hemotologic parameters is important with Campath. Patients who received Campath in the study are being monitored through the clinical trial, with close observation of hematologic parameters, and have been advised to watch for symptoms of thrombocytopenia-induced bleeding and to seek medical attention promptly if symptoms appear.

First-Time Generics - October 2005

	Generic Drug Name	Generic Manufacturer	Brand Name	Approval Date
1	AMLODIPINE BESYLATE TABLETS 2.5 MG (BASE), 5 MG (BASE), AND 10 MG (BASE)	MYLAN PHARMACEUTICALS, INC.	NORVASC TABLETS	10/3/2005
2	GLIMEPIRIDE TABLETS 1 MG, 2 MG, AND 4 MG	DR. REDDY'S LABORATORIES LIMITED	AMARYL TABLETS	10/6/2005
3	GLIMEPIRIDE TABLETS 1 MG, 2 MG, AND 4 MG	INVAGEN PHARMACEUTICALS, INC.	AMARYL TABLETS	10/6/2005
4	GLIMEPIRIDE TABLETS 1 MG, 2 MG, AND 4 MG	COREPHARMA LLC	AMARYL TABLETS	10/6/2005
5	GLIMEPIRIDE TABLETS 3 MG AND 6 MG	RANBAXY LABORATORIES LIMITED	AMARYL TABLETS	10/6/2005
6	GLIMEPIRIDE TABLETS 1 MG, 2 MG, 4 MG, AND 8 MG	RANBAXY LABORATORIES, INC.	AMARYL TABLETS	10/6/2005
7	GLIMEPIRIDE TABLETS 1 MG, 2 MG, AND 4 MG	TEVA PHARMACEUTICALS USA	AMARYL TABLETS	10/6/2005
8	RAMIPRIL CAPSULES 1.25 MG, 2.5 MG, 5 MG, AND 10 MG	COBALT PHARMACEUTICALS, INC.	ALTACE CAPSULES	10/24/2005
9	GLIPIZIDE AND METFORMIN HYDROCHLORIDE TABLETS 2.5 MG/250 MG, 2.5 MG/500 MG, AND 5 MG/500 MG	COREPHARMA LLC	METAGLIP TABLETS	10/27/2005

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